National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Survivorship

Version 1.2024 — March 29, 2024

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Clinical Trials: NCCN believes that the best management for any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Find an NCCN Member Institution: https://www.nccn.org/home/member-institutions.

NCCN Categories of Evidence and Consensus: All recommendations are category 2A unless otherwise indicated.

NCCN Categories of Evidence and Consensus.

Terminologies in all NCCN Guidelines are being actively modified to advance the goals of equity, inclusion, and representation.

Updates in Version 1.2024 of the NCCN Guidelines for Survivorship from Version 1.2023 include:

General Survivorship Principles

SURV-4

- 1st bullet revised: "...longer be involved in the survivor's care *and may also occur at younger ages than in the general population*."
- 2nd bullet revised: "... (eg, smoking, environmental exposures, health behaviors, human papillomavirus [HPV]), and mutagenic effects of cancer treatment. ~~Health behaviors should be modified as possible (eg, smoking cessation, weight management) to decrease the risk of subsequent malignancies~~."
- 3rd bullet revised: Treatment-related subsequent primary cancers vary with the type and intensity of ~~anti~~cancer treatment..."
- Bullet removed: Healthy lifestyle and behavioral counseling are important to reduce risk factors that may contribute to subsequent cancers (HL-1).

SURV-4A 1 of 5

- General:
  - New bullet added at the top: These treatment related screening and early detection recommendations are distinct from and should not replace surveillance for recurrence of the index cancer.
  - The "Treatment-Related Subsequent Primary Cancers by Treatment Exposure" tables (formerly SURV-C) were moved up in the algorithm to follow the section on "Screening for Subsequent New Primary Cancers" (SURV-4). Previously the table followed the "Survivorship Resources For Health Care Professionals And Survivors" pages (SURV-B).
    - ◊ New statement added to the table title: This table does not cover all populations, and additional cancer screenings may be warranted depending on clinical circumstances.
    - ◊ Radiation Therapy, Including Total Body Irradiation (TBI); Head and neck; Mucosal head and neck cancer
      - – Screening and Early Detection Recommendations revised: Annual head and neck exam *(including direct or indirect laryngoscopy as clinically indicated)*, and/or otolaryngology referral.
      - – Comments: Bullet added, For smoking-related cancer, evaluate indications for lung cancer screening

SURV-4A 3 of 5

- Radiation Therapy, Including Total Body Irradiation (TBI); Abdomen/Flank/Pelvic; Colorectal cancer; Comments revised:
  - New bullet added: Repeat colorectal cancer screening every 3 years after multi-target stool DNA test or every 5 years after colonoscopy. Consultation with primary care, gastroenterologist, or oncologist should be considered as clinically indicated.
  - New bullet added: Also see NCCN Guidelines for Colorectal Cancer Screening
  - Bullet removed: Repeat colorectal cancer screening based on findings, in consultation with primary care, gastroenterologist, or oncologist.
- Footnote c is new: Children's Oncology Group Long-Term Follow Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers – Version 6.0 (October 2023).

SURV-4A 4 of 5

- Transplant Conditioning Therapy (RT or chemotherapy); Hematopoietic Cell Transplantation; Screening and Early Detection Recommendations: New arrow sub-bullet added, Consider increased frequency/intensity of cancer screenings (eg, cervical) for immunocompromised individuals.
- Systemic Therapy; PARP Inhibitors Lutetium-octreotide; Screening and Early Detection Recommendations: New bullet added, Consider referral to hematology for work up for persistent cytopenias or leukopenias.
- Footnote d is new: Specific populations such as hematopoietic cell transplantation (HCT) survivors may have additional considerations for cancer screening.

Continued
UPDATES

Updates in Version 1.2024 of the NCCN Guidelines for Survivorship from Version 1.2023 include:

General Survivorship Principles (continued)

SURV-6

- Care providers are also encouraged to assess the following at regular intervals; Point #9 revised: Fertility concerns for adults of ~~childbearing potential~~ *reproductive age*

SURV-A 2 of 2

- Survivorship Assessment; Healthy Lifestyle; Provider Key section revised: If NO to question 23 or 24, or YES to question 25, OR if question 23a is less than 3 times per week, OR if body mass index (BMI) *is* not ~~in the healthy range~~ *between 18.5–24.9 kg/m²*, refer to HL-1

SURV-B 1 of 5 through SURV-B 5 of 5 Survivorship Resources For Health Care Professionals And Survivors

- General Online Information
  - Revised: National Cancer Institute: ~~Cancer Survivorship Research~~ *Office of Cancer Survivorship (OCS)*
    - ◊ Springboard Beyond Cancer removed from the informational bullet
    - ◊ Website updated: https://cancercontrol.cancer.gov/ocs
    - ◊ Websites removed:
      - – http://survivorship.cancer.gov
      - – https://survivorship.cancer.gov/springboard
- Integrative Therapies
  - Added: Society for Integrative Oncology: https://integrativeonc.org/
- Information About LGBTQ Individuals with Cancer
  - Added: National LGBT Cancer Project: https://www.lgbtcancer.org/
- Nutrition and Weight Management
  - Added: World Cancer Research Fund: Diet, Activity and Cancer Guidelines: https://www.wcrf.org/diet-activity-and-cancer/
  - Removed: LIVESTRONG MyPlate Calorie Counter: http://www.livestrong.com/myplate
- Cardiovascular Health
  - Removed: CardioOnc.org (database of cancer drugs and cardiac toxicities) (http://cardioonc.org/providers)
- Sleep Disorders
  - Added: The Society of Behavioral Sleep Medicine: https://www.behavioralsleep.org/
  - Added: U.S. Department of Veterans Affairs: CBT-i Coach: https://mobile.va.gov/app/cbt-i-coach

PREVENTIVE HEALTH

Healthy Lifestyles

HL-1

- 3rd bullet;
  - 4th arrow sub-bullet revised: Maintain a healthy diet high in vegetables, fruits, *beans/legumes,* and whole grains.
  - 7th arrow sub-bullet; New diamond sub-bullet added: Avoid secondary exposure to cigarette smoke.
  - 9th arrow and diamond sub-bullets revised
    - ◊ Strive for ~~at least 7–9 hours of~~ *sufficient* sleep on a regular basis (SSD-1). *Recommended total sleep duration*:
      - – ~~Younger adults require more sleep~~. *Adults: 7–9 hours*
      - – ~~Teenagers may require 9 or more hours of sleep~~. *Adolescents: 8–10 hours*
      - – *Older adults: 7–8 hours*

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Updates in Version 1.2024 of the NCCN Guidelines for Survivorship from Version 1.2023 include:

PREVENTIVE HEALTH

Healthy Lifestyles

HL-1A

- Footnote a revised: ~~Highly (sometimes referred to as "ultra") processed foods are made mostly or entirely from substances derived from foods and additives, with little or no intact food (eg, soft drinks, sweet or savory packaged snacks, reconstituted meat products [eg, sausage, chicken nuggets], prepared frozen dishes). Monteiro CA, et al. Public Health Nutr 2018;21:5-17.~~ *Highly (sometimes referred to as "ultra") processed foods are industrial formulations typically with 5 or more and usually many ingredients (eg, soft drinks, sweet or savory packaged snacks, reconstituted meat products [eg, sausage, chicken nuggets], prepared frozen dishes). Besides salt, sugar, oils, and fats, ingredients of ultra-processed foods include food substances not commonly used in culinary preparations, such as hydrolyzed protein, modified starches, and hydrogenated or interesterified oils, and additives whose purpose is to imitate sensorial qualities of unprocessed or minimally processed foods and their culinary preparations or to disguise undesirable qualities of the final product. (Martínez Steele E, et al. BMJ Open 2016;6:e009892)*.
- Reference is new: Paruthi S, et al. J Clin Sleep Med 2016;12:785-786.

Physical Activity

SPA-1

- 5th bullet revised: Avoid prolonged sedentary behavior (eg, sitting for long periods, *prolonged screen-based activities*)
- Footnote a: 2nd and 3rd bullet references updated

SPA-2

- Physical Activity Assessment; Assessment of comorbidities and treatment effects as appropriate
  - 12th bullet revised: Thrombocytopenia*/pancytopenia* and/or coagulopathies
  - New bullet added: Presence of limb prosthesis

SPA-3

- Risk Assessment For Physical Activity-Induced Adverse Events; 1st column; 2nd pathway; New bullet added: Presence of limb prosthesis.

SPA-A

- 6th bullet revised: ~~For survivors with peripheral neuropathy, resistance weight machines and/or training with resistance bands are recommended over free weights.~~ *If there is a concern that peripheral neuropathy may increase the risk of dropping free weights, survivors could consider utilizing weight machines and/or training with resistance bands*.

SPA-B

- Examples of Physical Activity: The activities for all three levels of exercise were alphabetized.

SPA-C

- Considerations for Specific Populations;
  - Survivors with established lymphedema; New arrow sub-bullet added: Survivors at risk for upper extremity lymphedema should be encouraged to perform arm/shoulder exercises (SLYMPH-1).
  - New bulleted section added for Presence of limb prosthesis or limb amputation
  - Survivors with peripheral neuropathy
    - ◊ 2nd arrow sub-bullet revised: "Consider alternative aerobic exercise (stationary biking, water aerobics, *yoga*)..."
    - ◊ 1st diamond sub-bullet revised: "Consider use of water shoes*/protective footwear* with aerobic exercise..."
    - ◊ New diamond sub-bullet added: Assistance with walking should be provided if alternative aerobic activities are not possible
  - Survivors with bone loss or bone metastases; New bullet added: Consider checking vitamin D levels and use of supplemental vitamin D if appropriate

Continued

Updates in Version 1.2024 of the NCCN Guidelines for Survivorship from Version 1.2023 include:

PREVENTIVE HEALTH

Nutrition and Weight Management

SNWM-1

- 1st bullet revised: "...as well as red and processed meats, alcohol, *dietary supplements,* and processed foods..."
- 3rd bullet; All survivors should be encouraged to; Arrow sub-bullets revised:
  - ....fruit, *beans/legumes*, and whole grains
  - ~~Eat~~ *Limit consumption of* processed meats such as ham, hot dogs, deli cuts, bacon, and sausage ~~sparingly if at all~~.
  - Limit consumption of ~~"fast foods" and other~~ processed foods that are high in fat...
  - ~~Track~~ *Monitor* calorie intake.
- 4th bullet; 1st arrow sub-bullet revised: Consider referral to a registered dietitian ~~or nutritionist~~
- 5th Bullet; Arrow sub-bullets revised
  - Fat: plant sources such as olive or canola oil, avocados, seeds and nuts, and ~~fatty~~ *cold water* fish
  - Protein: poultry, fish, legumes, low-fat dairy foods, *eggs,* and nuts
- Footnote "f" is new: Examples of "cold water fish" include mackerel, salmon, herring, and others

SNWM-2

- 1st bullet revised: All survivors should be encouraged to achieve and maintain a ~~normal~~ BMI *between 18.5 and 24.9 kg/m^2* and strive..."
- Arrow sub-bullets revised
  - *Intentional* weight gain should be a priority for survivors who have underweight. (SNWM-4)
  - *Intentional* weight loss should be a priority for survivors who have overweight/obesity.
    - ◊ Diamond sub-bullet revised: Weight gain after cancer diagnosis and treatment is common and ~~can~~ *may* exacerbate risk for functional decline, comorbidity, and possibly cancer recurrence or death, and ~~can~~ *may* reduce quality of life.
  - Weight maintenance should be a priority for survivors who have *a* ~~normal weight~~ *BMI between 18.5 and 24.9 kg/m^2*.
- 4th bullet revised: Providers should discuss strategies *and goal setting* for weight management...
  - ◊ Diamond sub-bullet revised: ~~Track~~ *Monitor* weight, diet, calories...
- Footnote h revised: Many hospitals ~~employ~~ *use* CSOs and those in private practice...

SNWM-3

- Footnote j revised: "...~~Normal~~ *Healthy* weight (BMI, 18.5–24.9 kg/m^2)..."
- Footnote l revised: For additional resources see the ASCO Toolkit on Obesity and Cancer: https://www.asco.org/sites/new-www.asco.org/files/content-files/blog-release/documents/2014-Obesity-Cancer-Guide-Oncology-Providers.pdf ~~and the "LIVESTRONG My Plate Calorie Tracker: http://www.livestrong.com/myplate~~." (Also for SNWM-4A)

SNWM-4

- Weight gain
  - 2nd bullet revised: Discuss increasing frequency of feeding *and portion size*
  - 5th bullet revised": "Consider referral to *registered* dietitian for individualized counseling
  - New bullets added
    - ◊ Optimize nutritional density and caloric quality of food
    - ◊ Consider appetite stimulants
    - ◊ Monitor weight regularly
- Weight maintenance
  - 1st bullet revised: Reinforce maintenance of ~~normal~~ *healthy* body weight throughout lifetime
  - Bullet added: Promote regular physical activity (SPA-1)

Continued
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Updates in Version 1.2024 of the NCCN Guidelines for Survivorship from Version 1.2023 include:

PREVENTIVE HEALTH

Nutrition and Weight Management

SNWM-4

- Weight loss
  - New bullet added: Promote regular physical activity (SPA-1)
  - 9th bullet revised: Refer to *registered* dietitian or weight management programs for individualized help as needed
  - Last bullet revised: Consider evaluation for bariatric surgery or pharmacologic therapy as appropriate ~~(if BMI ≥30 kg/m²)~~

General Principles of Supplement Use

SSUP-1

- 1st bullet revised: Supplement use is not recommended for most survivors, except in instances of documented deficiencies, inadequate diet, *previous gastrointestinal surgery that may cause deficiencies (eg, Roux-en-Y gastric bypass)*, or comorbid indications...
- 5th bullet revised: Refer survivors using supplements not prescribed by a medical provider to a registered ~~nutritionist/~~dietitian...

Immunizations and Infections

SIMIN-1

- General: Link to the NCCN COVID-19 Resources (https://www.nccn.org/covid-19) was removed from the algorithm.
- Footnote b revised: Also see: ~~Freedman MS, Ault K, Bernstein H. Advisory Committee on Immunization Practices recommended immunization schedule for adults aged 19 years or older - United States, 2021. MMWR Morb Mortal Wkly Rep 2021;70:193-196~~ *Murthy N, Wodi AP, McNally VV, et al. Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older - United States, 2024. MMWR Morb Mortal Wkly Rep 2024;73:11-15*. (Also for SIMIN-C)

SIMIN-2

- Footnote h revised: "...Travelers may find useful information at ~~https://wwwnc.cdc.gov/travel/yellowbook/2020/travelers-with-additional-considerations/immunocompromised-travelers~~ *https://wwwnc.cdc.gov/travel/yellowbook/2024/additional-considerations/immunocompromised-travelers*..."

SIMIN-3

- Recommended for all cancer survivors; Treatment: Tetanus, diphtheria, pertussis ~~(Tdap) vaccine~~ *vaccination*

SIMIN-3A

- Footnotes revised
  - Footnote q: Recommendations regarding COVID-19 vaccines are continually changing (https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html). For guidance about ~~COVID-19 vaccine usage in patients with cancer~~ *the management of concurrent COVID-19 and cancer, please see the NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections*. ~~please see NCCN: Cancer and COVID-19 Vaccination https://www.nccn.org/covid-19~~.
  - Footnote s: Recommended in high-risk patients or those with functional or anatomic asplenia. ~~Committee on Infectious Diseases. Pediatrics 2016;138:e20161890~~ *Mbaeyi SA, Bozio CH, Duffy J, et al. Meningococcal Vaccination: Recommendations of the Advisory Committee on Immunization Practices, United States, 2020. MMWR Recomm Rep 2020;69:1-41*.

Continued
UPDATES

Updates in Version 1.2024 of the NCCN Guidelines for Survivorship from Version 1.2023 include:

PREVENTIVE HEALTH

Immunizations and Infections

SIMIN-B **General Principles Of Vaccines In Cancer Survivors**

SIMIN-B 1 of 6

- Meningococcal conjugate vaccine, quadrivalent (MCV4); Population revised: ~~Splenectomized/functional asplenia survivors~~ *Survivors with surgical or functional asplenia*

SIMIN-B 2 of 6

- Vaccination in Survivors Who Had Cellular Therapy (ie, HCT, CAR T-cell therapy)
  - Measles, mumps, rubella (MMR) vaccine; Recommended Dose/Timing bullet revised: A 2-dose series of MMR vaccine should be administered 24 months after HCT and 8–11 months after the last dose of *intravenous immunoglobulin* ~~immune globulin~~ ~~intravenous~~ (IVIG)
  - COVID-19 vaccine; Recommended Dose/Timing bullet revised: Recommendations regarding COVID-19 vaccines are continually changing (https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html.) ~~For guidance about COVID-19 vaccine usage in patients with cancer, please see NCCN: Cancer and COVID-19 Vaccination: https://www.nccn.org/docs/default-source/covid-19/2021_covid-19_vaccination_guidance_v5-0.pdf?sfvrsn=b483da2b_78.~~ *For guidance on the management of concurrent COVID-19 and cancer, please see the NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections*. (Also for SIMIN-B 4 of 6)

SIMIN-B 3 of 6

- Vaccination in All Other Survivors
  - Pneumococcal vaccine; Population; New bullet added: Survivors with surgical or functional asplenia
  - Vaccine: *Haemophilus influenzae type b (Hib) vaccine* recommendations added to the table

SIMIN-B 4 of 6

- Vaccination in All Other Survivors
  - Meningococcal conjugate vaccine quadrivalent (MCV4); Population revised: Splenectomized/functional asplenia survivors changed to *Survivors with surgical or functional asplenia*

SIMIN-B 5 of 6

- References updated as follows:
  - Refrence 3 ~~Kobayashi M, Farrar JL, Gierke R, et al. Use of 15-Valent Pneumococcal Conjugate Vaccine and 20-Valent Pneumococcal Conjugate Vaccine Among U.S. Adults: Updated Recommendations of the Advisory Committee on Immunization Practices — United States, 2022. MMWR Morb Mortal Wkly Rep 2022;71;109-117~~ *Kobayashi M, Pilishvili T, Farrar JL, et al. Pneumococcal Vaccine for Adults Aged ≥19 Years: Recommendations of the Advisory Committee on Immunization Practices, United States, 2023. MMWR Recomm Rep 2023;72*:1-39.
  - Reference 4 ~~Dooling KL, Guo A, Patel M, et al. Recommendations of the Advisory Committee on Immunization Practices for use of herpes zoster vaccines. MMWR Morb Mortal Wkly Rep 2018;67:103-108. https://www.cdc.gov/mmwr/volumes/67/wr/mm6703a5.htm~~ *Anderson TC, Masters NB, Guo A, et al. Use of Recombinant Zoster Vaccine in Immunocompromised Adults Aged ≥19 Years: Recommendations of the Advisory Committee on Immunization Practices — United States, 2022. MMWR Morb Mortal Wkly Rep 2022;71:80-84.*
  - Reference 5 ~~Freedman MS, Ault K, Bernstein H. Advisory Committee on Immunization Practices recommended immunization schedule for adults aged 19 years or older - United States, 2021. MMWR Morb Mortal Wkly Rep 2021;70:193-196.~~ *Murthy N, Wodi AP, McNally VV, et al. Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older - United States, 2024. MMWR Morb Mortal Wkly Rep 2024;11;73:11-15*. (Also for SIMIN-C)
  - Refrence 6 is new: Briere EC, Rubin L, Moro PL, et al. Prevention and Control of Haemophilus influenzae Type b Disease: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2014;(RR01):1-14.

Continued

Updates in Version 1.2024 of the NCCN Guidelines for Survivorship from Version 1.2023 include:

PREVENTIVE HEALTH

Immunizations and Infections

SIMIN-B 6 of 6

- Footnote g revised: Administration of the flu vaccine to survivors with egg allergy symptoms (other than hives) should be done at a center that can manage severe allergic reactions *if an egg-based vaccine is used*. ~~Grohskopf LA, Alyanak E, Ferdinands JM, et al. Prevention and control of seasonal influenza with vaccines: Recommendations of the Advisory Committee on Immunization Practices - United States, 2021-2022 influenza season. MMWR Recomm Rep 2021;70:1-28~~ *Grohskopf LA, Blanton LH, Ferdinands JM, et al. Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023–24 Influenza Season. MMWR Recomm Rep 2023;72:1-25.* (Also for SIMIN-C)

SIMIN-C

- Principles of Influenza Vaccine(s)
  - 2nd bullet link updated: ~~https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8407757~~ https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/flu.html
  - Preferred Vaccines list revised as follows
    - ◊ Inactivated influenza vaccine (IIV)
      - – ~~Trivalent (IIV3), standard dose~~
      - – ~~Trivalent (IIV3), high dose~~
      - – Quadrivalent (IIV4), standard dose
      - – Quadrivalent ~~(IIV4)~~, high-dose (*HD-IIV4;* preferred ~~in~~ *option for* survivors ≥65 y)
      - – *Quadrivalent adjuvanted inactivated influenza vaccine (aIIV4; preferred option for survivors ≥65 y)*
    - ◊ Recombinant influenza vaccine (RIV)[a]
      - – ~~Trivalent (RIV3)~~
      - – Quadrivalent (RIV4*; preferred option for survivors ≥65 y*)

LATE EFFECTS/LONG-TERM PSYCHOSOCIAL AND PHYSICAL PROBLEMS

Cardiovascular Disease Risk Assessment

SCVD-1

- 4th bullet revised: Cancer treatments (immunotherapy, cytotoxic, *HCT,* and targeted systemic therapies, RT) can result...
- 7th bullet revised: Tools exist to help quantify atherosclerotic CVD (ASCVD) risk (eg, ASCVD risk score) *and thus determine appropriate risk reduction strategies*.
- Bullet removed: Consider referral to cardio-oncology or a cardiology specialist for high-risk survivors.

Anthracycline-Induced Cardiac Toxicity

SCARDIO-2

- Initial Clinical Assessment For Patients Who Have Received Previous Anthracycline Therapy; 3rd bullet; 2nd arrow sub-bullet revised: Other systemic therapy *(eg, anti-HER2 treatment)* and/or chest RT.
- Footnote d revised: "...shortness of breath when ~~sleeping~~ *laying flat (ie, orthopnea)*, waking up at night due to shortness of breath...

Continued
UPDATES

Updates in Version 1.2024 of the NCCN Guidelines for Survivorship from Version 1.2023 include:

LATE EFFECTS/LONG-TERM PSYCHOSOCIAL AND PHYSICAL PROBLEMS

Anthracycline-Induced Cardiac Toxicity

SCARDIO-3

- Treatment
  - Stage A; 3rd bullet revised: Consider referral ~~to cardiologist~~ for management
  - Stage B, Stage C, Stage D pathways; Bullet revised: Referral to ~~cardiologist~~ *cardiovascular specialist (ie, cardiologist, cardio-oncologist)* for management
- Footnote n revised: Consider referral to a cardiologist, ~~especially~~ *cardio-oncologist, survivorship specialist, or PCP for serial surveillance based on cardiotoxicity risk of cancer treatment regimen or* if additional anthracycline therapy or other cardiotoxic treatment is needed.

Anxiety, Depression, Trauma, and Distress

SANXDE-7

- Social/External Factors; New arrow sub-bullet added: Discrimination or marginalization because of race, ethnicity, sexual orientation, sexual identity, or disability status

Cognitive Function

SCF-1

- General Principles; 3rd bullet revised: "...cancer-associated cognitive dysfunction has been identified*, and screening tools*~~. Existing diagnostic tools~~ do not strongly correlate with patient reports of cognitive dysfunction.

SCF-3

- General Strategies for Management of Cancer-Associated Cognitive Dysfunction: New bullet added, Involve social support system to help with completion of tasks and activities

SCF-4

- Second-line Interventions; 1st bullet revised: "...and care for survivors who continue to have ~~memory~~ *cognitive* problems after rehabilitation

Fatigue

SFAT-1

- Considerations For Fatigue In Cancer Survivors
  - 1st bullet; 1st arrow sub-bullet revised: "Receipt of chemotherapy, radiation, endocrine, *immunotherapy,* targeted, and/or cellular therapies..."
  - New arrow sub-bullet added: Assessment and communication regarding fatigue and anticipated recovery after treatment should be done periodically.

Lymphedema

SLYMPH-1

- Footnotes revised
  - Footnote a: National Cancer Institute Lymphedema (PDQ)~~® Health Professional~~ *Patient* Version: ~~https://www.cancer.gov/about-cancer/treatment/side-effects/lymphedema/lymphedema-hp-pdq~~ *https://www.cancer.gov/about-cancer/treatment/side-effects/lymphedema*. (Also for SLYMPH-2A)
  - Footnote b: ~~International Society of Lymphology. Executive Committee. The Diagnosis and Treatment of Peripheral Lymphedema: 2016 Consensus Document of the International Society of Lymphology. Lymphology 2016;49:170-184.~~ *Executive Committee of the International Society of Lymphology. The diagnosis and treatment of peripheral lymphedema: 2020 Consensus Document of the International Society of Lymphology. Lymphology 2020;53:3-19. https://pubmed.ncbi.nlm.nih.gov/32521126/*

Continued

UPDATES

Updates in Version 1.2024 of the NCCN Guidelines for Survivorship from Version 1.2023 include:

LATE EFFECTS/LONG-TERM PSYCHOSOCIAL AND PHYSICAL PROBLEMS

Lymphedema

SLYMPH-3

- Screening; 1st bullet; 3rd arrow sub-bullet revised: Swelling*, tightness, or uncomfortable sensation* that interferes with daily activities
- Workup If Lymphedema Is Suspected; 1st bullet revised: Rule out recurrence of cancer*, infection, or deep vein thrombosis (DVT) of an extremity*

SLYMPH-A

- Survivor Lymphedema Education; 1st bullet; 3rd arrow sub-bullet revised: "...maintenance of skin integrity on the affected side*, manual drainage, and range of motion exercise*."
- Footnote b revised: For a complete list of lymphedema risk reduction practices, see the Position Statement from the National Lymphedema Network: ~~https://issuu.com/lymphnet/docs/risk_reduction~~ https://lymphnet.org/position-papers.
- Footnote c is new: Limb elevation can be used as an option for early-stage lymphedema for short-term improvement, but data are limited.

Pain

SPAIN-1

- 6th bullet; New arrow sub-bullet added: Hypnosis, meditation, acupuncture, cognitive restructuring, and behavioral activation can be considered to control pain and maximize function.
- The arrow sub-bullet "Physical modalities (heat, cold, massage, acupuncture, physical therapy, or occupational therapy) are useful and should be considered for some pain syndromes." was previously the 7th bullet.
- Footnote is new: Thompson T, Terhune DB, Oram C, et al. The effectiveness of hypnosis for pain relief: A systematic review and meta-analysis of 85 controlled experimental trials. Neurosci Biobehav Rev 2019;99:298-310.

SPAIN-2

- 4th Bullet: Link regarding pain patient agreements removed, https://nida.nih.gov/sites/default/files/SamplePatientAgreementForms.pdf

SPAIN-9

- GI/urinary/pelvic pain; Treatment; For GI pain (abdominal pain/cramping): *Bowel regimen* added as an option

Hormone-Related Symptoms

SHRS-1

- Principles of Menopause Symptom Management In Female Survivors; Treatment Options for Vasomotor Symptoms; Hormonal therapies; New arrow sub-bullet added: Survivors often use herbal supplements for vasomotor symptom management. However, some supplements may interfere with hormonal cancer treatments, and routine use of supplements is not recommended (SSUP-1). Providers should encourage survivors to discuss such therapies prior to use. (Also for SHRS-2A)

SHRS-A 1 of 2

- Non-Hormonal Pharmacologic Treatments And Dosing For Vasomotor Symptoms; New drug class entry and recommendations added for Selective neurokinin-3 (NK3) receptor antagonist

SHRS-B

- Principles Of Menopausal Hormone Therapy (MHT) Use In Female Survivors; 2nd bullet, New sub-bullets added
  - The tissue-selective estrogen complex (TSEC) conjugated estrogens/bazedoxifene is FDA-approved for treating menopausal symptoms in healthy post-menopausal survivors.
    - These drugs are contraindicated in survivors of hormonally dependent cancers.

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National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2024
Survivorship

NCCN Guidelines Index
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Discussion

Updates in Version 1.2024 of the NCCN Guidelines for Survivorship from Version 1.2023 include:

LATE EFFECTS/LONG-TERM PSYCHOSOCIAL AND PHYSICAL PROBLEMS

Sexual Health

SSH-3

- Male with concerns/issues regarding sexual health; Problems with ejaculation (premature, absent, delayed, or climacturia); Treatment Options; 4th bullet revised: "For climacturia: Empty bladder prior to sex, pelvic physical therapy, or ~~trial of imipramine~~ *use of condoms to catch urine*"

SSH-3A

- Footnote m revised: "...prostate cancer under therapy with androgen deprivation). *Exogenous testosterone therapy should not be prescribed to those who are currently trying to conceive. The long-term impact of exogenous testosterone on spermatogenesis should be discussed with patients who are interested in future fertility*."

Sleep Disorders

SSD-1

- 3rd column; H&P; Arrow sub-bullet; Comorbidities; Revised: Iron and ferritin levels *and when indicated transferrin saturation %*
- 4th column; Bottom pathway; Sleep disturbance and/or excessive sleepiness:
  - New bullet added: Sleep disordered breathing (includes obstructive sleep apnea [most common] and central sleep apnea)
  - Bullet removed: Obstructive sleep apnea

SSD-1A

- Footnote c revised: ~~Consider~~ *Medication review: Re-evaluate the need for* persistent use of sleep aids, pain medications, antiemetics, stimulants..."
- Footnote e revised: "Note that *sleep disordered breathing (eg*, obstructive sleep apnea*),* RLS, circadian rhythm sleep wake disorders, and parasomnias..."

SSD-2

- 3rd column; Top pathway; Evaluate for and address comorbid causes; New bullet added: Other sleep disorders

SSD-3

- Associated with observed apneas, snoring pathway; Diagnosis revised for Sleep Study: Obstructive sleep apnea changed to Sleep disordered breathing
- Associated with uncomfortable sensation; Treatment; Management options revised under "Initial preferred therapy"
  - Gabapentin enacarbil added
  - Enacarbil removed
- Footnote o revised: The following tools may be used to help identify individuals at high risk for *obstructive* sleep apneas...
- Footnote r revised: Sleep studies can be ~~done~~ *performed* as *an in*-laboratory polysomnography or as home sleep study. However, survivors with ~~known~~ *certain medical disorders (ie,* cardiac, ~~disease or~~ *respiratory*, neurologic ~~disease~~*)*, ~~who have used~~ *or currently on* opiates for cancer-related pain, may not be good candidates for ~~some~~ home sleep ~~tests~~ *studies*.
- Footnote t revised: The most common medical treatment for ~~obstructive sleep apnea~~ *sleep disordered breathing* is continuous positive airway pressure (CPAP).

Continued

Updates in Version 1.2024 of the NCCN Guidelines for Survivorship from Version 1.2023 include:

LATE EFFECTS/LONG-TERM PSYCHOSOCIAL AND PHYSICAL PROBLEMS

Sleep Disorders

SSD-A

- Other Sleep Interventions revised
  - 1st bullet: If survivor is not able to fall asleep within ~~45 minutes~~ *what feels like 20 minutes (survivor should not check the clock)* or...
  - Arrow sub-bullets:
    - ◊ Get up, go to a different location, but stay in a darkened room and do non-stimulating activity like ~~watching a relaxing TV show or~~ reading..."
    - ◊ "...reduce worrying (ie, write a "to do" list or set aside "worry time" *[eg, 10–15 mins] earlier in the day, not close to bedtime)*"

SSD-B

- Footnote b is new: There are paid and/or free guided, semi-guided, and unguided CBT-I digital resources available. See Survivorship Resources for Health Care Professionals and Survivors (SURV-B).

SSD-C

- Footnote d revised: "...and nutritional/herbal supplements ~~(eg, melatonin)~~. They do not have an FDA-approved indication..."

SSD-D

- Section title revised: ~~Iron Deficiency And~~ Restless Legs Syndrome
- New arrow sub-bullet added: Consider referral to specialist for refractory symptoms (See NCCN Guidelines for Palliative Care)
- New bullet added: Consider modification of lifestyle factors and medications that can exacerbate RLS symptoms
- Footnote c is new: Alcohol, nicotine, caffeine, centrally active antihistamines, SSRI, SNRI, and dopaminergic medications are associated with worsening of RLS symptoms.

ABBR-1 and ABBR-2

- The abbreviations pages were updated to reflect changes in the algorithm.

General Survivorship Principles

DEFINITION OF SURVIVORSHIP

- **An individual is considered a cancer survivor from diagnosis, through the balance of life.[a] This includes survivors living with cancer and those free of cancer. The panel recognizes that not all individuals with a history of cancer identify with the term "survivor." These guidelines are meant to be inclusive and use the term "survivor" to describe anyone with a history of cancer.**
- **These guidelines focus on the vast and persistent impact both the diagnosis and treatment of cancer have on the adult survivor. This includes the potential impact on physical and mental states, health behaviors, professional and personal identity, sexuality, and financial standing. It is appropriate to counsel on these impacts early in the treatment trajectory and at regular intervals thereafter.**
- **These guidelines are applicable to survivors across the continuum of care, including those on prolonged therapy, those with chronic cancers (eg, metastatic disease), and long-term survivors.**
- **The panel recognizes the growing population of individuals who are living with metastatic disease and that many aspects of these guidelines pertain to this population of survivors. This group is included in the definition of survivorship, and these guidelines are meant to be applied when helpful to meet the individuals' needs.**
- **The panel recommends reviewing the NCCN Guidelines for Survivorship in conjunction with the cancer-specific guidelines for individuals with metastatic disease. As more evidence is established for this population, more specific survivorship guidelines for individuals living with metastatic cancers may be developed.**

[a] Adapted with permission from the National Coalition for Cancer Survivorship as shown in the National Cancer Institute's Office of Cancer Survivorship Definitions web page, available at https://cancercontrol.cancer.gov/ocs/definitions.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

STANDARDS FOR SURVIVORSHIP CARE[b]

Care of the cancer survivor should include:

1. **Surveillance for cancer spread or recurrence, and screening for subsequent primary cancers (SURV-4)[c]**
2. **Monitoring long-term effects of cancer, including psychosocial, physical, and immunologic effects**
3. **Prevention and detection of late effects of cancer and therapy**
4. **Evaluation and management of cancer-related syndromes, with appropriate referrals for targeted intervention**
5. **Coordination of care between primary care providers and specialists to ensure that all of the survivor's health needs are met**
6. **Planning for ongoing survivorship care[d]:**
   - ◊ **Information on treatment received including all surgeries, radiation therapy (RT), and systemic therapies**
   - ◊ **Information regarding follow-up care, surveillance, and screening recommendations**
   - ◊ **Information on post-treatment needs, including information on acute, late, and long-term treatment-related side effects and health risks when possible (NCCN Guidelines for Treatment of Cancer by Site)**
   - ◊ **Delineation of roles of all health care providers (including oncologists, primary care physicians [PCPs], and subspecialists) in long-term survivorship care with coordinated timing of care and transfer of care as appropriate**
   - ◊ **Promotion of adherence to healthy behavior recommendations (HL-1)**
   - ◊ **Periodic assessment of ongoing needs and identification of appropriate resources**

[b] From Hewitt M, Greenfield S, Stovall E. From Cancer Patient to Cancer Survivor: Lost in Transition. Committee on Cancer Survivorship: Improving Care and Quality of Life, Institute of Medicine and National Research Council 2006. Available at: http://www.nap.edu/catalog/11468.html.

[c] Surveillance testing (eg, labwork, imaging, other studies) should be based on cancer diagnosis and individualized patient risk. A small excess risk of cancer has been linked to frequent radiographic imaging. Surveillance testing should be performed as per NCCN Guidelines for Treatment of Cancer by Site. Additional labwork, imaging, or other studies to evaluate for recurrence should be based on clinical presentation and judgment.

[d] Commission on Cancer: Optimal Resources for Cancer Care (2020 Standards): https://www.facs.org/-/media/files/quality-programs/cancer/coc/optimal_resources_for_cancer_care_2020_standards.ashx.

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GENERAL PRINCIPLES OF THE SURVIVORSHIP GUIDELINES

- **Cancer survivors include those who are initiating treatment, in ongoing treatment, have completed cancer treatment, or are in clinical remission. (Also see the NCCN Guidelines for Supportive Care Table of Contents)**
- **These guidelines provide screening, evaluation, and treatment recommendations for common consequences of cancer and cancer treatment. They can be used to optimize health and wellness for all survivors; however, they were created to assist health care professionals who work with survivors of adult-onset cancer in the post-treatment period, including those in both the oncology and primary care practices.**
- **The panel recognizes that many of the post-treatment issues covered in these Guidelines are best addressed before cancer treatment begins so that many problems can be prevented or minimized.**
- **These guidelines are designed to provide a framework for the general survivorship care and management of potential long-term and/or late effects of cancer and its treatment that survivors may experience.**
- **The NCCN Guidelines for Survivorship should be used as a supplement to the follow-up recommendations within the disease-specific guidelines. See the NCCN Guidelines for Treatment of Cancer by Site and NCCN Guidelines for Palliative Care for recommendations regarding metastatic disease.**
- **These guidelines, with the appropriate disease-specific guideline, provide a framework for the coordination of care between the survivor's health care providers to ensure that needs are appropriately addressed.**
- **The panel does not assume that all survivorship issues will be addressed at every visit. The panel recommends periodic screening assessments and appropriate follow-up care as clinically indicated.**
- **Referral to other health care disciplines/providers or community resources may be used to address several indications or identified issues with one intervention (eg, rehabilitation for fatigue, depression, and pain).**
- **The panel recommends stakeholders ensure the implementation of guideline-concordant survivorship care within their unique health systems.[1] Specifically, institutions are encouraged to determine how to systematically deliver the six key components of survivorship care (SURV-1).[1-3] There are several models of care that frame the implementation of survivorship care according to provider type(s), clinic type(s), patient risk, and other factors.[4-7] Engaging these models of care will facilitate implementation planning.[7] Panel members recommend institutions provide the resources necessary to plan, deliver, and evaluate their survivorship care program(s).[1-2]**
- **For survivorship issues related to younger populations, also see the NCCN Guidelines for Adolescent and Young Adult (AYA) Oncology and the Children's Oncology Group Long-Term Follow-up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers (www.survivorshipguidelines.org).**
- **For survivors treated with immunotherapy, ongoing surveillance for immune-mediated toxicities is warranted. See NCCN Guidelines for Management of Immunotherapy-Related Toxicities.**

[1] Jazieh AR, McClure JS, Carlson RW. Implementation Framework for NCCN Guidelines. J Natl Compr Canc Netw 2017;15:1180-1185.
[2] Commission on Cancer. American College of Surgeons Optimal Resources for Cancer Care: 2020 Standards. https://www.facs.org/media/whmfnppx/2020_coc_standards.pdf
[3] The Advisory Board Company: Oncology Round Table. The Survivorship Challenge. https://www.advisory.com/-/media/project/advisoryboard/advisory/topics/oncology/survivorship-challenge/Survivorship-Challenge.pdf
[4] Sussman J, Souter LH, Grunfeld E, et al. Models of Care for Cancer Survivorship 2017; Cancer Care Ontario Evidenced-Based Series 26-1;Version 2: https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/246
[5] Halpern MT, Viswanathan M, Evans TS, et al. Models of cancer survivorship care: Overview and summary of current evidence. J Oncol Pract 2015;11:e19-27.
[6] Jefford M, Howell D, Li Q, et al. Improved models of care for cancer survivors. Lancet 2022;399:1551-1560.
[7] ASCO Determining the Best Model for You: https://old-prod.asco.org/news-initiatives/current-initiatives/cancer-care-initiatives/survivorship-compendium/needs-assessment

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

SCREENING FOR SUBSEQUENT NEW PRIMARY CANCERS

- **Subsequent new primary malignant neoplasms may occur in survivors years after treatment when the survivor's oncologist may no longer be involved in the survivor's care and may also occur at younger ages than in the general population.**
- **The overall cancer rate in survivors is higher than in the general population. This increased risk is due to genetic susceptibilities (eg, hereditary cancer syndromes) and/or family history, shared etiologic exposures (eg, smoking, environmental exposures, health behaviors, human papillomavirus [HPV]), and mutagenic effects of cancer treatment.**
- **Treatment-related subsequent primary cancers vary with the type and intensity of cancer treatment and are associated in particular with RT and specific chemotherapeutic agents. For recommendations for screening considerations, see Principles of Screening for Treatment-Related Subsequent Primary Cancers (SURV-4A).**
- **Screening for subsequent primary cancers should be a shared responsibility between primary and oncology care physicians. For survivors living with metastatic disease, recommendations for screening should be tailored to the survivor's individualized risk and disease status. (See the NCCN Guidelines for Detection, Prevention, and Risk Reduction Table of Contents).**
- **Evidence suggests that excess lifetime radiation exposure from CT imaging may be associated with a mildly increased risk of developing a radiation-associated cancer. Use of radiologic studies to screen for recurrent cancer should be based on diagnosis and evidence that early detection of recurrence will improve cancer-related outcomes. Recommendations for surveillance imaging modality and frequency can be found in the NCCN Guidelines for Treatment of Cancer by Site.**
- **For familial assessment considerations that impact screening, see SURV-5.**

Note: All recommendations are category 2A unless otherwise indicated.
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PRINCIPLES OF SCREENING FOR TREATMENT-RELATED SUBSEQUENT PRIMARY CANCERS

- **As part of screening and early detection for subsequent primary cancers, history and physical exam (H&P) are recommended at least annually.**
- **Also see the NCCN Guidelines for Adolescent and Young Adult (AYA) Oncology and other NCCN Guidelines as referenced. For adult survivors of pediatric cancer, please reference the Children's Oncology Group Long-Term Follow Up Guidelines.**
- **These treatment related screening and early detection recommendations are distinct from and should not replace surveillance for recurrence of the index cancer.**

Treatment-Related Subsequent Primary Cancers by Treatment Exposure
(This table does not cover all populations, and additional cancer screenings may be warranted depending on clinical circumstances.)

Treatment Exposure (and body part affected, where noted)	Increased Subsequent Primary Cancer Risk	Screening and Early Detection Recommendations	Comments
Radiation Therapy, Including Total Body Irradiation (TBI)			
Cranial	Meningiomas	Imaging if clinically indicated due to signs or symptoms of disease	
	Skin cancer	Consider annual skin exam and/or dermatology referral	Counsel on sun safety and regular use of sunscreen (at least SPF 30)
Head and Neck	Mucosal head and neck cancer	Annual head and neck exam (including direct or indirect laryngoscopy as clinically indicated), and/or otolaryngology referral	• Counsel on avoidance of tobacco and heavy alcohol use • Based on age, consider HPV vaccination counseling as appropriate. (SIMIN-1) • For smoking-related cancer, evaluate indications for lung cancer screening
	Thyroid cancer	Annual neck exam	Neck ultrasound as clinically indicated
	Skin cancer	Consider annual skin exam and/or dermatology referral	Counsel on sun safety and regular use of sunscreen (at least SPF 30)
	Salivary gland cancers	Imaging if clinically indicated due to signs or symptoms of disease	
	Soft tissues sarcomas	Imaging if clinically indicated due to signs or symptoms of disease	

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Continued

PRINCIPLES OF SCREENING FOR TREATMENT-RELATED SUBSEQUENT PRIMARY CANCERS

Treatment-Related Subsequent Primary Cancers by Treatment Exposure
(This table does not cover all populations, and additional cancer screenings may be warranted depending on clinical circumstances.)

Treatment Exposure (and body part affected, where noted)	Increased Subsequent Primary Cancer Risk	Screening and Early Detection Recommendations	Comments
Radiation Therapy, Including Total Body Irradiation (TBI)–Continued			
Mantle/Chest	Breast cancer (assigned female at birth)[a]	Breast MRI and mammogram annually, starting at age 30 or 8 years after radiation, whichever occurs last, for exposure ≥10 Gy and <30 years old. See also NCCN Guidelines for Breast Cancer Screening and Diagnosis	• Risk starts to increase at about 8 years after exposure • Consider chemoprevention options (see NCCN Guidelines for Breast Cancer Risk Reduction)
	Skin cancer	Consider annual skin exam and/or dermatology referral	Counsel on sun safety and regular use of sunscreen (at least SPF 30)
	Soft tissue sarcomas	Imaging if clinically indicated due to signs or symptoms of disease	
	Lung cancer	Consider imaging if clinically indicated due to signs or symptoms of disease	• Smoking substantially increases risk. For survivors who smoke or have a history of smoking: ▸ Counsel on tobacco cessation as indicated ▸ Consider spiral CT scan or referral to lung cancer screening clinic for shared decision-making if screening criteria met (see NCCN Guidelines for Lung Cancer Screening) ▸ For survivors not meeting lung cancer screening criteria (especially survivors of Hodgkin lymphoma), consider chest imaging as clinically indicated
	Thyroid and parathyroid cancer	Imaging and/or testing if clinically indicated due to signs or symptoms of disease	

[a] Screening should be individualized based on risk factors and individual anatomy.

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Continued

PRINCIPLES OF SCREENING FOR TREATMENT-RELATED SUBSEQUENT PRIMARY CANCERS

Treatment-Related Subsequent Primary Cancers by Treatment Exposure
(This table does not cover all populations, and additional cancer screenings may be warranted depending on clinical circumstances.)

Treatment Exposure (and body part affected, where noted)	Increased Subsequent Primary Cancer Risk	Screening and Early Detection Recommendations	Comments
Radiation Therapy, Including Total Body Irradiation (TBI)–Continued			
Abdomen/Flank/Pelvic	Colorectal cancer	Colorectal cancer screening starting at age 30 or 5 years after radiation, whichever occurs last, for exposure ≥20 Gy[b]	• Repeat colorectal cancer screening every 3 years after multi-target stool DNA test or every 5 years after colonoscopy. Consultation with primary care, gastroenterologist, or oncologist should be considered as clinically indicated.[c] • Also see NCCN Guidelines for Colorectal Cancer Screening
	Skin cancer	Consider annual skin exam and/or dermatology referral	Counsel on sun safety and regular use of sunscreen (at least SPF 30)
	Soft tissue sarcomas	Imaging if clinically indicated due to signs or symptoms of disease	
Extremities	Skin cancer	Consider annual skin exam and/or dermatology referral	Counsel on sun safety and regular use of sunscreen (at least SPF 30)
	Soft tissue sarcomas	Imaging if clinically indicated due to signs or symptoms of disease	

[b] These recommendations are based on data from the treatment of children and adolescents as well as emerging data regarding the rising incidence of colorectal cancer in younger adults within the general population.
[c] Children's Oncology Group Long-Term Follow Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers – Version 6.0 (October 2023).

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PRINCIPLES OF SCREENING FOR TREATMENT-RELATED SUBSEQUENT PRIMARY CANCERS

Treatment-Related Subsequent Primary Cancers by Treatment Exposure
(This table does not cover all populations, and additional cancer screenings may be warranted.)

Treatment Exposure (and body part affected, where noted)	Increased Subsequent Primary Cancer Risk	Screening and Early Detection Recommendations	Comments
Transplant Conditioning Therapy (RT or chemotherapy)			
Hematopoietic Cell Transplantation[d]	• May increase the risk for a variety of hematologic or solid tumor cancers, including skin cancer, myelodysplastic syndrome/acute myeloid leukemia (MDS/AML), liver cancer, cervical cancer, or oral cancer • May increase the risk for lymphoproliferative disorders	• CBC if clinically indicated due to signs or symptoms of disease • Adhere to age-appropriate cancer screening recommendations ▸ Consider increased frequency/ intensity of cancer screenings (eg, cervical) for immunocompromised individuals • Consider annual skin exam and/or dermatology referral	• Chronic GVHD may increase the risk of certain subsequent malignancies[1,2] • Counsel on sun safety and regular use of sunscreen (at least SPF 30) • Counsel on importance of regular dental checkups
Systemic Therapy			
Alkylating Agents, Anthracyclines, Epipodophyllotoxins	Hematologic malignancies (eg, AML)	CBC if clinically indicated due to signs or symptoms of disease	
Alkylating Agents	Bladder cancer	Urine cytology if clinically indicated due to signs or symptoms of disease	When given in combination with pelvic radiation, risk is increased
Tamoxifen	Endometrial cancer	Assess vaginal pain or bleeding annually; If abnormal uterine bleeding, referral to gynecology for consideration of transvaginal ultrasound and biopsy[e]	Very little risk in premenopausal survivors; risk is primarily in postmenopausal survivors with a uterus.
PARP Inhibitors Lutetium-octreotide	MDS; AML	• CBC if clinically indicated due to signs or symptoms of disease • Consider referral to hematology for work up for persistent cytopenias or leukopenias	MDS and AML are rare; usually after long-term treatment[3,4]

[d] Specific populations such as hematopoietic cell transplantation (HCT) survivors may have additional considerations for cancer screening.
[e] If there is abnormal uterine bleeding in survivors in peri- and premenopausal age ranges, consider first checking estradiol levels, then do additional interventions if reasonable.

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REFERENCES

[1] Gunduz M, Ozen M, Sahin U, et al. Subsequent malignancies after allogeneic hematopoietic stem cell transplantation. Clin Transplant 2017;31.
[2] Rambhia PH, Conic RZ, Atanaskova-Mesinkovska N, et al. Role of graft-versus-host disease in the development of secondary skin cancers in hematopoietic stem cell transplant recipients: A meta-analysis. J Am Acad Dermatol 2018;79:378-380.e3.
[3] LaFargue CJ, Dal Molin GZ, Sood AK, Coleman RL. Exploring and comparing adverse events between PARP inhibitors. Lancet Oncol 2019;20:e15-e28.
[4] Strosberg JR, Caplin ME, Kunz PL, et al; NETTER-1 investigators. 177Lu-Dotatate plus long-acting octreotide versus high dose long-acting octreotide in patients with midgut neuroendocrine tumours (NETTER-1): final overall survival and long-term safety results from an open-label, randomised, controlled, phase 3 trial. Lancet Oncol 2021;22:1752-1763. Erratum in: Lancet Oncol 2022;23:e59.

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PRINCIPLES OF CANCER RISK ASSESSMENT AND COUNSELING

- **Periodic updating of family cancer history (when known) is recommended to reassess hereditary risk. Genetic testing guidelines and knowledge about hereditary cancer risk evolve over time and new family diagnoses may occur making periodic assessment important.**
- **Comprehensive family history including any prior genetic testing is the first step in genetic risk assessment.**
- **Many cancer survivors, particularly those diagnosed at younger ages, as well as those diagnosed with rare cancers, multiple primary cancers, or cancers associated with high-risk cancer syndromes, and those with one or more relatives with the same or related cancers are candidates for risk assessment per guidelines from NCCN and other expert groups. Genetic testing is recommended for appropriate survivors based on results of the risk assessment. (See General Testing Criteria [CRIT-1] from the NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic)**
  - **Criteria for formal genetic risk assessment and/or testing, and for care of patients with known germline mutations linked to an increased risk for cancer can be found in the following NCCN Guidelines:**
    - **NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic**
      - **Principles of Cancer Risk Assessment and Counseling (EVAL-A)**
      - **Pedigree: First-, Second, and Third-Degree Relatives of Proband (EVAL-B)**
    - **NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal**
    - **NCCN Guidelines for Gastric Cancer**
    - **NCCN Guidelines for Neuroendocrine and Adrenal Tumors**
    - **NCCN Guidelines for Thyroid Carcinoma**
    - **NCCN Guidelines for Prostate Cancer**
    - **NCCN Guidelines for Melanoma: Cutaneous**
  - **Genetic testing with multigene panels should be reconsidered in those with prior negative tests with limited sets of genes.**
  - **Consider referral for genetic risk assessment for patients who do not meet the criteria but who request it.**
- **Consider referral to genetic counseling services for risk assessment and/or testing if the survivor did not have a comprehensive evaluation at time of diagnosis.**
- **Genetic testing may also provide opportunities to identify and reduce risks in relatives of cancer survivors.**

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ASSESSMENT BY HEALTH CARE PROVIDER (ONCOLOGY OR PRIMARY CARE) AT REGULAR INTERVALS

- **A periodic assessment at least annually is recommended for all survivors to determine any needs and necessary interventions. For sample assessment, see SURV-A.**
- **Shared coordinated care between the oncology, primary care, and subspecialty care providers is encouraged. Depending on the cancer type and stage of disease, transition of care to a PCP may be done when deemed clinically appropriate with referral back to oncologic care as needed.**
- **Care providers are also encouraged to assess the following at regular intervals:**
  1. **Current disease status**
  2. **Functional/performance status**
  3. **Medication use (including over-the-counter [OTC] medications and supplements)**
  4. **Comorbidities**
  5. **Prior cancer treatment history and modalities used**
  6. **Family history**
  7. **Psychosocial factors**
  8. **Weight and health behaviors that can modify cancer and comorbidity risk (including tobacco/alcohol use)**
  9. **Fertility concerns for adults of reproductive age**
  10. **See the NCCN Guidelines for Treatment of Cancer by Site for disease-specific recommendations for surveillance/follow-up**

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SURVIVORSHIP ASSESSMENT (Patient Version)
Please answer the following questions:

Survivorship Concerns	Survivorship Care Survey
Cardiac Health	1. Do you have shortness of breath or chest pain after physical activities (eg, climbing stairs) or exercise? Yes/No 2. Do you have shortness of breath when lying flat, wake up at night needing to get air, or have persistent leg swelling? Yes/No
Anxiety, Depression, Trauma, and Distress	3. In the past two weeks, have you been bothered more than half the days by little interest or pleasure in doing things? Yes/No 4. In the past two weeks, have you been bothered more than half the days by feeling down, depressed, or hopeless? Yes/No 5. Has stress, worry, anger, fear of recurrence, or distress about effects of cancer treatment interfered with your life? Yes/No
Cognitive Function	6. Do you have difficulties with multitasking or paying attention? Yes/No 7. Do you have difficulties with remembering things? Yes/No 8. Does your thinking seem slow? Yes/No
Fatigue	9. Do you feel persistent fatigue despite a good night's sleep? Yes/No 10. Does fatigue interfere with your usual activities? Yes/No 11. How would you rate your fatigue on a scale of 0 (none) to 10 (extreme) over the past week? 0–10
Lymphedema	12. Since your cancer treatment, have you had any swelling, fatigue, heaviness, or fullness on the same side as your treatment that has not gone away? Yes/No
Pain	13. Have you had any pain in the past week? Yes/No 14. How would you rate your pain on a scale of 0 (none) to 10 (extreme) over the past week? 0–10
Hormone-Related Symptoms	15. Have you been bothered by hot flashes/night sweats? Yes/No 16. Have you been bothered by other hormone-related symptoms (ex, vaginal dryness, erectile dysfunction, urinary incontinence)? Yes/No
Sexual Health	17. Do you have any concerns regarding your sexual function, sexual activity, sexual relationships, or sex life? Yes/No 18. Are these concerns causing you distress? Yes/No
Fertility	19. Do you have concerns about fertility or family planning? Yes/No
Sleep Disorder	20. Are you having problems falling asleep, staying asleep, or waking up too early? Yes/No 21. Are you experiencing excessive sleepiness (ie, sleepiness or falling asleep in inappropriate situations or sleeping more during a 24-hour period than in the past)? Yes/No 22. Have you been told that you snore frequently or that you stop breathing during sleep? Yes/No
Healthy Lifestyle	23. Do you engage in regular physical activity or exercise, such as brisk walking, jogging, weight/resistance training, bicycling, swimming, etc.? Yes/No ▸ 23a. If you answered "Yes," how often? 24. Excluding white potatoes, do you eat at least 2½ cups of fruits and/or vegetables each day? Yes/No 25. Do you have concerns about your weight? Yes/No 26. Do you take vitamins or other supplements? Yes/No
Immunizations and Infections	27. Have you received your flu vaccine this flu season? Yes/No 28. Are you up to date on your vaccines? Yes/No/Don't know
Employment/ Return to Work	29. Do you have concerns about how cancer and/or cancer therapy has affected your ability to work? Yes/No

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SURVIVORSHIP ASSESSMENT[a] (Provider Key)

Based on the survivor's answers to the assessment questions, refer to the detailed recommendations indicated below:

Survivorship Concerns	Survivorship Care Survey	Provider Key
Cardiac Health	Questions 1–2	If YES to any question, refer to SCVD-1
Anxiety, Depression, Trauma, and Distress	Questions 3–5	If YES to any question, refer to SANXDE-1
Cognitive Function	Questions 6–8	If YES to any question, refer to SCF-1
Fatigue	Questions 9–11	If YES to either question 9 or 10, or a rating of >3 to question 11, refer to SFAT-1
Lymphedema	Questions 12	If YES to question 12, refer to SLYMPH-1
Pain	Questions 13–14	If YES to question 13 and a rating of >4 to question 14, refer to SPAIN-1
Hormone-Related Symptoms	Questions 15–16	If YES to any question, refer to SHRS-1
Sexual Health	Questions 17–18	If YES to any question, refer to SSH-1
Fertility	Question 19	If YES, refer to SF-1
Sleep Disorder	Questions 20–22	If YES to any question, refer to SSD-1
Healthy Lifestyle	Questions 23–26	If NO to question 23 or 24, or YES to question 25, OR if question 23a is less than 3 times per week, OR if body mass index (BMI) is not between 18.5–24.9 kg/m^2, refer to HL-1 If YES to question 26, refer to SSUP-1
Immunizations and Infections	Questions 27–28	If NO to question 27, or NO or DON'T KNOW to question 28, refer to SIMIN-1
Employment and Return to Work	Question 29	If YES to question 29, refer to SWORK-1

[a] The tool can be used to guide providers to topics within the guidelines that require more in-depth assessment based on survivor response. While this instrument has not yet been piloted or validated, validated questions have been included when possible.

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SURVIVORSHIP RESOURCES FOR HEALTH CARE PROFESSIONALS AND SURVIVORS[a]

General Online Information	
National Coalition for Cancer Survivorship (NCCS)	http://www.canceradvocacy.org
American Association for Cancer Research (AACR)	http://www.aacr.org
(ACS) • Survivorship information • Cancer Survivors Network • National Cancer Survivorship Resource Center • Physical side effects information, including sexual health	http://www.cancer.org/index http://www.cancer.org/treatment/survivorshipduringandaftertreatment/index http://csn.cancer.org http://www.cancer.org/SurvivorshipCenter http://www.cancer.org/treatment/treatmentsandsideeffects/physicalsideeffects/index
American Institute for Cancer Research (AICR): Survivorship information • Survivorship information • Nutrition, physical activity, and weight management	http://www.aicr.org/patients-survivors
American Society of Clinical Oncology (ASCO) • Survivorship information for patients • Tools and resources for oncology providers	http://www.cancer.net/survivorship https://www.asco.org/news-initiatives/current-initiatives/cancer-care-initiatives/survivorship-compendium
Cancer Care: Free, professional support services for anyone affected by cancer	www.cancercare.org
Be The Match	https://bethematch.org
Centers for Disease Control and Prevention (CDC): Survivorship information	https://www.cdc.gov/cancer/survivors/index.htm
Leukemia & Lymphoma Society (LLS): Survivorship information	https://www.lls.org/managing-your-cancer
LIVESTRONG	http://www.livestrong.org
National Cancer Institute: Office of Cancer Survivorship (OCS) • Facing Forward series, designed to educate cancer survivors, family members, and health care providers about the challenges associated with life after cancer treatment	https://cancercontrol.cancer.gov/ocs http://cancercontrol.cancer.gov/ocs/resources/ffseries.html
National Comprehensive Cancer Network (NCCN) NCCN Guidelines for Patients: Survivorship	https://www.nccn.org/patientresources/patient-resources/guidelines-for-patients
MedlinePlus: Current accurate information by cancer site	http://www.nlm.nih.gov/medlineplus/cancers.html
Oncology Nursing Society: Putting Evidence Into Practice	https://www.ons.org/explore-entrance
General Help Lines	
American Cancer Society	1.800.227.2345 http://www.cancer.org
Cancer Support Community	1.888.793.9355 http://www.cancersupportcommunity.org
LIVESTRONG SurvivorCare	1.855.220.7777
National Cancer Institute's Cancer Information Service	1.800.4.CANCER

[a] There are many smart phone/tablet/mobile device apps, web-based programs, DVDs, and TV programs available to help survivors with various aspects of health care and wellness.

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Continued

SURVIVORSHIP RESOURCES FOR HEALTH CARE PROFESSIONALS AND SURVIVORS[a] (CONTINUED)

Other Survivorship Guidelines	
Children's Oncology Group: Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers	http://www.survivorshipguidelines.org
Survivorship Care Planning	
ASCO Cancer Treatment Summaries	http://www.cancer.net/survivorship/follow-care-after-cancer-treatment/asco-cancer-treatment-and-survivorship-care-plans
Integrative Therapies	
National Institutes of Health Office of Dietary Supplements	https://ods.od.nih.gov/factsheets/list-all
National Center for Complementary and Integrative Resources for Health Care Providers	https://nccih.nih.gov/health/providers
Society for Integrative Oncology	https://integrativeonc.org/
Legal and Employment Issues	
Americans with Disabilities Act	www.ada.gov
The ADA National Network	https://adata.org
ASCO Cancer.net: Working When You Have Cancer: An Expert Q&A	https://www.cancer.net/blog/2018-12/working-when-you-have-cancer-expert-qa
Cancer and Careers: Patient information about working and dealing with cancer	http://www.cancerandcareers.org/en
Cancer Legal Resource Center	https://thedrlc.org/cancer
Job Accommodation Network (JAN)	www.askjan.org
National Cancer Institute: Going Back to Work	https://www.cancer.gov/about-cancer/coping/day-to-day/back-to-work
National Coalition for Cancer Survivorship (NCCS) Employment Rights • Employment Rights, Working It Out" • "What Cancer Survivors Need To Know About Health Insurance"	http://www.canceradvocacy.org/resources/employment-rights https://canceradvocacy.org/wp-content/uploads/Working_It_Out.pdf https://canceradvocacy.org/wp-content/uploads/2013/01/Health-Insurance.pdf
NCCN Employer Tool Kit	https://www.nccn.org/business-policy/business/employer-resources/employer-toolkit
ACS: • Understanding Health Insurance • Returning to Work After Cancer Treatment	https://www.cancer.org/treatment/finding-and-paying-for-treatment/understanding-health-insurance.html https://www.cancer.org/treatment/finding-and-paying-for-treatment/understanding-financial-and-legal-matters/working-during-and-after-treatment/returning-to-work-after-cancer-treatment.html
Social Security Administration	https://www.ssa.gov/disability
Triage Cancer	https://triagecancer.org

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Continued

SURVIVORSHIP RESOURCES FOR HEALTH CARE PROFESSIONALS AND SURVIVORS[a] (CONTINUED)

Information About LGBTQ Individuals with Cancer	
CDC Lesbian, Gay, Bisexual, and Transgender Health	https://www.cdc.gov/lgbthealth/index.htm
National LGBT Cancer Network	https://cancer-network.org https://cancer-network.org/welcoming-spaces
National LGBT Cancer Project	https://www.lgbtcancer.org/
Menopause and Sexual Health	
The North American Menopause Society	http://www.menopause.org
American College of Obstetricians and Gynecologists (ACOG)	https://www.acog.org
International Society for the Study of Women's Sexual Health (ISSWSH)	https://www.isswsh.org
Physical Activity	
ACS • Nutrition and Physical Activity Guidelines for Cancer Survivors, Patient Page • "Physical Activity and the Cancer Patient" guide	https://acsjournals.onlinelibrary.wiley.com/doi/epdf/10.3322/caac.21721 http://www.cancer.org/treatment/survivorshipduringandaftertreatment/stayingactive/physical-activity-and-the-cancer-patient
American College of Sports Medicine (ACSM): • ACSM ProFinder: Search for Certified Professionals • ACSM Guidelines for Exercise and Cancer	https://www.acsm.org/get-stay-certified/find-a-pro https://www.acsm.org/blog-detail/acsm-certified-blog/2019/11/25/acsm-guidelines-exercise-cancer-download
Cancer Supportive and Survivorship Care: Exercise: A Cancer Survivor's Tool For Wellness	http://www.cancersupportivecare.com/whyexercise.html
LIVESTRONG at the YMCA	http://www.livestrong.org/YMCA
SilverSneakers: A program that helps older adults live healthy, active lifestyles	https://www.silversneakers.com

[a] There are many smart phone/tablet/mobile device apps, web-based programs, DVDs, and TV programs available to help survivors with various aspects of health care and wellness.

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Continued

SURVIVORSHIP RESOURCES FOR HEALTH CARE PROFESSIONALS AND SURVIVORS[a] (continued)

Nutrition and Weight Management	
ASCO Obesity and Cancer: A Guide for Oncology Providers	https://www.asco.org/sites/new-www.asco.org/files/content-files/blog-release/documents/2014-Obesity-Cancer-Guide-Oncology-Providers.pdf
ASCO/Cancer.Net Managing Your Weight After a Cancer Diagnosis: A Guide for Patients and Families	https://www.cancer.net/sites/cancer.net/files/weight_after_cancer_diagnosis.pdf
Cancer Nutrition Consortium: Nutritional Guidance & Support	https://www.cancernutrition.org
National Heart, Lung, and Blood Institute • Guideline for the Management of Overweight and Obesity in Adults • 3 Steps to Initiate Discussion About Weight Management With Your Patients	http://www.nhlbi.nih.gov/health-pro/guidelines/in-develop/obesity-evidence-review http://www.nhlbi.nih.gov/health/prof/heart/obesity/aim_kit/steps.pdf
National Institute of Diabetes and Digestive and Kidney Diseases Body Weight Planner	https://www.niddk.nih.gov/health-information/weight-management/body-weight-planner?dkrd=hispt0903
New American Plate	http://www.aicr.org/new-american-plate
Oncology Nutrition Dietetic Practice Group of the Academy of Nutrition and Dietetics	http://www.oncologynutrition.org
World Cancer Research Fund: Diet, Activity and Cancer Guidelines	https://www.wcrf.org/diet-activity-and-cancer/
Cardiovascular Health	
American Heart Association/American Stroke Association Tools	https://millionhearts.hhs.gov/tools-protocols/tools.html
Oral and Dental Health	
National Institute of Dental and Craniofacial Research: Oral Complications of Cancer Treatment	http://www.nidcr.nih.gov/oralhealth/Topics/CancerTreatment/OralComplicationsCancerOral.htm

[a] There are many smart phone/tablet/mobile device apps, web-based programs, DVDs, and TV programs available to help survivors with various aspects of health care and wellness.

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Continued

SURVIVORSHIP RESOURCES FOR HEALTH CARE PROFESSIONALS AND SURVIVORS[a] (continued)

Sleep Disorders	
National Cancer Institute Sleep Disorders (PDQ)–Health Professional Version	https://www.cancer.gov/about-cancer/treatment/side-effects/sleep-disorders-hp-pdq
The Society of Behavioral Sleep Medicine	https://www.behavioralsleep.org/
U.S. Department of Veterans Affairs: CBT-i Coach	https://mobile.va.gov/app/cbt-i-coach
Smoking Cessation	
ACS: Smoking cessation support	http://www.cancer.org/healthy/stayawayfromtobacco/index
ASCO: Tobacco Cessation and Control Resources	https://old-prod.asco.org/news-initiatives/current-initiatives/prevention-survivorship/tobacco-cessation-control
North American Quitline Consortium	http://map.naquitline.org
U.S. Federal Government: Smoking cessation support	http://www.smokefree.gov
Suicide Prevention and Other Psychosocial Issues	
988 Suicide and Crisis Lifeline	https://988lifeline.org Call or text 988
American Psychosocial Oncology Society (APOS) Helpline	1.866.276.7443 http://apos-society.org
Cancer Support Community–Cancer Support Helpline	1.888.793.9355 https://www.cancersupportcommunity.org/cancer-support-helpline
Veterans Affairs/Department of Defense Practice Guidelines: Assessment and Management of Patients at Risk for Suicide	https://www.healthquality.va.gov/guidelines/MH/srb/VASuicidePreventionPocketGuidePRINT508FINAL.pdf
NCCN Guidelines for Patients: Distress During Cancer Care	https://www.nccn.org/patientresources/patient-resources/guidelines-for-patients
Anxiety and Depression Association of America • Mobile app • Pocket SAFE-T Card	https://adaa.org https://adaa.org/find-help/support/mental-health-apps https://adaa.org/sites/default/files/SMA09-4432.pdf
Substance Abuse and Mental Health Services Administration	https://www.samhsa.gov/find-treatment

[a] There are many smart phone/tablet/mobile device apps, web-based programs, DVDs, and TV programs available to help survivors with various aspects of health care and wellness.

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Preventive Health

GENERAL PRINCIPLES OF HEALTHY LIFESTYLES

- Healthy lifestyle habits have been associated with improved overall health and quality of life. For some cancers, a healthy lifestyle has been associated with a reduced risk of recurrence and death.
- Cancer prehabilitation[1,2] is appropriate for many newly diagnosed survivors prior to initiating treatment with surgery or chemotherapy. Referrals to physical therapy or exercise oncology specialists should be considered.
- For optimal health, all survivors should be encouraged to set incremental as well as ultimate goals for diet, physical activity, and weight management. At a minimum all survivors should be encouraged to:
  - Achieve and maintain a healthy body weight throughout life (SNWM-2).
  - Avoid inactivity.
  - Engage in physical activity (eg, exercise, take the stairs, park in the back of parking lot) daily (SPA-1).
  - Maintain a healthy diet high in vegetables, fruits, beans/legumes, and whole grains.
  - Limit intake of red and cured meats and highly processed foods,[a,b] particularly those high in fats and sugars (SNWM-1).
  - Drink alcohol sparingly if at all (SNWM-1).
  - Discontinue use of cigarettes, other tobacco products (including hookah), and e-cigarettes (NCCN Guidelines for Smoking Cessation).
    - Avoid secondary exposure to cigarette smoke.
  - Practice sun safety
    - Utilize a sunscreen with an SPF of at least 30 that protects against UVA and UVB rays and is water resistant.
    - Apply sunscreen generously and reapply every 2 hours or after swimming/excessive sweating.
    - Consider using physical barriers whenever possible (ie, hats, shirts with sleeves, avoiding direct sun during peak hours).
    - Do not use tanning beds.
    - Avoid sunburns.
    - Seek shade and wear protective clothing (ie, hats and long-sleeved garments) if outside for prolonged periods of time or during peak direct sun hours.
  - Strive for sufficient sleep on a regular basis (SSD-1).[3] Recommended total sleep duration:
    - Adults: 7–9 hours[4,5]
    - Adolescents: 8–10 hours[4,5]
    - Older adults: 7–8 hours[4,5]
  - Follow up with PCP regularly.
    - Adhere to age-appropriate and treatment-associated health screening, preventive measures (SIMIN-1), and cancer screening recommendations (NCCN Guidelines for Detection, Prevention, & Risk Reduction).
  - Obtain nutrients from food sources rather than relying on dietary supplements. Routine use of dietary supplements is not recommended for the purposes of cancer control (SSUP-1).
- A multidisciplinary approach (including but not limited to clinicians, physical therapists, dieticians, social workers, and patient navigators) should be utilized to:
  - Assess individual and community-level barriers to meeting the healthy lifestyle recommendations.
  - Support patients in developing strategies to overcome challenges throughout the continuum of survivorship care (from diagnosis to long-term survivorship).
  - Consider specialty referrals to supportive programs offered by medical centers or the community (ie, Livestrong at the YMCA).

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Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Footnotes on (HL-1A)
References on (HL-1A)

FOOTNOTES AND REFERENCES FOR GENERAL PRINCIPLES OF HEALTHY LIFESTYLES

Footnotes

[a] Highly (sometimes referred to as "ultra") processed foods are industrial formulations typically with 5 or more and usually many ingredients (eg, soft drinks, sweet or savory packaged snacks, reconstituted meat products [eg, sausage, chicken nuggets], prepared frozen dishes). Besides salt, sugar, oils, and fats, ingredients of ultra-processed foods include food substances not commonly used in culinary preparations, such as hydrolyzed protein, modified starches, and hydrogenated or interesterified oils, and additives whose purpose is to imitate sensorial qualities of unprocessed or minimally processed foods and their culinary preparations or to disguise undesirable qualities of the final product. (Martínez Steele E, et al. BMJ Open 2016;6:e009892).

[b] Consumption of highly-processed foods is associated with an increased risk of cancer. Fiolet T, et al. BMJ 2018;360:k322.

References

[1] Michael CM, et al. Cancer Med 2021;10:4195-4205.
[2] Mina DS, et al. Front Oncol 2021;10:598425.
[3] Watson NF, et al. J Clin Sleep Med 2015; 38:843-844.
[4] Hirshkowitz M, et al. Sleep Health 2015;1:40-43.
[5] Paruthi S, et al. J Clin Sleep Med 2016;12:785-786.

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GENERAL PRINCIPLES OF PHYSICAL ACTIVITY

- **Physical activity and exercise recommendations should be tailored to individual survivor's abilities and preferences.**
- **When it is deemed unsafe or impractical for a survivor to participate in a home exercise program due to specific impairments or need for supervision, referral to skilled therapy (eg, physical and/or occupational therapy) should be made.**
- **Physical activity for cancer survivors[a,b]:**
  - **Survivors should strive for at least 150 minutes of weekly activity with an ultimate goal of 300 minutes or more of moderate-intensity[c] activity or 75 minutes of vigorous-intensity[c] activity or equivalent combination spread out over the course of the week.**
  - **Engage in two to three sessions per week of strength/resistance training that include major muscle groups (SPA-A).**
  - **Stretch major muscle groups prior to aerobic/endurance exercises and at least 2 days per week on days that exercises on those muscle groups are not performed.**
  - **Core exercises and balance training are recommended especially for older survivors and those at risk for falls.**
- **Engage in general physical activity daily (eg, take the stairs, park in the back of parking lot).**
  - **Physical activity includes exercise, daily routine activities, and recreational activities.**
- **Avoid prolonged sedentary behavior (eg, sitting for long periods, prolonged screen-based activities).**
  - **Schedule movement/activity breaks regularly.**
  - **Stand or move while talking on the phone, using the computer, or watching television.**

[a] Additional resources for physical activity in cancer survivors:
- Rock CL, Thomson CA, Sullivan KR, et al. American Cancer Society nutrition and physical activity guideline for cancer survivors. CA Cancer J Clin 2022;73:230-262.
- Rock CL, Thomson C, Gansler T, et al. American Cancer Society guideline for diet and physical activity for cancer prevention. CA Cancer J Clin 2020;70:245-271
- Piercy KL, Troiano RP, Ballard RM, et al. The physical activity guidelines for Americans. JAMA 2018;320:2020-2028.
- Campbell KL, Winters-Stone KM, Wiskemann J, et al. Exercise guidelines for cancer survivors: Consensus statement from international multidisciplinary roundtable. Med Sci Sports Exerc 2019;51:2375-2390.
- Patel AV, Friedenreich CM, Moore SC, et al. American College of Sports Medicine roundtable report on physical activity, sedentary behavior, and cancer prevention and control. Med Sci Sports Exerc 2019;51:2391-2402.

[b] All exercise should be preceded by a light-intensity aerobic warm-up and stretching.

[c] Light physical activity: No noticeable change in breathing pattern; Moderate exercise: Can talk, but not sing; Vigorous exercise: Can say a few words without stopping to catch a breath (see Examples of Physical Activity [SPA-B]).

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PHYSICAL ACTIVITY ASSESSMENT

Ask about prior and current participation in physical activity and assess level of current physical activity at regular intervals

→

Focused clinical evaluation:
- Weight/body mass index (BMI)
- Blood pressure
- Functional status
- Assess baseline level of activity prior to diagnosis and current level of activity[d]
- Barriers to physical activity as assessed by survivor
  - Environmental (eg, home, gym access, outdoor space, physical safety)
  - Financial
  - Physical limitations
  - Time/competing demands
  - Motivation level
  - Social support
  - Stress
- Review of systems
- Disease status

Assessment of modifiable barriers to physical activity:
- Pain
- Fatigue
- Emotional distress
- Nutritional deficits/imbalance
- Medications/side effects

→

Assessment of comorbidities and treatment effects as appropriate:
- Cardiovascular disease (CVD) (including cardiomyopathy)
- Pulmonary disease
- Arthritis/musculoskeletal issues
- History of major musculoskeletal surgery
- Lymphedema
- Peripheral neuropathy
- Bone health/bone strength (including presence of bone metastases)
- Incontinence or bowel/bladder symptoms
- Presence of stoma or ostomy
- Fall risk assessment
- Need for assistive devices (cane, walker, brace, etc)
- Thrombocytopenia/pancytopenia and/or coagulopathies
- Steroid myopathy
- Presence of limb prosthesis

→

Determine risk level for exercise-induced adverse events (SPA-3)

[d] Ask survivor about duration, intensity, and frequency of activity. For example, see Godin G, Shepard RJ. Godin Leisure-Time Exercise Questionnaire. Med Sci Sports Exerc 1997;29:S36-S38. (https://journals.lww.com/acsm-msse/Fulltext/1997/06001/Godin_Leisure_Time_Exercise_Questionnaire.9.aspx)

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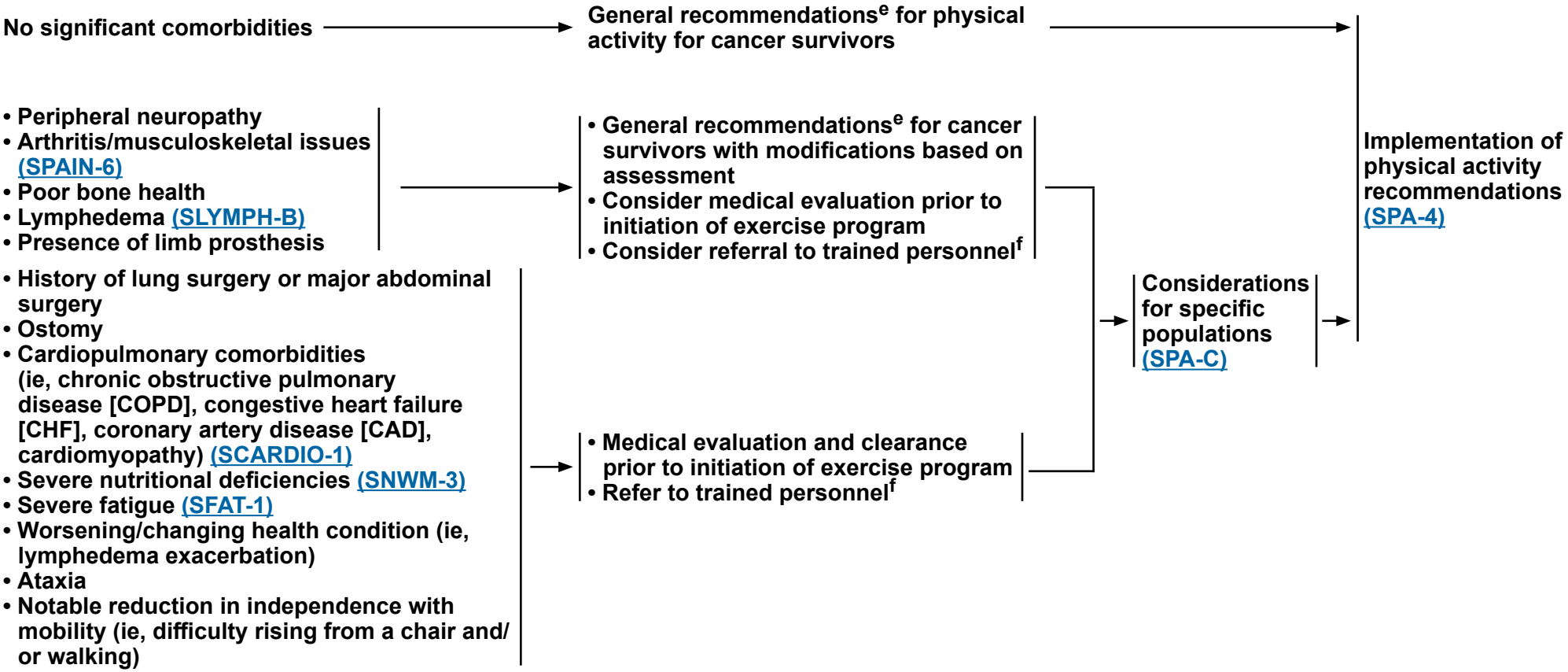
RISK ASSESSMENT FOR PHYSICAL ACTIVITY-INDUCED ADVERSE EVENTS



[e] General Principles of Physical Activity (SPA-1).

[f] Trained personnel can include physical and occupational therapists, certified exercise professionals, and rehabilitation specialists. Specialized training in working with survivors is available for both physical therapists and exercise professionals: ACSM [http://www.acsm.org/get-stay-certified] and American Physical Therapy Association [APTA] Oncology section [http://oncologypt.org].

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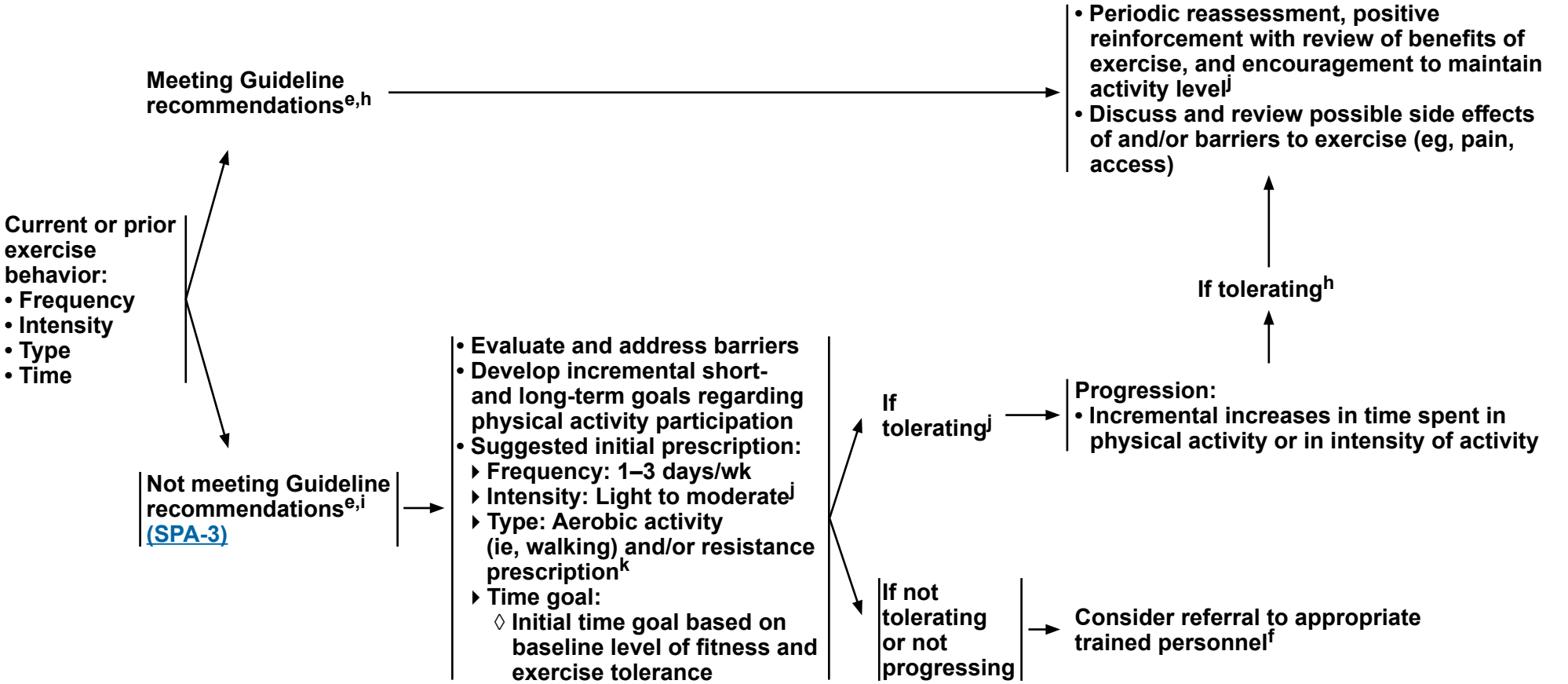
IMPLEMENTATION OF RECOMMENDATIONS[g]



[e] General Principles of Physical Activity (SPA-1).

[f] Trained personnel can include physical and occupational therapists, certified exercise professionals, and rehabilitation specialists. Specialized training in working with survivors is available for both physical therapists and exercise professionals (ACSM [http://www.acsm.org/get-stay-certified] and APTA Oncology section [http://oncologypt.org]).

[g] Reproduced and adapted with permission from Jones LW, Eves ND, Peppercorn J. Pre-exercise screening and prescription guidelines for cancer patients. Lancet Oncol 2010;11:914-916.

[h] If tolerating minimum guideline recommendations, consider encouragement of variation within exercise program or physical activities.

[i] Patients with comorbidities may need additional evaluation before doing more rigorous activity.

[j] Examples of Physical Activity and Strategies to Increase Physical Activity (SPA-B).

[k] Guidance for Resistance Training Recommendations (SPA-A).

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GUIDANCE FOR RESISTANCE TRAINING RECOMMENDATIONS

- **Health benefits of resistance training include improvement in muscle strength and endurance, improvements in functional status, and maintenance/improvement in bone density.**
- **Core and strength training are important to maintain balance and minimize fall risk.**
- **All major muscle groups (chest, shoulders, arms, back, core, and legs) should be incorporated into a resistance training program.**
- **Resistance training prescription**
  - **Frequency: 2–3 times/wk with adequate rest between sessions**
  - **Intensity: 2–3 sets of 10–15 repetitions per set; consider increasing weight amount as tolerated when 3 sets of 10–15 repetitions becomes easy**
  - **Rest: 2- to 3-minute rest period between sets and exercises**
  - **For survivors who wish to start resistance training, refer to trained personnel or exercise specialist if available.[a]**
- **Utilize weight amount that would allow for performance of 10–15 repetitions.**
- **If there is a concern that peripheral neuropathy may increase the risk of dropping free weights, survivors could consider utilizing weight machines and/or training with resistance bands.**
- **For survivors at risk for or with lymphedema, see SLYMPH-B.**

[a] Trained personnel can include physical and occupational therapists, certified exercise professionals, and rehabilitation specialists. Specialized training in working with survivors is available for both physical therapists and exercise professionals (ACSM [http://www.acsm.org/get-stay-certified] and APTA Oncology section [http://oncologypt.org]).

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EXAMPLES OF PHYSICAL ACTIVITY		
Light Exercise[a] **(No noticeable change in breathing pattern)** **• Activity-promoting video game** **• Bowling** **• Child care** **• Leisurely biking at 5 miles/hour or less** **• Light housework (light sweeping, dusting)** **• Playing catch** **• Restorative yoga** **• Tai chi** **• Walking (slow)**	**Moderate Exercise[b]** **(Can talk, but not sing)** **• Ballroom/line dancing** **• Baseball, softball, volleyball** **• Biking on level ground or with few hills** **• Doubles tennis** **• General gardening** **• Moderate-intensity yoga (ie, Vinyasa)** **• Pickleball** **• Pilates** **• Using a manual wheelchair** **• Water aerobics** **• Walking (brisk)**	**Vigorous Exercise[b]** **(Can say a few words without stopping to catch a breath)** **• Aerobic/fast dancing** **• Biking faster than 10 miles/hour** **• Boxing** **• Heavy gardening** **• High-intensity yoga** **• Hiking uphill** **• Jogging** **• Jumping rope** **• Martial arts** **• Pickleball** **• Running** **• Running sports (basketball, hockey, soccer)** **• Singles tennis** **• Stair climbing** **• Swimming (fast pace or laps)** **• Walking (race paced)**

[a] From the National Heart, Lung, and Blood Institute (http://www.nhlbi.nih.gov/health/public/heart/obesity/lose_wt/phy_act.htm) and the Compendium of Physical Activities (https://sites.google.com/site/compendiumofphysicalactivities).
[b] Reproduced and adapted from U.S. Department of Health and Human Services. Move Your Way. Washington, DC: U.S. Department of Health and Human Services. https://health.gov/moveyourway. Accessed March 16, 2020.

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Continued

STRATEGIES TO INCREASE PHYSICAL ACTIVITY
• Physician recommendation
• Referral to trained personnel or exercise specialist if available
• Supervised exercise program or classes
• Telephone counseling
• Motivational interviewing[c]
• Evaluate readiness to change, importance of change, and self-efficacy, utilizing behavior change techniques (eg, action planning, feedback and monitoring, habit formation and tracking)
• Cancer survivor-specific materials and resources (SURV-B 3 of 5)
• Set SMART (specific, measurable, achievable, realistic, timebound) short- and long-term goals[1]
• Consider use of pedometer or wearable fitness tracker to monitor activity goals (eg, obtain at least 7000–10,000 steps per day[2])
• Encourage social support (exercise buddy, group)

Footnotes
[c] Consider referral to trained personnel.

References
[1] Rethorn ZD, Covington K, Cook CE, Bezner JR. J Orthop Sports Phys Ther 2022;52:236-242.
[2] Paluch AE, Bajpai S, Bassett DR, et al. The Lancet Public Health 2022;7:e219-e228.

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CONSIDERATIONS FOR SPECIFIC POPULATIONS[a]

- **Survivors with established lymphedema:**
  - **For workup and treatment of established lymphedema (SLYMPH-3)**
  - **For considerations regarding physical activity in survivors with established lymphedema (SLYMPH-B)**
  - **Survivors at risk for upper extremity lymphedema should be encouraged to perform arm/shoulder exercises (SLYMPH-1)**

- **Survivors with ostomy:[1]**
  - **Empty ostomy bag before engaging in exercise**
  - **Weight lifting/resistance exercises should start with low resistance and progress slowly under the guidance of trained exercise professionals[b]**
  - **Modify core exercises to minimize excess intra-abdominal pressure and avoid Valsalva maneuvers, as ostomy survivors may be at risk for parastomal hernias.**
  - **Use ostomy protector when engaging in contact sports or where there is a risk of a trauma to the ostomy.**
  - **Discuss hydration strategies prior to, during, and after physical activity in survivors with ileostomies, as dehydration is possible given ostomy placement and output.**

- **Presence of limb prosthesis or limb amputation:**
  - **Referral to trained personnel (eg, physical therapist) to develop a physical activity recommendation program to support the survivor**
  - **Ensure proper fit of limb prosthesis and understanding of proper use**
  - **Encourage assistive device use as necessary**

- **Survivors with peripheral neuropathy:**
  - **Stability, balance, and gait should be assessed before engaging in exercise; consider balance training under the care of a trained professional**
  - **Consider alternative aerobic exercise (stationary biking, water aerobics, yoga) rather than walking if neuropathy affects stability**
    - ◊ **Consider use of water shoes/protective footwear with aerobic exercise to minimize risk of skin breakdown**
    - ◊ **Assistance with walking should be provided if alternative aerobic activities are not possible**
  - **Resistance training recommendations:**
    - ◊ **Monitor discomfort in hands when using hand-held weights**
    - ◊ **Consider using dumbbells with soft/rubber coating, and/or wear padded gloves (eg, cycling gloves)**
    - ◊ **Consider resistance training machines**

- **Survivors with bone loss or bone metastases:**
  - **Avoid exercises that place high load on fragile skeletal sites**
  - **Minimize fall risk**
  - **Refer for medical evaluation if bone pain develops**
  - **Consider weight-bearing exercises to improve bone density[2]**
  - **Consider checking vitamin D levels and use of supplemental vitamin D if appropriate**

- **Older adults:**
  - **Assess baseline fitness and functional status**
  - **Recommend core exercises and balance training**
  - **See NCCN Guidelines for Older Adult Oncology**

Footnotes

[a] When possible, survivors in these populations should initiate an exercise program under supervision by trained personnel.

[b] Trained personnel can include physical and occupational therapists, certified exercise professionals, and rehabilitation specialists. Specialized training in working with survivors is available for both physical therapists and exercise professionals:ACSM [http://www.acsm.org/get-stay-certified] or APTA Oncology section [http://oncologypt.org].

References

[1] Campbell KL, Winters-Stone KM, Wiskemann J, et al. Exercise guidelines for cancer survivors: Consensus statement from international multidisciplinary roundtable. Med Sci Sports Exerc 2019;51:2375-2390.

[2] Zhang S, Huang X, Zhao X, et al. Effect of exercise on bone mineral density among patients with osteoporosis and osteopenia: A systematic review and network meta-analysis. J Clin Nurs 2021;31:2100-2111.

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GENERAL PRINCIPLES OF NUTRITION

- Assess dietary pattern for daily intake of fruits, vegetables, and whole grains, as well as red and processed meats, alcohol, dietary supplements, and processed foods or beverages with added fats and/or sugars.
- Assess timing of meals and snacking habits, portion size, frequency of eating out, and use of added fats and/or sugars to foods or beverages.
- All survivors should be encouraged to:
  - Follow a predominantly nutrient-rich plant-based diet, including vegetables, fruit, beans/legumes, and whole grains.[a,b,1]
  - Make informed choices about food to ensure variety and adequate nutrient intake.
  - Limit consumption of red meat such as beef, pork, or lamb to no more than 18 ounces (cooked) per week.
  - Limit consumption of processed meats such as ham, hot dogs, deli cuts, bacon, and sausage.[c]
  - Limit consumption of processed foods that are high in fat, starches, or sugars such as chips, cookies, candy bars, desserts, processed baked goods, sugary cereals, and fried foods.
  - Limit refined sugars to <6 tsp (25 g) for a 2000-calorie daily diet and <9 tsp (38 g) for a 3000-calorie daily diet. One medium cookie has about 2 tsp of sugar; a 12-oz can of a soft drink has about 10 tsp.
  - Monitor calorie intake.
    - ◊ Self-monitoring of food and beverage intake has been shown to be an effective strategy for weight management.
    - ◊ Prolonged periods of fasting may impair adequate caloric and nutrient intake.
  - Drink alcohol sparingly if at all.[2,d] Lower levels of alcohol consumption are associated with a lower risk of cancer.
- For patients desiring further recommendations for dietary guidelines:
  - Consider referral to a registered dietitian.
  - The USDA approximate food plate volumes (https://www.myplate.gov) are:
    - ◊ Vegetables and fruits should comprise half the volume of food on the plate
    - ◊ Vegetables: 30% of plate; fruits 20% of plate
    - ◊ Whole grains: 30% of plate
    - ◊ Protein: 20% of plate
- Recommended sources of dietary components:
  - Fat: plant sources such as olive or canola oil, avocados, seeds and nuts, and cold water fish[e,f]
  - Carbohydrates: fruits, vegetables, whole grains, and legumes
  - Protein: poultry, fish, legumes, low-fat dairy foods, eggs, and nuts
- While the risks and benefits of soy foods for cancer survivors have been debated for many years, most studies to date show that moderate consumption of soy foods (up to 3 servings per day) are beneficial in promoting overall health and survival, with the strongest evidence existing for the prevention of lung cancer and reduction of breast cancer recurrence.[g,3]

References on (SNWM-1A)
Footnotes on (SNWM-1A)

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GENERAL PRINCIPLES OF NUTRITION
FOOTNOTES AND REFERENCES

Footnotes

[a] Recommendation for healthy food portion sizes can be found on the AICR New American Plate website (https://www.aicr.org/cancer-prevention/food-facts/aicrs-new-american-plate) as well as the USDA “My Plate” website (https://www.myplate.gov).

[b] Encourage the use of healthy recipes from resources such as the American Cancer Society’s “Find Healthy Recipes” website: http://www.cancer.org/healthy/eathealthygetactive/eathealthy/findhealthyrecipes/maindishes/index.

[c] Consumption of processed meats is associated with an increased risk of colorectal and gastric cancers (Bouvard V, et al. Carcinogenicity of consumption of red and processed meat. Lancet Oncol 2015;16:1599-1600).

[d] There are some cancers for which survivors should abstain from alcohol. These include liver, esophageal, breast, colon, and head and neck cancers. For some survivors, there may be an increased risk of certain cancers; however, data are limited, especially on risk of recurrence. Recommend drinking alcohol sparingly, if at all (Goding Sauer A, et al. Cancer Epidemiol 2021;71:101893).

[e] These types of fats should be prioritized over saturated fats and used in moderation in the context of weight loss strategies.

[f] Examples of "cold water fish" include mackerel, salmon, herring, and others.

[g] AICR. Soy: Intake Does Not Increase Risk for Breast Cancer Survivors (https://www.aicr.org/cancer-prevention/food-facts/soy).

References

[1] AICR: https://www.aicr.org/cancer-prevention/how-to-prevent-cancer.

[2] Rock CL, Thomson CA, Sullivan KR, et al. American Cancer Society nutrition and physical activity guideline for cancer survivors. CA Cancer J Clin 2022;72:230-262.

[3] Yang WS, Va P, Wong MY, et al. Soy intake is associated with lower lung cancer risk: results from a meta-analysis of epidemiologic studies. Am J Clin Nutr 2011;94:1575-1583.

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GENERAL PRINCIPLES OF WEIGHT MANAGEMENT

- **All survivors should be encouraged to achieve and maintain a BMI between 18.5 and 24.9 kg/m^2 and strive for metabolic health.**
  - **Intentional weight gain should be a priority for survivors who have underweight. (SNWM-4)**
  - **Intentional weight loss should be a priority for survivors who have overweight/obesity.**
    - ◊ **Weight gain after cancer diagnosis and treatment is common and may exacerbate risk for functional decline, comorbidity, and possibly cancer recurrence or death, and may reduce quality of life.**
  - **Weight maintenance should be a priority for survivors who have a BMI between 18.5 and 24.9 kg/m^2.**
- **In conjunction with primary care, survivors should be assessed for metabolic health and body composition independently of BMI.**
- **Weight management includes a three-pronged approach: caloric management, physical activity, and behavior modification.**
- **Providers should discuss strategies and goal setting for weight management and optimal metabolic health, including how to achieve low overall body fat and higher amounts of muscle mass.**
  - ◊ **Practice portion control.**
  - ◊ **Make informed food choices through routine evaluation of food labels.**
  - ◊ **Incorporate physical activity, particularly strength training, to assure optimal lean body mass (SPA-1).**
  - ◊ **Monitor weight, diet, calories, and physical activity routines (eg, journaling, mobile phone apps).**
- **Referrals to registered dietitians, especially those who are Certified Specialists in Oncology Nutrition (CSO) and members of the Oncology Nutrition Dietetic Practice Group of the Academy of Nutrition and Dietetics, should be considered.[h]**
- **There is no current evidence to support the use of weight loss supplements in cancer survivors.**

[h] Many hospitals use CSOs and those in private practice can be accessed via the Academy of Nutrition and Dietetics locator at www.eatright.org.

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NUTRITION AND WEIGHT MANAGEMENT ASSESSMENT[i]

- Evaluate weight status based on BMI criteria[j]
- Evaluate involuntary weight change[k]

→

Clinical evaluation:
- Assess current dietary and physical activity habits and ask about:
  - Daily food intake and eating habits
  - Physical activity habits
  - Willingness to address weight (if necessary) and past strategies used to change[l]
  - Barriers to nutrition and weight management:
    - ◊ Access to healthful, nutrient-dense foods
    - ◊ Financial and socioeconomic issues
    - ◊ Time
  - Appetite and changes in eating patterns

→

Assess treatment effects and medical issues:
- Effects of treatment
  - Gastrointestinal (GI) dysmotility
  - Swallowing issues/ dysphagia
  - Dysgeusia/change in taste
  - Oropharyngeal anatomic changes
  - Bowel dysfunction
  - Digestive enzyme insufficiency
  - GI tract reconstruction/anastomoses
- Comorbidities:
  - CVD
  - Diabetes
  - Renal disease
  - Liver disease
  - Mood disorders (eg, anxiety and depression)
  - Thyroid dysfunction
  - GI disease
- Medication use
- Dental health
- Supplement use
- Psychosocial distress and fear of recurrence

→

INTERVENTIONS

- Discuss "General Principles of Nutrition" (SNWM-1)
- Discuss "General Principles of Weight Management" (SNWM-2)
- Discuss "General Principles of Physical Activity" (SPA-1)

→

Additional Nutrition and Weight Management Interventions (SNWM-4)

[i] Coordination with PCPs and other involved providers is recommended.
[j] The following BMI calculator from the CDC may be used: http://www.cdc.gov/healthyweight/assessing/bmi/adult_bmi/english_bmi_calculator/bmi_calculator.html.
BMI is calculated using the following formula: weight in pounds (lb) x 703 / height in inches squared. The weight categories are as follows: Underweight (BMI, <18.5 kg/m2), Healthy weight (BMI, 18.5–24.9 kg/m^2), Overweight (BMI, 25–29.9 kg/m2), Obese (BMI, ≥30 kg/m2).
[k] Consider workup for disease recurrence in the setting of cachexia or significant involuntary weight loss/gain >5% within 3 months.
[l] For additional resources see the ASCO Toolkit on Obesity and Cancer: https://www.asco.org/sites/new-www.asco.org/files/content-files/blog-release/documents/2014-Obesity-Cancer-Guide-Oncology-Providers.pdf.

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GOAL	ADDITIONAL NUTRITION AND WEIGHT MANAGEMENT INTERVENTIONS[i,l]
Weight gain[m] →	• Manage contributing treatment effects and risk factors as clinically indicated ▸ Dental health and risk factors for poor oral intake ▸ Swallowing disorder, taste/smell disorders, and GI motility as appropriate ▸ Offer smoking cessation assistance as appropriate (NCCN Guidelines for Smoking Cessation) ▸ Contributing psychosocial factors (SANXDE-1) ▸ Barriers to access of healthy food such as living too far from grocery store, lack of transportation, or lack of resources to prepare food • Discuss increasing frequency of feeding and portion size • Discuss avoiding fluid intake with meals • Encourage foods that are both high in calories and nutrient-dense (eg, avocados, nuts) • Consider referral to registered dietitian for individualized counseling • Optimize nutritional density and caloric quality of food • Consider appetite stimulants • Monitor weight regularly
Weight maintenance →	• Reinforce maintenance of healthy body weight throughout lifetime • Monitor weight regularly[n] • Limit foods that are high in calories, particular those that provide relatively few nutrients such as sugar-sweetened beverages and foods with high amounts of fats and sugars • Practice portion control through plate and serving size awareness • Promote regular physical activity (SPA-1)
Weight loss[l] →	• Manage contributing treatment effects and risk factors as clinically indicated ▸ Contributing psychosocial factors, including depression (SANXDE-1) ▸ Barriers to access of healthy food such as living too far from grocery store, lack of transportation, or lack of resources to prepare food • Monitor weight regularly[n] • Recommend weight loss of no more than 2 lb per week and no more than 1 lb per week in survivors >64 years • Limit foods that are high in calories, particularly those with relatively few nutrients such as sugar-sweetened beverages and foods with high amounts of fats and sugars • Substitute high-calorie foods with low-calorie, nutrient-dense foods such as water-rich/low-starch vegetables, broth-based soups, whole grains, fresh fruits for desserts, and beverages such as water, unsweetened tea, and black coffee • Practice portion control by using smaller plates and restricting intake to one serving • Promote regular physical activity (SPA-1) • Refer to community resources or PCP • Refer to registered dietitian or weight management programs for individualized help as needed[o] • Consider evaluation for bariatric surgery or pharmacologic therapy[p] as appropriate

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Footnotes on SNWM-4A

FOOTNOTES FOR SNWM-4

[i] Coordination with PCPs and other involved providers is recommended.
[l] For additional resources see the ASCO Toolkit on Obesity and Cancer: https://www.asco.org/sites/new-www.asco.org/files/content-files/blog-release/documents/2014-Obesity-Cancer-Guide-Oncology-Providers.pdf.
[m] Modification of diet and dietary components should be done on an individual basis.
[n] Daily monitoring has been shown to be associated with improved weight loss (Steinberg, et al. J Acad Nur Diet 2015;115:511-518 and Zheng Y, et al. Int J Obes (Lond) 2016;40:1392-1396).
[o] Strongly consider for survivors with negligible weight loss from diet and exercise interventions.
[p] The safety and efficacy of these drugs in cancer survivors is unknown. Lifestyle modifications are preferred over pharmacologic therapy.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

GENERAL PRINCIPLES OF SUPPLEMENT USE

- **Supplement use is not recommended for most survivors, except in instances of documented deficiencies, inadequate diet, previous gastrointestinal surgery that may cause deficiencies (eg, Roux-en-Y gastric bypass), or comorbid indications (eg, osteoporosis, ophthalmologic disorders, cirrhosis).**
- **Little data exist to support the use of vitamins or other dietary supplements for the purposes of cancer control, recurrence, or prevention.**
- **Taking vitamin supplements does not replace the need for adhering to a healthy diet. All efforts should be made to obtain nutrients from dietary intake.[a]**
- **Providers should assess supplement use at regular intervals. Ask about reasons for supplement use and supplement ingredients.[b]**
- **Refer survivors using supplements not prescribed by a medical provider to a registered dietitian, preferably one with oncology credentials, or other cancer care team members such as integrative medicine or clinical pharmacist.**
- **Survivors of certain cancers are at risk for vitamin deficiencies based on their cancer treatment. Deficiencies should be assessed and repleted as needed (for example, see GAST-I 2 of 3 the NCCN Guidelines for Gastric Cancer).**

[a] Referral to registered dietitians, especially those who are CSO, should be considered for guidance in supplement use, if deemed necessary.
[b] Consider use of available resources for information on supplements (see SURV-B 2 of 3).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

GENERAL PRINCIPLES OF IMMUNIZATIONS

- **These principles apply to cancer survivors, including those with hematologic or solid tumor malignancies and those post transplant.**
- **Clinicians should consider and encourage the administration of inactivated vaccines (eg, influenza) or vaccines made of purified antigens (eg, pneumococcus), bacterial components (eg, diphtheria-tetanus-pertussis), or genetically engineered recombinant antigens (eg, hepatitis B [HepB]) in all cancer and transplant survivors. In the absence of known harm, administration of inactivated vaccines with the hope of achieving some protection may be worthwhile. The usual doses and schedules are recommended.[a,b,c]**
  - **Recommended Immunization Schedule for Adults Aged 19 Years or Older, United States: https://www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf**
- **Vaccines as a strategy to prevent infection represents a unique challenge in cancer and transplant survivors. Vaccines may not trigger protective immune responses in actively immunocompromised individuals or in survivors with residual immune deficits. In addition, certain vaccines such as those that are live attenuated (eg, measles, mumps, rubella [MMR]) are contraindicated in actively immunosuppressed individuals because of a proven or theoretical increased risk of prolonged shedding and disease from the live organism present in the vaccine; other live attenuated vaccines might also be contraindicated in survivors' close contacts. When other vaccine options exist, they should be preferred over live attenuated vaccines in survivors (eg, recombinant zoster vaccine [RZV]).**
- **Ideally, clinicians should have administered all indicated vaccines to patients before initiation of cancer treatment (if possible, at least 2 weeks before cancer treatment).[d]**
  - **Inactivated or recombinant vaccines should be administered 2 or more weeks before cancer treatment and 3 or more months after cancer chemotherapy. While this schedule is preferred, the inactivated influenza vaccine (IIV) can be administered during cancer treatment.**
  - **Live viral vaccines[e] can be administered 4 or more weeks before cancer treatment or 3 or more months after cancer chemotherapy, but consultation with an infectious disease specialist or physician familiar with vaccination in survivors and/or patients with cancer is strongly recommended.**
  - **COVID-19 vaccine is recommended as appropriate. See https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html**
- **In survivors who received anti–B-cell antibody therapy, vaccination should be delayed for at least 6 months after chemotherapy and the last dose of such therapy.**

[a] National Center for Immunization and Respiratory Diseases. General recommendations on immunization — recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2011;60:1-64. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21293327.
[b] Also see: Murthy N, Wodi AP, McNally VV, et al. Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older - United States, 2024. MMWR Morb Mortal Wkly Rep 2024;73:11-15.
[c] Rubin LG, Levin MJ, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clin Infect Dis 2014;58:309-318.
[d] Cancer treatment includes chemotherapy, surgery, treatment with immunosuppressive drugs, radiation, and splenectomy.
[e] Vaccines Contraindicated or to Be Used With Caution in Actively Immunocompromised Survivors or In Close Contacts of Immunocompromised Survivors (SIMIN-A).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

RISK ASSESSMENT AND SCREENING

Risk factors for infections:
- **Underlying disease and/or comorbidities**
- **Splenectomy**
- **Ongoing or recent exposures (ie, <3 months)**
  - **Cytotoxic chemotherapy**
  - **Monoclonal antibodies (eg, rituximab, alemtuzumab)**
  - **Radiation**
  - **Corticosteroids**
- **Prior cellular therapies**
  - **HCT[f]**
  - **Chimeric antigen receptor (CAR) T-cell therapy**
- **Prior/current exposure to endemic infections or epidemics**
- **Blood transfusion history**

→

INTERVENTIONS

- **Education on infection prevention practices**
  - **Safe pet care/avoidance of zoonosis[g]**
  - **Travel precautions[h]**
  - **Gardening precautions[i]**
  - **Proper hand hygiene[j]**
- **Vaccines[e,k]**
  - **Assess overall immune system viability and history of allergic reactions to vaccines**
    - ◊ **Baseline white blood cell count (WBC) should be adequate before starting vaccinations, unless elevated due to disease status**
    - ◊ **Patient should not be on immunosuppressive drugs[l] or chemotherapy**
    - ◊ **Ongoing infection should not be present**
- **Antimicrobial prophylaxis (See NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections)**

→ **SIMIN-3**

[e] Vaccines Contraindicated or to Be Used With Caution in Actively Immunocompromised Survivors or In Close Contacts of Immunocompromised Survivors (SIMIN-A).
[f] HCT includes peripheral blood stem cell transplantation, bone marrow transplantation, and cord blood transplantation.
[g] Safe pet care tips include washing hands with soap and running water after handling animal feces. If possible, survivors at high risk for immune suppression should avoid direct contact with animal feces and other bodily secretions. Survivors with elevated risk of infection and those who are immunocompromised are at higher risk for zoonoses and should use extra caution.
[h] Travel precautions include education on the need for pre-travel vaccines, prophylaxis against specific infections, and education on how to prevent waterborne, airborne, and zoonotic infections. Travelers may find useful information at https://wwwnc.cdc.gov/travel/yellowbook/2024/additional-considerations/immunocompromised-travelers or by consulting a travel clinic.
[i] Examples of gardening precautions include:
- Wearing gloves to avoid skin cuts/punctures that could have delayed healing and to avoid thorns that can have fungus or staphylococcus/streptococcus.
- Wearing a protective mask to avoid spores. (For guidelines on physical activity, see SPA-1)

[j] For proper hand hygiene, see the CDC "Clean Handwashing: Clean Hands Save Lives" campaign: https://www.cdc.gov/handwashing.
[k] For dosing and schedule, see General Principles of Vaccines in Cancer Survivors (SIMIN-B).
[l] Patients should not be on immunosuppressive drugs including ≥0.5 mg/kg of prednisone or equivalent, or greater than a combination of two immunosuppressive medications given concurrently.

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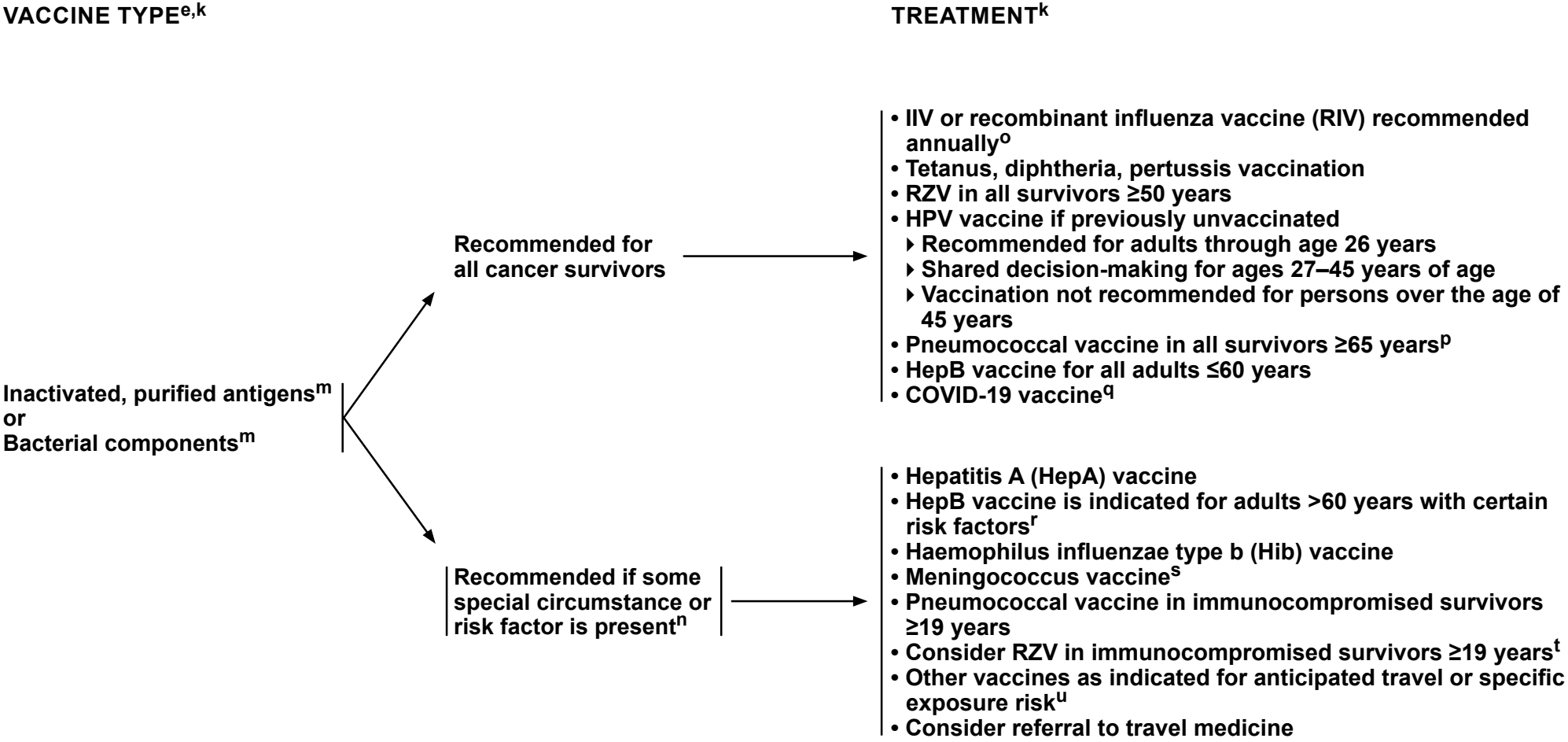
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.



Footnotes on SIMIN-3A

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

FOOTNOTES FOR SIMIN-3

[e] Vaccines Contraindicated or to Be Used With Caution in Actively Immunocompromised Survivors or In Close Contacts of Immunocompromised Survivors (SIMIN-A).

[k] For dosing and schedule, see General Principles of Vaccines in Cancer Survivors (SIMIN-B).

[m] Inactivated or purified antigens or bacterial components should be administered beginning at least 3 months after cytotoxic chemotherapy or RT and 6 months after HCT (a dose of IIV can be given as early as 4 months after HCT, but a second dose should be considered in this situation).

[n] These vaccines should be considered if there are unique circumstances such as functional or anatomic asplenia or in a survivor's lifestyle, upcoming travel, or local epidemic or risks that merit their use. Please consult with an infectious disease or travel medicine specialist. Vaccination precautions for survivors who had cellular therapy can be found on SIMIN-B.

[o] Principles of Influenza Vaccine(s) (SIMIN-C).

[p] General Principles of Vaccines in Cancer Survivors (SIMIN-B).

[q] Recommendations regarding COVID-19 vaccines are continually changing (https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html). For guidance about the management of concurrent COVID-19 and cancer, please see the NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections.

[r] For a list of risk factors for hepatitis B, see the CDC's Hepatitis B Vaccination of Adults: https://www.cdc.gov/hepatitis/hbv/vaccadults.htm.

[s] Recommended in high-risk patients or those with functional or anatomic asplenia. Mbaeyi SA, Bozio CH, Duffy J, et al. Meningococcal Vaccination: Recommendations of the Advisory Committee on Immunization Practices, United States, 2020. MMWR Recomm Rep 2020;69:1-41.

[t] Anderson TC, et al. MMWR Morb Mortal Wkly Rep 2022;71:80-84.

[u] For travel-related vaccine recommendations, see the CDC website at https://wwwnc.cdc.gov/travel.

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VACCINES CONTRAINDICATED OR TO BE USED WITH CAUTION IN ACTIVELY IMMUNOCOMPROMISED SURVIVORS OR TO BE USED WITH CAUTION IN CLOSE CONTACTS OF IMMUNOCOMPROMISED SURVIVORS[1]
Live attenuated vaccines[a] • Measles, mumps, rubella (MMR) • Oral typhoid • Yellow fever • Rotavirus[b] • Nasal influenza vaccine • Varicella vaccine (single or combined with MMR)

Footnotes

[a] Severe complications have followed vaccination with live attenuated vaccines among immunocompromised patients. They should not be offered to an actively immunocompromised or transplant survivor or their close contacts, unless cleared by a clinician experienced in vaccine use or by an infectious disease specialist. If a live attenuated vaccine is inadvertently administered to a survivor's close contact, close contact with the survivor should be avoided for 2 to 6 weeks following vaccination depending on the type of administered vaccine.

[b] Immunocompromised survivors should avoid handling diapers of children who have been vaccinated with rotavirus vaccine for 4 weeks after vaccination.

References

[1] Rubin LG, Levin MJ, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clin Infect Dis 2014;58:309-318.

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Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

GENERAL PRINCIPLES OF VACCINES IN CANCER SURVIVORS

Vaccination in Survivors Who Had Cellular Therapy (ie, HCT,[a] CAR T-cell therapy)[1]

- **For infection concerns and recommended prophylaxis for immune-targeted agents, see NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections.**
- **Live viral vaccines should not be administered to HCT survivors with active graft-versus-host disease (GVHD) or ongoing immunosuppression. They should only be administered to HCT survivors without active GVHD or ongoing immunosuppression following consultation with an infectious disease specialist.**
- **There is a lack of comprehensive data regarding the use of vaccines after CAR T-cell therapy. Due to the significant immune suppression post CAR T-cell therapy, recommendations for vaccination should be individualized to the survivor based on the type of CAR T-cell therapy the survivor received.**
- **The following vaccines can be administered to survivors who had cellular therapy:**

Vaccine	Population	Recommended Dose/Timing
Influenza vaccine[2] (Principles of Influenza Vaccine(s) [SIMIN-C])	All cellular therapy survivors	1 dose annually, starting 6 months after HCT and starting 4 months after if there is a community outbreak of influenza as defined by the local health department
Pneumococcal vaccine[3,b]	• Adult cellular therapy survivors ≥65 years • Adult cellular therapy survivors who are immunocompromised	• PCV20 or PCV15 is recommended: ▸ 1 dose of 20- or 15-valent pneumococcal conjugate vaccine (PCV20 or PCV15) if never vaccinated against pneumococcus ▸ When PCV15 is used, it should be followed by a dose of PPSV23 at least 1 year later • Adults who have only received PPSV23 may receive a PCV (either PCV20 or PCV15) ≥1 year after their last PPSV23 dose • Adults with previous PCV13 who have not completed their recommended pneumococcal vaccine series with PPSV23 can receive one dose of PCV20 if PPSV23 is not available.
Haemophilus influenzae type b (Hib) vaccine	All cellular therapy survivors	3 doses of Hib vaccine should be administered 6–12 months after HCT
Meningococcal conjugate vaccine, quadrivalent (MCV4)	Survivors with surgical or functional asplenia	2-dose series at least 8 weeks apart and revaccinate every 5 years if risk remains
	• Consider in cellular therapy survivors in outbreak situations or in endemic areas	1 dose and revaccinate every 5 years if risk remains
Tetanus, diphtheria, pertussis vaccine (DTaP/Td or Tdap/DT/Td)	All cellular therapy survivors	• 3 doses of DTaP vaccine should be administered 6–12 months after HCT (administer the first 2 doses at least 4 weeks apart and the third dose 6–12 months after the second) • This 3-dose regimen should be followed by Td boosters every 10 years • Alternatively, 1 dose of Tdap and 2 doses of DT or 1 dose of Tdap and 2 doses of Td can be given
Hepatitis A (HepA) vaccine	All cellular therapy survivors	• 2 doses of single-antigen HepA vaccine or • 3-dose series of combination HepA and HepB vaccine

Footnotes on (SIMIN-B 5 of 6) References on (SIMIN-B 5 of 6)

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Continued

GENERAL PRINCIPLES OF VACCINES IN CANCER SURVIVORS

Vaccination in Survivors Who Had Cellular Therapy (ie, HCT,[a] CAR T-cell therapy)[1] (continued)

Vaccine	Population	Recommended Dose/Timing
Hepatitis B (HepB) vaccine	All cellular therapy survivors	• 2 doses of HepB vaccine, recombinant (adjuvanted) given at least 4 weeks apart or 3 doses of HepB vaccine administered 6–12 months after HCT • 3 doses of a different HepB vaccine (at 0, 1, and 6 months) 40 mcg/mL • If a post-vaccination anti-hepatitis B surface antigen (anti-HBsAg) concentration of ≥10 mIU/mL is not obtained, a second series of HepB vaccine is recommended • First dose of HepB vaccine (after which anti-HBsAg is tested) using high dose (40 µg) should be administered
Inactivated polio vaccine (IPV)	All cellular therapy survivors	3 doses of IPV vaccine should be administered 6–12 months after HCT
HPV vaccine	• Recommended for adults ≤26 years • Shared decision-making for ages 27–45 years of age • Vaccination not recommended for persons >45 years	3 doses of HPV vaccine 6–12 months after HCT (https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/hpv.html)
Measles, mumps, rubella (MMR) vaccine	Measles-seronegative adolescent and adult cellular therapy survivors with neither chronic GVHD nor ongoing immunosuppression	• MMR vaccine should be avoided within 4 weeks before HCT • A 2-dose series of MMR vaccine should be administered 24 months after HCT and 8–11 months after the last dose of intravenous immunoglobulin (IVIG)
Recombinant zoster vaccine (RZV)[4]	• Survivors aged ≥50 years • Consider in cellular therapy survivors ≥19 years[c]	• A 2-dose series of RZV should be administered 24 months after HCT and 8–11 months after the last dose of IVIG • In survivors who have previously received the live attenuated zoster vaccine, immunization with RZV should be considered. The recombinant vaccine should not be given less than 2 months after receiving the live attenuated vaccine
COVID-19 vaccine	All cellular therapy survivors	• Recommendations regarding COVID-19 vaccines are continually changing (https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html.) • For guidance on the management of concurrent COVID-19 and cancer, please see the NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections.

Footnotes on (SIMIN-B 5 of 6)

References on (SIMIN-B 5 of 6)

Note: All recommendations are category 2A unless otherwise indicated.
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Continued

GENERAL PRINCIPLES OF VACCINES IN CANCER SURVIVORS

Vaccination in All Other Survivors[5]

- **The following vaccines can be administered to survivors of hematologic or solid tumor malignancies who did not receive cellular therapy (except those receiving anti–B-cell antibodies):[d]**

Vaccine	Population	Recommended Dose/Timing
Influenza vaccine (Principles of Influenza Vaccine(s) [SIMIN-C])	All survivors	Annually
Pneumococcal vaccine[3,b]	• Adult survivors ≥65 years • Adult survivors who are immunocompromised • Survivors with surgical or functional asplenia	• PCV20 or PCV15 is recommended: ▸ 1 dose of 20- or 15-valent pneumococcal conjugate vaccine (PCV20 or PCV15) if never vaccinated against pneumococcus ▸ When PCV15 is used, it should be followed by a dose of PPSV23 at least 1 year later • Adults who have only received PPSV23 may receive a PCV (either PCV20 or PCV15) ≥1 year after their last PPSV23 dose • Adults with previous PCV13 who have not completed their recommended pneumococcal vaccine series with PPSV23 can receive one dose of PCV20 if PPSV23 is not available.
Haemophilus influenzae type b (Hib) vaccine[6]	• Survivors with surgical or functional asplenia • Survivors living with HIV infection	3 doses of Hib vaccine should be administered
Tetanus, diphtheria, pertussis vaccine (Td/Tdap)	• Adult survivors <65 years of age who have not received Tdap previously • Adult survivors <65 years of age for whom vaccine status is unknown	• Substitute 1-time dose of Tdap for Td booster • Boost with Td or Tdap booster every 10 years
	• All other survivors	• Td or Tdap booster every 10 years

References on (SIMIN-B 5 of 6)

Footnotes on (SIMIN-B 5 of 6)

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Continued

GENERAL PRINCIPLES OF VACCINES IN CANCER SURVIVORS

Vaccination in All Other Survivors[5]

• The following vaccines can be administered to survivors of hematologic or solid tumor malignancies who did not receive cellular therapy (except those receiving anti–B-cell antibodies)[d]:

Vaccine	Population	Recommended Dose/Timing
HPV vaccine	• Recommended for adults ≤26 years • Shared decision-making for ages 27–45 years of age • Vaccination not recommended for persons >45 years	For dosing and schedules see https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/hpv.html
Recombinant zoster vaccine (RZV)[4]	Survivors aged ≥50 years[c]	A 2-dose series of RZV is recommended
Meningococcal conjugate vaccine quadrivalent (MCV4)	Survivors with surgical or functional asplenia	2-dose series at least 8 weeks apart and revaccinate every 5 years if risk remains
Hepatitis B (HepB) vaccine	Adult survivors ≤60 years	• 2 doses of HepB vaccine, recombinant (adjuvanted) given at least 4 weeks apart or • 3 doses of a different HepB vaccine (at 0, 1, and 6 months) 40 mcg/mL
COVID-19 vaccine	All survivors	• Recommendations regarding COVID-19 vaccines are continually changing (https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html.) • For guidance on the management of concurrent COVID-19 and cancer, please see the NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections.

Footnotes on (SIMIN-B 5 of 6)

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FOOTNOTES FOR GENERAL PRINCIPLES OF VACCINES IN CANCER SURVIVORS
(SIMIN-B 1 OF 6 TO SIMIN-B 4 OF 6)

Footnotes

[a] HCT includes peripheral blood stem cell transplantation, bone marrow transplantation, and cord blood transplantation.
[b] There are data on immune response to PCV-13 post HCT, but not yet for PCV15 or PCV20. Kobayashi M, Farrar JL, Gierke R, et al. MMWR Morb Mortal Wkly Rep 2022;71;109-117.
[c] Consider RZV in immunocompromised survivors ≥19 years (Anderson TC, et al. MMWR Morb Mortal Wkly Rep 2022;71:80-84).
[d] In survivors who received anti–B-cell antibody therapy, the above vaccines can be given, but should be delayed for at least 6 months after chemotherapy and the last dose of such therapy.

References

[1] Rubin LG, Levin MJ, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clin Infect Dis 2014;58:309-318.
[2] Walti CS, Loes AN, Shuey K, et al. Humoral immunogenicity of the seasonal influenza vaccine before and after CAR-T-cell therapy: a prospective observational study. J Immunother Cancer 2021;9:e003428.
[3] Kobayashi M, Pilishvili T, Farrar JL, et al. Pneumococcal Vaccine for Adults Aged ≥19 Years: Recommendations of the Advisory Committee on Immunization Practices, United States, 2023. MMWR Recomm Rep 2023;72:1-39.
[4] Anderson TC, Masters NB, Guo A, et al. Use of Recombinant Zoster Vaccine in Immunocompromised Adults Aged ≥19 Years: Recommendations of the Advisory Committee on Immunization Practices — United States, 2022. MMWR Morb Mortal Wkly Rep 2022;71:80-84.
[5] Murthy N, Wodi AP, McNally VV, et al. Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older - United States, 2024. MMWR Morb Mortal Wkly Rep 2024;11;73:11-15.
[6] Briere EC, Rubin L, Moro PL, et al. Prevention and Control of Haemophilus influenzae Type b Disease: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2014;(RR01):1-14.

Continued

Note: All recommendations are category 2A unless otherwise indicated.
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GENERAL PRINCIPLES OF VACCINES IN CANCER SURVIVORS

Vaccines Considered Safe for Cancer and Transplant Survivors and Close Contacts[e]	
Inactivated or purified antigens or bacterial components[f]	**Recombinant viral antigens**

• Influenza: inactivated influenza virus vaccine[g]
  ▸ Trivalent (IIV3), standard dose
  ▸ Trivalent (IIV3), high dose
  ▸ Quadrivalent (IIV4), standard dose
• Pneumococcus:
  ▸ Pneumococcal conjugate vaccine (PCV)
  ▸ Pneumococcal polysaccharide vaccine (PPSV)
• Meningococcus[6]:
  ▸ Quadrivalent meningococcal conjugate vaccine (MCV4: serotypes A, C, W, Y)
  ▸ Meningococcal vaccine (serotype B)
• Tetanus, diphtheria, pertussis (Td/Tdap)
• Hepatitis A (HepA)
• Haemophilus influenzae type b (Hib)
	• Hepatitis B (HepB)
	• Human papillomavirus (HPV)
	• Recombinant trivalent influenza vaccine (RIV3)[e]
	• Recombinant zoster vaccine (RZV)

Footnotes

[e] Ideally, clinicians should have administered all indicated vaccines to patients at least 2 weeks before initiation of cancer treatment (ie, chemotherapy, surgery, treatment with immunosuppressive drugs, radiation, splenectomy).

[f] For patients traveling to endemic countries, vaccines such as typhoid bacterial capsular polysaccharide, IPV, Japanese encephalitis, and rabies virus are recommended by the CDC (www.cdc.gov).

[g] Administration of the flu vaccine to survivors with egg allergy symptoms (other than hives) should be done at a center that can manage severe allergic reactions if an egg-based vaccine is used. Grohskopf LA, Blanton LH, Ferdinands JM, et al. Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023–24 Influenza Season. MMWR Recomm Rep 2023;72:1-25.

References

[6] Mbaeyi SA, Bozio CH, Duffy J, et al. Meningococcal vaccination: Recommendations of the Advisory Committee on Immunization Practices, United States, 2020. MMWR Recomm Rep 2020;69:1-41.

Note: All recommendations are category 2A unless otherwise indicated.
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PRINCIPLES OF INFLUENZA VACCINE(S)[1,2]

- **Annual influenza vaccination is recommended[2] for all cancer and transplant survivors. Live attenuated influenza vaccines should be avoided in these individuals unless they have been cleared to do so by an infectious disease specialist or physician familiar with vaccination in this population.**
- **For a summary of recommendations for prevention and control of influenza with vaccines, see: https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/flu.html**
- **Components of the influenza vaccine are determined each year by the World Health Organization (WHO) according to reports of the most common influenza viruses that are likely to circulate that year.**
- **Influenza vaccines can be inactivated or recombinant. They may contain standard or higher doses of the antigen. They can be trivalent or quadrivalent.**

Preferred Vaccines

- **Inactivated influenza vaccine (IIV)**
  - **Quadrivalent (IIV4), standard dose**
  - **Quadrivalent, high-dose (HD-IIV4; preferred option for survivors ≥65 y)**
  - **Quadrivalent adjuvanted inactivated influenza vaccine (aIIV4; preferred option for survivors ≥65 y)**
- **Recombinant influenza vaccine (RIV)[a]**
  - **Quadrivalent (RIV4; preferred option for survivors ≥65 y)**

To date, there is no evidence that one vaccine is superior to any other vaccine.

Footnotes

[a] Administration of the flu vaccine to survivors with egg allergy symptoms (other than hives) should be done at a center that can manage severe allergic reactions if an egg-based vaccine is used. Grohskopf LA, Blanton LH, Ferdinands JM, et al. Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023–24 Influenza Season. MMWR Recomm Rep 2023;72:1-25.

References

[1] Murthy N, Wodi AP, McNally VV, et al. Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older - United States, 2024. MMWR Morb Mortal Wkly Rep 2024;11;73:11-15.

[2] Grohskopf LA, Blanton LH, Ferdinands JM, et al. Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023–24 Influenza Season. MMWR Recomm Rep 2023;72:1–25.

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Late Effects/Long-Term Psychosocial and Physical Problems

PRINCIPLES OF CARDIOVASCULAR DISEASE RISK ASSESSMENT

- **CVD remains a leading cause of death in cancer survivors. CVD-related comorbidity and mortality may detrimentally affect patients with cancer and survivors with short- and long-term sequelae. Counseling regarding cardiovascular risk factors and lifestyle modifications are paramount in cancer survivors and patients with favorable prognoses. The risk of CVD-related death varies with years from diagnosis, with most survivors being at greatest risk 5 or more years after diagnosis and completion of curative therapy.**
- **Referral to a cardiologist or cardio-oncologist in patients at elevated CVD risk should be considered at any stage of the cancer journey.[e]**
- **Shared risk factors for both cancer and CVD (ie, smoking, poor health behaviors) contribute to the development of CVD and structural heart disease or heart failure, a concept that becomes especially relevant to cancer survivors. Attention and counseling regarding shared risk factors may improve cancer- and cardiovascular-related outcomes.**
- **Cancer treatments (immunotherapy,[a] cytotoxic, HCT, and targeted systemic therapies,[b] RT) can result in diverse cardiovascular issues, including cardiomyopathy, hypertension, hyperlipidemia, cardiac arrhythmia, myocardial infarction, carotid stenosis after head and neck and mantle radiation, and cerebrovascular accidents.**
  - **Survivors treated with anthracyclines are at increased risk for heart failure (SCARDIO-1).**
  - **Androgen or estrogen deprivation therapy may elevate cardiovascular risk.[c]**
- **Most CVDs (such as atherosclerosis) develop over time as a result of well-defined risk factors such as hypertension, hyperlipidemia, use of tobacco products, obesity, and diabetes. Control of these risk factors can decrease the risk of subsequent cardiovascular events.**
- **Survivors should be assessed throughout the survivorship continuum for:**
  - **Pre-existing and emerging CVD (eg, CAD, CHF, peripheral vascular disease, arrhythmias including atrial fibrillation) and CVD risk factors (eg, hypertension, dyslipidemia, obesity, cigarette/tobacco use, diabetes mellitus), with intervention for modifiable risk factors as necessary**
  - **Cancer treatment history (eg, regimen/dose,[b] radiation field, dose/volume)**
  - **Diet and exercise habits**
- **Tools exist to help quantify atherosclerotic CVD (ASCVD) risk (eg, ASCVD risk score[d]) and thus determine appropriate risk reduction strategies.**
- **Survivors should be counseled on any increased risk of CVD they may have based on prior treatment, comorbidity, or CVD risk factors and on the ABCDEs of CVD Prevention (see Table 1 on SCVD-2).**
- **Cooperation and shared care with primary care providers, and cardiovascular specialists as needed, is key to optimizing cardiac and vascular outcomes in cancer survivors.**

[a] Drobni ZD, Alvi RM, Taron J, et al. Association between immune checkpoint inhibitors with cardiovascular events and atherosclerotic plaque. Circulation 2020;142:2299-2311.
[b] HER2-directed therapy, VEGF signaling pathway inhibitors, cisplatin, anthracyclines, and androgen or estrogen deprivation therapy are possible CVD risk factors.
[c] Okwuosa TM, Morgans A, Rhee JW, et al. Impact of hormonal therapies for treatment of hormone-dependent cancers (breast and prostate) on the cardiovascular system: Effects and modifications: A scientific statement from the American Heart Association. Circ Genom Precis Med 2021;14:14:e000082.
[d] The ASCVD Risk Estimator Plus from the American College of Cardiology is available at http://tools.acc.org/ascvd-risk-estimator-plus/#!/calculate/estimate.
[e] Armenian SH, Lacchetti C, Barac A, et al. Prevention and monitoring of cardiac dysfunction in survivors of adult cancers: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol 2017;35:893-911.

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PRINCIPLES OF CARDIOVASCULAR DISEASE RISK ASSESSMENT[e]

Table 1: ABCDEs to Promote Cardiovascular Wellness in Cancer Survivors[f]	
A	• Awareness of risks and presentation of heart disease • Assessment of CVD and cardiovascular risk • Aspirin use as appropriate (indicated for secondary prevention; clinician-survivor discussion required for primary prevention with careful weighing of benefits and risks)[g]
B	• Blood pressure monitoring/management (with clinician-survivor discussion regarding the use of hypertension treatment and blood pressure goals)
C	• Cholesterol assessment/management (with clinician-survivor discussion regarding the use of statin therapy for primary prevention and lipid profile goals) • Cigarette/tobacco cessation (NCCN Guidelines for Smoking Cessation)
D	• Diet and weight management (SNWM-1) • Dose (cumulative) of anthracyclines and/or radiation to heart • Diabetes mellitus prevention/treatment
E	• Exercise (SPA-1)[h] • Echocardiogram (ECHO) and/or electrocardiogram (ECG) based on individual risk

[e] Armenian SH, Lacchetti C, Barac A, et al. Prevention and monitoring of cardiac dysfunction in survivors of adult cancers: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol 2017;35:893-911.
[f] Adapted with permission from Montazeri K, Unitt C, Foody JM, et al. ABCDE Steps to Prevent Heart Disease in Breast Cancer Survivors. Circulation 2014;130:e157-e159.
[g] U.S. Preventive Services Task Force; Davidson KW, Barry MJ, Mangione CM, et al. Aspirin use to prevent cardiovascular disease: U.S. Preventive Services Task Force Recommendation Statement. JAMA 2022;327:1577-1584.
[h] Gilchrist SC, Barac A, Ades PA, et al. Cardio-oncology rehabilitation to manage cardiovascular outcomes in cancer patients and survivors: A scientific statement from the American Heart Association. Circulation 2019;139:e997-e1012.

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PRINCIPLES OF ANTHRACYCLINE-INDUCED CARDIAC TOXICITY[a]

- **Cancer treatments can result in diverse cardiovascular issues (SCVD-1). This algorithm focuses specifically on heart failure or cardiomyopathy that may arise from anthracycline therapy. Other systemic therapies may also cause cardiomyopathy (eg, HER2-targeted therapies), and some of the concepts presented in these recommendations may apply to these other cardiomyopathies.**
- **Anthracycline-induced heart failure/cardiomyopathy may take years or even decades to manifest. Data suggest that signs of cardiac dysfunction can be seen prior to the development of symptoms. If detected early, anthracycline-induced heart failure/cardiomyopathy may be responsive to cardioprotective medications, although prospective studies evaluating these medications are lacking.**
- **Survivors may have risk factors that predispose them to heart failure. Some survivors may have structural heart disease (such survivors are considered to have Stage B heart failure) even if they have no actual symptoms. A history of anthracycline exposure is a risk factor that predisposes survivors to develop cardiomyopathy[b] (SCARDIO-3).**
- **Having a history of anthracycline exposure plus additional cardiovascular risk factors increases the risk of developing cardiomyopathy and heart failure. It is encouraged that heart failure risk factors, including hypertension, dyslipidemia, and diabetes be addressed in coordination with primary care.**
- **The risk for cardiovascular problems varies greatly depending on the type of anthracycline used and the cumulative dose received.[c]**
- **For this algorithm, the panel has placed an emphasis on early recognition and prevention of clinical heart failure, as well as early treatment of patients at risk with appropriate cardioprotective medications to prevent cardiac remodeling over time. Therefore, for high-risk survivors, the panel emphasizes the need for a thorough clinical screening for heart failure within one year after completion of anthracycline therapy.**

[a] Armenian SH, Lacchetti C, Barac A, et al. Prevention and monitoring of cardiac dysfunction in survivors of adult cancers: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol 2017;35:893-911.
[b] Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013;62:e147-e239.
[c] High cumulative anthracycline dose is defined as cumulative doxorubicin dose at or higher than or equal to 250 mg/m^2 or equivalent.

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INITIAL CLINICAL ASSESSMENT FOR PATIENTS WHO HAVE RECEIVED PREVIOUS ANTHRACYCLINE THERAPY

- H&P
  - Assess for signs and symptoms of heart failure[d,e]
  - Assess patient's ability to perform routine and desired activities of daily living (ADLs)
  - Look for signs of volume overload
- Review medications, alcohol use, and other substance use
- Review oncologic history
  - Review total cumulative dose of anthracycline
  - Other systemic therapy (eg, anti-HER2 treatment) and/or chest RT
- Evaluate for presence of heart failure risk factors
  - Hypertension
  - Dyslipidemia
  - Diabetes mellitus
  - Family history of cardiomyopathy
  - Age >65 years
  - High cumulative anthracycline dose[f]
  - Low-normal left ventricular ejection fraction (LVEF) (50%–54%) at baseline
  - History of other cardiovascular comorbidities (ie, atrial fibrillation, known CAD, baseline evidence of structural heart disease)
  - Smoking
  - Obesity
  - Physical inactivity

→

- Cardiovascular risk factor management (SCVD-1)[g]
- Consider two-dimensional ECHO with doppler flow study within 1 year after completion of anthracycline therapy for survivors with[e,h,i]:
  - High cumulative anthracycline dose[f]
  - Low cumulative anthracycline dose and 1 or more heart failure risk factors

→

No evidence of structural heart disease, but symptomatic[d] →
- Workup for other causes of symptoms
- Referral to other specialties (eg, pulmonology or cardiology)

No evidence of structural heart disease and asymptomatic or No ECHO performed and asymptomatic → **Stage A (SCARDIO-3)**

Evidence of structural heart disease (asymptomatic or symptomatic[d]):
- Left ventricular (LV) dysfunction
- LV hypertrophy
- Valvular disease
- LV dilatation and/or wall thinning

→ **Determine stage of cardiomyopathy (heart failure) (SCARDIO-3)**

[d] Signs and symptoms of heart failure include: shortness of breath or chest pain after physical activity or exercise, shortness of breath when laying flat (ie, orthopnea), waking up at night due to shortness of breath, and swelling in the legs.
[e] Patients with symptoms of heart failure should undergo an ECHO.
[f] High cumulative anthracycline dose is defined as cumulative doxorubicin dose ≥250 mg/m^2 or equivalent.
[g] Encourage primary care provider involvement in treatment of cardiovascular risk factors and encourage routine follow-up in coordination with primary care provider.
[h] Referral to cardiologist/cardio-oncologist if there are echocardiographic abnormalities and/or any cardiovascular symptoms or concerns.
[i] For survivors of certain cancer types, longer-term cardiovascular surveillance may be needed. Please see the NCCN Guidelines for Treatment of Cancer by Site for specific monitoring recommendations.

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STAGES OF CARDIOMYOPATHY (HEART FAILURE)[j]	TREATMENT	SURVEILLANCE
Stage A **(No structural disorder of the heart, but at risk of developing heart failure)[j,k,l]** • **Patients may have any of the following:** ▸ **History of potentially cardiotoxic chemotherapy[m] (including anthracyclines)** ▸ **History of chest irradiation (especially mantle and left-sided)** ▸ **Hypertension, CAD, diabetes mellitus** ▸ **History of alcohol use disorder, personal history of rheumatic fever, family history of cardiomyopathy**	→ • **Address underlying risk factors (hypertension, lipids, cigarette/tobacco use, obesity, metabolic syndrome, diabetes)[g]** • **Recommend regular physical activity and healthy diet habits (HL-1)** • **Consider referral for management[n]**	→ **Reassess based on symptoms**
Stage B **(Structural heart disease but no signs or symptoms of heart failure)[j]** • **Patients may have any of the following:** ▸ **LV hypertrophy** ▸ **LV dilatation or hypocontractility** ▸ **Asymptomatic valvular heart disease** ▸ **Previous myocardial infarction**	→ • **Measures under Stage A as appropriate** • **Referral to cardiovascular specialist (ie, cardiologist, cardio-oncologist) for management**	
Stage C **Signs and symptoms of heart failure with underlying structural heart disease[j]**	→ **Referral to cardiovascular specialist (ie, cardiologist, cardio-oncologist) for management**	
Stage D **Advanced structural heart disease and marked symptoms of heart failure at rest despite maximal medical therapy and requiring specialized interventions[j]**	→	

[g] Encourage primary care provider involvement in treatment of cardiovascular risk factors and encourage routine follow-up in coordination with primary care provider.
[j] Yancy CW, et al. Circulation 2013;128:e240-e327.
[k] Consider use of biomarkers in select patients at high risk for heart failure (Stage A) (Discussion).
[l] Any patient who has received potentially cardiotoxic chemotherapy and/or chest radiation (and specifically anthracycline-based chemotherapy) should be considered Stage A cardiomyopathy.
[m] For a list of potentially cardiotoxic chemotherapy agents, see Moslehi JJ. N Engl J Med 2016;375:1457-1467.
[n] Consider referral to a cardiologist, cardio-oncologist, survivorship specialist, or PCP for serial surveillance based on cardiotoxicity risk of cancer treatment regimen or if additional anthracycline therapy or other cardiotoxic treatment is needed.

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GENERAL PRINCIPLES OF ANXIETY, DEPRESSION, TRAUMA, AND DISTRESS

- **The NCCN Guidelines for Distress Management define distress as "a multifactorial unpleasant emotional experience of a psychological (ie, cognitive, behavioral, emotional), social, spiritual, and/or physical nature that may interfere with the ability to cope effectively with cancer, its physical symptoms, and its treatment." The NCCN Guidelines for Survivorship complement the NCCN Guidelines for Distress Management.**

- **Survivors of cancer and its treatment are at elevated risk for mental health issues such as fear of recurrence, distress, anxiety, and depression that may persist for many years after diagnosis.[a]**
  - **Fear of recurrence can lead to increased symptoms when surveillance testing or follow-up appointments are scheduled and increased anxiety when physical symptoms occur that may or may not be similar to those experienced during the cancer diagnosis.**
  - **Medical, psychosocial, environmental, and psychiatric health factors may affect the mood of cancer survivors and need to be considered when screening for distress, anxiety, and depression in survivors and deciding on treatment (SANXDE-6).**
  - **Recurrent worry, fear, thoughts, or images related to cancer events should be distinguished from obsessive compulsive disorders. Repetitive, persisting thoughts, images, or behaviors or mental acts that a person is compelled to perform, aimed at reducing intense anxiety or preventing a dreaded event require psychiatric referral for evaluation and treatment.**
  - **Monitor distress, especially at times of new diagnoses, transitions in care, cancer surveillance, significant loss, other major life events, and with social isolation.**
    - ◊ **Survivors may not appear to be distressed and should be encouraged to inform their health care provider when they are feeling increased distress, worry, anxiety, or depression. See NCCN Distress Thermometer Screening Tool (DIS-A).**
    - ◊ **Screening for anxiety, depression, trauma, and distress should be a part of routine care. The panel recommends using validated measures such as the PHQ-9 for depression, GAD-7 for anxiety, PC-PTSD-5 for trauma (also see Trauma Screening [SANXDE-D]), NCCN Distress Thermometer Screening Tool (DIS-A), or PROMIS measures.**
  - **Clinical assessments should include and evaluate psychosocial aspects of a survivor's background, including trauma (SANXDE-7).**
  - **Caregivers and all family members of the survivor, including younger children, are vulnerable to the same psychosocial stresses and symptoms as survivors, though often at different times or for different reasons. If needs are observed, they can be offered resources and referred for evaluation.**
- **This algorithm is intended for oncologists and other health care providers to screen for distress, anxiety, and depression in cancer survivors, to provide steps for addressing these concerns with survivors, and to facilitate decisions about referral to specialists.**
  - **The algorithm is not intended as a psychiatric diagnosis and treatment tool.**
  - **The algorithm focuses on more common mood disorders after cancer. It does not screen or address treatment for psychiatric conditions such as bipolar disorders, schizophrenia, personality disorders, or obsessive compulsive disorders. Diagnosis and management of these disorders should be done by a mental health professional (See NCCN Guidelines for Distress Management).**

- **Decisions about treatment and referral will depend on the acuteness of onset of symptoms, their intensity, and safety of the survivor and others (SANXDE-6 and SANXDE-A).**

[a] Lu D, Andersson TM, Fall K, et al. Clinical diagnosis of mental disorders immediately before and after cancer diagnosis: a nationwide matched cohort study in Sweden. JAMA Oncol 2016;1188-1196.

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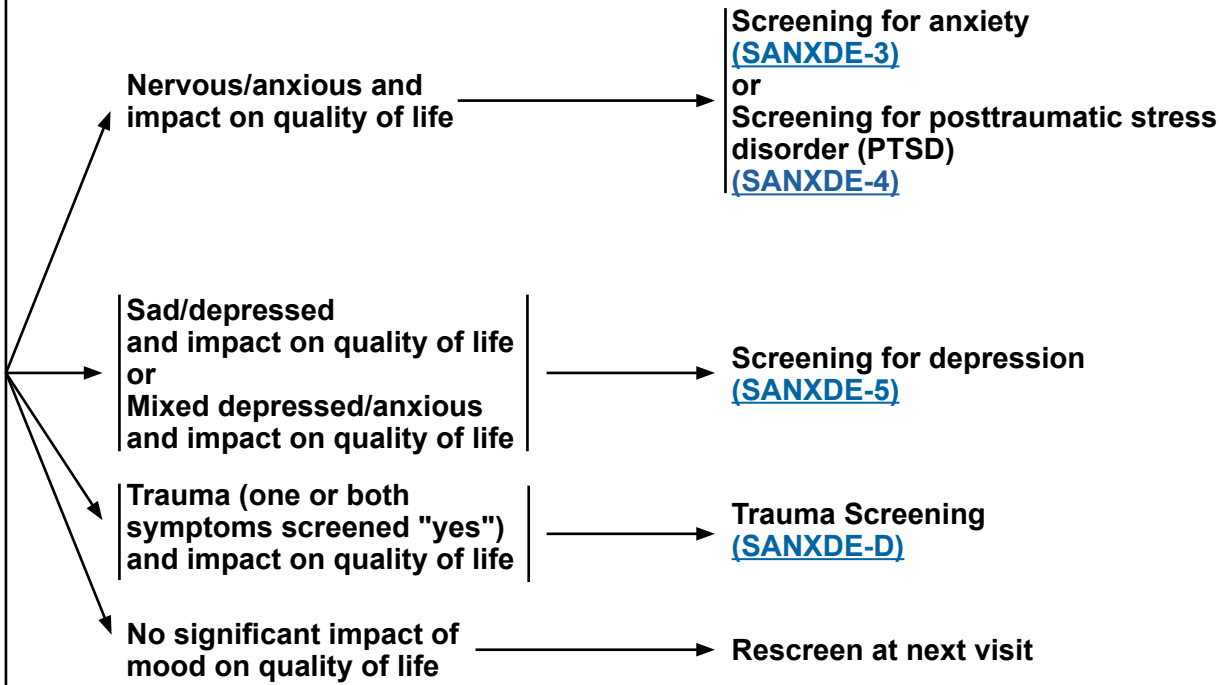
SCREENING: ANXIETY, DEPRESSION, AND TRAUMA

Screening questions[b] to be asked at regular intervals, especially when there is a change in clinical status or treatment, or patient presents with multiple somatic complaints[c]:

- **In the past 2 weeks, on more days than not have you:**
  - **Nervous/anxious**
    - ◊ **had worries or fears related to your cancer?**
    - ◊ **felt nervous, or worried about other things?**
    - ◊ **had trouble controlling your worry?**
  - **Sad/depressed**
    - ◊ **had less interest or enjoyment in activities than usual?**
    - ◊ **felt sad or depressed?**
  - **Trauma screening**
    - ◊ **had nightmares or thoughts about your cancer, your treatment, or other effects of treatment when you did not want to?**
    - ◊ **tried hard not to think about events or effects related to your cancer or went out of your way to avoid situations that reminded you of those events?**
- **Additional screening for impact of mood on quality of life if "Yes" to any of the above:**
  - **had difficulty functioning or withdrawn from daily activities because of these (above-mentioned) feelings or problems?**
  - **had trouble sleeping (eg, staying asleep, falling asleep, getting too much sleep)?[b]**
  - **had difficulty concentrating?[b]**



[b] A positive response to any of the questions should result in further assessment. However, if a patient has an isolated problem with sleep or concentration in the absence of other symptoms, see (SSD-1) or (SCF-1).

[c] If the NCCN Distress Thermometer is used as a primary screening tool, these questions would follow for those survivors with an elevated level of distress.

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SCREENING: ANXIETY AND PANIC[d]

Anxiety
Excessive anxiety and worry that is difficult to control and ≥3 of the following:
- **Restless or on edge**
- **Easily fatigued**
- **Difficulty concentrating or mind going blank**
- **Irritability**
- **Muscle tension**
- **Sleep disturbance**

Panic
Sudden intense fear or discomfort that peaks within minutes and ≥4 of the following[e]:
- **Palpitations, pounding heart**
- **Sweating**
- **Trembling or shaking**
- **Sensations of shortness of breath or smothering**
- **Chest pain or discomfort**
- **Nausea or abdominal distress**
- **Feeling dizzy, lightheaded, unsteady**
- **Chills or heat sensations**
- **Paresthesias (numbness or tingling)**
- **Feelings of unreality or being detached from oneself**
- **Fear of losing control**
- **Fear of dying**

DIAGNOSIS

≥3 symptoms and persisting more than 6 months: Consider general anxiety disorder, PTSD symptoms, or adjustment disorder → **Safety evaluation[g]** → **See Evaluation (SANXDE-7) or Refer to mental health services for evaluation and treatment[h]**

<3 symptoms and/or persisting less than 6 months: Adjustment disorder[f] with anxious or mixed mood or Other anxiety disorder → **Screening (SANXDE-6)**

Panic disorder → **Safety evaluation[g]** → **See Evaluation (SANXDE-7) or Refer to mental health services for evaluation and treatment[h]**

[d] The following additional tools may be used for individual intensive screening for a specific problem: Anxiety, GAD-7; Panic: Brief Patient Health Questionnaire, item 2 a-e. Both tools can be found at http://www.phqscreeners.com.
[e] Consideration should be taken for evaluation of other medical causes to rule out alternative etiologies.
[f] Development of emotional or behavioral symptoms in response to an identifiable stressor(s) occurring within 3 months of the onset of the stressor(s). [American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed). Arlington, VA: American Psychiatric Publishing.]
[g] Safety Evaluation for Anxiety and Depression (SANXDE-A).
[h] Psychiatrist, psychologist, advanced practice clinician, and/or social worker.

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SCREENING: POSTTRAUMATIC STRESS SYMPTOMS OR DISORDER (PTSD)[i,j]

- **Screen for PTSD symptoms using PC-PTSD-5**
  See Trauma Screening (SANXDE-D)
- **Assess risk factors for PTSD (SANXDE-B)**
- **Diagnosis of PTSD requires symptoms from each of the following 4 categories**
  - **Exposure to traumatic events (eg, cancer diagnosis, treatment)[k] and the following symptoms that cause clinically significant distress or impairment in social interactions, capacity to work, or other functioning for more than 1 month:**
    - ◊ **Re-experiencing: repeated, disturbing memories, dreams, or flashbacks (minimum 1 symptom)**
    - ◊ **Persistent avoidance: avoidance of distressing memories, thoughts, feelings, or external reminders of the cancer experience (minimum 1 symptom)**
    - ◊ **Negative alterations in mood or cognition: exaggerated negative beliefs about oneself or the world, feeling detached or estranged from others, lack of positive emotions, feelings of fear, horror, anger, guilt, or shame (minimum 2 symptoms)**
    - ◊ **Arousal: hypervigilance (being super alert or watchful or on guard), difficulty concentrating, sleep disturbance, aggressiveness, risky or self-destructive behavior (minimum 2 symptoms)**

→

DIAGNOSIS

- **Posttraumatic stress symptoms impacting quality of life**
- **Consider adjustment disorder/distress (SANXDE-6)**

→ **Safety evaluation[g]** →

See Evaluation (SANXDE-7)
or
Refer to mental health services for evaluation and treatment[h]

[g] Safety Evaluation for Anxiety and Depression (SANXDE-A).
[h] Psychiatrist, psychologist, advanced practice clinician, and/or social worker.
[i] For a complete list of screening symptoms review the American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Arlington, VA: American Psychiatric Publishing.
[j] Also see Risk Factors for PTSD (SANXDE-B).
[k] Person may directly experience the traumatic event, witness the event, learn of the event occurring to a close family member or friend, or experience repeated or extreme exposure to aversive details of the trauma. Life-threatening illness or cancer or debilitating medical condition is not necessarily a traumatic event, but may be in some cases. A history of PTSD prior to a cancer diagnosis increases risk for symptoms of PTSD to be associated with cancer treatment if experiences remind the survivor of a prior traumatic event. A future trauma may also evoke traumatic cancer memories increasing posttraumatic stress symptoms.

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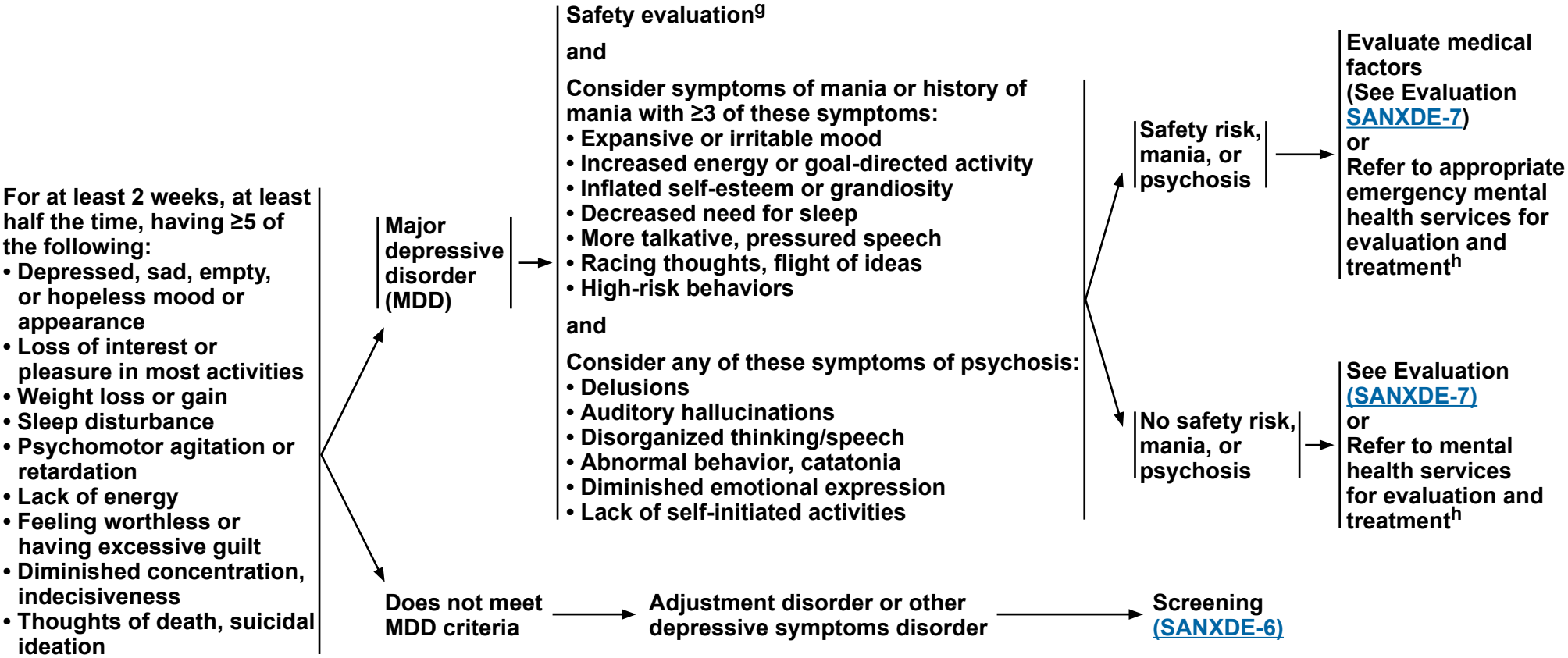
SCREENING: DEPRESSION[i,l,m] DIAGNOSIS



[g] Safety Evaluation for Anxiety and Depression (SANXDE-A).
[h] Psychiatrist, psychologist, advanced practice clinician, and/or social worker.
[i] For a complete list of screening symptoms review the American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Arlington, VA: American Psychiatric Publishing.
[l] The following additional tools may be used for individual intensive screening for a specific problem: Screening Tools: PHQ-9 or PHQ-2. The PHQ-2 is comprised of the first two items of the PHQ-9 and can be used as an initial depression screening. If the patient responds affirmatively to either of these two items, the remaining 7 items are asked (available at: www.phqscreeners.com and http://www.commonwealthfund.org/usr_doc/PHQ2.pdf).
[m] When screening, also take into consideration a survivor's cultural differences at presentation (eg, somatization as expression of emotional distress).

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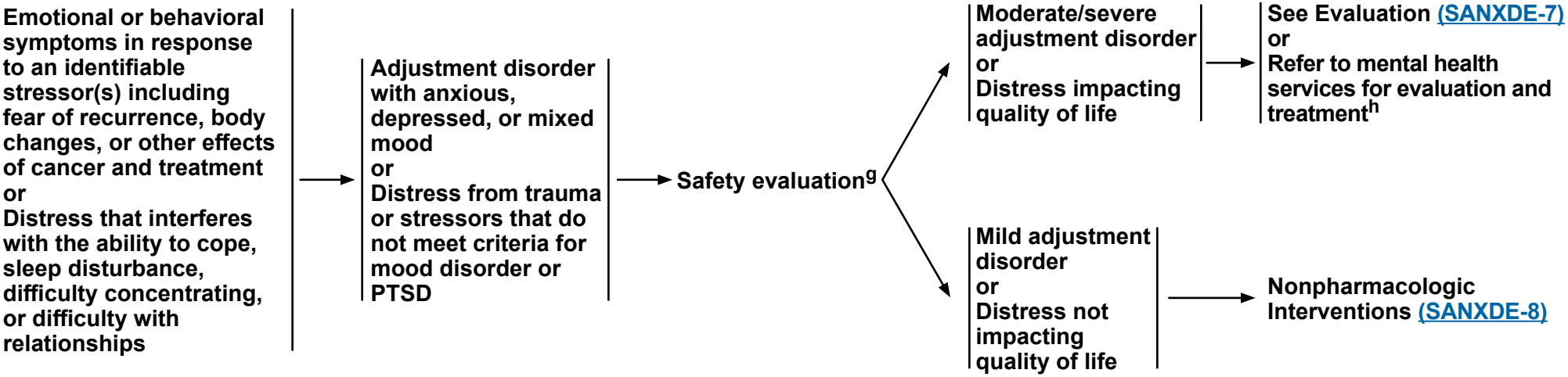
SCREENING: ADJUSTMENT DISORDER/DISTRESS[i,n]

DIAGNOSIS



[g] Safety Evaluation for Anxiety and Depression (SANXDE-A).
[h] Psychiatrist, psychologist, advanced practice clinician, and/or social worker.
[i] For a complete list of screening symptoms review the American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed). Arlington, VA: American Psychiatric Publishing.
[n] The following additional tool may be used for screening distress level: NCCN Distress Thermometer Screening Tool [DIS-A]. A score of ≥4 indicates moderate/severe distress: "On a scale of 0–10 how much distress have you been experiencing in the past week, including today with 0 = No Distress and 10 = Extreme Distress?"

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EVALUATION: ANXIETY, DEPRESSION, TRAUMA, AND DISTRESS[o]

Medical Factors (H&P Exam)

- General review:
  - Illness status/progression
  - Medication changes/side effects
  - Presence of new or poorly controlled symptoms (ie, pain, nausea, constipation)
  - Status of coexisting medical conditions
  - Substance use disorder
  - History of prior mental health problems including depression, anxiety, phobias, panic, psychoses, or suicide attempt
  - History of childhood or adult trauma prior to or after cancer diagnosis
  - Fatigue level (SFAT-1)
  - Functional status
  - Current coping strategies
  - Sexual health (SSH-1)
  - Infertility
  - Other medical factors including cognitive function (SCF-1)
- Laboratory studies to consider:
  - Metabolic studies
  - Infection workup
  - Anemia with underlying deficiencies
  - Endocrine/hormonal status
- Other studies as clinically indicated:
  - Neurologic:
    - ◊ Central nervous system (CNS) imaging
    - ◊ Neuropsychological testing
  - Cardiac: ECG, ECHO, stress test (SCARDIO-1)
  - Pulmonary function tests
  - Sleep evaluation (SSD-1)

→

Psychiatric/Emotional Factors

- Identify content of distress including recurrence, health problems, body and sexuality changes, financial burden, or other concerns
- Symptom review based on the Survivorship Anxiety Depression, Trauma, and Distress screening recommendations (See SANXDE-2 through SANXDE-6); evaluate for anticipation/fear of recurrence in the setting of:
  - Active surveillance by oncology team
  - New symptoms or findings suggestive of recurrence
  - Transitions in surveillance and care
- Consider other major psychiatric disorders

→

Social/External Factors

- Environmental stressors and non–cancer-related factors:
  - Social isolation, living alone
  - Family and caregiver conflicts, roles, and responsibilities
  - Spouse, intimate partner relationship
  - Financial problems and limited insurance coverage
  - Employment concerns
  - Limited access to medical care
  - Adolescents, younger adults, lack of connection with peers
  - History of abuse (ie, emotional, physical, sexual)
  - Spiritual, religious, or existential concerns
  - Discrimination or marginalization because of race, ethnicity, sexual orientation, sexual identity, or disability status.
  - Other stresses

→

Management and Treatment (SANXDE-8)
or
For mania, psychosis, extensive psychiatric history, or moderate to high safety risk
- **Refer for psychiatric evaluation and treatment**

[o] These are general factors/principles that affect anxiety, depression, trauma, distress, and adjustment that need to be considered when evaluating survivors.

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ANXIETY, DEPRESSION, TRAUMA, AND DISTRESS: MANAGEMENT AND TREATMENT

NONPHARMACOLOGIC INTERVENTIONS

- **For all survivors:**
  - Address treatable contributing factors
    - ◊ Pain, sleep disturbance, fatigue, toxic metabolic/endocrine/other medical comorbidities, substance use disorder
  - Provide reassurance that symptoms of worry, stress, fear of recurrence, anxiety, and depression are common problems among cancer survivors and that these symptoms can be treated
  - Provide support and education to patient and family regarding normal recovery phases after treatment, common stresses, distress and fears, and strategies for managing uncertainty and distress
  - Provide resources for social support networks and specific social, emotional, spiritual, intimacy, and practical problem needs, including online and mobile phone apps. Consider referral to social work services, patient navigator, and/or financial navigator (if available) (SURV-B).
  - Develop a plan for regular physical activity and healthy nutrition (HL-1).

- For adjustment disorder or distress without safety risk, mania, or psychosis:
  (See DIS-10 and DIS-17 in the NCCN Guidelines for Distress Management):
  - Refer to a therapist, preferably one with psycho-oncology training if available (ie, psychologist, psychiatrist, social worker, advanced practice clinician, licensed therapist):
    - ◊ Cognitive behavioral therapy (CBT) (eg, mindfulness, behavioral activation, structured CBT) can be effective for distress, fear of recurrence, trauma symptoms, insomnia, or other symptoms related to distress and can be delivered as individual therapy, in structured groups, or with digital modalities (category 1)
    - ◊ Social work for complex psychosocial factors
    - ◊ Supportive normalizing of survivor's experience
    - ◊ Existential therapy related to values, meaning, and purpose in life
  - Consider referral to chaplain for spiritual support for religious conflict, concerns about death and afterlife, guilt, grief, and meaning and purpose in life
  - Consider referral for integrative therapies (ie, mindfulness meditation, imagery/hypnosis, yoga)
  - Consider referral for couples, family, caregiver, or relationship counseling/support

- For moderate to severe intensity major depression, generalized anxiety, panic, or PTSD symptoms:
  - Refer for evaluation and treatment by a mental health professional[h]
  - Consider pharmacologic and/or nonpharmacologic treatments

- For substance use disorder[p]:
  - Safety evaluation (SANXDE-A)
  - See DIS-21 in the NCCN Guidelines for Distress Management
  - Refer to substance use disorder specialist

[h] Psychiatrist, psychologist, advanced practice clinician, and/or social worker.
[p] For additional resources, see SURV-B 4 of 4.

- Reevaluate symptoms and function at next visit
- Revise referrals and interventions if symptoms are persistent or increased

Consider pharmacologic interventions (SANXDE-9)

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

ANXIETY, DEPRESSION, TRAUMA, AND DISTRESS: MANAGEMENT AND TREATMENT

PHARMACOLOGIC INTERVENTIONS[q]

- Consider referral to mental health professional[r]
- First-line treatment: (SANXDE-C and SANXDE-E)
  - Selective serotonin reuptake inhibitors (SSRIs)
    - ◊ Consider for concomitant hot flashes
  - Serotonin-norepinephrine reuptake inhibitors (SNRIs):
    - ◊ Consider for concomitant pain or neuropathic pain
    - ◊ Consider for concomitant hot flashes
  - Inform survivor of potential side effects
  - Counsel survivor that it may take up to 2 to 6 weeks at a therapeutic dose for SSRIs and SNRIs to take effect
  - Benzodiazepines (ie, clonazepam, lorazepam):
    - ◊ For acute anxiety relief or while waiting for antidepressant to take effect
    - ◊ Adjust dose once SSRIs or SNRIs are fully effective and symptoms are partially or completely abated
  - Counsel survivor that symptoms of withdrawal may occur should any of the above-mentioned medications be abruptly discontinued
    - ◊ Withdrawal symptoms may include restlessness, akathisia, GI upset, dizziness, tingling, sleep disruption
    - ◊ More common with venlafaxine, paroxetine
    - ◊ Withdrawal effects can be avoided with slow taper
    - ◊ Withdrawal effects may be life-threatening and may require a mental health specialist
- Inquire about use of OTC medications
- Consider drug-drug interactions
- Medications not recommended as first-line treatments: tricyclics, tetracyclics, serotonin modulators, monoamine oxidase inhibitors

→

- Follow up with survivor by phone or visit about medication effects and mood in 2–4 weeks
- Reevaluate distress and function at next visit, within 4–8 weeks
- Monitor for increased suicidal thoughts or plans and other side effects
- Increase dose if within therapeutic dosing range and distress remains elevated and side effects are manageable
- Reinforce treatment adherence
- Consider drug switch if there are adverse effects or side effects that impact adherence
- Refer to a prescribing mental health professional for diagnostic evaluation if distress is persistent, increased, or other mood change, or medication management is not stable and effective in 8–12 weeks
- Choose once daily dosing, if possible, to improve adherence

[q] Principles of Pharmacologic Interventions (SANXDE-C).
[r] Psychiatrist, psychologist, or advanced practice clinician.

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SAFETY EVALUATION[a]

DANGER TO SELF OR OTHERS OR INABILITY TO CARE FOR SELF

Consider at elevated risk if survivor:

Has an organized plan for suicide or homicide

OR

Has suicidal or homicidal thoughts and, based on clinical judgment, the survivor is at imminent risk of harm to self or others

- **Consider the following risk factors:**
  - **Psychosocial risk factors**
    - ◊ **Previous attempts at suicide or self-injury (eg, cutting or burning)**
    - ◊ **Personality disorder or bipolar disorder with impulsivity, irritation, agitation, or aggression**
    - ◊ **New trauma or change in major stress or trauma**
    - ◊ **Family history or other exposure to suicide**
    - ◊ **Isolation**
    - ◊ **Recent loss of important person or relationship breakdown**
    - ◊ **Depression**
    - ◊ **Loss of rational thinking**
    - ◊ **Fear of death or dying due to pain and suffering**
    - ◊ **Feeling hopeless or loss of control**
    - ◊ **Perceives self as a burden**
    - ◊ **Access to firearms/weapons**
    - ◊ **Financial instability**
    - ◊ **Alcohol or other substance use disorder**
  - **Demographic risk factors**
    - ◊ **Male**
    - ◊ **Age (especially young adults and older adults)**
    - ◊ **No spouse or live-in partner**
  - **Medical risk factors**
    - ◊ **Chronic illness/pain or recent change in health status**
    - ◊ **Non-adherence to treatment or difficulty making treatment decisions**
    - ◊ **Sleep disorder (SSD-1)**
    - ◊ **Poor physical and emotional function, including disability**
    - ◊ **Access to potentially lethal medications (ie, opioids, benzodiazepines, antidepressants)**
    - ◊ **Substance use disorder**

→

CONSIDER PROTECTIVE FACTORS TO BALANCE WITH RISKS:

- **Psychosocial protective factors**
  - **Personal resources that increase resilience, environmental support, or coping**
  - **Strong interpersonal bonds to family/ community**
  - **Reasonably safe and stable environment**
  - **Seeks help**
  - **Good impulse control and coping/problem-solving skills**
  - **Sense of belonging, sense of identity, and good self-esteem**
  - **Cultural, spiritual, and religious beliefs about the meaning and value of life**
  - **Identification of future goals**
  - **Identifies reasons for living**
  - **Responsibility to/bonds with family, pets or others; living with family**
  - **Supportive social network or family**
  - **Belief that suicide is immoral; high spirituality**
  - **Engaged in work or school**
  - **Engaged in enjoyable activities**
  - **Access to health care with support of ongoing medical and mental health relationships**
- **Demographic protective factors**
  - **Married, child-rearing responsibilities**
  - **Employed**

→ **Determine risk level (SANXDE-A 2 of 3)**

[a] For further information on screening and responding to suicide risk, see https://www.healthquality.va.gov/guidelines/MH/srb/VASuicidePreventionPocketGuidePRINT508FINAL.pdf or SAFE-T Card: https://adaa.org/sites/default/files/SMA09-4432.pdf

Note: All recommendations are category 2A unless otherwise indicated.
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ACUTE (URGENT/EMERGENT) INTERVENTIONS

Lower risk based on:
- Suicidal ideation with no plan, no thoughts of danger to others
- Clinical judgment based on assessment of risk factors and protective factors

→

Develop safety plan with survivor and family
- Immediate referral for mental health evaluation based on urgency
- Regular follow-up and monitoring until psychiatric care is in place
- Address underlying conditions and risk factors
- Have survivor agree to contact a health care provider or call, text, or chat 988 Suicide & Crisis Lifeline; or call 911; or go to the nearest emergency room if suicidal thoughts increase or change
- Provide contact information for local crisis hotlines or counselors. (SURV-B)

Elevated risk of danger to self or others based on:
- Suicidal or homicidal thoughts with plan and/or with multiple other risk factors or
- Clinical judgment based on assessment of risk factors and protective factors
- Inability to care for self

→

Emergency intervention:
- Evaluate availability of firearms, weapons, medications, and other potentially lethal methods of suicide and arrange to have them secured
- If off-site and threat is to others or patient is agitated or threatening:
  - Call 911 and/or
  - Identify a caregiver who is with patient to take to emergency room; call 911; or call, text, or chat 988 Suicide & Crisis Lifeline and/or
  - Follow state mental health emergency plan
- If on-site and patient becomes agitated or threatening:
  - Involve other staff/security, keep door open, call 911, and maintain direct observation of patient
  - Assess environmental risks for harm to self or others, such as sharp objects as well as items that could be used for hanging
  - Refer to emergency psychiatric evaluation procedures on-site
  - Identify and follow any state reporting or other requirements

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SAFETY EVALUATION	ACUTE (URGENT/EMERGENT) INTERVENTIONS
DANGER FOR ABUSE OR NEGLECT OF VULNERABLE PERSON (CHILD, OLDER ADULT, PERSON UNABLE TO CARE FOR SELF): • Self-report or observation of risk for or actual physical, sexual, health care, or financial abuse	→ Determine acuity, involve social work or emergency services, and follow mandatory reporting requirements • Refer to urgent social work or emergency room for full evaluation of risks and options • Follow state laws for reporting abuse
SUBSTANCE USE DISORDER • Self-report, caregiver/family report, or observation of misuse of medications or of altered mental status potentially related to drug or alcohol use	→ See Substance-Related and Addictive Disorders (DIS-21) section in the NCCN Guidelines for Distress Management

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RISK FACTORS FOR PTSD

- **Physical**
  - **Recurrence of cancer**
  - **Intensive treatment (eg, HCT, intensive care unit stay)**
  - **Unrelieved chronic pain or physical dysfunction**
  - **Advanced disease**
  - **Younger age**
- **Psychosocial**
  - **Exposure to previous trauma (eg, combat, sexual assault, major loss)**
  - **History of mental health issues prior to cancer**
  - **Poor coping skills (eg, using avoidance)**
  - **Lower income and/or less education**
  - **Less social support**
- **Significant change in life stressors including health, interpersonal, financial, and occupational**

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PRINCIPLES OF PHARMACOLOGIC INTERVENTIONS

Special Pharmacologic Considerations for Concomitant Problems:

- Substance use
  - Minimize use of benzodiazepines
  - Alternatives for sedation and acute anxiety are low-dose atypical neuroleptics (ie, olanzapine, quetiapine) or gabapentin
- Pain syndromes (eg, neuropathy) (SPAIN-1)
  - SNRIs
  - Tricyclic antidepressants (TCAs)
    - ◊ Amitriptyline has sedating properties that may or may not be desirable
    - ◊ Nortriptyline and desipramine have the fewest side effects
- Fatigue (SFAT-1)
  - Consider less-sedating antidepressants such as bupropion
  - Consider bright white light therapy[1]
  - Evidence for psychostimulant effects for depression and fatigue are limited and mixed (SFAT-5)
- Insomnia
  - See Sleep Disorders (SSD-1)

Caveats (SANXDE-E):

- Review side effects with patient, noting that some may be beneficial (sedation, arousal, or weight gain and appetite stimulation)
- Monitor QT interval on ECG at initiation and dose increases with neuroleptics and citalopram
- Monitor for serotonin toxicity with use of any serotonergic agent
- Monitor for anticholinergic effects that can worsen cognition and other side effects (eg, dry mouth or other mucosa)
- Blood pressure should be monitored with venlafaxine and treated appropriately
- Recommend using non-CYP2D6– or non-CYP3A4–inhibiting options when possible[a]
- Use psychotropics with cytochrome P450 interactions with caution in survivors taking tamoxifen or other medications metabolized through CYP2D6 or CYP3A4 pathways[a,b] (SANXDE-E)
  - Fluoxetine[a,2,3]
  - Paroxetine[a,2,3]
  - Sertraline[a,2,3]
  - Bupropion
  - Fluvoxamine
  - Duloxetine
  - Clomipramine
- Refer to specialist if first-line treatment is unsuccessful or if there are complicating factors such as chronic pain or substance use disorder

Footnotes

[a] Evidence generally does not support the clinical significance of the inhibitory activity of SSRIs, SNRIs, or other antidepressants on tamoxifen's or other CYP2D6- or CYP3A4-metabolized agent's anticancer effects in terms of increased recurrence or mortality rates. However, pharmacokinetic/pharmacogenetic studies do indicate reduced availability of endoxifen in lower CYP2D6 metabolizers taking tamoxifen.[2,3] SSRIs, and in particular paroxetine, block conversion of tamoxifen to active metabolites through CYP2D6.

[b] Antidepressants that are strong CYP3A4 inhibitors or inducers may interact with some cancer prevention or maintenance drugs other than tamoxifen, such as tyrosine kinase inhibitors, monoclonal antibodies, or mTOR inhibitors.

References

[1] Johnson JA, et al. J Cancer Surviv 2018;12:206-215.
[2] Haque R, et al. J Natl Cancer Inst 2015;108:djv337.
[3] Wedret JJ, et al. Ment Illn 2019;11:8115.

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Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

TRAUMA SCREENING[1,2,3]

In the past two weeks, have you…

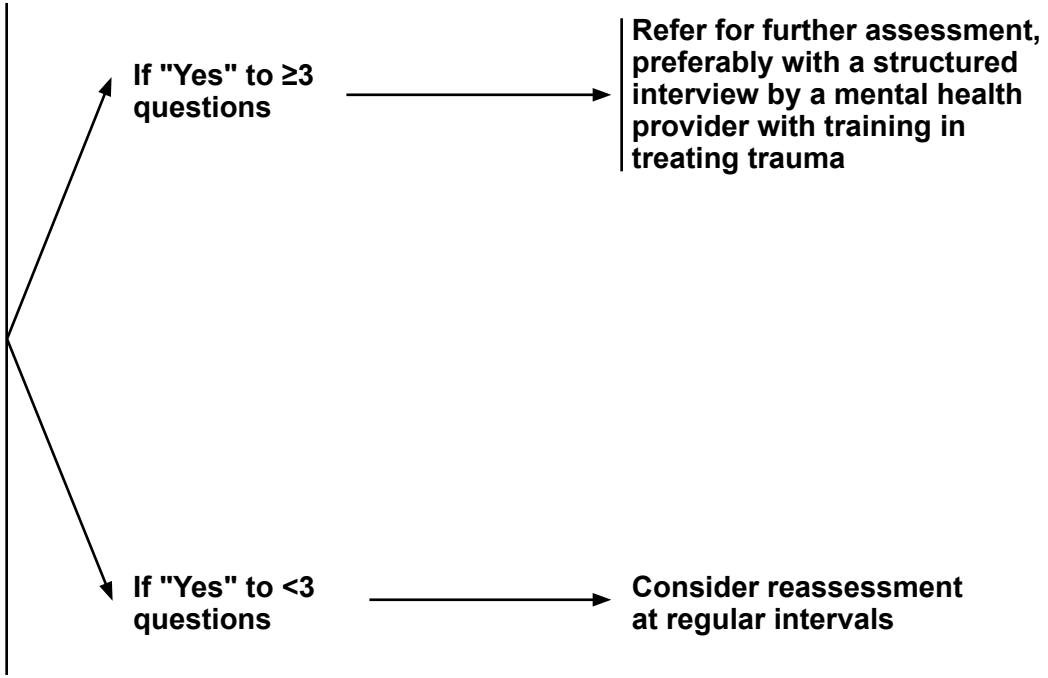
1. Had nightmares or thoughts about your cancer or treatment when you did not want to?
YES NO

2. Tried hard not to think about events related to your cancer or went out of your way to avoid situations that reminded you of those events?
YES NO

3. Been constantly on guard, watchful, or easily startled?
YES NO

4. Felt numb or detached from people, activities, or your surroundings?
YES NO

5. Felt guilty or unable to stop blaming yourself or others for events during your cancer treatment or any problems the event(s) may have caused?
YES NO



[1] Reproduced and adapted from Prins A, Bovin MJ, Kimerling R, et al. (2015). Primary Care PTSD Screen for DSM-5 (PC-PTSD-5) [Measurement instrument]. Available at https://www.ptsd.va.gov.
[2] The PC-PTSD-5 is designed to identify individuals with probable PTSD. Available at https://www.ptsd.va.gov/professional/assessment/documents/pc-ptsd5-screen.pdf.
[3] Prins A, et al. J Gen Intern Med 2016;31:1206-1211.

Note: All recommendations are category 2A unless otherwise indicated.
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First-Line Antidepressants for Depression or Anxiety in Adults[a,b,†]

Drug	Usual Starting Dose PER DAY TOTAL (mg)[c]	Extreme Dose Range PER DAY TOTAL (mg)	Severity of Side Effects Scale: 0 = none; 1 = slight; 2 = low; 3 = moderate; 4 = high								CYP450 Interaction Modulator Potential[d]	Notes
			Antichol	Drowsiness	Insomnia/ agit	↓ BP	QTc	GI	↑ Weight	Sexual		
Selective serotonin reuptake inhibitors												
Citalopram	20	10–40[e]	0	0	1	1	1	1	1	3	CYP2D6 mild	Caution with imatinib. May prolong QTc at higher doses
Escitalopram	10	5–30	0	0	1	1	1	1	1	3	CYP2D6 mild	May prolong QTc at higher doses
Fluoxetine	20	10–80	0	0	2	1	1	1	0	3	CYP2D6 **strong**; CYP3A4 **moderate**	Caution with tamoxifen, imatinib; long half-life
Paroxetine	20	10–50	1	1	1	2	0–1	1	2	4	CYP2D6 **strong**	Caution with tamoxifen, tyrosine kinase inhibitors, and monoclonal antibodies (eg, imatinib)
Paroxetine CR	25	12.5–62.5	1	1	1	2	0–1	1	2	4	CYP2D6 **strong**	
Sertraline	50	25–300	0	0	2	1	0–1	2	1	3	CYP2D6 **moderate**; CYP3A4 **moderate**	Inhibits CYP2D6 only at high doses
Serotonin-norepinephrine reuptake inhibitor												
Desvenlafaxine[f,g]	50	50–400	0	0	1	0	0	2	0	1	CYP2D6 mild	
Duloxetine	30–60	30–120	0	0	1	0	0	2	0–1	1	CYP2D6 **moderate**	May improve neuropathic pain
Venlafaxine[g]	37.5 BID	37.5 BID – 125 TID	0	1	1	0	1	2	0	3	CYP2D6 mild	Safe with tamoxifen; may improve hot flashes; short half-life so withdrawal can occur more readily with short-acting preparation
Venlafaxine XR[g]	75	37.5–350	0	1	1	0	1	2	0–1	3	CYP2D6 mild	
Atypical agents												
Bupropion	100 BID	200–450 total per day, max 150/dose	0	0	2	0	1	1	0	0	CYP2D6 **strong**	Caution with sorafenib, tamoxifen; can be helpful for energizing; contraindicated if seizure history or bulimia; used for smoking cessation
Bupropion SR 12 hr	150	150–200 BID	0	0	1	0	1	1	0	0	CYP2D6 **strong**	
Bupropion XL 24 hr	150	150–450	0	0	1	0	1	1	0	0	CYP2D6 **strong**	
Mirtazapine	15	7.5–60	1	4	0	0	1	0	4	1	CYP2D6 mild	Safe with tamoxifen; may improve nausea, hot flashes, appetite, insomnia

† BID twice daily; TID, three times daily; Antichol, anticholinergic; Insomnia/agit, insomnia/agitation; ↓ BP, orthostatic hypotension; QTc, QTc prolongation; GI, gastrointestinal; ↑ weight, weight gain; sexual, sexual dysfunction. Note: All SSRIs and SNRIs are associated with transient nausea and GI discomfort upon initiation or dose increase.

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Footnotes on (SANXDE-E 2 of 2)

FOOTNOTES FOR FIRST-LINE ANTIDEPRESSANTS FOR DEPRESSION OR ANXIETY IN ADULTS

[a] Information extracted from:

- Simon G, Rush AJ. Unipolar major depression in adults: Choosing initial treatment. UpToDate, accessed 11/30/2020: https://www.uptodate.com/contents/unipolar-major-depression-in-adults-choosing-initial-treatment?search=antidepressants&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2.
- Caraci F, Crupi R, Drago F, Spina E. Metabolic drug interactions between antidepressants and anticancer drugs: focus on selective serotonin reuptake inhibitors and hypericum extract. Curr Drug Metab 2011;12:570-577.
- Mehta RD, Roth AJ. Psychiatric considerations in the oncology setting. CA Cancer J Clin 2015;65:300-314.
- Miguel C, Albuquerque E. Drug interaction in psycho-oncology: antidepressants and antineoplastics. Pharmacology 2011;88:333-339.
- Wedret JJ, Tu TG, Paul D, et al. Interactions between antidepressants, sleep aids and selected breast cancer therapy. Ment Illn 2019;11:8115.

[b] These recommendations do not apply to bipolar depression.

[c] Starting doses for older adults, those with renal or hepatic compromise, drug-sensitive survivors, or those with low BMI may be half the usual starting dose.

[d] Hypericum extract (ie, St. John's wort) can reduce the plasma concentrations of tyrosine kinase inhibitors and monoclonal antibodies by inducing both CYP3A4 and P-glycoprotein (P-gp).

[e] Citalopram: maximum dose of 20 mg is recommended for those aged >60 years or those with hepatic insufficiency or if taking drugs with CYP3A4 metabolism or other interacting medications that can increase levels.

[f] Desvenlafaxine: no evidence that doses >50 mg per day provide any additional benefit.

[g] Desvenlafaxine and venlafaxine may cause persistent dose-related increases in blood pressure (primarily diastolic) and heart rate. Monitor blood pressure regularly.

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COGNITIVE FUNCTION FOLLOWING CANCER TREATMENT

General Principles

- **Growing evidence supports the validity of the patient-reported experience of cognitive dysfunction associated with cancer diagnosis and treatments.**
- **Neuropsychological testing and brain imaging have demonstrated abnormalities in patients diagnosed with and treated for cancer.**
- **Currently no effective brief screening tool for cancer-associated cognitive dysfunction has been identified, and screening tools do not strongly correlate with patient reports of cognitive dysfunction. The Mini-Mental State Examination (MMSE)[a] and similar screening tools lack adequate sensitivity for the more subtle decline in cognitive performance most commonly seen in cancer survivors.**
- **There is limited evidence to guide management of this condition.**
- **Patients benefit from validation of their symptom experience, a thorough evaluation of this concern and related issues, and education.**
- **Cognitive concerns should be systematically assessed using self report.**
- **Providers need to be aware that self-report of cognitive concerns, or the lack thereof, is not a surrogate for measurement of the presence or absence of impairment in cognitive function.**
- **Imaging studies may not be helpful, except to rule out structural abnormalities as indicated by high-risk illness, or focal neurologic deficits or comorbidities.**
- **Patients who report cognitive impairment should be screened for potentially reversible factors that may contribute to cognitive impairment (ie, depression, sleep disturbance, fatigue, delirium).**
- **These guidelines address cognitive function of survivors with non-CNS malignancies who did not have CNS-directed therapies.**

[a] Folstein MF, Folstein SE, McHugh PR. “Mini-mental state”: A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-198.

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COGNITIVE FUNCTION ASSESSMENT

Focused History:

- Focal neurologic deficits
- High risk or known metastatic disease/brain primary
- Onset, temporality
- Age (a risk factor for developing cognitive deficiency)
- Trajectory over time
- Cancer treatment history
- Prescription medications/OTC medications and supplements
- Education attainment
- Caregiver assessment of cognitive function
- Nature of impairments per patient; clarifying questions may include:
  - Do you have difficulty paying attention? Multitasking?
  - Do you frequently leave tasks incomplete?
  - Do you have difficulty finding words?
  - Do you have difficulty remembering things?
  - Do you need to use more prompts like notes or reminders than you used to?
  - Does it take you longer to think through problems; does your thinking seem slower?
  - Do you notice an impact on functional performance? Job performance?
- Assessment of medical history that may impact cognitive function

Assessment of Contributing Factors:

- Medications/side effects
- Emotional distress
  - Depression/anxiety (see SANXDE-1 and NCCN Guidelines for Distress Management)
- Symptom burden
  - Pain (SPAIN-1)
  - Fatigue (SFAT-1)
  - Sleep disturbance (SSD-1)
- Comorbidities
- Use of alcohol and other agents that alter cognition
- New-onset vitamin deficiencies and endocrinopathies (eg, thyroid-stimulating hormone (TSH), B_1, B_{12}, D)

SPECIALIZED EVALUATION

Neuroimaging

Cancer-Associated Cognitive Dysfunction Interventions (SCF-3)

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CANCER-ASSOCIATED COGNITIVE DYSFUNCTION INTERVENTIONS

Patient/Family Education and Counseling
- Validation of experience of cognitive dysfunction associated with cancer diagnosis and treatment
- Reassurance that cancer-associated cognitive dysfunction is often not a progressive neurologic disorder like progressive dementias[b]
- Support self-management and coping strategies

→

General Strategies for Management of Cancer-Associated Cognitive Dysfunction
- Teach enhanced organizational strategies (ie, using memory aids like notebooks and planners, keeping items in the same place, using reminder notes, smart phone technology)
- Encourage patients to do the most cognitively demanding tasks at the time of day when energy levels are highest
- Provide information about relaxation or stress management skills for daily use
- Recommend routine physical activity (HL-1)
- Recommend limiting use of alcohol and other agents that alter cognition and sleep
- Consider meditation, yoga, mindfulness-based stress reduction, and cognitive training (ie, brain games)
- Involve social support system to help with completion of tasks and activities
- For older adults also see the cognitive function section in the NCCN Guidelines for Older Adult Oncology (OAO-F)
- Optimize management of:
  - Depression or emotional distress (See appropriate survivorship guidelines or NCCN Guidelines for Distress Management)
  - Sleep disturbance (SSD-1)
  - Fatigue (SFAT-1)
  - Contributing symptoms such as pain (SPAIN-1)
  - Medical comorbidities

→ **Specific Interventions (SCF-4)**

[b] Cognitive dysfunction may be progressive in survivors of CNS cancers or those who had CNS-directed therapies.

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CANCER-ASSOCIATED COGNITIVE DYSFUNCTION-SPECIFIC INTERVENTIONS

FIRST-LINE INTERVENTIONS

- **Neuropsychological evaluation/testing and recommendations[c]**
- **Cognitive rehabilitation**
  - **Occupational therapy[d]**
  - **Speech therapy**
  - **Neuropsychologist**
- **Psychotherapy**
- **Recommend routine physical activity (HL-1)**

SECOND-LINE INTERVENTIONS

- **Consider referral to a clinician with expertise in memory or cognitive concerns for further evaluation and care for survivors who continue to have cognitive problems after rehabilitation**
- **Consider trial use of medications (methylphenidate, modafinil, or donepezil)[e]**

[c] Neuropsychological evaluation and intervention may be therapeutic and validating. Evaluation may also be necessary if an individual is pursuing disability benefits and cognitive impairment is a contributing factor to work limitation.
[d] Occupational therapy strategies focus on improvement of cognitive functioning and may be most effective for an individual who notes the impact of specific functional limitations (ie, word finding, comprehension or task completion, quality-of-life or role expectations).
[e] Overall the evidence for these medications is lacking, but there may be some benefit in select survivors or certain clinical scenarios.

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DEFINITION OF CANCER-RELATED FATIGUE

- **Cancer-related fatigue is a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning. (See the NCCN Guidelines for Cancer-Related Fatigue.)**

CONSIDERATIONS FOR FATIGUE IN CANCER SURVIVORS

- **Fatigue is a common complaint in individuals undergoing cancer therapy and can be a persistent problem for some cancer survivors in the months and years after cancer diagnosis.**
  - **Receipt of chemotherapy, radiation, endocrine, immunotherapy, targeted, and/or cellular therapies are predisposing factors for cancer-related fatigue, but it can be seen in some patients who are treated with surgery alone.**
  - **The time-course of fatigue is unique to the survivor and their treatment plan. However, many cancer survivors report that fatigue may be a disruptive symptom months or years after treatment ends.**
  - **Fatigue that initially presents months after the completion of adjuvant therapy or fatigue that worsens over this period warrants additional evaluation.**
  - **Assessment and communication regarding fatigue and anticipated recovery after treatment should be done periodically.**
- **Fatigue is a subjective experience that should be systematically assessed using patient self-reports and other sources of data for cancer survivors in the months and years after diagnosis.**
- **Patients and family/caregiver(s) should be informed that management of fatigue is an integral part of total health care and that fatigue can persist following treatment.**
- **Medical care contracts should include reimbursement for the management of fatigue.**
- **Disability insurance should include coverage for the continuing effects of fatigue.**
- **Referral to rehabilitation services including physical therapy, occupational therapy, and physical medicine should be considered for survivors with fatigue in the months and years after cancer diagnosis.**
- **Also see the NCCN Guidelines for Cancer-Related Fatigue.**

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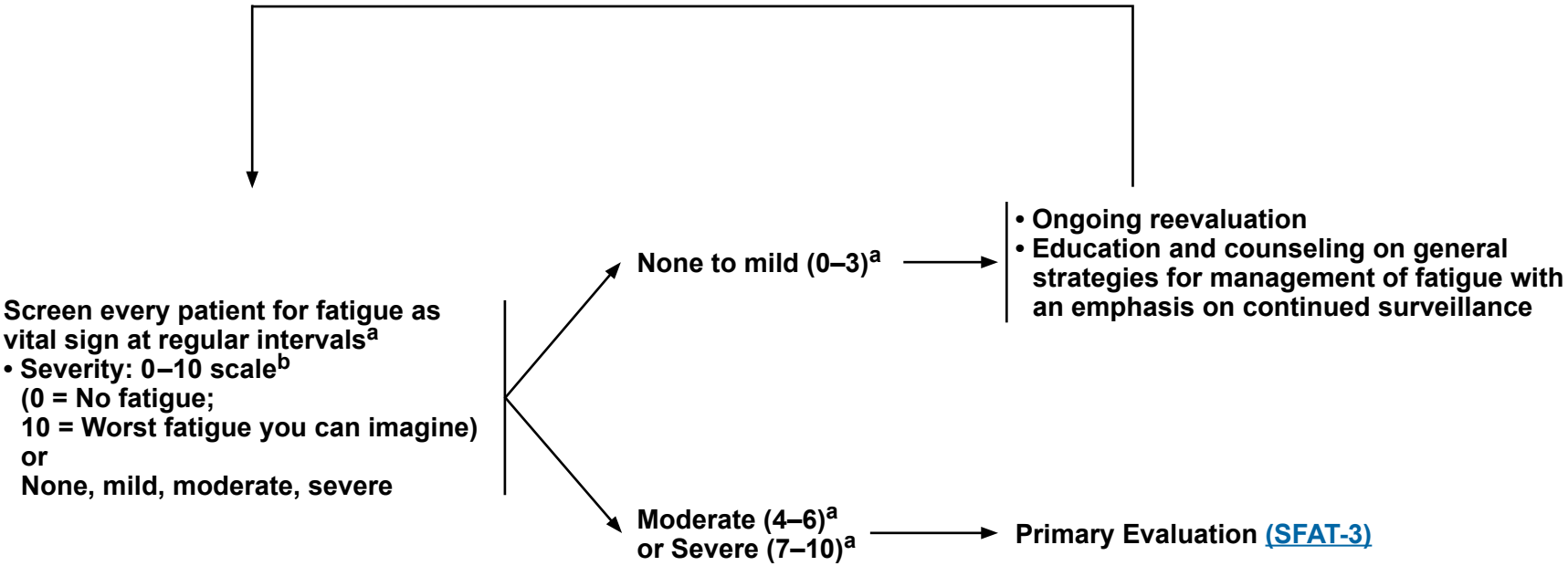
SCREENING



[a] Recommended screen and re-evaluation: "How would you rate your fatigue on a scale of 0–10 over the past 7 days?"
[b] Butt Z, Wagner LI, Beaumont JL, et al. Use of a single-item screening tool to detect clinically significant fatigue, pain, distress, and anorexia in ambulatory cancer practice. J Pain Symptom Manage 2008;35:20-30.

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PRIMARY EVALUATION FATIGUE SCORE: MODERATE OR SEVERE (4–10)

EVALUATION

H&P:
- Focused fatigue history
  - Onset, pattern, duration
  - Change over time
  - Associated or alleviating factors
  - Interference with function
- Evaluate disease status
  - Evaluate risk of recurrence based on stage, pathologic factors, and treatment history
  - Perform review of systems to determine if other symptoms substantiate suspicion for recurrence
- Assessment of treatable contributing factors:
  - Comorbidities
    - ◊ Alcohol/substance use disorder
    - ◊ Organ dysfunction[c]
    - ◊ Infection
    - ◊ Anemia
    - ◊ Arthritis
  - Prescribed or OTC medications (eg, sleep aids, pain medications, antiemetics)
  - Emotional distress- screen for anxiety and depression (SANXDE-1)
  - Sleep disturbance (eg, insomnia, sleep apnea, vasomotor symptoms, restless legs syndrome [RLS]) (SSD-1)
  - Pain (SPAIN-1)
  - Nutritional issues
    - ◊ Weight/caloric intake changes (SNWM-1)
  - Deconditioning/loss of muscle mass
  - Physical inactivity or sedentary behavior

→

Laboratory Evaluation:
- Consider performing laboratory evaluation based on presence of other symptoms, onset, and severity of fatigue
  - CBC with differential
    - ◊ Compare end-of-treatment hemoglobin/hematocrit with current values
    - ◊ Assess other cell lines (WBC and platelets)
  - Comprehensive metabolic panel
    - ◊ Assess electrolytes
    - ◊ Assess hepatic and renal function
  - Endocrine evaluation
    - ◊ TSH, especially in patients who have received prior head/neck, torso, or breast radiation
    - ◊ Consider more comprehensive evaluation or referral to specialist if other symptoms present
    - ◊ Cortisol stimulation test, if history of prolonged steroid use

→

Other Diagnostic Testing:
- Consider radiologic assessment only if high risk of disease recurrence OR if accompanying signs and symptoms suggest presence of metastatic disease
- Consider cardiac testing (ECHO) for patients treated with an anthracycline (SCARDIO-1), trastuzumab, bevacizumab, other VEGF- or HER2-targeted therapy, or other therapy known to cause cardiac dysfunction
- Chest x-ray and oxygen saturation testing for pulmonary complaints[d]

→ **Treatment of Contributing Factors (SFAT-4)**

[c] Cardiac, endocrine (eg, hypothyroidism, hypogonadism, adrenal insufficiency), GI, pulmonary, renal, and/or hepatic dysfunction.
[d] Refer to a pulmonologist for pulmonary complaints.

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TREATMENT OF CONTRIBUTING FACTORS

- **Treat contributing factors:**
  - **Medications/side effects**
  - **Pain (SPAIN-1)**
  - **Emotional distress (SANXDE-1) and NCCN Guidelines for Distress Management**
  - **Anemia**
    - ◊ **Treat iron, B_{12}, folate deficiency, if present**
    - ◊ **Consider referral/further evaluation for anemia or cytopenias**
  - **Sleep disturbance (SSD-1)**
  - **Nutritional deficit/imbalance**
  - **Comorbidities**

→ **Interventions for Cancer Survivors (SFAT-5)**

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INTERVENTIONS FOR CANCER SURVIVORS

Patient/Family Education and Counseling

Provide information about patterns of fatigue during and after treatment
- Self-monitoring of fatigue levels
- Energy prioritization
  - Set priorities
  - Plan and pace activities
  - Schedule activities at times of peak energy

→

Physical Activity

- Maintain adequate levels of physical activity (category 1) (SPA-1 and SPA-4)
- Survivors at higher risk of injury (eg, those living with neuropathy, cardiomyopathy, lymphedema, or other long-term effects of therapy or other comorbidities) should be referred to a physical therapist or exercise specialist
- Make use of local resources to help patients increase exercise (eg, aerobics, strength training, yoga)
  - Community exercise programs or classes, preferably those focused on cancer survivors
  - Exercise professional certified by the ACSM
  - For patients with fatigue interfering with function, consider referral to a physical therapist or physiatrist

→

Other Interventions[e]

- Psychosocial interventions (category 1)
  - CBT[f]/Behavioral therapy (category 1)
  - Mindfulness-based stress reduction (category 1)
  - Psycho-educational therapies/Educational therapies (category 1)
  - Supportive expressive therapies (category 1)[g]
- Nutrition consultation
- CBT[f] for insomnia (CBT-I) (category 1) (SSD-1)
  - Stimulus control
  - Sleep restriction
  - Sleep hygiene
- Acupuncture
- Bright white light therapy[h]
- Massage therapy (category 1)

→

Pharmacologic[i]

Consider psychostimulants[j] (methylphenidate[k]) after ruling out other causes of fatigue and if other interventions are unsuccessful

[e] Interventions should be culturally specific and tailored to the needs of patients and families along the illness trajectory, because not all patients may be able to integrate these options due to variances in individual circumstances and resources.
[f] A type of psychotherapy that focuses on recognizing and changing maladaptive thoughts and behaviors to reduce negative emotions and facilitate psychological adjustment.
[g] Supportive expressive therapies (such as support groups, counseling, and journal writing) facilitate expression of emotion and foster support from one or more people.
[h] Bright white light therapy of 1250–10,000 lux is most frequently self-administered in the early morning for 30–40 minutes. Timing needs to be adjusted for those who sleep during the day. Xiao P, et al. J Pain Symptom Manage 2022;63:e188-e202.
[i] Pharmacologic interventions remain investigational, but have been reported to improve symptoms of fatigue in some patients.
[j] Psychostimulants are at times used to treat cancer-related fatigue. A number of studies have evaluated their efficacy in the setting of active treatment and results have been mixed. There are extremely limited data regarding the use of these agents in the post-treatment setting.
[k] Methylphenidate should be used cautiously and should not be used until treatment- and disease-specific morbidities have been characterized or excluded. Optimal dosing and schedule have not been established for use of psychostimulants in patients with cancer.

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DEFINITION AND STAGES OF LYMPHEDEMA[a,b]

- **Definition: Lymphedema occurs when lymph fluid accumulates in the interstitial tissue, causing swelling of the limb or other areas such as the neck, trunk, or genitals. It is a common side effect of cancer treatment, occurring on the same side of the body as the cancer treatment, as a result of dysfunction of the lymphatic system.**
- **Stage 0 (latent/subclinical): Lymphatic dysfunction without swelling; subtle symptoms, such as a feeling of heaviness or fatigue in the limb, may be present.**
- **Stage 1 (spontaneously reversible): Accumulation of fluid and protein causing swelling; pitting edema may be evident; increased girth, heaviness, and/or stiffness of affected area. For the limbs, swelling is relieved with elevation.**
- **Stage 2 (irreversible): Spongy tissue consistency, with pitting edema that becomes less evident as swelling increases; tissue fibrosis causing hardness and increase in size. For the limbs, swelling is not relieved with elevation.**
- **Stage 3 (lymphostatic elephantiasis): Severe dry, scaly, thickened skin; increased swelling and girth of affected area; can be debilitating. In the limbs, fluid leakage and blisters are common. Fungal infection and papilloma may occur. Pitting can be absent due to progressive deposition of fat and fibrosis, which is the hallmark of later stage lymphedema.**

[a] National Cancer Institute Lymphedema (PDQ)–Patient Version https://www.cancer.gov/about-cancer/treatment/side-effects/lymphedema
[b] Executive Committee of the International Society of Lymphology. The diagnosis and treatment of peripheral lymphedema: 2020 Consensus Document of the International Society of Lymphology. Lymphology 2020;53:3-19. https://pubmed.ncbi.nlm.nih.gov/32521126/

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PRINCIPLES OF LYMPHEDEMA

- **Lymphedema is a potential side effect after the treatment of cancer resulting from damage to the lymphatic system. Approximately 3 in 4 cases of lymphedema are diagnosed within 3 years of treatment; however, it can develop anytime in the life of the survivor. Depending on stage of diagnosis, lymphedema can be an acute or chronic condition. It can impact any area of the body (eg, arms, legs, face, trunk, groin).**
- **Swelling on the same side as the cancer treatment is a universal symptom of lymphedema. Additional initial symptoms may include sensation of heaviness, fatigue, fullness or tightness in the skin, or pain. Symptoms including decreased range of motion or function and thickening of the skin may occur in later stages.[a]**
- **Survivors who had surgery, radiation, or chemoradiation to the axillary, supraclavicular, cervical, or pelvic inguinal lymph node system are at risk for the development of lymphedema. Sentinel node biopsy also increases the risk of lymphedema, although it poses less risk than complete dissection.**
- **BMI ≥30 kg/m^2, localized infection, increased number of nodes removed, and higher initial extent of disease raise the risk of lymphedema development.**
- **If possible, pretreatment limb measurement of both sides should be performed as a baseline for survivors with treatment-related or individual risk factors, preferably by a trained lymphedema specialist.**
- **Early detection/diagnosis and early referral are key for optimal lymphedema management because stages 0 and 1 are reversible, whereas stages 2 and 3 are less responsive to treatment. Therefore, survivors at risk for lymphedema should be regularly screened for lymphedema by symptom assessment, clinical exam, and, if available, bioimpedance spectroscopy. Patients should be educated about early symptoms and signs of lymphedema including fullness, tightness, heaviness, and pain.**
- **Lymphedema may cause or exacerbate psychological distress (SANXDE-1).**
- **Survivors at risk for lymphedema and those with lymphedema are at a higher risk of localized infection in the affected area. These infections can require hospitalization for IV antibiotics. Therefore, survivors with or at risk for lymphedema should be educated to inform their medical provider immediately for signs of infection in the affected area.**
- **Progressive weight training under supervision and physical activity are not associated with exacerbation or development of lymphedema.[c,d,e]**
- **Observational studies have demonstrated that air travel, venipuncture, and blood pressure measurement (via arm cuff) are not associated with exacerbation or development of lymphedema, and precautionary measures are likely unnecessary.[f,g] In the absence of high-level data, the panel recommends medical procedures such as venipuncture and blood pressure measurements be done on the non–at-risk limb; however, if necessary, procedures may be done using the at-risk limb.[h] More research is needed to determine the effect of these procedures on the risk of lymphedema.**

Footnotes on SLYMPH-2A

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FOOTNOTES FOR SLYMPH-2

[a] National Cancer Institute Lymphedema (PDQ)–Patient Version https://www.cancer.gov/about-cancer/treatment/side-effects/lymphedema
[c] Campbell KL, Winters-Stone KM, Wiskemann J, et al. Exercise guidelines for cancer survivors: Consensus statement from international multidisciplinary roundtable. Med Sci Sports Exerc 2019;51:2375-2390.
[d] Irwin M, ed. ACSM's Guide to Exercise and Cancer Survivorship. Champaign, IL: The American College of Sports Medicine; 2012.
[e] National Lymphedema Network. Position Paper: Exercise 2013. https://issuu.com/lymphnet/docs/exercise.
[f] Asdourian MS, Skolny MN, Brunelle C, et al. Precautions for breast cancer-related lymphoedema: risk from air travel, ipsilateral arm blood pressure measurements, skin puncture, extreme temperatures, and cellulitis. Lancet Oncol 2016;17:e392-405.
[g] Ahn S, Port ER. Lymphedema precautions: Time to abandon old practices? J Clin Oncol 2016;34:655-658.
[h] National Lymphedema Network. Position Paper: Lymphedema Risk Reduction Practices 2012: https://issuu.com/lymphnet/docs/risk_reduction.

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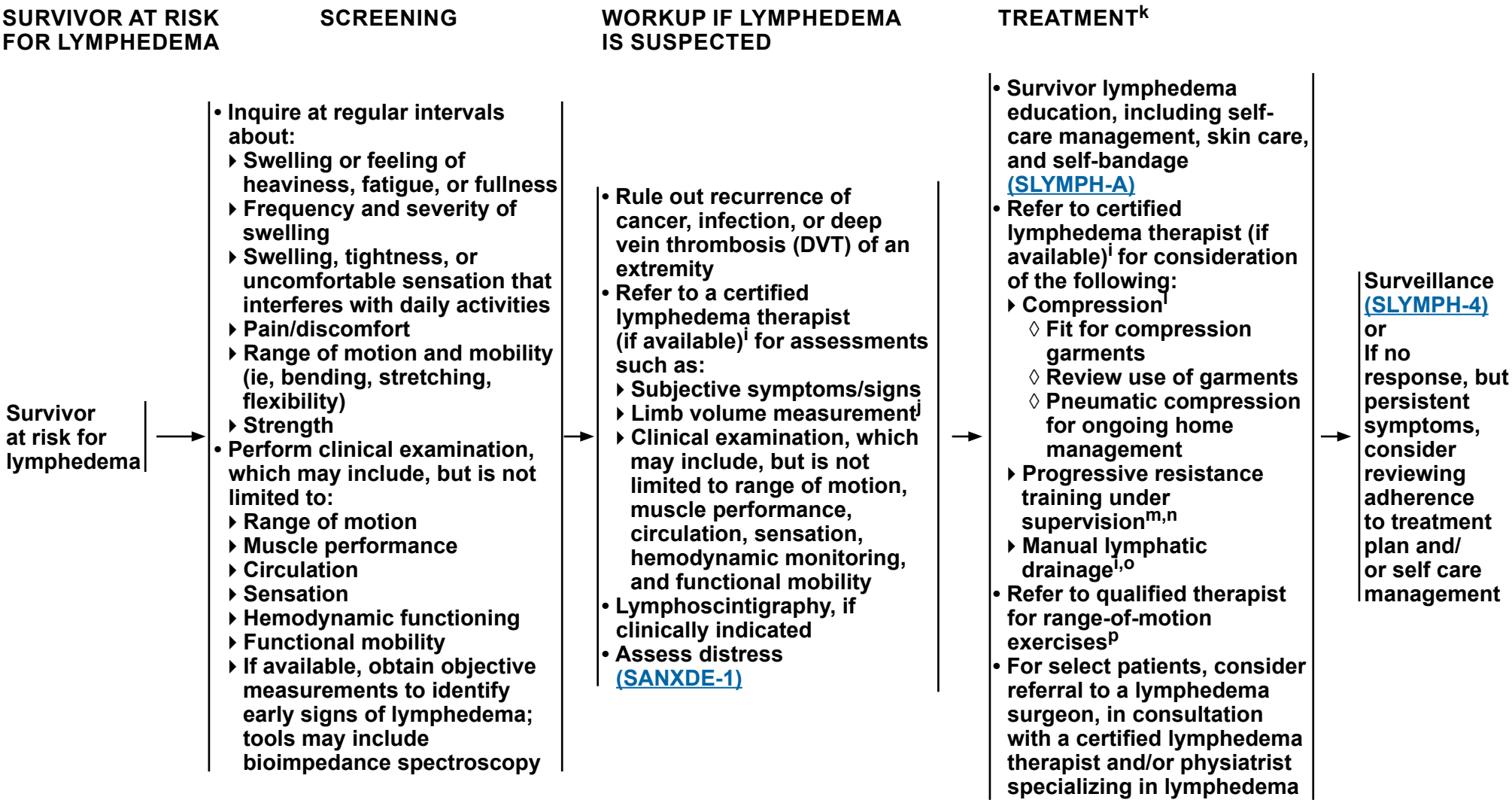

Footnotes on (SLYMPH-3A)

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FOOTNOTES FOR LYMPHEDEMA TREATMENT (SLYMPH-3)

[i] Certified lymphedema therapists can be located using the following resource: https://www.clt-lana.org/therapists. NCCN recommends attention to evidence-based practice and specialized training for lymphedema management.

[j] If baseline measurement is not available, measure unaffected contralateral limb as a reference.

[k] Lymphedema Management: The Comprehensive Guide for Practitioners. Joachim Ernst Zuther, Steve Norton (Autoren) Buch | Hardcover 592 Seiten; 2017 | 4th New edition; Thieme Medical Publishers Inc (Verlag); 978-1-62623-433-8 (ISBN); Chapter 5.

[l] Compression garments should be prescribed. Optimally, they should be fitted and measured by a certified lymphedema therapist.

[m] If a certified therapist is not available, survivors with lymphedema can perform resistance training with a professional trainer who has knowledge of cancer-related physical activity principles. Weights should be slowly progressed as tolerated, and lymphedema should be evaluated periodically.

[n] Aerobic exercise or other forms of physical activity as tolerated. See Principles of Physical Activity for Survivors with or At Risk for Lymphedema (SLYMPH-B).

[o] If a certified lymphedema therapist is not available, consider referral to appropriate provider for treatment.

[p] Trained personnel can include physical and occupational therapists, certified exercise professionals, and rehabilitation specialists. Specialized training in working with survivors is available for both physical therapists and exercise professionals: ACSM [http://www.acsm.org/get-stay-certified] and APTA Oncology section [http://oncologypt.org].

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SURVEILLANCE

Follow-up with treatment team as clinically indicated

- **Inquire about fit and age of compression garments**
- **Replace compression garments as clinically indicated**
- **Check range of motion**
- **Inquire about performance of prescribed exercises**
- **Inquire about self-care management**
- **Continue survivor lymphedema education (SLYMPH-A)**
- **Continue treatment as clinically indicated (SLYMPH-3)**
- **Assess for distress (SANXDE-1)**

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SURVIVOR LYMPHEDEMA EDUCATION

- **Survivors should be educated regarding:**
  - **Signs and symptoms of lymphedema and the importance of rapid reporting to the treatment team.**
  - **Signs and symptoms of infection (eg, redness, pain, skin streaking/warm to touch) in the affected area and the importance of rapid reporting to the treatment team.**
  - **Self-care management: Infection prevention measures,[a] risk reduction strategies,[b] maintenance of skin integrity on the affected side, manual drainage, and range of motion exercise[c]**
  - **Consideration of compression garments, manual lymphatic drainage, and pneumatic compression for ongoing home management**
- **Survivors should also be informed that:**
  - **Progressive weight training under supervision and physical activity are not associated with exacerbation or development of lymphedema[1,2,3] (SLYMPH-B).**
    - ◊ **Progressive resistance training under supervision may improve lymphedema symptoms. However, caution is advised in this population, and survivors with or at risk for lymphedema should discuss physical activity plans with a lymphedema specialist before starting a program that involves strength or resistance training (SLYMPH-B).**
    - ◊ **Water exercise under supervision may be an option to consider after assessing any skin integrity and/or incision issues, although evidence that water exercise helps decrease lymphedema symptoms is limited.[4]**
  - **Studies have demonstrated that air travel, venipuncture, and blood pressure measurement (via arm cuff) are not associated with exacerbation or development of lymphedema, and precautionary measures are likely unnecessary.[5,6] However, medical procedures such as venipuncture and blood pressure measurements should be done on the non–at-risk arm/limb if possible.[7] If necessary, procedures may be done using the at-risk arm/limb.**

Footnotes

[a] Risk of infections can be reduced by safe pet care and gardening techniques (SIMIN-2).
[b] For a complete list of lymphedema risk reduction practices, see the Position Statement from the National Lymphedema Network: https://lymphnet.org/position-papers.
[c] Limb elevation can be used as an option for early-stage lymphedema for short-term improvement, but data are limited.

References

[1] Campbell KL, Winters-Stone KM, Wiskemann J, et al. Exercise guidelines for cancer survivors: Consensus statement from international multidisciplinary roundtable. Med Sci Sports Exerc 2019;51:2375-2390.
[2] Irwin M, ed. ACSM's Guide to Exercise and Cancer Survivorship. Champaign, IL: The American College of Sports Medicine; 2012.
[3] National Lymphedema Network. Position Paper: Exercise 2013. https://issuu.com/lymphnet/docs/exercise.
[4] Lindquist H, Enblom A, Dunberger G, et al. Water exercise compared to land exercise or standard care in female cancer survivors with secondary lymphedema. Lymphology 2015;48:64-79.
[5] Asdourian MS, Skolny MN, Brunelle C, et al. Precautions for breast cancer-related lymphoedema: risk from air travel, ipsilateral arm blood pressure measurements, skin puncture, extreme temperatures, and cellulitis. Lancet Oncol 2016;17:e392-405.
[6] Ahn S, Port ER. Lymphedema precautions: Time to abandon old practices? J Clin Oncol 2016;34:655-658.
[7] National Lymphedema Network. Position Paper: Lymphedema Risk Reduction Practices 2012: https://issuu.com/lymphnet/docs/risk_reduction.

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PRINCIPLES OF PHYSICAL ACTIVITY FOR SURVIVORS WITH OR AT RISK FOR LYMPHEDEMA

- **Lymphedema is not a contraindication for physical activity, and no special precautions are required if participating in cardiovascular/aerobic exercise or strength training of unaffected limbs.**
- **Continued full use of the extremity and range-of-motion exercises are encouraged to maintain strength and range of motion even in the presence of lymphedema.**
- **Progressive strength training:**
  - **Gradually increase resistance by smallest increment possible with monitoring.**
  - **Consider referral to lymphedema specialist for evaluation prior to starting a physical activity program that involves the affected or at-risk limb.**
  - **Compression garments may be required during training sessions.**
  - **When possible, survivors should work with trained exercise professionals[1] and initiate exercises involving affected body part in consultation with a certified lymphedema therapist and/or physiatrist specializing in lymphedema management. Avoid exercise in the setting of an acute injury or infection of the affected area.**
- **Survivors should undergo baseline and periodic evaluation for development or exacerbation of lymphedema.**
- **Survivors should stop exercise and see a lymphedema specialist if exacerbation of lymphedema occurs.**

[1] Trained personnel can include physical and occupational therapists, certified exercise professionals, and rehabilitation specialists. Specialized training in working with survivors is available for both physical therapists and exercise professionals (ACSM [http://www.acsm.org/get-stay-certified] or APTA Oncology section [http://oncologypt.org]).

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GENERAL PRINCIPLES OF PAIN MANAGEMENT

- **Comprehensive pain assessment should be done to determine the etiology of the pain.**
  - **If the pain is new and acute, differential diagnosis should include cancer recurrence or progressive disease.**
  - **If the pain is chronic, a specific pain syndrome should be identified if possible.**
- **Conduct a discussion with the patient and caregivers regarding realistic treatment goals, including improvement in function, side effects of pain regimen and, if on opioids, safe opioid use, as well as pain relief.**
- **Non-cancer pain in cancer survivors should be treated congruent with pain diagnosis, with opioids remaining the last resort. In addition to non-cancer–related pain, differential diagnosis should include cancer recurrence or progressive disease. Consider referring to primary care service for management of non-cancer pain.**
- **Use a multimodality approach to pain management if those resources are available.**
- **Non-opioid adjuvant analgesics are appropriate as primary therapy for many pain syndromes.**
- **Non-pharmacologic interventions can be used as the sole treatment for pain, or as adjuncts to pharmacologic therapy.**
  - **Physical modalities (heat, cold, massage, acupuncture, physical therapy, or occupational therapy) are useful and should be considered for some pain syndromes.**
  - **Hypnosis,[a] meditation, acupuncture, cognitive restructuring, and behavioral activation can be considered to control pain and maximize function.**
- **Opioid treatment is sometimes necessary, and the lowest appropriate dose should be used for the shortest amount of time possible.**
- **Psychological support of the survivor with chronic pain is necessary, and referral to psychosocial services should be considered for survivors in distress (SANXDE-1).**
- **Consider referral to a specialist for survivors who might benefit from further pain interventions. This could include referral to interventional pain, physical medicine and rehabilitation, palliative care, pain specialist, urology, gynecology, orthopedic surgery, gastroenterology, or other appropriate consultants.**
  - **If these resources are available, consider referral as early as possible during the course of treatment planning.**
- **Opioids and pregnancy:**
  - **Ensure appropriate opioid prescribing and screening for opioid use disorder (OUD) for survivors of childbearing potential.**
  - **If a survivor on chronic opioids is pregnant or wants to become pregnant, do not stop opioids abruptly but coordinate further pain management with the obstetrician. If the survivor has OUD and takes buprenorphine for addiction and/or pain, provide access to addiction services without stopping buprenorphine. OUD can cause preterm birth, stillbirth, and neonatal abstinence syndrome.**
- **The panel acknowledges the legalization of medical marijuana for various conditions in multiple states. However, there are presently not enough data to make any guideline recommendations regarding use in cancer survivors.**
- **Also see the NCCN Guidelines for Adult Cancer Pain.**

[a] Thompson T, Terhune DB, Oram C, et al. The effectiveness of hypnosis for pain relief: A systematic review and meta-analysis of 85 controlled experimental trials. Neurosci Biobehav Rev 2019;99:298-310.

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PRINCIPLES OF OPIOID USE IN LONG-TERM SURVIVORS

- **When opioids are appropriate and necessary, establish treatment goals with survivors and caregivers and use the lowest effective opioid dose for the shortest period of time possible.**
- **Provide survivor and caregiver education on safe opioid use, risks including risk of psychological and/or physical dependence and addiction, safe storage, and disposal.**
- **Consider prescribing naloxone and educate the patient and the caregivers on its use. Instruct caregivers to call 911 Emergency Service if naloxone is administered.**
- **Functional outcomes are important measures for patients on opioid therapy. The expected outcome (ie, improvement in function and/or pain) and terms of monitoring for outcomes, adherence, and safety should be clearly discussed with survivors and caregivers, agreed upon, and documented upon initiation and continuation of chronic therapy. Consider establishing pain treatment agreements/contracts in consultation with state and/or institutional requirements. Pain treatment agreements can be a useful tool in the overall strategy to manage opioid use and long-term pain in survivors[b].**
- **Re-evaluate the effectiveness, safety, and necessity of opioids at regular intervals.**
  - **If the expected outcome is not achieved, other treatment alternatives should be considered. If opioids are no longer appropriate, recommend gradual tapering of opioids to help avoid symptoms of withdrawal (see PAIN-G 3 of 13 in the NCCN Guidelines for Adult Cancer Pain).**
- **Address medical-related issues due to chronic or high-dose opioids.**
  - **Endocrine/hypopituitary abnormalities**
    - ◊ **Testosterone deficiency**
  - **Manage opioid adverse effects (ie, constipation, nausea, pruritus, delirium, motor and cognitive impairment, respiratory depression, sedation) (see PAIN-H in the NCCN Guidelines for Adult Cancer Pain).**
- **Monitor for aberrant drug-taking behaviors[c] and for signs of substance use disorder (see PAIN-G 6 of 13 in the NCCN Guidelines for Adult Cancer Pain).**
  - **If there is evidence of aberrant opioid use, verbalize concerns to the survivor and refer as early as possible to pain specialist, palliative care, physiatry, and/or substance use disorder/mental health specialists.**
  - **Engage caregivers or people living with the survivor if possible.**
- **The panel endorses the ASCO Policy Brief on Opioid Therapy and Access to Treatment (2016), particularly as it relates to weighing the risks/benefits of opioid treatment.**
- **If opioids are indicated, advocacy to ensure access to the appropriate opioid regimen may be needed to address possible insurance, pharmacy, and other barriers as well as survivors' and caregivers' concerns about addiction.**

[b] Chou R, et al. J Pain 2009;10:113-130.
[c] Aberrant behaviors may include family member using drugs prescribed to the survivor.

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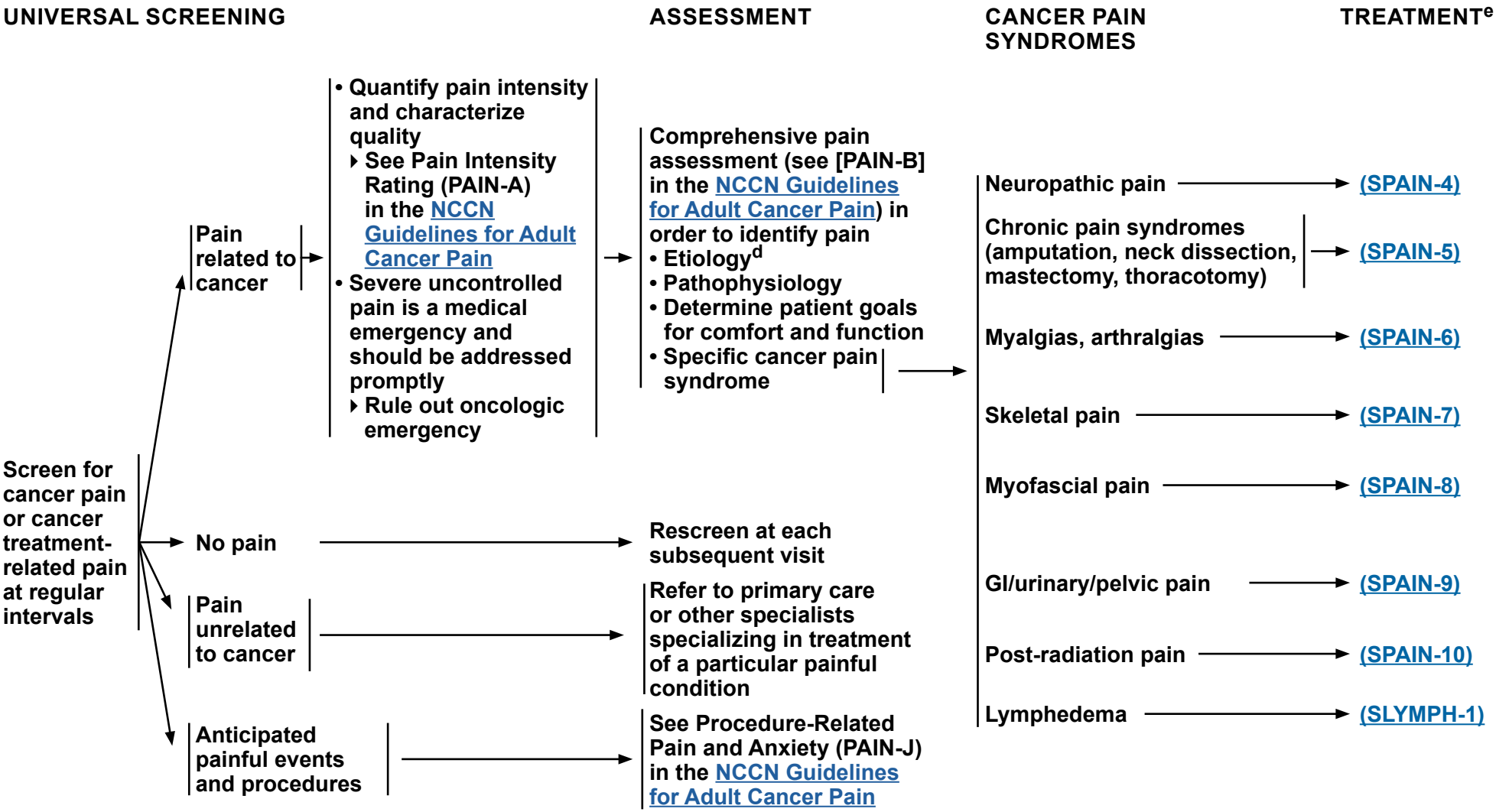

[d] Referral to PCP for non-cancer treatment-related workup and pain management (ie, rheumatoid arthritis) and consider the possibility of pain due to cancer recurrence.
[e] General Principles of Pain Management (SPAIN-1).

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CANCER PAIN SYNDROME	TREATMENT
Neuropathic pain[f] **• Paresthesias (tingling or prickling)** **• Shooting, "electrical"** **• Numbness** **• Allodynia (pain with non-painful stimulus)**	**• General measures:** **▸ Pharmacologic** **◊ Non-opioid/Adjuvant analgesics** **(See [PAIN-E] in the NCCN Guidelines for Adult Cancer Pain)** **– Antidepressants: SNRIs (including duloxetine[g], TCAs, anticonvulsants** **◊ Topicals** **– Patches (ie, lidoderm, capsaicin)** **– Creams/gels: Diclofenac topical gel** **– Compounded creams (eg, combinations of lidocaine, baclofen, ketamine, and amitriptyline)** **▸ Non-pharmacologic** **◊ CBT and psychosocial support** **(See [PAIN-C] in the NCCN Guidelines for Adult Cancer Pain)** **◊ Physical modalities** **– Heat** **– Ice** **– Acupuncture** **– Transcutaneous electrical nerve stimulation (TENS) unit** **• For moderate or severe pain, opioids and dual-action opioid agonist/noradrenaline reuptake inhibitor[h,i]** **See (PAIN-3, PAIN-4, and PAIN-5) in the NCCN Guidelines for Adult Cancer Pain** **• Consider referral to pain management services, interventional specialist,[j] physical therapy, physical medicine and rehabilitation, integrative services, and/or palliative care as appropriate**

[f] Also see NCCN Guidelines for Adult Cancer Pain and Loprinzi CL, et al. J Clin Oncol 2020;38:3325-3348.
[g] Duloxetine has the most evidence for treating neuropathic pain.
[h] Principles of Opioid Use in Long-Term Survivors (SPAIN-2).
[i] Initiating opioids in cancer survivors should be carefully considered if other interventions are unsuccessful.
[j] Scrambler therapy can be considered. Loprinzi C, et al. Support Care Cancer 2020;28:1183-1197.

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CANCER PAIN SYNDROME	TREATMENT	ADDITIONAL INTERVENTIONS
Chronic pain syndrome (amputation, neck dissection, mastectomy, thoracotomy) →	• General measures: ▸ Non-opioids/Adjuvant analgesics See (PAIN-E) in the NCCN Guidelines for Adult Cancer Pain ▸ Psychosocial support and behavioral interventions See (PAIN-C) in the NCCN Guidelines for Adult Cancer Pain • For moderate to severe pain: ▸ Opioids[h,i] See (PAIN-3, PAIN-4, and PAIN-5) in the NCCN Guidelines for Adult Cancer Pain • Consider referral to pain management services, interventional specialist, orthopedic services, physical therapy, physical medicine and rehabilitation, integrative services, and/or palliative care as appropriate	→ Specific chronic pain syndromes[k] →

Specific chronic pain syndromes[k] →

- For post-amputation syndrome:
  - ▸ Physical therapy for desensitization
    - ◊ Consider mirror therapy
  - ▸ Cognitive therapy
  - ▸ Upper extremities:
    - ◊ Consider stellate ganglion block
  - ▸ Lower extremities:
    - ◊ Consider lumbar sympathetic block
  - ▸ Neuromas:
    - ◊ Consider phenol/alcohol block
- For post-radical neck dissection syndrome:
  - ▸ Physical therapy for stretching, range of motion
  - ▸ Myofascial release
  - ▸ Soft tissue massage
  - ▸ Trigger point injections
  - ▸ Possible botulinum toxin injection
- For post-mastectomy or post-thoracotomy syndrome:
  - ▸ Physical therapy or structured exercise
  - ▸ Intercostal nerve block
  - ▸ TENS unit
  - ▸ Possible botulinum toxin injection

[h] Principles of Opioid Use in Long-Term Survivors (SPAIN-2).
[i] Initiating opioids in cancer survivors should be carefully considered if other interventions are unsuccessful.
[k] There are other postoperative pain syndromes and many treatment measures can be used across syndromes. Also consider referral to appropriate specialist.

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CANCER PAIN SYNDROME	TREATMENT
Myalgias, Arthralgias	• Nonpharmacologic ▸ Physical activity (category 1 for aromatase inhibitor [AI]-induced arthralgia) ▸ Heat (ie, paraffin wax, hot pack) ▸ Cold pack ▸ Aquatic therapy ▸ Ultrasonic stimulation[l] ▸ Massage ▸ Acupuncture (category 1 for AI-induced arthralgia) ▸ Yoga • Pharmacologic[m] ▸ SNRIs (category 1 for AI-induced arthralgia) ▸ TCAs ▸ Anticonvulsant drugs (ie, gabapentin, pregabalin) ▸ Acetaminophen ▸ COX-2 inhibitors ▸ Nonsteroidal anti-inflammatory drugs (NSAIDs) ▸ Muscle relaxants • Consider referral to pain management services, interventional specialist, physical therapy, physical medicine and rehabilitation, orthopedic services, and/or palliative care

[l] Ultrasonic stimulation is a type of heat treatment that can penetrate directly to the bone and should be used with caution. It is not recommended for patients with multiple myeloma or bone metastases.
[m] Consider switching to an alternative AI or tamoxifen for AI-induced arthralgia.

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CANCER PAIN SYNDROME

Skeletal pain[n] →

TREATMENT

- **For vertebral compression:**
  - **General measures:**
    - ◊ **Bisphosphonates or other antiresorptive medications if appropriate**
    - ◊ **NSAIDs**
    - ◊ **Muscle relaxants**
    - ◊ **Consider vertebral augmentation (ie, vertebroplasty, kyphoplasty)**
    - ◊ **Acetaminophen**
    - ◊ **COX-2 inhibitors**
  - **Consider referral to pain management services, interventional specialist, physical therapy, physical medicine and rehabilitation, orthopedic services, and/or palliative care**
  - **For acute vertebral compression:**
    - ◊ **Opioids[h,i]**
    - ◊ **Bracing (ie, thoracolumbar sacral orthosis [TLSO], Jewett brace)**
    - ◊ **Limited bed rest**
    - ◊ **Weight-bearing exercises when pain improves**
    - ◊ **Physical therapy**
  - **For chronic vertebral compression:**
    - ◊ **Weight-bearing exercises**
    - ◊ **Physical therapy – thoracic and lumbar stabilization exercises**
    - ◊ **Consider medial branch blocks and radiofrequency ablation for post-compression arthritic pain**
- **For avascular necrosis:**
  - **Physical therapy – based on weight-bearing and range-of-motion restrictions**
  - **Opioids[h]**
  - **Muscle relaxants if myofascial component**
  - **Core decompression**
  - **Joint replacement as clinically indicated**
  - **Nerve ablation evaluation and bracing for patients who are not joint replacement candidates**
- **For osteonecrosis of the jaw:**
  - **Referral to oral surgeon**
  - **Anti-convulsants**
  - **SNRIs**
  - **Opioids[h]**

[h] Principles of Opioid Use in Long-Term Survivors (SPAIN-2).
[i] Initiating opioids in cancer survivors should be carefully considered if other interventions are unsuccessful.
[n] For skeletal metastases and/or bone pain, see (PAIN-D) in the NCCN Guidelines for Adult Cancer Pain. Consider orthopedic/surgical referral.

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CANCER PAIN SYNDROME	TREATMENT
Myofascial pain	• Nonpharmacologic ▸ Physical activity ▸ Range-of-motion exercises ▸ Strengthening exercises ▸ Soft tissue/myofascial release massage ▸ Ultrasonic stimulation[l] ▸ Acupuncture or acupressure • Pharmacologic ▸ Topical ointments (ketamine) and patches (ie, lidocaine, capsaicin) ▸ NSAIDs ▸ Anticonvulsant drugs ▸ SNRIs ▸ Acetaminophen ▸ COX-2 inhibitors • For muscle cramps or spasms, check electrolytes, calcium and magnesium levels, and hydration status • Consider referral to pain management services, interventional specialist, physical therapy, physical medicine and rehabilitation, and/or palliative care for services such as trigger point injections

[l] Ultrasonic stimulation is a type of heat treatment that can penetrate directly to the bone and should be used with caution. It is not recommended for patients with multiple myeloma or bone metastases.

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CANCER PAIN SYNDROME	TREATMENT
GI/urinary/pelvic pain →	• For GI pain (abdominal pain/cramping): ▸ Adequate hydration ▸ Consider referral to gastroenterologist ▸ Bowel regimen • For chronic pelvic pain[o]: ▸ Consider referral to specialist in pelvic floor pain such as urologist, gynecologist, or physical medicine and rehabilitation ▸ Consider physical therapy for pelvic floor exercises ▸ Adequate hydration ▸ Bowel regimen ▸ Dorsal column stimulation for chronic cystitis and chronic pelvic pain • For dyspareunia: (SSH-2) ▸ Consider referral to gynecologist or sexual health specialist • For refractory GI/urinary/pelvic pain: ▸ Consider referral to pain management services, interventional specialist, physical therapy, physical medicine and rehabilitation, and/or palliative care

[o] Multidisciplinary treatment for chronic pelvic pain is preferred if available.

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CANCER PAIN SYNDROME	TREATMENT
Post-radiation pain • Pain may be acute or appear months or years after radiation • Radiation may lead to scarring, adhesions, or fibrosis ▸ Differentiate fibrosis from recurrent tumor • Radiation to a localized area of the body (ie, head and neck, breast) may cause a chronic pain syndrome in that area	→ • Treat according to specific cancer pain syndrome guidelines, if appropriate (See SPAIN-3 for list of cancer pain syndromes) • Physical therapy • Pain medication (appropriate to the etiology) • Surgical lysis of adhesions may be indicated in extreme circumstances • Consider referral to pain management services, interventional specialist, physical therapy, physical medicine and rehabilitation, orthopedic services, and/or palliative care for post-radiation pain including after stereotactic body RT (SBRT)

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PRINCIPLES OF MENOPAUSE SYMPTOM MANAGEMENT IN FEMALE SURVIVORS[a]

Menopause

- Many survivors may experience symptoms whether or not they have ovarian function.
- In survivors with prior chemotherapy or pelvic radiation exposure or survivors on tamoxifen, serial estradiol levels may be useful to confirm current menopausal status.
- In non-cancer populations, primary ovarian insufficiency or early menopause may be associated with specific menopause-related health risks (see below). There are limited data in cancer survivors.
- Peri- or premenopausal survivors
  - For survivors who have become amenorrheic and later develop bleeding, serial estradiol levels can be useful to determine return of ovarian function. Other markers including follicle-stimulating hormone (FSH), anti-Müllerian hormone (AMH), and inhibin may provide additional information on ovarian status in cancer survivors with prior chemotherapy or those on tamoxifen, but alone are not reliable to ensure menopausal status.
  - Survivors who have become amenorrheic and are sexually active should be counseled on the need for contraception to prevent unintended pregnancy if they do not meet the definition of menopause and if their sexual activity could result in pregnancy.
  - Menopause is defined as no menses for one year in the absence of prior chemotherapy or tamoxifen use, or no menses after surgical removal of all ovarian tissue.

Menopausal Signs and Symptoms

- Vasomotor symptoms (ie, hot flashes/night sweats)
- Vaginal dryness
- Urogenital complaints
- Sexual dysfunction
- Sleep disturbance
- Mood disturbance and depression
- Cognitive dysfunction
- Arthralgias/myalgias
- Fatigue

Menopause-Related Health Risks

- Osteoporosis/bone fractures
- Cardiovascular disease
- Cognitive change

Treatment Options for Vasomotor Symptoms (SHRS-4)

- Non-hormonal options
  - Prescription alternatives (SHRS-A)
  - OTC options
  - Integrative therapies
  - Lifestyle modifications (HL-1)
- Hormonal therapies (relatively contraindicated in survivors of hormonally mediated cancers; use with caution in those with increased genetic cancer risk) (SHRS-B)
  - Combination estrogen and progestins (for survivors with an intact uterus) or estrogen alone (for survivors without a uterus)
  - Survivors often use herbal supplements for vasomotor symptom management. However, some supplements may interfere with hormonal cancer treatments, and routine use of supplements is not recommended (SSUP-1). Providers should encourage survivors to discuss such therapies prior to use.

[a] Sexual function and management of hormone-related symptoms are important aspects of quality of life for all cancer survivors. The recommendations here are intended for cisgender survivors based on the availability of data in this population, but should be followed for transgender and intersex survivors as applicable, with the involvement of the appropriate health care specialists.

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PRINCIPLES OF MANAGEMENT OF HORMONAL SYMPTOMS IN MALE SURVIVORS[a]

- **Survivors who have received RT, chemotherapy, or surgery for non-prostate malignancies may have hypogonadism and should be evaluated for biochemical evidence of hypogonadism (ie, testosterone free and total, LH, prolactin) and treated with testosterone for hormone-related symptoms.**
- **Survivors of prostate cancer who have no evidence of recurrent disease may have symptoms of hypogonadism or have prior history of hypogonadism. These patients should be evaluated for biochemical evidence of hypogonadism. When to initiate treatment for low testosterone in prostate cancer survivors or resume treatments for those who had pre-existing hypogonadism is controversial and should be coordinated with the patient's PCP (ie, surgeon, oncologist, radiation oncologist).**
- **Androgen deprivation therapy (ADT) is the main therapeutic approach to metastatic prostate cancer, and may be used as adjuvant or neoadjuvant therapy in the treatment of prostate cancer.**
- **Survivors who are receiving ADT may experience hormone-related symptoms and sexual dysfunction. These patients should not receive androgens (eg, testosterone).**
- **ADT-related symptoms and health risks:**
  - **Acute kidney injury**
  - **Anemia**
  - **Arthralgias/myalgias**
  - **CVD[b]**
    - ◊ **Prolongation of QT/QTc interval**
  - **Cognitive dysfunction**
  - **Decreased muscle (sarcopenia) and increased body fat**
  - **Decreased penile size**
  - **Mood disturbance and depression**
  - **Diabetes mellitus (new onset)**
    - ◊ **Reduced insulin sensitivity**
  - **Fatigue**
  - **Gynecomastia**
  - **Osteoporosis/bone fractures**
  - **Sexual dysfunction[c]**
  - **Sleep disturbance**
  - **Testicle atrophy**
  - **Thinning body hair[d]**
  - **Vasomotor symptoms (ie, hot flashes/night sweats)[e]**
  - **Venous thromboembolic disease**

[a] Sexual function and management of hormone-related symptoms are important aspects of quality of life for all cancer survivors. The recommendations here are intended for cisgender survivors based on the availability of data in this population, but should be followed for transgender and intersex survivors as applicable, with the involvement of the appropriate health care specialists.
[b] ADT may increase cardiovascular morbidity and mortality, notably in the first 6 months of therapy and in individuals with two or more prior cardiovascular events. An increase in serum LDL cholesterol, HDL cholesterol, and triglycerides may also be seen.
[c] ADT-related sexual dysfunction includes loss of libido, loss of nocturnal and morning erections, and varying degrees of erectile dysfunction.
[d] Although facial and body hair decrease, some bald individuals may have some regrowth of scalp hair.
[e] Hot flashes may be associated with nausea and sweating and may occur during sleep.

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PRINCIPLES OF MANAGEMENT OF HORMONAL SYMPTOMS IN MALE SURVIVORS[a]

Treatment Options for Vasomotor Symptoms (SHRS-6)

- **Non-hormonal options**
  - **Prescription alternatives (SHRS-A)**
  - **OTC options**
  - **Integrative therapies**
  - **Lifestyle modifications (HL-1)**
- **Hormonal therapies (relatively contraindicated in survivors of hormonally mediated cancers; use with caution in those with increased genetic cancer risk)**
  - **Androgens (eg, testosterone)**
    - ◊ **Contraindicated in individuals with carcinoma of the breast or known or suspected prostate cancer**
  - **Medroxyprogesterone acetate (a progestin)**
  - **Cyproterone acetate (an antiandrogen)**
  - **Estrogen (eg, diethylstilbestrol)**
  - **Survivors often use herbal supplements for vasomotor symptom management. However, some supplements may interfere with hormonal cancer treatments, and routine use of supplements is not recommended (SSUP-1). Providers should encourage survivors to discuss such therapies prior to use.**

[a] Sexual function and management of hormone-related symptoms are important aspects of quality of life for all cancer survivors. The recommendations here are intended for cisgender survivors based on the availability of data in this population, but should be followed for transgender and intersex survivors as applicable, with the involvement of the appropriate health care specialists.

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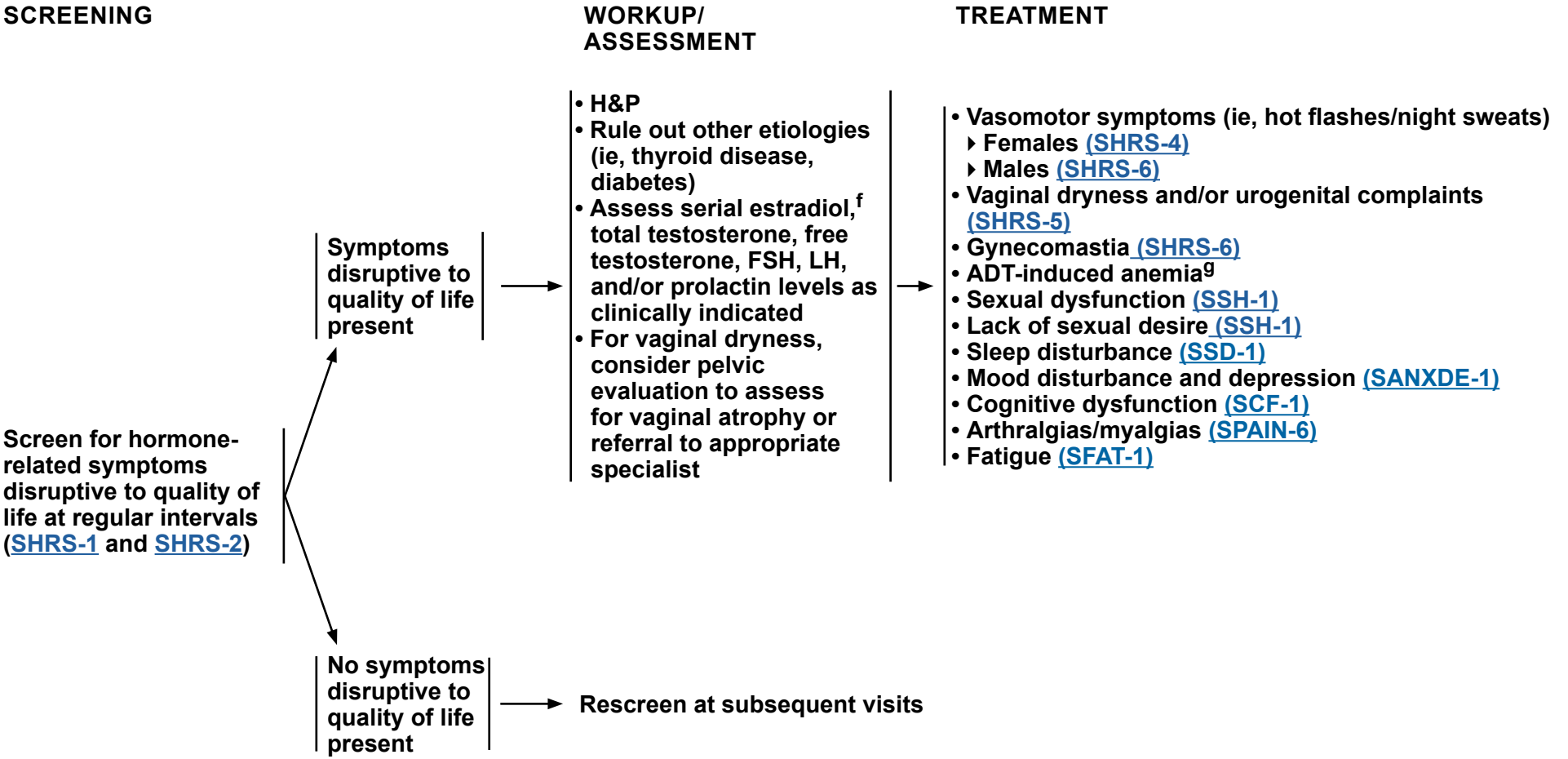

[f] For peri- or premenopausal survivors who have become amenorrheic and later develop bleeding, serial estradiol levels can be useful to determine return of ovarian function. Other markers including FSH, AMH, and inhibin may provide additional information on ovarian status in cancer survivors with prior chemotherapy or those on tamoxifen, but alone are not reliable to ensure menopausal status.

[g] ADT-associated anemia is generally responsive to blood transfusions and erythropoietin and should be treated as per the NCCN Guidelines for Hematopoietic Growth Factors.

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MENOPAUSE SYMPTOM	TREATMENT
Vasomotor symptoms (ie, hot flashes/night sweats) disruptive to quality of life in females[a]	**• Menopausal hormone therapy (MHT) or other hormonal therapies in appropriate candidates[h,i] with referral to appropriate specialist for MHT dosing and management** **• Non-hormonal pharmacologic treatments[j]** **▸ Categories include antidepressants,[k] anti-convulsants, neuropathic pain relievers, certain anti-hypertensives, and certain antimuscarinic anticholinergic agents** **• Non-pharmacologic treatments[l]** **▸ Weight loss if survivor has obesity or overweight (SNWM-1)** **▸ Acupuncture** **▸ Exercise/physical activity (SPA-1)** **▸ Lifestyle modifications[m] (HL-1)** **▸ Integrative therapies including CBT, yoga, and hypnosis** **• If no response after 2 or 3 lines of therapy, consider referral to specialists as appropriate**

[a] Sexual function and management of hormone-related symptoms are important aspects of quality of life for all cancer survivors. The recommendations here are intended for cisgender survivors based on the availability of data in this population, but should be followed for transgender and intersex survivors as applicable, with the involvement of the appropriate health care specialists.

[h] Principles of Menopausal Hormone Therapy (MHT) Use In Survivors (Females) (SHRS-B).

[i] MHT is generally contraindicated in survivors of hormonally mediated cancers. Custom-compounded bioidentical hormone therapy is not recommended. There is a lack of data supporting claims that custom-compounded bioidentical hormones are a safer and more effective alternative to standard hormone therapies. In fact, they may be harmful.

[j] Non-Hormonal Pharmacologic Treatments and Dosing (SHRS-A).

[k] Lower doses of antidepressants are often effective if the intent is to treat hot flashes (SHRS-A).

[l] Data are limited on the effectiveness and safety of phytoestrogens, botanicals, and dietary supplements in survivors of some cancers. The panel consensus is that the efficacy and safety data for these treatments are too limited to make a recommendation for use (Discussion).

[m] Drinking alcohol may cause hot flashes. Individual responses to alcohol may vary. If alcohol is a trigger, consider limiting intake.

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MENOPAUSE SYMPTOM	TREATMENT
Vaginal dryness	• Non-hormonal treatments[n] ▸ Vaginal moisturizers, vaginal gels, hyaluronic acid (category 2B), oils (category 2B) • Lubricants for sexual activity[o] • Local estrogen treatment[p] (ie, rings, suppositories, creams) (category 2B) ▸ Limited data in breast cancer survivors suggest minimal systemic absorption with rings and suppositories. Therefore, if estrogen-based treatment is warranted, rings and suppositories are preferred over creams for survivors of hormonally sensitive tumors. • Other topical hormones[p] (ie, testosterone,[q] dehydroepiandrosterone [DHEA][r]) • Consider referral to appropriate specialist for management • For vaginal pain or discomfort, see SSH-2
Urogenital complaints (females)[a]	• Local estrogen treatment[p] • Referral to appropriate specialist for management

[a] Sexual function and management of hormone-related symptoms are important aspects of quality of life for all cancer survivors. The recommendations here are intended for cisgender survivors based on the availability of data in this population, but should be followed for transgender and intersex survivors as applicable, with the involvement of the appropriate health care specialists.
[n] Recommend as first-line therapy if vaginal dryness is not too severe.
[o] Survivors should be cautioned that some lubricants may be irritating to the area of application.
[p] Vaginal estrogen and vaginal testosterone preparations can be used in managing vaginal atrophy, but safety has not been established for use in patients with or survivors of estrogen-dependent cancers.
[q] Although compounded testosterone vaginal creams are often used, there is a lack of data showing efficacy or safety in cancer survivors.
[r] Vaginal DHEA should be used with caution in survivors with a history of hormonally mediated cancers because safety in this population is unknown.

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ADT-RELATED SYMPTOMS	TREATMENT
Vasomotor symptoms (ie, hot flashes/night sweats) disruptive to quality of life in males[a]	• **Modification to ADT (NCCN Guidelines for Prostate Cancer)** • **Pharmacologic treatments** ▸ **Hormonal therapy in appropriate candidates[s] with referral to appropriate specialist for dosing and management** ◊ **Medroxyprogesterone** ◊ **Cyproterone acetate** ◊ **Estrogen (eg, diethylstilbestrol)** ▸ **Non-hormonal therapies[t]** ◊ **Venlafaxine** ◊ **Gabapentin** • **Non-pharmacologic treatments[u]** ▸ **Acupuncture** ▸ **Exercise/physical activity (SPA-1)** ▸ **Lifestyle modifications[m] (HL-1)** ▸ **CBT** ▸ **Weight loss if survivor has obesity or overweight (SNWM-1)** • **If no response after 2 or 3 lines of therapy, consider referral to specialists as appropriate**
Gynecomastia	• **Prophylactic radiation (must be delivered prior to development of breast tissues)** • **Tamoxifen** • **Reduction mammoplasty**

[a] Sexual function and management of hormone-related symptoms are important aspects of quality of life for all cancer survivors. The recommendations here are intended for cisgender survivors based on the availability of data in this population, but should be followed for transgender and intersex survivors as applicable, with the involvement of the appropriate health care specialists.

[m] Drinking alcohol may cause hot flashes. Individual responses to alcohol may vary. If alcohol is a trigger, consider limiting intake.

[s] Testosterone is contraindicated in individuals with carcinoma of the breast or known or suspected prostate cancer.

[t] Non-Hormonal Pharmacologic Treatments and Dosing for Vasomotor Symptoms (SHRS-A).

[u] Data are limited on the effectiveness and safety of phytoestrogens, botanicals, vitamin E, and dietary supplements in survivors of some cancers. The panel consensus is that the efficacy and safety data for these treatments are too limited to make a recommendation for use (Discussion).

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NON-HORMONAL PHARMACOLOGIC TREATMENTS AND DOSING FOR VASOMOTOR SYMPTOMS[a]

Class	Drug	Commonly Used Daily Dose for Management of Vasomotor Symptoms	Comments (For maximum benefit, may increase to higher doses after a week as tolerated)
Antidepressants[b]	Venlafaxine[c] (SNRI) (preferred)	75 mg	Start at lowest dose possible (25 mg or 37.5 mg) and increase as tolerated
	Desvenlafaxine (SNRI)	100 mg	Start at lowest dose possible (25 mg or 50 mg) and increase as tolerated
	Escitalopram (SSRI)	20 mg	• Start at lowest dose possible (10 mg) and increase as tolerated
	Citalopram (SSRI)	20 mg	• Start at lowest dose possible (10 mg) and increase as tolerated
	Sertraline (SSRI)[d]	50 mg	• Start at lowest dose possible (25 mg) and increase as tolerated • Limited data on effectiveness • Use with caution for survivors on tamoxifen
	Paroxetine (SSRI)[d]	Low-dose 7.5 mg or Standard paroxetine short acting up to 20 mg, controlled release up to 25 mg	• Low-dose (7.5 mg) paroxetine is an FDA-approved alternative to hormones for hot flashes • Use with caution for survivors on tamoxifen
	Fluoxetine (SSRI)[d]	20 mg	• Start at lowest dose possible (10 mg) and increase as tolerated • Limited data on effectiveness • Use with caution for survivors on tamoxifen
Anti-convulsants	Gabapentin[c] (preferred)	900 mg (typically 300 mg 3 times a day)	• Start at lowest dose possible (100 mg or 300 mg) and increase as tolerated • Consider starting at night time as this drug tends to cause sedation
	Pregabalin	150–300 mg	Start at lowest dose possible (25 mg) and increase as tolerated
Alpha-agonist hypertensive	Clonidine	0.1 mg (oral or transdermal)	Transdermal preparations may have fewer side effects
Antimuscarinic anticholinergic	Oxybutynin[1]	5–10 mg	Start with 2.5–5 mg BID, typically used for overactive bladder and may cause urinary retention along with other anticholinergic side effects
Selective neurokinin-3 (NK3) receptor antagonist	Fezolinetant	45 mg PO once daily with or without food	• An FDA-approved alternative to hormones for the treatment of moderate to severe vasomotor symptoms due to menopause. • Side effects: Risk for elevated LFT's. Perform LFTs prior to initiation. • In the original trials, patients with breast cancer were excluded.

Footnotes on SHRS-A 2 of 2
References on SHRS-A 2 of 2

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FOOTNOTES AND REFERENCES FOR SHRS-A 1 OF 2

Footnotes

[a] For long-term care or maintenance and/or if lack of response, consider referral to appropriate health care specialist. A gradual tapering of dose rather than an abrupt discontinuation of drug is recommended when discontinuing these treatments.

[b] Anticipated clinical response of SSRIs/SNRIs for hormone-related symptoms tends to be more rapid than the typical response for depression. For additional information, see First-Line Antidepressants for Depression or Anxiety in Adults (SANXDE-E).

[c] Venlafaxine and gabapentin have been studied for the treatment of hormone-related symptoms in males, but data are limited. The other therapies have been used but not tested in males.

[d] Evidence generally does not support the clinical significance of the inhibitory activity of SSRIs, SNRIs, or other antidepressants on tamoxifen's or other CYP2D6- or CYP3A4-metabolized agent's anticancer effects in terms of increased recurrence or mortality rates. However, pharmacokinetic/pharmacogenetic studies do indicate reduced availability of endoxifen in lower CYP2D6 metabolizers taking tamoxifen. SSRIs, and in particular paroxetine, block conversion of tamoxifen to active metabolites through CYP2D6.

References

[1] Leon-Ferre RA, et al. JNCI Cancer Spectr 2019;4:pkz088.

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National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2024
Survivorship: Hormone-Related Symptoms

NCCN Guidelines Index
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Discussion

PRINCIPLES OF MENOPAUSAL HORMONE THERAPY (MHT) USE IN FEMALE SURVIVORS[a]

- **MHT is the most effective therapy for management of vasomotor symptoms.**

- **General recommendations are to use the lowest dose possible to control symptoms.**
  - **Combination estrogen and progestins (for survivors with an intact uterus) or estrogen alone (for survivors without a uterus)**
    - ◊ **Formulations of hormones include oral, transdermal, vaginal ring, and intrauterine device.**
  - **The tissue-selective estrogen complex (TSEC) conjugated estrogens/bazedoxifene is FDA-approved for treating menopausal symptoms in healthy post-menopausal survivors.**
    - ◊ **These drugs are contraindicated in survivors of hormonally dependent cancers.**

- **If MHT is used, refer to appropriate specialist for MHT dosing and management.**

- **For young cancer survivors experiencing menopause at an early age, consider oral contraceptives or MHT for symptom relief and potential cardiac and bone benefits as long as not contraindicated.**

- **Relative contraindications for MHT in cancer survivors mirror those for the general population and include:**
  - **History of hormonally mediated cancers (high-risk endometrial and most breast)**
  - **History of abnormal vaginal bleeding**
  - **Active or recent history of thromboembolic event**
  - **Pregnancy**
  - **Active liver disease**

- **Caution in:**
  - **Survivors with coronary heart disease or hypertension**
  - **Survivors at increased genetic risk for cancers**
  - **Survivors who smoke, especially if >35 years**

- **Approach to treatment should be individualized based on risks and benefits.**

[a] Sexual function and management of hormone-related symptoms are important aspects of quality of life for all cancer survivors. The recommendations here are intended for cisgender survivors based on the availability of data in this population, but should be followed for transgender and intersex survivors as applicable, with the involvement of the appropriate health care specialists.

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DIAGNOSTIC EVALUATION[a]

- Ask about sexual health at regular intervals (See screening questions on SURV-A)
- Discuss treatment-associated infertility and refer to fertility specialist if indicated[b,c]

Screening questions do not indicate an issue → **Re-evaluate and discuss potential impact of treatment on sexual health at future visits**

Screening questions indicate an issue, but survivor does not want to discuss at oncology visit → **Refer to sexual health specialist, if survivor is interested[e] and Re-evaluate and discuss potential impact of treatment on sexual health at future visits**

- Screening questions indicate an issue and survivor wants to discuss further
- Consider use of a screening tool[d]

→

- H&P
- Review oncologic history (ie, diagnosis/stage, surgeries, systemic treatment, local RT, endocrine therapy)
- Discuss treatment-related impact on sexual health ideally before planned procedures and/or systemic therapy
- Assess for signs or symptoms of estrogen or androgen deprivation or refer to appropriate specialist
- Review medical history for conditions associated with sexual dysfunction (eg, depression [see SANXDE-1 and Distress Thermometer Screening Tool (DIS-A) in the NCCN Guidelines for Distress Management], diabetes, hypertension)
- Assess total morning testosterone as indicated
- Review medication list for drugs that impact sexual health (eg, SSRIs, beta blockers)

→

- See Treatment for Females (SSH-2) or for Males (SSH-3)
- Appropriate referrals for:
  - Psychotherapy
  - Sexual/couples counseling
  - Gynecologic care
  - Urology care
  - Sexual health specialist, if available[e]
  - Sex therapist, if available[f]

Footnotes on (SSH-1A)

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FOOTNOTES FOR SSH-1

[a] Sexual function and management of hormone-related symptoms are important aspects of quality of life for all cancer survivors. The recommendations here are intended for cisgender survivors based on the availability of data in this population, but should be followed for transgender and intersex survivors as applicable, with the involvement of the appropriate health care specialists.

[b] For information regarding fertility preservation for patients with cancer, see NCCN Guidelines for Adolescent and Young Adult (AYA) Oncology and Oktay K, et al. J Clin Oncol 2018;36:1994-2001; Burns KC, et al. Cancer 2018;124:1867-1876; and Hampe ME, Rhoton-Vlasak AS. J Assist Reprod Genet 2020;37:717-729.

[c] Principles of Fertility (SF-1)

[d] There are a number of validated tools to assess sexual concerns in cancer survivors. Common tools that may be used include:

- Brief Symptom Checklist [Brief Sexual Symptom Checklist for Women (SSH-A)]
- Sexual Health Inventory for Men (SHIM) (SSH-B)
- Arizona Sexual Experience Scale
- Female Sexual Functioning Index (FSFI), including a breast-specific adaptation of the FSFI (http://www.fsfiquestionnaire.com/)
- PROMIS Sexual Function and Satisfaction Measure (SexFS)

[e] Sexual health specialists may come from a range of backgrounds, including primary care, gynecology, urology, oncology, psychology, and/or rehabilitation medicine. Whenever possible, survivor should be referred to an appropriate local resource for further sexual health evaluation.

[f] Referral to a sex therapist certified by the American Association of Sexuality Educators, Counselors and Therapists (AASECT) (https://www.aasect.org/).

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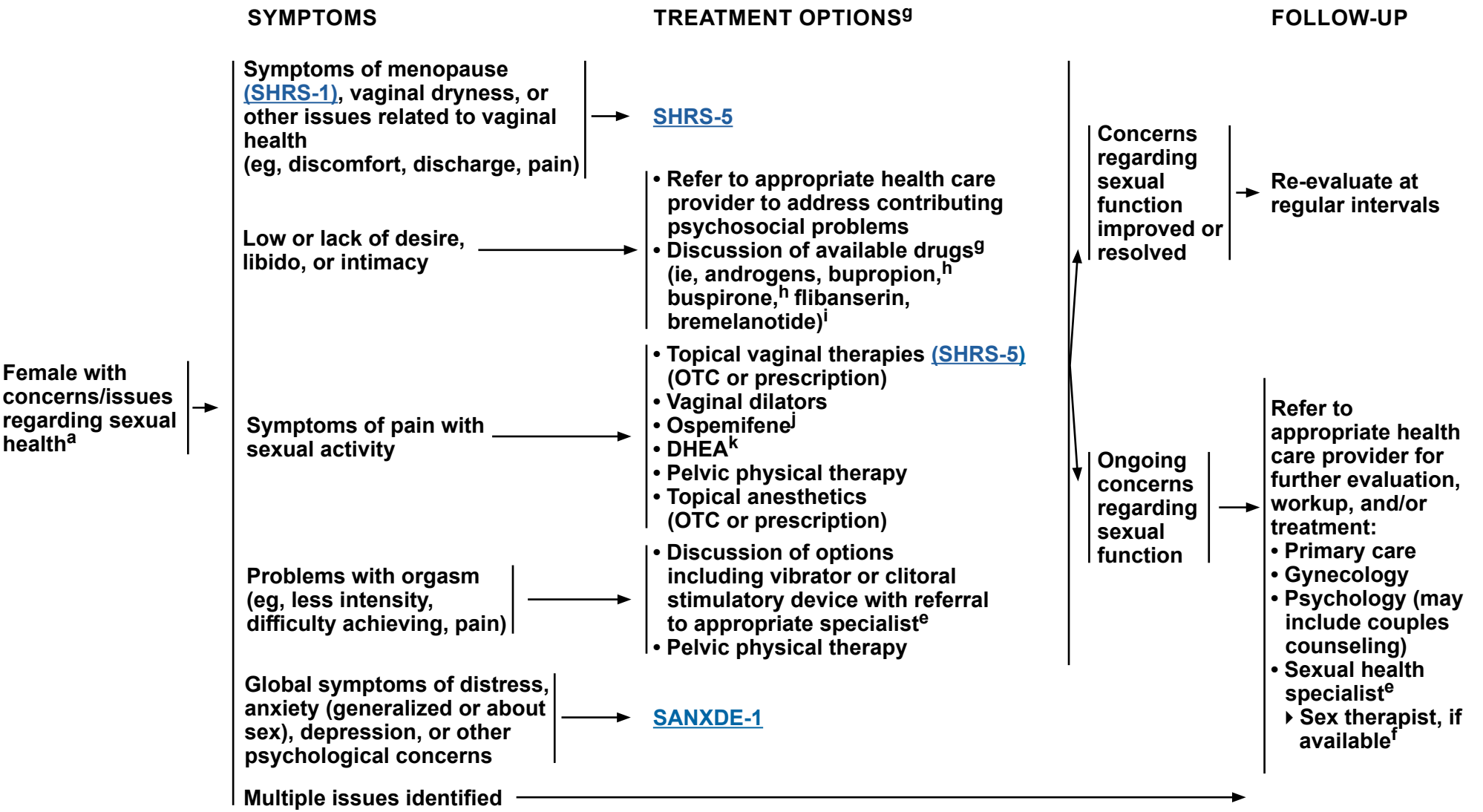

Footnotes on (SSH-2A)

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

FOOTNOTES FOR FEMALE WITH CONCERNS/ISSUES REGARDING SEXUAL FUNCTION

[a] Sexual function and management of hormone-related symptoms are important aspects of quality of life for all cancer survivors. The recommendations here are intended for cisgender survivors based on the availability of data in this population, but should be followed for transgender and intersex survivors as applicable, with the involvement of the appropriate health care specialists.

[e] Sexual health specialists may come from a range of backgrounds, including primary care, gynecology, urology, oncology, psychology, and/or rehabilitation medicine. Whenever possible, survivor should be referred to an appropriate local resource for further sexual health evaluation.

[f] Referral to a sex therapist certified by the AASECT (https://www.aasect.org).

[g] Discuss risk/benefits of prescription medications if not contraindicated for cancer type or refer to appropriate health care provider (eg, sexual health specialist) for prescription and/or treatment as necessary.

[h] Bupropion and buspirone may be considered as off-label treatments for hypoactive sexual desire disorder, despite limited safety and efficacy data.

[i] There is a lack of data showing a benefit of sildenafil in female sexual arousal or of flibanserin and androgens in cancer survivors. In addition, there is a lack of safety data for the use of androgen-based therapy in survivors of hormonally mediated cancers.

[j] Currently ospemifene is contraindicated in survivors with a history of estrogen-dependent cancers.

[k] DHEA should be used with caution in survivors with a history of estrogen-dependent cancers.

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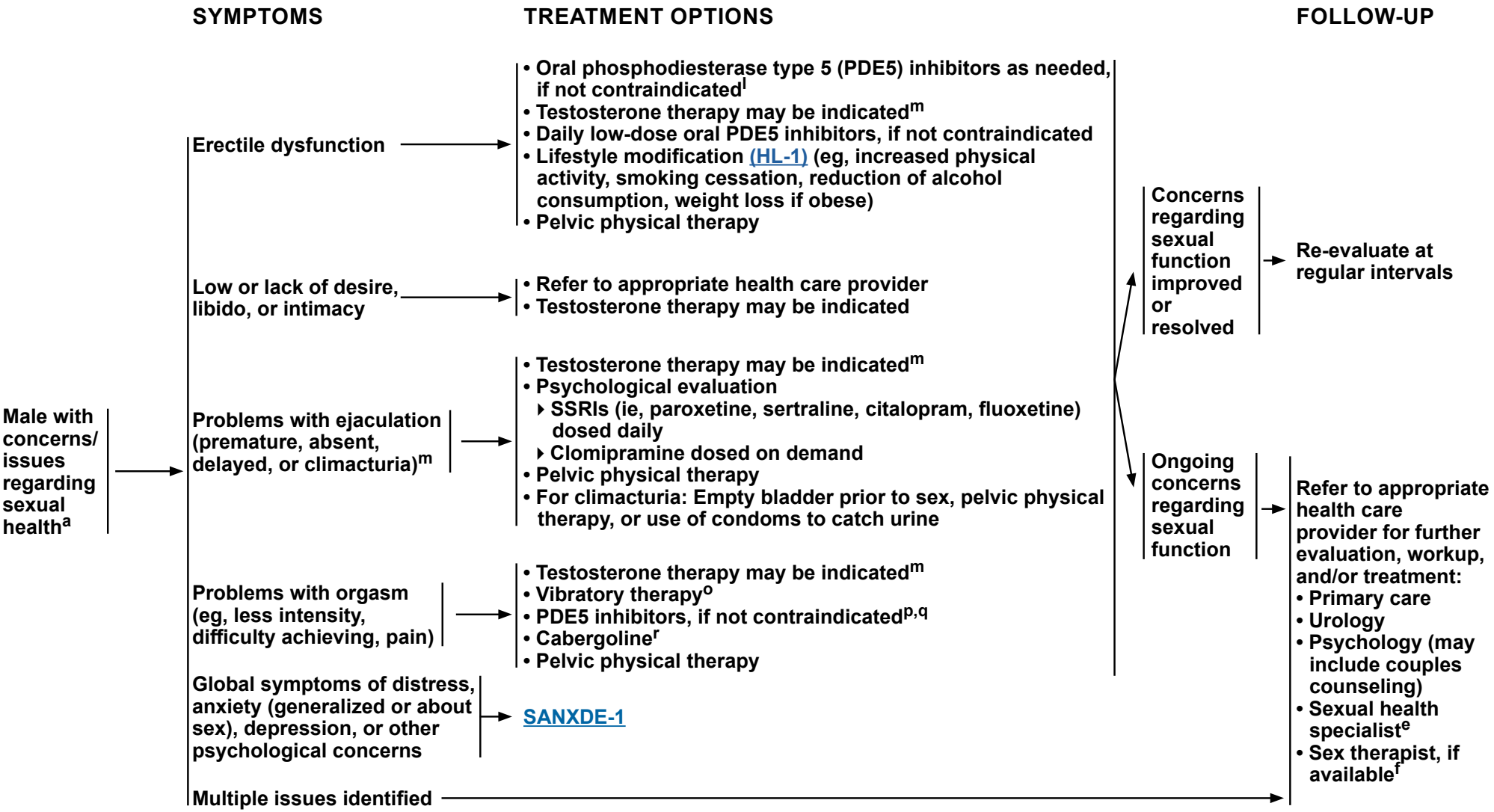

Footnotes on (SSH-3A)

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

FOOTNOTES FOR SSH-3

[a] Sexual function and management of hormone-related symptoms are important aspects of quality of life for all cancer survivors. The recommendations here are intended for cisgender survivors based on the availability of data in this population, but should be followed for transgender and intersex survivors as applicable, with the involvement of the appropriate health care specialists.

[e] Sexual health specialists may come from a range of backgrounds, including primary care, gynecology, urology, oncology, psychology, and/or rehabilitation medicine. Whenever possible, survivor should be referred to an appropriate local resource for further sexual health evaluation.

[f] Referral to a sex therapist certified by the AASECT (https://www.aasect.org/).

[l] Dosing should be titrated to optimal effect.

[m] If total morning testosterone <300 ng/dL (repeat second morning total testosterone and free testosterone, LH, and prolactin), then testosterone therapy may be indicated. Testosterone therapy should only be used if not contraindicated by primary oncologic diagnosis (eg, prostate cancer on active surveillance, prostate cancer under therapy with androgen deprivation). Exogenous testosterone therapy should not be prescribed to those who are currently trying to conceive. The long-term impact of exogenous testosterone on spermatogenesis should be discussed with patients who are interested in future fertility.

[n] Clavell-Hernández J, et al. Sex Med Rev 2018;6:124-134.

[o] Nelson CJ, et al. Urology 2007;69:552-555.

[p] Pavlovich CP, et al. BJU Int 2013;112:844-851.

[q] Montorsi F, et al. J Urol 2004;172:1036-1041. Erratum in: J Urol 2005;173:664.

[r] Hollander AB, et al. Sex Med 2016;4:e28-33.

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BRIEF SEXUAL SYMPTOM CHECKLIST FOR WOMEN[a,b]

Please answer the following questions about your overall sexual function:

1. Are you satisfied with your sexual function?

__ Yes __No
If no, please continue.

2. How long have you been dissatisfied with your sexual function?

3a. The problem(s) with your sexual function is:
(mark one or more)

__1 Problem with little or no interest in sex
__2 Problem with decreased genital sensation (feeling)
__3 Problem with decreased vaginal lubrication (dryness)
__4 Problem reaching orgasm
__5 Problem with pain during sex
__6 Other:

3b. Which problem is most bothersome? (circle)
1 2 3 4 5 6

4. Would you like to talk about it with your doctor?
__Yes __No

[a] Reprinted with permission from Hatzichristou D, Rosen RC, Derogatis LR, et al. Recommendations for the clinical evaluation of men and women with sexual dysfunction. J Sex Med 2010;7:337-348.

[b] Sexual health and related concerns can be difficult for survivors to discuss with their providers. Examples of sexual health screeners have been provided to help facilitate a discussion regarding a survivor's symptoms and/or sexual health history.

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SEXUAL HEALTH INVENTORY FOR MEN (SHIM)[a,b]

Sexual health is an important part of an individual's overall physical and emotional well-being. Erectile dysfunction, also known as impotence, is one type of very common medical condition affecting sexual health. Fortunately, there are many different treatment options for erectile dysfunction. This questionnaire is designed to help you and your doctor identify if you may be experiencing erectile dysfunction. If you are, you may choose to discuss treatment options with your doctor.

Each question has several possible responses. Circle the number of the response that best describes your own situation.

Please be sure that you select one and only one response for each question.

OVER THE PAST 6 MONTHS:

1. How do you rate your confidence you could get and keep an erection?		**Very Low**	**Low**	**Moderate**	**High**	**Very High**
		1	**2**	**3**	**4**	**5**
2. When you had erections with sexual stimulation, how often were your erections hard enough for penetration (entering your partner)?	**No Sexual Activity**	**Almost Never or Never**	**A Few Times (Much Less Than Half The Time)**	**Sometimes (About Half the Time)**	**Most Times (Much More Than Half The Time)**	**Almost Always or Always**
	0	**1**	**2**	**3**	**4**	**5**
3. During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?	**Did Not Attempt Intercourse**	**Almost Never or Never**	**A Few Times (Much Less Than Half The Time)**	**Sometimes (About Half the Time)**	**Most Times (Much More Than Half The Time)**	**Almost Always or Always**
	0	**1**	**2**	**3**	**4**	**5**
4. During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?	**Did Not Attempt Intercourse**	**Extremely Difficult**	**Very Difficult**	**Difficult**	**Slightly Difficult**	**Not Difficult**
	0	**1**	**2**	**3**	**4**	**5**
5. When you attempted sexual intercourse, how often was it satisfactory for you?	**Did Not Attempt Intercourse**	**Almost Never or Never**	**A Few Times (Much Less Than Half The Time)**	**Sometimes (About Half the Time)**	**Most Times (Much More Than Half The Time)**	**Almost Always or Always**
	0	**1**	**2**	**3**	**4**	**5**

PROVIDER KEY: Add the numbers corresponding to questions 1–5.

TOTAL: _____

The SHIM further classifies ED severity with the following breakpoints: 1–7: Severe ED 8–11: Moderate ED 12–16: Mild to Moderate ED 17–21: Mild ED

[a] Reproduced and modified with permission from Cappelleri JC, Rosen RC. The Sexual Health Inventory for Men (SHIM): a 5-year review of research and clinical experience. Int J Impot Res 2005;17:307-319.

[b] Sexual health and related concerns can be difficult for survivors to discuss with their providers. Examples of sexual health screeners have been provided to help facilitate a discussion regarding a survivor's symptoms and/or sexual health history.

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PRINCIPLES OF FERTILITY[1]

- **The risks of treatment-induced infertility should be discussed with all reproductive-aged survivors at the time of cancer diagnosis.**
- **Survivor-centered care is important. The survivor's goals regarding fertility and discussions regarding the risks of treatment-induced infertility should be discussed and documented in the medical chart.**
- **Prior to initiation of cancer treatments, available options for fertility preservation should be discussed and/or referrals made to the appropriate specialists for those patients wishing to preserve fertility.**
- **Fertility preservation procedures prior to cancer treatment are the most effective way to preserve fertility in cancer survivors.**
  - **Fertility preservation procedures include in vitro fertilization (IVF) with oocyte or embryo cryopreservation, ovarian tissue preservation, and sperm cryopreservation.**
  - **Data show that ovarian tissue cryopreservation is currently only about 40% successful. There is a much greater success with traditional IVF with oocyte or embryo cryopreservation.**
  - **In addition to fertility preservation procedures, gonadotropin-releasing hormone (GnRH) agonists should be offered during chemotherapy to breast cancer survivors in order to preserve ovarian function.**
- **If possible, reproductive organs should be shielded during RT.**
- **If survivors have a change in their cancer treatment, the impact of treatment on potential infertility should be discussed again and/or referrals made to the appropriate specialists.**
- **Once cancer treatment is complete, clinicians and survivors should not assume that the survivor is infertile, and survivors interested in fertility should be assessed by a fertility specialist.**
- **For survivors of breast cancer, pregnancy is considered safe and the hormonal environment associated with pregnancy is not thought to increase the risk of breast cancer recurrence. Prior breast cancer treatment does not increase the future risk of congenital malformations. General recommendations have traditionally been to wait until the survivor is disease free for 2 years before attempting to conceive, whether naturally or via assisted reproductive technologies, because of the higher risk of recurrence within that time.**
- **For additional information regarding fertility preservation for patients with cancer, see:**
  - **NCCN Guidelines for Adolescent and Young Adult (AYA) Oncology**
  - **NCCN Guidelines for Breast Cancer**

[1] Oktay K, Harvey BE, Partridge AH, et al. Fertility preservation in patients with cancer: ASCO Clinical Practice Guideline Update. J Clin Oncol 2018;36:1994-2001.

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SCREENING

Screening/assessment questions[a] to be asked at regular intervals, especially when there is a change in clinical status or treatment:

- **Are you having problems falling asleep, staying asleep, waking up too early, or with poor sleep quality?**
- **Are you experiencing excessive sleepiness (sleepiness or falling asleep in inappropriate situations or sleeping more during a 24-hour period than in the past)?**
- **Have you been told that you snore frequently or stop breathing during sleep?**

No concerns for sleep disorder/disturbance → **Re-evaluate at subsequent visits/post therapy**

Concerns for sleep disorder/disturbance[b] →

H&P

- **Assessment of treatable or modifiable contributing factors:**
  - **Comorbidities**
    - ◊ **Alcohol and/or substance use disorder**
    - ◊ **Obesity**
    - ◊ **Cardiac dysfunction**
    - ◊ **Respiratory disorders**
    - ◊ **Endocrine dysfunction (eg, hypothyroidism)**
    - ◊ **Anemia**
      - – **Iron and ferritin levels and when indicated transferrin saturation %**
    - ◊ **Emotional distress: screen for anxiety and depression (See SANXDE-1 and NCCN Guidelines for Distress Management)**
    - ◊ **Neurologic disorders including chemotherapy-induced peripheral neuropathy**
    - ◊ **Psychiatric disorders**
  - **Medications[c]**
  - **Vasomotor symptoms (see SHRS-4 [females] and SHRS-6 [males])**
  - **Review sleep/wake timing and/or sleep log/diary**
  - **Review caffeine intake**
  - **Review history of cancer treatments**
  - **Pain (SPAIN-1)**
  - **Fatigue (SFAT-1)**
  - **Shift work**
  - **Current coping strategies (eg, relaxation techniques, meditation)**

Insomnia symptoms (difficulty falling asleep staying asleep, or waking up too early)[d]:
- **Duration ≥3 months**
- **Occurring at least 3 times per week**

→ **SSD-2**

Sleep disturbance and/or excessive sleepiness[d]
- **Hypersomnias**
- **Sleep disordered breathing (includes obstructive sleep apnea [most common] and central sleep apnea)[e]**
- **RLS[e,f]**

→ **SSD-3**

Footnotes on (SSD-1A)

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FOOTNOTES FOR SSD-1

[a] The following additional tools may be used for individual intensive screening to assess sleep quality: PSQI https://www.sleep.pitt.edu/instruments/#psqi; PROMIS SLEEP http://www.healthmeasures.net/index.php?option=com_instruments&view=measure&id=183&Itemid=992; and Epworth Sleepiness Scale, Johns MW. Sleep 1991;14:540-545.

[b] Patients may have more than one sleep disorder.

[c] Medication review: Re-evaluate the need for persistent use of sleep aids, pain medications, antiemetics, stimulants, antidepressants, anti-psychotics, sedative/hypnotics, opioids, OTC sleep aids, or antihistamines.

[d] In the differential diagnosis of insomnia or excessive sleepiness symptoms, consider parasomnias or circadian rhythm sleep wake disorders and referral to a sleep specialist.

[e] Note that sleep disordered breathing (eg, obstructive sleep apnea), RLS, circadian rhythm sleep wake disorders, and parasomnias may also present with symptoms of insomnia.

[f] RLS is also known as Willis-Ekbom disease.

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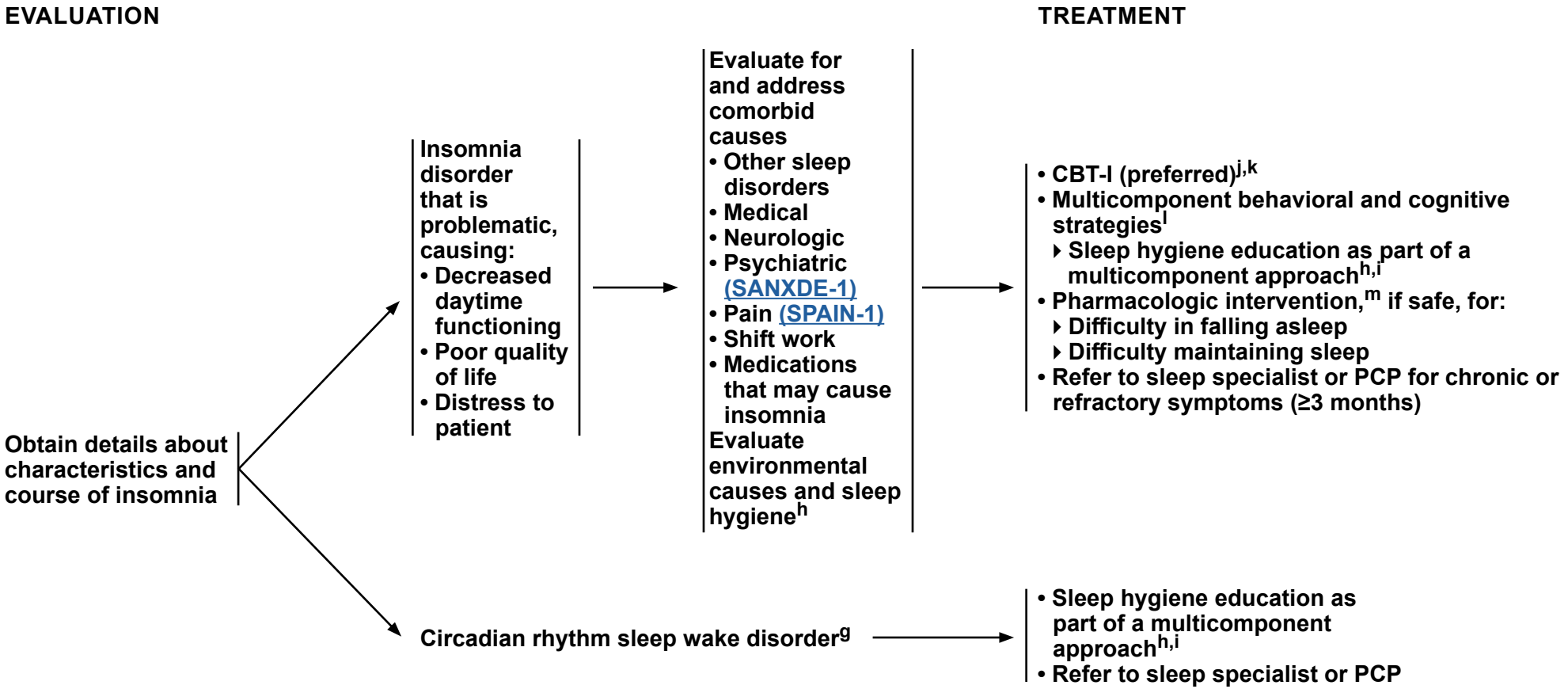

[g] Circadian rhythm sleep wake disorder: A chronic or recurrent pattern of sleep-wake rhythm disruption due primarily to an alteration of the circadian timing system or to a misalignment with the sleep-wake schedule required by an individual's physical environment or social/work schedules.
[h] General Sleep Hygiene Measures (SSD-A).
[i] Sleep hygiene alone has not been shown to be effective, but should be part of the initial treatment of all survivors with sleep disorders and as a prevention strategy for insomnia disorder. Sleep hygiene alone is not the recommended treatment for insomnia, but should be used in conjunction with other treatments such as CBT-I and/or pharmacotherapy. Use of general sleep hygiene measures should not delay other interventions or referral to a specialist, especially if quality of life is impacted or if sleep problems (eg, insomnia) are severe. (Edinger JD, et al. J Clin Sleep Med 2021;17:255-262).
[j] Cognitive Behavioral Therapy for Insomnia (SSD-B).
[k] CBT-I is preferred over pharmacologic interventions as first-line therapy.
[l] Strategies such as tai chi and mindfulness therapy may be beneficial.
[m] Principles for Choosing an FDA-Approved Hypnotic (SSD-C).

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National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2024
Survivorship: Sleep Disorders

NCCN Guidelines Index
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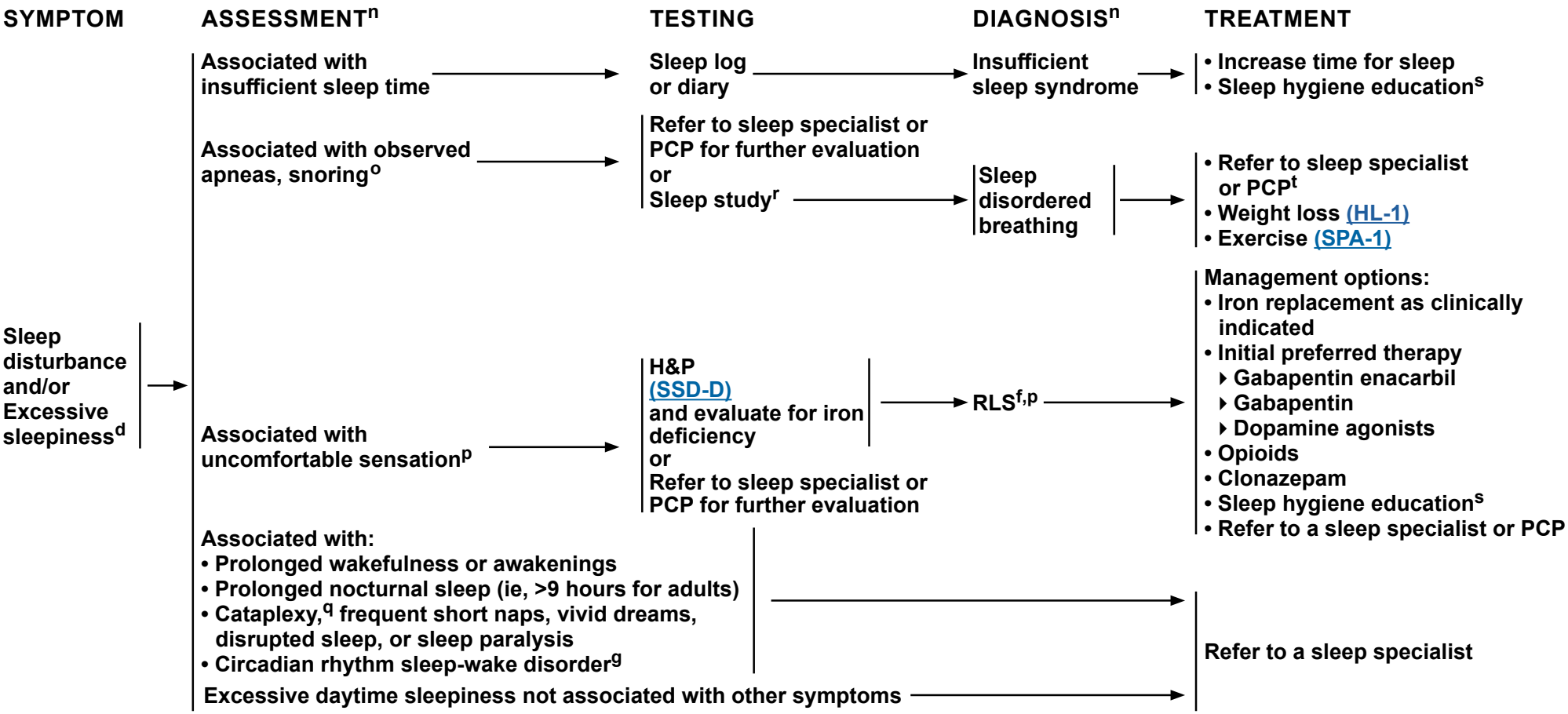

[d] In the differential diagnosis of insomnia or excessive sleepiness symptoms, consider parasomnias or circadian rhythm sleep wake disorders and referral to a sleep specialist.
[f] RLS is also known as Willis-Ekbom disease.
[g] Circadian rhythm sleep wake disorder: A chronic or recurrent pattern of sleep-wake rhythm disruption due primarily to an alteration of the circadian timing system or to a misalignment with the sleep-wake schedule required by an individual's physical environment or social/work schedules.
[n] For other less frequent syndromes, refer to a sleep specialist.
[o] The following tools may be used to help identify individuals at high risk for obstructive sleep apneas: STOP Questionnaire (Chung F, et al. Anesthesiology 2008;108:812-821) and Berlin Questionnaire (https://www.ncbi.nlm.nih.gov/books/NBK424168/bin/appb-fm1.pdf).
[p] Essential Diagnostic Criteria for Restless Legs Syndrome (SSD-D).
[q] Cataplexy: Sudden loss of muscle tone, typically triggered by strong emotions, such as laughter or anger. Cataplexy is the most specific diagnostic feature of narcolepsy.
[r] Sleep studies can be performed as an in-laboratory polysomnography or as home sleep study. However, survivors with certain medical disorders (ie, cardiac, respiratory, neurologic), or currently on opiates for cancer-related pain, may not be good candidates for home sleep studies.
[s] General Sleep Hygiene Measures (SSD-A).
[t] The most common medical treatment fo sleep disordered breathing is continuous positive airway pressure (CPAP).

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GENERAL SLEEP HYGIENE[a,1,2,3]

- **Maintain a regular bedtime and waketime every day.**
- **Engage in regular physical activity in the morning and/or afternoon (SPA-1). Avoid moderate to strenuous physical activity within 3 hours of bed time.**
- **Exposure to daytime bright light, particularly in the morning.**
- **Reduce exposure to bright light (ie, computer, phone screens, light sources close to the eye) within a few hours before bedtime and during the night.**
- **Avoid heavy meals and limit fluid intake within 3 hours of bedtime.**
- **Avoid alcohol and nicotine too close to bedtime.**
- **Limit caffeine consumption and avoid caffeine consumption at least 4 hours before bedtime.**
- **Enhance sleep environment (dark, quiet room; comfortable temperature).**
- **Avoid looking at the clock when awake during the night.**
- **If necessary, limit daytime sleep to 1 short nap per day in the afternoon (no longer than 30 min).**
- **Turn off electronics and light-emitting sources at bedtime.**

Other Sleep Interventions

- If survivor is not able to fall asleep within what feels like 20 minutes (survivor should not check the clock) or if they wake up in middle of night and can't fall back to sleep, consider using the following sleep strategy:
  - Get up, go to a different location, but stay in a darkened room and do non-stimulating activity like reading a relaxing non-stimulating book. Once survivor feels sleepy again they should try to go to bed. The goal is to help the body associate the bed with sleeping.
- Other sleep interventions include the use of:
  - Sleep apps, meditation apps, breathing exercises, and strategies to reduce worrying (ie, write a "to do" list or set aside "worry time" [eg, 10–15 mins] earlier in the day, not close to bedtime)

Footnote

[a] Sleep hygiene alone has not been shown to be effective, but should be part of the initial treatment of all survivors with sleep disorders and as a prevention strategy for insomnia disorder. Sleep hygiene alone is not the recommended treatment for insomnia, but should be used in conjunction with other treatments such as CBT-I and/or pharmacotherapy. Use of general sleep hygiene measures should not delay other interventions or referral to a specialist, especially if quality of life is impacted or if sleep problems (eg, insomnia) are severe (Edinger JD, et al. J Clin Sleep Med 2021;17:255-262).

References

[1] National Heart, Lung, and Blood Institute Working Group on Insomnia. Insomnia: Assessment and Management in Primary Care. 1998. NIH Publication. 98-4088.
[2] Kupfer DJ, Reynolds CF. Management of insomnia. N Engl J Med 1997;336:341-346.
[3] Lippmann S, Mazour I, Shahab H. Insomnia: therapeutic approach. South Med J 2001;94:866-873.

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COGNITIVE BEHAVIORAL THERAPY FOR INSOMNIA (CBT-I)[a,b,1]

Strategy	Goal
CBT-I[2] or internet-based cognitive behavioral therapy for insomnia	**Challenge survivor's maladaptive beliefs and misconceptions about sleep disturbances**
Stimulus control	**Associate the bed/bedroom as a place for sleep or sexual activity only**
Sleep restriction	**Improve sleep continuity by:** **• Limiting time spent in bed[c]** **• Maintaining a regular sleep schedule by keeping a standard bedtime and wake time every day**
Relaxation training	**• Reduce physiologic and cognitive arousal at bedtime** **• Techniques include progressive muscular relaxation, deep breathing, meditation, yoga, and biofeedback** **• Visualization**

Footnotes

[a] The American Academy of Sleep Medicine (AASM) includes a strong recommendation for multicomponent CBT-I and conditional recommendations for stimulus control, sleep restriction, and relaxation therapy as single-component therapy options for the treatment of insomnia. Edinger JD, Arnedt JT, Bertisch SM, et al. J Clin Sleep Med 2021;17:255-262.

[b] There are paid and/or free guided, semi-guided, and unguided CBT-I digital resources available. See Survivorship Resources for Health Care Professionals and Survivors (SURV-B).

[c] Match total amount of time spent in bed to the actual amount of time spent sleeping (no less than 5 hours).

References

[1] Data from Bootzin RR and Perlis ML. Nonpharmacologic treatments of insomnia. J Clin Psychiatry 1992;53(suppl):37-41.

[2] Johnson JA, Rash JA, Campbell TS, et al. A systematic review and meta-analysis of randomized controlled trials of cognitive behavior therapy for insomnia (CBT-I) in cancer survivors. Sleep Med Rev 2016;27:20-28.

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PRINCIPLES FOR CHOOSING AN FDA-APPROVED HYPNOTIC AS SECOND-LINE THERAPY[a-f]:

- **Does the patient have difficulty initiating or maintaining sleep?**
- **Does the patient have both sleep onset and sleep maintenance difficulty?**

AGENT	HELPS WITH SLEEP INITIATION	INCREASES TOTAL SLEEP TIME	INDICATED FOR SLEEP INITIATION AND MAINTENANCE
Zolpidem	+	+	–
Zolpidem CR	+	+	+
Zaleplon	+	–	–
Eszopiclone	+	+	+
Ramelteon	+	±	–
Temazepam	+	+	+
Doxepin (3–6 mg)	–	+	+
Suvorexant	+	+	+
Lemborexant	+	+	+
Daridorexant	+	+	+

[a] These agents should only be used after all other methods have been deemed unsuccessful. CBT-I is the preferred first-line treatment option (SSD-2).
[b] Data from the Physicians' Desk Reference ed 66). Montvale, NJ: PDR Network, LLC; 2012.
[c] Inform patients that taking hypnotic medications may cause complex sleep-related behaviors (eg, sleep driving, sleep eating).
[d] Other commonly used medications for insomnia include sedating medications such as antidepressants (eg, trazodone, mirtazapine), antihistamines, atypical anti-psychotics, other benzodiazepine receptor agonists, and nutritional/herbal supplements. They do not have an FDA-approved indication for the treatment of insomnia, and do not have enough data to be recommended for routine use. Trazodone is one of the most commonly used medications for insomnia, but due to paucity of evidence of its long-term efficacy and safety, it is not recommended for routine use (Kansagara D, et al. Ann Intern Med 2016;165:892; Sateia MJ, et al. J Clin Sleep Med 2017;13:307-349; Wilt TJ, et al. Ann Intern Med 2016;165:103-112).
[e] Most of these agents, with the exception of ramelteon, doxepin, suvorexant, and lemborexant are benzodiazepine receptor agonists and can be associated with dependence, misuse, and withdrawal. Assessment for the continued need of hypnotics is recommended every 1–3 months.
[f] Refer to package insert for specifics regarding potential for drug-drug interactions, side effects, risk of dependency, black box warnings, or other problems with these drugs.

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ESSENTIAL DIAGNOSTIC CRITERIA FOR RESTLESS LEGS SYNDROME[a]

- **An urge to move the legs usually accompanied by uncomfortable and unpleasant sensations in the legs, and sometimes the arms or other body parts.**
- **The urge to move or unpleasant sensations begin or worsen during periods of rest or inactivity such as lying or sitting.**
- **The urge to move or unpleasant sensations are partially or totally relieved by movement, such as walking or stretching.**
- **The symptoms are more pronounced in the evening or night or may only occur in the evening or night.**

RESTLESS LEGS SYNDROME

- **Iron deficiency is a secondary cause of RLS and can also exacerbate symptoms.**
- **Treatment with iron replacement in survivors with documented iron deficiency can improve symptoms.**
  - **Recommend taking iron replacement with vitamin C (eg, orange juice) to enhance the absorption of oral iron.**
  - **Goal ferritin level is 50–75 µg/L or until alleviation of symptoms.[b]**
  - **Consider referral to specialist for refractory symptoms** **(See NCCN Guidelines for Palliative Care)**
- **Consider modification of lifestyle factors and medications that can exacerbate RLS symptoms.[c]**

[a] Reproduced with permission from Allen RP, Picchietti D, Hening WA, et al. Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology. A report from the restless legs syndrome diagnosis and epidemiology workshop at the National Institutes of Health. Sleep Med 2003;4:101-119.
[b] Winkelman JW, Armstrong MJ, Allen RP, et al. Practice guideline summary: Treatment of restless legs syndrome in adults: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology 2016;87:2585-2593.
[c] Alcohol, nicotine, caffeine, centrally active antihistamines, SSRI, SNRI, and dopaminergic medications are associated with worsening of RLS symptoms.

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GENERAL PRINCIPLES OF WORKING AND RETURNING TO WORK AFTER A CANCER DIAGNOSIS

- **These recommendations related to working and returning to work apply to survivors who are post active treatment as well as persons living chronically with cancer. However, discussions about work are ideally best had before treatment begins so that treatment recommendations can take work needs into consideration if possible.**
- **Symptoms affecting work may wax and wane with a survivor's treatments or disease status, especially if they are living chronically with cancer or the consequences of cancer treatment. Some survivors might start and stop working more than once.**
- **Most existing literature focuses on unemployment and/or those who do not return to work. However, underemployment and/or work limitations due to cancer or side effects are also common.**
- **Employment helps to protect survivors from financial toxicity and, at least in the United States, is frequently tied to health insurance access. This can be a main reason survivors work even when/if they are not fully recovered.**
- **Employment is an important source of personal interaction, normalcy, and social support. The psychosocial effects/advantages derived from work may include a sense of purpose, emotional well-being, link to identity, improved quality of life, connection with others, and distraction.**
- **Some populations are at increased risk for difficulties related to work (based on factors such as gender, age, race, ethnicity, cancer type, cancer stage, rural residence, educational attainment, etc). The increased difficulties in these populations are more likely for survivors with physically or cognitively demanding jobs or jobs with limited flexibility in scheduling or tasks. Additionally, patients with cancer may experience discrimination as a result of diagnosis/illness, and this may be a consideration for some individuals in decisions surrounding employment.**
- **Survivors should be offered information to help them understand their likely ability to work, take into account their finances and personal/family needs, and discuss potential work accommodations with their employers.[1]**
- **Clinicians should regularly re-evaluate work-related concerns post active cancer treatment or for persons living chronically with cancer.**
  - **Periodically identify goals and barriers regarding work with survivor (SWORK-3).**
  - **A team approach may be needed. Consider early involvement of social work, primary care, physical therapy/occupational therapy, cancer rehabilitation, and/or career counseling services, if available.**
  - **Employment disability forms are not typically well-suited to cancer. However, clinicians should consider the survivor's needs for flexibility in tasks and hours, and other workplace accommodations as a starting point for filling out the necessary forms.**

[1] U.S. Department of Justice, Civil Rights Division; Americans with Disabilities Act (ADA). Guide to Disability Rights Laws. https://www.ada.gov/resources/disability-rights-guide/

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

EVALUATION/ASSESSMENT

- Discuss survivor's concerns, needs, goals, and desires related to work
- Assess abilities required for job (eg, cognitive tasks, long periods of standing, use of hands)
- Assess barriers
  - Assess practical concerns regarding employment (eg, transportation, caregiving responsibilities, health insurance coverage, financial toxicity)
  - Assess treatable contributing symptoms:
    - ◊ Fatigue (SFAT-1)
    - ◊ Pain/neuropathy (SPAIN-1)
    - ◊ Musculoskeletal/neurologic issues (eg, joint/extremity mobility, deconditioning/loss of muscle mass, sensory neuropathy)
    - ◊ Cognitive dysfunction (SCF-1)
    - ◊ Anxiety, depression, distress (SANXDE-1)
    - ◊ Vision/hearing changes
  - Assess comorbid conditions:
    - ◊ Organ dysfunction[a]
    - ◊ Hematologic dysfunction/Infection risk[b]
    - ◊ Alcohol/substance use

→

TREATMENT OF CONTRIBUTING FACTORS[c]

- Treat contributing symptoms
  - Fatigue (SFAT-1)
  - Pain/neuropathy (SPAIN-1)
  - Cognitive dysfunction (SCF-1)
  - Anxiety, depression, distress (See SANXDE-1 and NCCN Guidelines for Distress Management)
  - Musculoskeletal/neurologic issues
  - Vision/hearing
- Treat comorbidities

→ Additional Interventions for Survivors (SWORK-3)

[a] Organ dysfunction resulting from cancer or cancer treatment that may most impact work includes cardiac (SCARDIO-1), pulmonary, and GI.
[b] The majority of solid tumor survivors do not have an increased infection risk. However, infection risk should be assessed in post-transplant survivors.
[c] Treat contributing symptoms/comorbidities with appropriate pharmacologic interventions and/or referrals as needed.

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ADDITIONAL INTERVENTIONS FOR CANCER SURVIVORS

SURVIVOR/FAMILY EDUCATION AND COUNSELING

- Help survivor identify goals with regards to working and barriers to those goals
- Discuss coping strategies for the psychosocial impacts of cancer and cancer treatment
- Provide guidance about expected duration/ management of symptoms or comorbidities limiting employment and return to work
- Recommend that survivors find out about their employer's Human Resources policies
- Provide resources to understand options and communicate with employer (SURV-B 2 of 5)
  - Include community-based, national, and online career counseling resources

→

OTHER INTERVENTIONS

- Refer as appropriate:
  - Vocational/occupational rehabilitation specialist
  - Physical or occupational therapist
  - Psychologist
  - State vocational rehabilitative services
  - Neuropsychology evaluation
  - Social worker
  - Financial counselor
  - Patient navigator
- Pharmacologic intervention for underlying causal symptom(s) as indicated (SWORK-2)

→

Periodic re-evaluation (SWORK-2)

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ABBREVIATIONS

AASECT	American Association of Sexuality Educators, Counselors and Therapists
AASM	American Academy of Sleep Medicine
ACOG	American College of Obstetricians and Gynecologists
ACS	American Cancer Society
ACSM	American College of Sports Medicine
ADA	Americans with Disabilities Act
ADT	androgen deprivation therapy
ADL	activities of daily living
AI	aromatase inhibitor
AICR	American Institute for Cancer Research
AMH	anti-Müllerian hormone
AML	acute myeloid leukemia
APOS	American Psychosocial Oncology Society
APTA	American Physical Therapy Association
ASCO	American Society of Clinical Oncology
ASCVD	atherosclerotic cardiovascular disease
BMI	body mass index
BP	blood pressure
CAD	coronary artery disease
CAR	chimeric antigen receptor
CBC	complete blood count
CBT	cognitive behavioral therapy
CBT-I	cognitive behavioral therapy for insomnia
CDAP	continuous positive airway pressure
CDC	Centers for Disease Control and Prevention
CHF	congestive heart failure
CNS	central nervous system
COPD	chronic obstructive pulmonary disease
CSO	Certified Specialists in Oncology Nutrition
CVD	cardiovascular disease
DTap/ Td	diptheria, tetanus, and acellular pertussis
DHEA	dehydroepiandrosterone
DVT	deep vein thrombosis
ECG	electrocardiogram
ECHO	echocardiogram
ED	erectile dysfunction
FSFI	Female Sexual Functioning Index
FSH	follicle-stimulating hormone
GI	gastrointestinal
GnRH	gonadotropin releasing hormone
GVHD	graft-versus-host disease
H&P	history and physical
HBsAg	hepatitis B surface antigen
HCT	hematopoietic cell transplant
HepA	hepatitis A
HepB	hepatitis B
HD-IIV	High-dose inactivated influenza vaccine
Hib	haemophilus influenzae type b
HPV	human papillomavirus
IIV	inactivated influenza vaccine
IPV	inactivated polio vaccine
ISSWSH	International Society for the Study of Women's Sexual Health
IVIG	intravenous immunoglobulin
IVF	in vitro fertilization
LFT	liver function test
LGBT	lesbian, gay, bisexual, transgender, and queer
LH	luteinizing hormone
LLS	Leukemia and Lymphoma Society
LV	left ventricular
LVEF	left ventricular ejection fraction

ABBREVIATIONS

MCV4	quadrivalent meningocccal conjugate vaccine
MDD	major depressive disorder
MDS	myelodysplastic syndrome
MHT	menopausal hormone therapy
MMR	measles, mumps, rubella
MMSE	Mini-Mental State Examination
NCCS	National Coalition for Cancer Survivorship
NSAID	nonsteroidal anti-inflammatory drug
NK3	neurokinin-3
OCS	Office of Cancer Survivorship
OTC	over-the-counter
OUD	opioid use disorder
PCP	primary care physician
PCV	pneumococcal conjugate vaccine
PDE5	phosphodiesterase type 5
PDQ	Physician Data Query
PPSV	pneumococcal polysaccharide vaccine
PTSD	post-traumatic stress disorder
QTc	corrected QT interval
RIV	recombinant influenza vaccine
RIV3	recombinant trivalent influenza vaccine
RLS	restless legs syndrome
RZV	recombinant zoster vaccine
SBRT	stereotactic body radiation therapy
SexFS	Sexual Function and Satisfaction Measure
SHIM	sexual health inventory for men
SMART	specific, measurable, achievable, realistic, timebound
SNRI	serotonin-norepinephrine reuptake inhibitor
SPF	sun protection factor
SSRI	selective serotonin reuptake inhibitor
TBI	total body irradiation
TCA	tricyclic antidepressant
TENS	transcutaneous electrical nerve stimulation
TLSO	thoracolumbar sacral orthosis
TSEC	tissue-selective estrogen complex
TSH	thyroid-stimulating hormone
USDA	United States Department of Agriculture
UVA	ultraviolet A
UVB	ultraviolet B
WBC	white blood cell

NCCN Categories of Evidence and Consensus	
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

All recommendations are category 2A unless otherwise indicated.

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National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2024
Survivorship

Discussion

This Discussion corresponds to the NCCN Guidelines for Survivorship. Last updated on 07/14/2020.

Table of Contents

Overview

The number of cancer survivors in the United States increased from approximately 3 million in 1971 to more than 16.9 million in 2019.[1-3] This number is predicted to surpass 22 million by 2030.[3] This striking increase is generally attributed to rising cancer incidence rates (mainly resulting from an aging population), earlier detection, and better treatment.

Approximately 64% of survivors were 65 years of age or older in 2019.[3] Only 5% are younger than 40 years, and survivors of childhood cancer constitute between 0.5% and 3.0% of the survivor population.[4,5] In fact, an estimated 1 of every 5 persons older than 65 years is a cancer survivor. The most common cancer sites in the survivor population are breast, prostate, colon/rectum, and melanoma, together accounting for approximately 58% of survivors.[4] Approximately 64% of survivors were diagnosed 5 or more years ago, whereas 15% of survivors were diagnosed 20 or more years ago, and approximately 5% have survived 30 years or longer.[4]

Unfortunately, many of these cancer survivors experience physical and/or psychosocial late and/or long-term effects of cancer and its treatment, which can be severe, debilitating, and sometimes permanent. Survivors may be discharged from the care of their oncologist and feel isolated and scared. Furthermore, their primary care physicians (PCPs), who may now be responsible for their care, often do not know how best to care for the specific concerns and needs of cancer survivors.[6] ASCO's statement, "Achieving High-Quality Cancer Survivorship Care," cites a need for standardized, evidence-based practice guidelines for the management of treatment effects and health promotion of survivors.[7] ASCO, NCCN, ACS, and other groups that are working in parallel hope to provide this guidance.[8-12]

The NCCN Survivorship Panel is comprised of a multidisciplinary panel of experts that includes at least one oncologist, bone marrow transplant clinician, gynecologist, urologist, infectious disease specialist, cardiologist, PCP, psychologist, nutrition scientist, nurse, epidemiologist, social worker, and patient advocate. The panel has defined general principles of cancer survivorship to help guide the recommendations that form the basis for these guidelines.[13]

Literature Search Criteria and Guidelines Update Methodology

Prior to the update of this version of the NCCN Guidelines for Survivorship, an electronic search of the PubMed database was performed to obtain key literature in the field of cancer survivorship, using the following search terms: (("neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "cancer"[All Fields]) AND ("survivors"[MeSH Terms] OR "survivors"[All Fields] OR "survivor"[All Fields])) OR (("neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "cancer"[All Fields]) AND ("survivorship"[All Fields])). The PubMed database was chosen because it remains the most widely used resource for medical literature and indexes peer-reviewed biomedical literature.[14]

The search results were narrowed by selecting studies in humans published in English. Results were confined to the following article types: Clinical Trial, Phase II; Clinical Trial, Phase III; Practice Guideline; Randomized Controlled Trial; Meta-Analysis; Systematic Reviews; and Validation Studies.

The data from key PubMed articles and articles from additional sources deemed as relevant to these guidelines and discussed by the panel have been included in this version of the Discussion section (eg, e-publications ahead of print, meeting abstracts). Recommendations for which high-level

evidence is lacking are based on the panel's review of lower-level evidence and expert opinion.

The complete details of the Development and Update of the NCCN Guidelines are available on the NCCN website (www.NCCN.org).

General Principles of These Guidelines

These NCCN Guidelines for Survivorship provide screening, evaluation, and treatment recommendations for common consequences of cancer and cancer treatment to aid health care professionals who work with survivors of adult-onset cancer, including those in specialty cancer survivor clinics and primary care practices. These guidelines are focused on options to maintain and enhance wellness in cancer survivors who are receiving or have completed active therapy, including those receiving treatment for years, those who may be in remission, and those who are cured. These guidelines are designed to provide a framework for the management of long-term and/or late effects of cancer and its treatment. The guidelines focus on the vast and persistent impact both the diagnosis and treatment of cancer can have on the adult survivor's health, physical and mental states, health behaviors, professional and personal identity, sexuality, and financial standing.

The panel acknowledges that there is a growing population of cancer survivors with chronic cancer. This group includes those with incurable disease who are receiving systemic therapy continuously and those who may be on treatment intermittently. Although these guidelines do not address the specific needs of survivors with chronic cancer (eg, psychosocial issues related to living for years with a terminal diagnosis and uncertainty about the future; how to handle comorbid conditions and disease prevention, screening, and treatment in the setting of limited life expectancy; managing discussions around new drugs and early-stage clinical trials),[15] many of the recommendations in these guidelines are relevant to this population (eg, those around fatigue, anxiety, depression). The panel emphasizes that these guidelines may be used to guide the management of all cancer survivors – not just those who have completed treatment, but also the population with chronic cancer.

These guidelines should be used as a supplement to the follow-up recommendations within the disease-specific guidelines (see NCCN Guidelines for Treatment of Cancer by Site, available at www.NCCN.org) and should provide a framework for the coordination of care between the survivor's health care providers to ensure that needs are appropriately addressed.

These guidelines are not intended to provide guidance for the care of survivors of childhood cancer (detailed guidelines for the care of childhood cancer survivors are available from the Children's Oncology Group at http://www.survivorshipguidelines.org/). For survivorship issues related to younger populations, please also see the NCCN Guidelines for Adolescent and Young Adult (AYA) Oncology (available at www.NCCN.org). For survivors treated with immunotherapy, ongoing surveillance for immune-mediated toxicities is warranted (see the NCCN Guidelines for Management of Immunotherapy-Related Toxicities, available at www.NCCN.org).

For this version of the NCCN Guidelines for Survivorship, the panel focused on the preventive health issues including healthy lifestyle behaviors, immunizations and prevention of infection, and cardiovascular disease (CVD) risk assessment and modification. The panel also focused on several common issues of survivors: 1) anthracycline-induced cardiac toxicity; 2) anxiety, depression, trauma, and distress; 3) cognitive decline; 4) fatigue; 5) lymphedema; 6) hormone-related symptoms; 7) pain; 8) female and male sexual dysfunction; and 9) sleep disorders. Additional topics will be addressed in subsequent updates.

Cancer Survivors

The NIH adapted the definition of a cancer survivor from the National Coalition for Cancer Survivor and states: “An individual is considered a cancer survivor from the time of diagnosis, through the balance of their life. There are many types of survivors, including those living with cancer and those free of cancer. This term is meant to capture a population of those with a history of cancer rather than to provide a label that may or may not resonate with individuals.”[16]

The Effects of Cancer and Its Treatment

For some survivors, the consequences of cancer are minimal; these patients can return to a normal life after the completion of treatment. In fact, most cancer survivors report being in good general health and experience good to excellent quality of life.[17,18] Also, a survey of 659 survivors of breast, colorectal, and prostate cancers found that a majority do not suffer from psychologic morbidity or have a large number of unmet supportive care needs.[19,20] Other studies have similarly found that most survivors enjoy a high quality of life without a large number of cancer-related symptoms.[21,22]

However, many survivors do experience physical and/or psychosocial effects of cancer and its treatment.[23-25] Some sequelae become evident during anticancer treatment (long-term effects), whereas others may not manifest for months or years after active therapy (late effects). The problems can range from mild to severe, debilitating, or even life-threatening. Some problems are temporary or improve with time, whereas other problems are progressive or permanent. This topic has been well reviewed.[18,26]

A literature review suggests that at least 50% of survivors experience some late effects of cancer treatment.[26] The most common problems in cancer survivors are depression, pain, and fatigue.[27] The exact prevalence of various effects of cancer and its treatment are hard to quantify, because few studies have addressed these issues in a longitudinal fashion, comparing patients with and without a history of cancer to differentiate between the effects of cancer and the effects of aging.[18] In general, the prevalence of late effects in cancer survivors is believed to have increased over time, likely because anticancer interventions have become more complex and intense with combinations of surgery, radiation, chemotherapy, hormone therapy, and targeted biologics.[28]

Physical Effects

Physical effects of cancer and its treatment in cancer survivors include pain, musculoskeletal issues, fatigue, lack of stamina, urinary and bowel problems, lymphedema, premature menopause, cognitive deficits, diabetes, and sexual dysfunction.[18,29-32] The effects of cancer treatment on the heart and bone are also well known.[33-36] The type of physical effects depends mainly on the treatment received. For example, radiation to the pelvis can be associated with bowel, urinary, and sexual dysfunction and increased risk for subsequent primary malignancies.[37,38] The ACS Study of Cancer Survivors II found that 38% of survivors reported at least one unmet need in the physical domain (eg, pain, sexual dysfunction).[24]

Subsequent Primary Cancers

Importantly, the overall incidence of subsequent primary cancers in survivors is higher than in the general population because of genetic susceptibilities (eg, hereditary cancer syndromes), shared causative factors (eg, smoking, obesity, environmental exposures, human papillomavirus [HPV] infection), and/or the mutagenic effects of cancer treatment.[39-50] In fact, subsequent cancers accounted for 18% of all cancers diagnosed in the United States between 2009 and 2013.[51] Treatment-related subsequent primary cancers vary with the type and intensity of anticancer treatment and are associated in particular with radiation and specific chemotherapeutic agents.[52-58] These subsequent

malignancies are especially well studied in long-term survivors of childhood cancers.[59-62] Studies by individual cancer type show that the incidence of subsequent unrelated cancers ranges from 2% in survivors of malignant lymphoma to 30% in survivors of small cell lung cancer (SCLC).[26] Another study of more than 2 million cancer survivors in the SEER database identified the highest risk for subsequent primary cancers in survivors of bladder cancer (34% at 20 years).[63] Overall, this study found that 8.1% of survivors of cancers diagnosed after age 18 years develop a subsequent malignancy within a mean follow-up of 7.1 years, with 55% of these survivors dying as a result of the subsequent cancer.

Screening for subsequent primary cancers should be a shared responsibility between primary and oncology care physicians (see the NCCN Guidelines for Detection, Prevention, & Risk Reduction, available at www.NCCN.org). In addition, lifestyle modifications that reduce the risk of subsequent primary cancers (eg, smoking cessation, physical activity, weight loss) should be encouraged.[64] Finally, referral to genetic risk assessment and/or testing should be considered for appropriate candidates, such as those with a cancer diagnosis at a young age or with multiple primary cancers, to identify those with a potential increased risk for subsequent malignancies.[65] Family cancer history should be periodically updated to reassess hereditary risk, because it should not be assumed that all cancer survivors were assessed at diagnosis. Genetic testing guidelines and knowledge about hereditary cancer risk evolve over time, and new family diagnoses may occur making periodic assessment important. Genetic risk assessment is appropriate for all survivors of breast cancer, epithelial ovarian cancer, high-grade prostate cancer, pancreatic cancer, and colorectal or endometrial cancer diagnosed at age 50 years or younger. Many other survivors of rare cancers, cancers diagnosed at young ages, multiple primary cancers, or those with one or more relatives with the same or related cancers are also candidates for risk assessment per guidelines from NCCN and other expert groups.

Genetic counseling and testing is recommended for appropriate survivors based on results of the risk assessment. Referral to genetic risk assessment and/or testing should be considered for appropriate candidates when available to identify those with an increased risk for subsequent malignancies. Genetic testing may also provide opportunities to identify and reduce risks in relatives of cancer survivors. Several NCCN Guidelines (available at www.NCCN.org) include criteria for genetic risk assessment and testing, and management recommendations for patients with known germline mutations linked to an increased risk for cancer, as listed above in these guidelines.

Psychosocial Effects

Cancer can have positive effects on a significant portion of individuals, including strengthened relationships, a sense of gratitude or empowerment, and an increased appreciation for life.[66-72] Many survivors, however, experience psychologic distress after active treatment, and some experience a combination of positive and negative psychologic effects. Distress can result from the fear of recurrence or death or secondary to physical, social, or practical problems.[66,69,73] In fact, as many as 19% of survivors meet the criteria for post-traumatic stress disorder (PTSD).[66,69,74-76] Practical and social problems of survivors include issues surrounding employment, finances, and health and life insurance.[66,77-80]

Fear of Recurrence

As many as 70% of post-treatment cancer survivors report high levels of fear of cancer recurrence, which can cause significant and enduring distress.[69,81-84] In addition, caregivers report distress from fear of cancer recurrence in their loved one.[85] These fears and their associated distress may cause survivors and their caregivers to either avoid appropriate surveillance or to demand more intense surveillance than evidence supports.[84] In addition, survivors with high levels of fear of recurrence are more likely to be depressed and have a lower quality of life.[86]

Employment Issues and Return to Work

Cancer and its treatment often have an adverse effect on work status, performance, and satisfaction.[87] Survivors often take long breaks from or even leave their jobs during treatment, and returning to work after cancer treatment can be critical to restoring normalcy to the lives of survivors. However, survivors may be left with disabilities or late/long-term effects that decrease their employment prospects or ability to perform at their previous levels. Several studies have shown that unemployment rates for survivors are higher than for the general population.[87-90] Furthermore, those survivors who do return to work often encounter difficulties, such as physical or cognitive limitations, fatigue, depression, anxiety, and perceived or real discrimination.[87,91,92]

Several studies have addressed factors that predict a delayed return to work.[93-99] For example, a French population-based study revealed that clinical factors, such as severity of the cancer, receipt of chemotherapy, or the experience of adverse effects, were associated with a delay in return to work.[97] In addition, a systematic review of cohort studies found that survivors who were older, had a lower education level, or had a lower income were less likely to return to work.[98] Another systematic review identified factors related to the person (eg, symptoms, coping, motivation), environmental supports (eg, family, workplace), and occupation (eg, type of work, job flexibility) that impacted successful return to work after cancer treatment.[100]

Some interventions to enhance return-to-work in cancer survivors have been studied (eg, psycho-education, physical training, vocational counseling), although additional research in this area is greatly needed.[101-104] Multidisciplinary interventions that combine vocational counseling with other elements (eg, patient education, patient counseling, behavioral training, physical exercises) may increase rates of return-to-work compared to usual care.

Financial Burden

The LIVESTRONG 2012 Survey found that approximately 33% of working-age survivors went into debt and 3% had filed for bankruptcy.[105] The ACS Study of Cancer Survivors II found that 20% of survivors reported unmet financial needs.[24] A study in Washington state found that patients with cancer have a 2.6-fold increased risk of bankruptcy.[106] In another study, 38% of patients with stage III colon cancer reported financial hardship resulting from cancer treatment, defined as accruing debt, selling or refinancing a home, borrowing money from friends or family, or experiencing a ≥20% decline in annual income.[107] Another study found that, in addition to the average >$16,000 excess economic burden that patients feel in the early phases of cancer treatment, survivors (>1 year from diagnosis) have an average annual excess economic burden that exceeds $4,000.[108,109] Much of this excess burden was because of excess medical expenditures. A more recent study found that the excess annual health care expenditures of cancer survivors averaged about $4400, and that the total mean annual direct health care expenditure for cancer survivors increased by about $1000 in the period from 2009 to 2010 to the period from 2015 to 2016.[109] Other recent studies also found that cancer survivors have greater out-of-pocket expenses and are more likely to experience material hardship than those without a history of cancer.[110,111] Younger cancer survivors seem to be particularly vulnerable to the financial effects of cancer.[111-113]

Clearly, with lost wages and increased expenses, the financial burden on many cancer survivors is great. Recent data suggest that patients belonging to racial and ethnic minorities are more likely to suffer financial hardship after cancer treatment.[114,115] Furthermore, the financial burden associated with cancer treatment and survivorship can lower health-related quality of life, increase psychologic distress, and impact adherence to prescribed medications.[116-119]

Standards for Survivorship Care

In 2005, the Institute of Medicine (IOM) (now known as the National Academy of Medicine [NAM]) and the National Research Council compiled a report entitled, "From Cancer Patient to Cancer Survivor: Lost in Transition."[28] The NCCN Survivorship Panel adapted the essential components of survivorship care from the report:

1. Prevention of new and recurrent cancers and other late effects
2. Surveillance for cancer spread, recurrence, or subsequent cancers
3. Assessment of late psychosocial, physical, and immunologic effects
4. Intervention for consequences of cancer and treatment (eg, medical problems, symptoms, psychologic distress, financial and social concerns)
5. Coordination of care between primary care providers and specialists to ensure that all of the survivor's health needs are met
6. Planning for ongoing survivorship care (see below)

In addition, the IOM report discusses the importance of policies that ensure access to and health insurance coverage for all aspects of survivorship care, including psychosocial services. Cancer survivors with untreated distress have poorer compliance with surveillance screenings and are less likely to exercise and quit smoking.[120] A 2008 IOM report, "Cancer Care for the Whole Patient: Meeting Psychosocial Health Needs,"[121] concluded that psychosocial screening and care should be a part of the new standard for quality cancer care and should be integrated into routine care across the trajectory of cancer, which includes the period after active treatment. See the NCCN Guidelines for Distress Management (available at www.NCCN.org) and *Anxiety and Depression* below for recommendations on screening for and treating distress.

In September 2011, the LIVESTRONG Foundation convened a meeting of experts and stakeholders in the survivorship field to define essential elements of survivorship care. After 2 days of consensus building, the group agreed on the following elements that all medical settings must provide for cancer survivors, either directly or through referral (http://images.livestrong.org/downloads/flatfiles/what-we-do/our-approach/reports/ee/EssentialElementsBrief.pdf):

1. Survivorship care plan, psychosocial care plan, and treatment summary
2. Screening for new cancers and surveillance for recurrence
3. Care coordination strategy that addresses care coordination with PCPs and primary oncologists
4. Health promotion education
5. Symptom management and palliative care

The 2020 Commission on Cancer (CoC) of the American College of Surgeons' accreditation standards for hospital cancer programs (https://www.facs.org/quality-programs/cancer/coc/standards/2020) has a patient-centered focus that recommends and encourages, but does not require, the development and dissemination of a survivorship care plan for all patients completing primary therapy. The current standard requires the development and implementation of a survivorship program directed at meeting the ongoing needs of survivors treated with curative intent. More information can be found on its website.

Implementation of these standards for survivorship care has been challenging, and reasons for the difficulties have been described.[122-124] To move toward the goal of personalized pathways to ensure that all cancer survivors receive all essential components of care, an ACS-ASCO summit identified the following necessary strategies: 1) developing candidate care delivery models; 2) conducting implementation studies to model the effects of personalized follow-up care pathways on survivor outcomes, workforce and health care resources, and utilization and costs; 3) developing

guidelines to inform the personalized care pathway delivery; and 4) identifying and filling research gaps.[123]

Models of Survivorship Care and the Role of Primary Care Providers

Various models have been proposed to facilitate the implementation of all the essential components of survivorship care for the growing population of post-treatment cancer survivors. These include survivorship clinics within academic or community cancer centers, community survivorship clinics run by primary care clinicians, and survivorship care in the primary care setting.[125-130] In each case, survivorship care is delivered by either physicians or by advanced practice clinicians such as nurse practitioners.[131] Each model has advantages and disadvantages, and no one model is clearly the best for all situations.

With the population of cancer survivors growing at a rapid pace, the demand for follow-up care is expected to increase. An increasing proportion of this care will likely be performed by primary care teams. In fact, a systematic review identified specific needs of cancer survivors in the primary care setting, including psychosocial needs, cancer/survivor information needs, and medical needs.[132] Because studies have shown that primary care providers often do not know how best to care for the specific concerns and needs of cancer survivors,[6,133-138] education for primary health care providers regarding appropriate survivorship care will be increasingly important.[139]

A study in the Netherlands found that patients with cancer 2 to 5 years after diagnosis increased their number of consultations with primary care compared with age- and sex-matched controls without cancer by 15% for colorectal cancer ($P < .05$), 24% for breast cancer ($P < .001$), and 33% for prostate cancer ($P < .001$).[140] These survivors also had more chronic conditions than controls. Although an American study using the SEER-Medicare database showed a smaller increase in primary care use by breast cancer survivors (10% increase in year 4 after diagnosis; $P < .05$),[141] these results show that PCPs are providing a substantial amount of survivorship care. In fact, according to IOM analyses of the 2001 and 2002 National Ambulatory Medical Care Survey and the National Hospital Ambulatory Medical Care Survey, approximately one-third of the more than 36 million cancer-related visits to physicians' offices were made to primary care.[28] Furthermore, a nationally representative survey by NCI and the ACS found that >50% of PCPs provide survivors with cancer-related follow-up care, often with co-management by oncologists.[142]

In a survey of survivors regarding their preferences for follow-up care, most participants said that the PCP should only provide care if the responsibility was shared with the oncologist.[143] One of the reasons commonly cited for this preference was that survivors believe their PCPs lack the needed expertise to deal with their specific issues. In addition, survivors cited a desire for continuity of care. Additional surveys of survivors of breast cancer in the United States and of survivors of breast, colorectal, and prostate cancer in the United Kingdom found similar preferences for oncologist-driven follow-up care over PCP follow-up care.[144,145] Importantly, however, two randomized trials comparing survivorship care administered by PCPs (provided guidelines outlining appropriate follow-up care) versus oncologists found no difference in disease-related outcomes, including survival.[146,147]

Survivorship Care Planning

Because primary care offices are in fact already caring for cancer survivors, it is critical for information to be shared between oncology and primary care teams. Good communication at the oncology/primary care interface may allow survivors to feel they have the continuity of care they desire.

Some data suggest that treatment summaries and survivorship care plans lead to improvements in outcomes for survivors, such as having fewer emotional concerns and more often reporting that their needs have been met.[148,149] However, a randomized controlled trial of 408 survivors of breast cancer that assessed the effects of survivorship care plans found no differences on patient-reported outcomes, including cancer-specific distress, between patients who received a discharge visit and a care plan and those who received only a discharge visit.[150,151] Criticisms of this trial, including the relevance of its outcome measures, have been published.[152-154] Another trial randomized 221 survivors of stage I–III colorectal cancer to usual care or usual care plus a supportive care package that included a survivorship care plan, educational materials, a needs assessment, an end-of-treatment session, and three follow-up telephone calls.[155] No effects on distress, supportive care needs, or quality of life were seen, although survivors in the care plan group were more satisfied with their care. In addition, a trial in which 12 hospitals were randomized to usual care or to patient-tailored, automated survivorship care plans found that the receipt of a care plan was associated with an increase in symptoms, concern about illness, and emotional impact.[156] No differences in satisfaction with information or care were evident.

More recent population-targeted randomized controlled trials are lending some support for the benefits of survivorship care planning. One randomized controlled trial tested the role of survivorship care plans in 212 low-income, predominantly Latina survivors of stage 0–III breast cancer.[157] Survivors in the intervention group received the care plan with a treatment summary and a 1-hour counseling session with a trained, bilingual, bicultural nurse who encouraged patient empowerment; the care plan and treatment summary were also delivered to the health care providers of survivors in the intervention group. Patient-reported physician implementation of recommended survivorship care (eg, for depression, hot flashes), the primary trial outcome, was greater in the intervention group than in the usual care group (P = .003). Patient adherence to recommended survivorship care, the secondary outcome, was also greater for the intervention group, but did not reach statistical significance (P = .07). Whereas this trial provides support for the benefits of survivorship care plans, it is impossible to separate the effects of the care plan and the intensive counseling session, and the applicability of the findings to other populations is unknown. Another randomized controlled trial examined the efficacy of mailing a personalized survivorship care plan, which was designed with qualitative input of hematopoietic cell transplant survivors and briefly reviewed in a telehealth call by a trained non-professional.[149] The study randomized 458 hematopoietic cell transplant survivors 1 to 5 years after transplant to receive the survivorship care plan or delayed survivorship care plan. After 6 months, the survivorship-care-plan recipients reported reduced cancer-specific distress and improved general mental health, although they did not report higher levels of confidence in survivorship information when compared with the delayed care plan recipients as hypothesized. In this study, about two-thirds of survivors reported that they found the survivorship care plan useful in helping them understand their treatments and side effects, and helpful in managing their health. Another randomized trial found that a survivorship care plan, discussed in consultation with a physician who had received skills training, increased patient knowledge about their disease and increased adherence to certain health promotion recommendations.[158] A third trial did not see an increase in survivors' knowledge after provision of a survivorship care plan.[159] At this time, definitive data supporting the benefits of survivorship care plans are still insufficient.[160]

A survey that included a nationally representative sample of 1130 oncologists found that fewer than 5% of them provide a written survivorship care plan to survivors.[161] The survey also included 1020 PCPs, who were nine times more likely (95% CI, 5.74–14.82) to have survivorship discussions with survivors if they received a written care plan.

More recent surveys have reported that 35% to 40% of survivors receive a written follow-up care plan and/or a written treatment summary.[162,163]

ASCO released a clinical expert statement on cancer survivorship care planning in 2014.[164] The group of experts identified barriers to the successful implementation of survivorship care planning (including the time it takes to complete one, the lack of reimbursement for doing so, and the uncertainty as to whose responsibility it is to prepare the plan) and revised the ASCO survivorship care plan template to help address some of these barriers. In addition, a pilot study assessed the use of electronic health records (EHRs) to reduce the time and effort involved with creating care plans.[165] Although many plan elements required manual entry by the oncologist, the median time to complete the plans was only 3 minutes (range 2–12 minutes). Another group reported on a similar initiative to facilitate generation of care plans using EHRs.[166] Care plan creation took a mean 12 minutes (range 10–15 minutes). However, a study in which EHR-based treatment summaries were abstracted and cross-checked revealed that 30% contained ≥1 omissions, and 10% contained ≥1 errors, indicating that autopopulation systems will require manual double-checking to ensure accuracy.[167] Thus, providing a survivorship care plan is time-consuming and resource-intensive and could have unforeseen harms.[154,168]

Because definitive evidence that survivorship care plans improve outcomes is lacking, the NCCN Survivorship Panel currently recommends planning for ongoing survivorship care, but does not mandate the use of survivorship care plans. The planning should include:

- Information on treatment received including all surgeries, radiation therapy, and systemic therapies
- Information regarding follow-up care**,** surveillance, and screening recommendations
- Information on post-treatment needs, including information regarding acute, late and long-term treatment-related effects, and health risks when possible (See NCCN Guidelines for Treatment of Cancer by Site)
- Delineation regarding roles of oncologists, PCPs, and subspecialty care physicians in long-term care and timing of transfer of care if appropriate
- Healthy behavior recommendations
- Periodic assessment of ongoing needs and identification of appropriate resources

Data from ongoing trials will help inform future recommendations.

Surveillance for Cancer Recurrence

Screening for cancer recurrence is an important aspect of survivorship care. In general, this surveillance is performed by the oncology team. When surveillance is overseen by the primary care team, the oncologist should provide evidence-based recommendations based on currently available guidelines. Specific recommendations for surveillance testing vary between cancer site and stage and individualized patient risk and are not addressed in these guidelines. Please see individual NCCN Guidelines for Treatment of Cancer by Site (available online at www.NCCN.org) for disease-specific surveillance recommendations. Additional lab work, imaging studies, or other studies to evaluate for recurrence should be based on clinical presentation and judgment. The use of radiologic imaging studies (ie, CT) should be based on evidence that early detection of recurrence will improve cancer-related outcomes, because evidence suggests that excess radiation exposure associated with CT imaging may be associated with an increased risk of developing a radiation-associated cancer.[169,170]

Assessment for Effects of Cancer and Its Treatment

All survivors should be assessed at least annually for symptoms related to cancer and prior cancer treatment, with appropriate follow-up care as clinically indicated. This assessment can be done by the oncologist or PCP. Shared, coordinated care between the oncology, primary care, and subspecialty care providers is encouraged. Depending on the cancer type and stage of disease, transition of care to primary care may be done when deemed clinically appropriate, with referral back to oncologic care as needed. The panel does not assume that all survivorship issues will be addressed at every visit.

Some tools that screen for long-term and late physical and psychosocial effects of cancer and its treatment in survivors have been validated.[171-176] In addition, the NCCN Survivorship Panel created a sample screening instrument that is guideline-specific and can be self-administered or administered by an interviewer. This assessment tool was developed specifically for use in combination with the NCCN Guidelines for Survivorship to help providers deliver necessary and comprehensive survivorship care. Although this instrument has not yet been piloted or validated, the answers can be used to guide providers to topics within the guidelines that require more in-depth assessment via validated tools and/or clinical evaluation.

In addition to screening by history and physical examination, care providers should assess the following at regular intervals:

1. Current disease status
2. Functional/performance status
3. Medication use (including over-the-counter medications and supplements)
4. Comorbidities
5. Prior cancer treatment history and modalities used
6. Family history
7. Psychosocial factors
8. Weight and health behaviors that can modify cancer and comorbidity risk (including cigarette/tobacco, alcohol use)
9. Disease-specific recommendations for surveillance/follow-up (see NCCN Guidelines for Treatment of Cancer by Site, at www.NCCN.org)

This information can also inform about the patient's risk for specific late or long-term effects, including risks for subsequent primary cancers and comorbidities. For example, patients who received pelvic irradiation or surgery are at risk for sexual dysfunction; patients with a history of brain metastasis or cranial irradiation have an elevated risk for cognitive dysfunction. In general, those who underwent more intensive therapy are at higher risk for multiple late and/or long-term effects. Survivors undergoing certain treatments, such as mantle field radiation or certain systemic therapies, may be at increased risk for subsequent malignancies. Those survivors who continue to smoke are at increased risk for smoking-related comorbidities and subsequent primary cancers.

Reassessment

Survivors should be followed and reassessed at regular intervals, depending on the nature and severity of late and long-term effects being treated. At each time point, assessment of disease status and ongoing effects of cancer and its treatment should be addressed. In addition, survivors should be periodically rescreened for the development of new late and long-term effects of cancer and its treatment. The outcomes of any interventions for ongoing effects of cancer and its treatment should be evaluated regularly based on best practices and available resources. Outcome assessment may include survivor satisfaction with the effectiveness of the intervention in reducing symptom burden, adequate pain control, receipt of recommended immunizations and preventive care,

and improved adherence to guideline recommendations for health behaviors.

Survivorship Research

The IOM survivorship report cites a paucity of longitudinal cohort studies linking specific cancer types or treatments with specific late effects, making it difficult to predict risk for individual patients.[28] Research is needed to increase understanding of the prevalence of, mechanisms of, and risks factors for late and long-term effects of cancer and its treatment. In addition, research is needed to better define interventions that relieve symptoms, restore function, and improve the quality of life of survivors.[177] Finally, research can help better define optimal follow-up and surveillance schedules for cancer survivors after treatment.[178,179]

An ASCO survey report highlighted several key gaps in current survivorship research.[180] For instance, more research pertaining to survivors >65 years of age, to survivors of cancers other than breast, and to long-term survivors (>5 years) is needed. In addition, research focused on patterns and quality of survivorship care is lacking. A study of NIH survivorship grants in fiscal year 2016 showed a need for research including more diverse cancer types, older and longer-term survivors, and more ethnoculturally diverse populations of survivors.[181]

In June 2012, the ACS, CDC, LIVESTRONG Foundation, and NCI held a joint meeting and created an action plan to facilitate the translation of survivorship research into survivorship care.[182] The plan is driven by collaboration between researchers, survivors, clinicians, and public health professionals; the use of technology, such as EHRs; analysis of information from the viewpoints of multiple stakeholders; and the integration and synthesis of knowledge using systematic reviews and meta-analyses.

Recommendations for Preventive Health

Analysis of data from the Behavioral Risk Factor Surveillance System (BRFSS) indicates that a large proportion of cancer survivors have significant comorbidities, smoke, are obese, and/or do not engage in physical activity.[183] Analysis of data from other studies, including the National Health Interview Survey, showed similar results.[184-187] Separate surveys by the ACS and the CDC found that 9.3% and 17% of survivors smoke, respectively.[186,188] In addition, many survivors forego recommended cancer screenings (ie, colorectal and cervical screening) and follow-up surveillance[189-191] or demand more intense surveillance than evidence supports.[84]

Healthy Lifestyles

Healthy lifestyle habits, such as engaging in routine physical activity, maintaining a healthy diet and weight, and avoiding cigarette/tobacco use, have been associated with improved health outcomes and quality of life. For some cancers, a healthy lifestyle has been associated with a reduced risk of recurrence and death.[192-199] In fact, the maintenance of a healthy lifestyle is associated with a decrease in premature death in cancer survivors.[200] Therefore, survivors should be encouraged to achieve and maintain a healthy lifestyle, including attention to weight management, physical activity, metabolic health, and dietary habits. Setting incremental goals for diet, physical activity, and weight management should be advised. Survivors should be counseled to limit alcohol intake and avoid or stop using cigarette/tobacco products, with emphasis on tobacco cessation if the survivor is a current smoker or user of smokeless tobacco (see the NCCN Guidelines for Smoking Cessation, available at www.NCCN.org).[201] Clinicians should also advise survivors to practice sun safety habits as appropriate, such as using a broad-spectrum sunscreen, avoiding peak sun hours, and using physical barriers. Survivors should also be encouraged to get an adequate amount of sleep. Finally, survivors should be encouraged to see a PCP regularly and adhere to age-

appropriate and treatment-associated health screenings, preventive measures (eg, immunizations), and cancer screening recommendations.

The panel made specific recommendations regarding physical activity, weight management, nutrition, and supplement use, which are discussed herein. Although achieving all of these healthy lifestyle goals may be difficult for many survivors, even small reductions in weight among overweight or obese survivors or small increases in physical activity among sedentary individuals are thought to yield meaningful improvements in cancer-specific outcomes and overall health.[202] Clinicians should assess individual and community-level barriers to meeting the healthy lifestyle recommendations and support patients in developing strategies to overcome challenges.

Physical Activity

During cancer treatment, many survivors become deconditioned and can develop impaired cardiovascular fitness because of the direct and secondary effects of therapy.[203] Randomized trials have shown that exercise training is safe, tolerable, and effective for most survivors. Structured aerobic and resistance training programs after treatment can improve cardiovascular fitness and strength and can have positive effects on balance, body composition, fatigue, emotional well-being, and quality of life.[204-216] The effectiveness of exercise is especially well studied in patients with early-stage breast cancer. Survivors of breast cancer who exercise have improved cardiovascular fitness and therefore an increased capacity to perform daily life functions, resulting in a better quality of life.[214,215,217-219] Furthermore, a study of adult survivors of childhood Hodgkin lymphoma found that vigorous exercise was associated with a reduction in the risk of major cardiovascular events after a median follow-up of 11.9 years.[220] In fact, the finding was dose-dependent, and survivors who reported ≥9 metabolic equivalent (MET) h/wk experienced a 51% reduction in risk compared with those reporting <9 MET h/wk (*P* = .002). A similar study in patients with breast cancer found a similar reduction in the risk of cardiovascular events with ≥9 MET h/wk.[221]

In addition, observational studies have consistently found that physical activity is linked to decreased cancer incidence and recurrence and increased survival for certain tumor types.[209,222-239] For example, one meta-analysis of 6 studies including more than 12,000 survivors of breast cancer found that post-diagnosis physical activity reduced all-cause mortality by 41% (*P* < .00001) and disease recurrence by 24% (*P* = .00001).[226] Data from other meta-analyses primarily consisting of observational studies of survivors of colorectal, ovarian, non-small cell lung, brain, prostate, and breast cancers show that physical activity is associated with decreased all-cause mortality and/or cancer-specific mortality.[224,227,236,240] In fact, analyses of data from 986 survivors of breast cancer from the National Runners' and Walkers' Health Studies found that mortality decreased with increased rates of energy expenditure.[237] Evidence in other disease sites is less robust, but also suggests survival benefits associated with exercise in survivors after treatment.[240]

Data also support the idea that inactivity/sedentary behavior is a risk factor for cancer incidence and mortality and impacts mood and quality of life in survivors, independent of the level of an individual's recreational or occupational physical activity.[192,241-247] For example, in a cohort of more than 2000 survivors of nonmetastatic colorectal cancer, those who spent more leisure time sitting had a higher mortality than those who spent more time in recreational activity.[192]

Evaluation and Assessment for Physical Activity

Survivors should be asked about readiness for participation in and their current level of physical activity at regular intervals. The Godin Leisure-Time Exercise Questionnaire is one tool that can be used to assess a survivor's exercise behavior, with a modified version also able to assess daily time in moderate-to-vigorous activity.[248,249]

For survivors who are not meeting the guideline recommendations (see later discussion), barriers to physical activity should be discussed and addressed, if possible. Common barriers include not having enough time to exercise, not having access to an acceptable exercise environment, uncertainty about safety of exercise post-treatment, lack of knowledge regarding appropriate activities, and physical limitations.[250] Alleviation of pain, fatigue, distress, or nutritional deficits can facilitate the initiation of an exercise program.

Risk Assessment for Exercise-Induced Adverse Events

Exercise is considered safe for most survivors.[214,215,251] However, a significant portion of survivors may have comorbid conditions or risk factors that make them unable to safely exercise without trained supervision.[252] Therefore, a risk assessment is required for all survivors before prescribing a specific exercise program.[214,253] The type of cancer, treatment modalities received, and the number and severity of comorbidities determine risk levels.[251] Thus, disease and treatment history, late and long-term effects, and comorbidities should be assessed. A standardized pre-participation screening questionnaire, such as the Physical Activity Readiness Questionnaire for Everyone (PAR-Q+),[254] can also be considered to identify patients for whom unsupervised physical activity is likely safe versus those for whom it may pose undue risk.

Survivors with peripheral neuropathy, poor bone health, arthritis, or musculoskeletal issues are considered to be at moderate risk for exercise-induced adverse events. Stability, balance, and gait should be assessed in survivors with peripheral neuropathy and possibly in survivors with poor bone health before they engage in exercise, and exercise choice should be made based on the results (ie, stationary bike or water aerobics for survivors with poor balance). In addition, balance training can be recommended for patients at risk for falls. Moderate-risk survivors can often follow the general recommendations for physical activity; however, medical clearance and/or referrals to trained personnel such as a physical or occupational therapist, certified exercise professional, or rehabilitation specialist can also be considered. Specialized training in working with survivors is available for both physical therapists and exercise professionals through the American College of Sports Medicine (ACSM; http://www.acsm.org/get-certified) and the American Physical Therapy Association (APTA) Oncology section (http://oncologypt.org/). Survivors should be encouraged to use an ACSM- or APTA-certified trainer when available.

Lymphedema is not a contraindication for physical activity, and no special precautions are required for cardiovascular/aerobic exercise or strength training of unaffected limbs (see *Survivor Lymphedema Education,* below).[255-260] Progressive resistance training under supervision is recommended as part of treatment for survivors with lymphedema (see *Treatment of Lymphedema,* above).

Survivors at high risk for exercise-associated adverse events include those with a history of lung surgery or major abdominal surgery, an ostomy, cardiopulmonary comorbidities (eg, chronic obstructive pulmonary disease [COPD], congestive heart failure [CHF], coronary artery disease [CAD], cardiomyopathy), ataxia, severe nutritional deficiencies, severe fatigue, or worsening/changing physical condition (eg, lymphedema exacerbation). These survivors should receive medical evaluation and clearance prior to initiation of an exercise program and referral to trained personnel for a supervised exercise program.[251] In general, exercise should be individualized to the participant based on current exercise level and medical factors and should be increased in terms of intensity, duration, and frequency as tolerated.

Physical Activity Recommendations for Survivors

Both the ACS and the ACSM have made physical activity recommendations for cancer survivors.[212,261] In addition, the panel also

considered the physical activity guidelines for Americans published by the Department of Health and Human Services (HHS) and those on diet and physical activity for the prevention of cancer by the ACS.[262,263] The panel supports the recommendations by these groups and has adapted them as follows:

1. Physical activity and exercise recommendations should be tailored to individual survivors' abilities and preferences.
2. Survivors who are able should be encouraged to engage in daily physical activity, including exercise, routine activities, and recreational activities.
3. All survivors should be encouraged to limit sedentary behavior (eg, sitting for long periods) and return to daily activities as soon as possible.
4. Physical activity for cancer survivors:
    - Overall volume of weekly activity should be at least 150 to 300 minutes of moderate-intensity activity or 75 minutes of vigorous-intensity activity, or an equivalent combination spread out over the course of the week;
    - Individuals should engage in 2 to 3 sessions per week of strength training (see *Resistance Training*, below) that include major muscle groups; and
    - Major muscle groups should be stretched at least 2 days per week on days that other exercises are performed.

The panel acknowledges that most survivors do not meet these exercise recommendations, and a significant portion reports that they perform no leisure-time activity.[183,264] However, the evidence suggests that even light-intensity physical activity can improve physical functioning in survivors.[265] For survivors who are inactive, clinicians should not advise the immediate initiation of a high-intensity, high-frequency program.[266,267] Instead, the panel suggests that clinicians provide sufficient information to encourage survivors to avoid a sedentary lifestyle.[253] Survivors and providers should work together to address barriers to physical activity and develop incremental short- and long-term physical activity goals. These goals may include incremental increases in time spent in physical activity or in intensity of activity over time. The panel suggested a possible initial physical activity prescription (starting inactive survivors with 1 to 3 light-/moderate-intensity sessions of 20 minutes or more per week), with progression based on tolerance.[266] For survivors tolerating the minimum guideline recommendations, clinicians should consider encouraging incremental increases in time spent in physical activity or in intensity of activity. Walking and using a stationary bike are safe for virtually all survivors.

Resistance Training

The health benefits of resistance training include improvement in muscle strength and endurance, improvements in functional status, and maintenance/improvement in bone density. Core and strength training is important to maintain balance and minimize fall risk. Studies in survivors have shown improvements in lean body mass, muscular function, and upper body strength, and a slowing of physical function deterioration.[268-273] A recent systematic review of 15 studies of resistance training interventions during and/or after cancer treatment concluded that meaningful improvements in physiologic and quality-of-life outcomes can be achieved.[270] A similar review of 11 randomized controlled trials came to similar conclusions.[273] One recent study that included 2863 cancer survivors found resistance exercise to be associated with a 33% lower risk of all-cause mortality (95% CI, 0.45–0.99), independent of aerobic exercise.[274]

All major muscle groups (chest, shoulders, arms, back, core, and legs) should be incorporated into a resistance training program. For survivors who do not currently engage in resistance training, referral to trained personnel or an exercise specialist is recommended if available. Clinicians

should recommend 2 to 3 sets of each exercise at a weight that allows the performance of 10 to 15 repetitions; however, individualizing recommendations for resistance and strength training is important. Survivors can consider increasing the weight when 3 sets of 10 to 15 repetitions become easy.

Interventions to Increase Physical Activity

Dozens of studies have looked at the efficacy of a variety of behavioral and exercise interventions for increasing exercise behavior in cancer survivors.[211,214,275-277] However, data comparing different interventions are limited, and there is currently no "best" physical activity program for cancer survivors.[278-281] Several studies have examined the physical activity and counseling preferences of survivors, with the goal of informing possible strategies to best encourage increased activity in this population.[282-284]

The panel suggests several strategies to help increase physical activity. These strategies include a simple recommendation from a physician, physical therapist, and/or certified exercise physiologist.[285-287] In addition, participation in supervised exercise programs or classes or enlisting the support of an exercise group or buddy may be helpful for survivors.[288-291] In addition, setting short- and long-term goals and considering the use of a pedometer or wearable activity tracker to monitor these goals (eg, achieving 10,000 steps per day) can be helpful.[292-301] Print materials, telephone counseling, motivational interviewing, and theory-based behavioral approaches (discussed in *Health Behavioral Change*, below) are other strategies that may be effective for increasing physical activity in the survivor population.[289,296,302-307] Combination approaches (eg, oncologist recommendation plus exercise DVDs, pedometers, exercise diaries, exercise education sessions) may also increase exercise participation in survivors.[308]

Nutrition and Weight Management

Weight gain after cancer diagnosis and treatment is common, and the prevalence of obesity in the survivor population is greater than in the general population and has increased at a faster rate.[309-311] The vast majority of studies on weight and weight gain in survivors have been performed in survivors of breast cancer, but some studies have also been done in survivors of other cancers. Weight gain or being overweight or obese can exacerbate a survivor's risk for functional decline, comorbidity, and cancer recurrence or death, and can reduce quality of life.[309,312-320] For example, a systematic review and meta-analysis of studies in survivors of breast cancer found a correlation between higher body mass index (BMI) and higher risk of total and breast cancer-specific mortality.[314] Additionally, a meta-analysis demonstrated that this risk for increased breast cancer mortality is predominantly confined to the pre- and perimenopausal, hormone receptor-positive population.[321] A retrospective study of survivors of stage II and III colon cancer enrolled in NSABP trials from 1989 to 1994 showed that survivors with a BMI of 35 kg/m^2 or greater had an increased risk of disease recurrence and death.[193,197] In addition, some evidence suggests that weight loss or gain increases mortality risk in survivors, suggesting that weight maintenance is optimal.[322]

ASCO published a position statement on obesity and cancer.[323] The ASCO panel established an initiative to reduce the impact of obesity on cancer through education, tools, and resources for clinicians by promoting research (eg, in health behavioral change) and advocating for policies that can help patients with cancer manage their weight.

Nutrition and Weight Management Assessment

The BMI of survivors should be evaluated at regular intervals. A BMI of 18.5 to 24.9 kg/m^2 is considered ideal. It is important to inform patients of their weight status, particularly if they are underweight (BMI <18.5), overweight (BMI = 25–29.9), or obese (BMI ≥30), and discuss the

importance of interventions to attain a normal body weight and avoid weight gain in adulthood. The panel notes, however, that BMI should be considered in context of body composition. For more muscular survivors, waist circumference may be a better measure of overall disease risk. A larger waist circumference increases risk for diabetes, hypertension, and CVD.[324]

Current dietary and physical activity habits and potential barriers to physical activity or a healthful diet of those in high-risk groups should be ascertained either by the oncologist or other appropriate allied health personnel (eg, nurses, dietitians). In addition, effects of cancer treatment and other medical issues, including psychosocial distress and fear of recurrence, should be assessed and addressed as necessary.

Weight Management for Survivors

Providers should discuss strategies to prevent weight gain for normal and overweight/obese survivors. Clinicians should reinforce the importance of maintaining a normal body weight throughout life and encourage all cancer survivors to achieve and maintain a normal BMI and strive for metabolic health. In conjunction with primary care, survivors should be assessed for metabolic health, body composition, and BMI. Regardless of BMI, all survivors should be advised about the panel's nutrition, weight management, and physical activity recommendations (see pages SNWM-1, SNWM-2, and SPA-1 in the algorithm, above). Contributing treatment effects and risk factors should be managed as clinically indicated. In addition, a workup for disease recurrence should be considered in the setting of involuntary weight loss or gain of >5% within 3 months or if cachexia is present.

For additional resources, see the ASCO Tool Kit on Obesity and Cancer (https://www.asco.org/practice-policy/cancer-care-initiatives/prevention-survivorship/obesity-cancer) and the LIVESTRONG MyPlate Calorie Tracker (http://www.livestrong.com/myplate/).

Recommendations for Normal Weight Survivors

In addition to discussing nutrition, weight management, and physical activity, clinicians should reinforce the importance of maintaining a normal weight throughout life in survivors with a BMI in the normal range. In particular, the importance of avoiding high-calorie, low-nutrient foods (eg, regular soft drinks, sugary desserts, fried foods) and focusing on lower-calorie, high-nutrient foods (eg, vegetables [especially those lower in starch], broth-based soups, fresh fruit for desserts, and beverages such as water, unsweetened tea, and black coffee) is especially important.

Recommendations for Overweight/Obese Survivors

Survivors with a BMI in the overweight or obese range should be engaged in discussions about nutrition, weight management, and physical activity, as outlined in these guidelines. In addition, clinicians should specifically discuss portion control; substituting high-calorie foods with low-calorie, healthful, nutrient-dense foods; and tracking diet, calories, and physical activity. Clinicians should also refer overweight/obese survivors to a PCP or appropriate hospital-based or community resources. Furthermore, contributing psychosocial factors should be assessed and addressed. Referrals can also be made to a registered dietitian, especially those who are Certified Specialists in Oncology Nutrition (CSO) or members of the Oncology Nutrition Dietetic Practice Group of the Academy of Nutrition and Dietetics. Diet, exercise, and behavioral modification are the cornerstones of weight management; however, in cases of morbid obesity, pharmacologic agents or bariatric surgery can be considered with appropriate referral to primary care and other providers. Of note, the safety and efficacy of weight loss drugs or bariatric surgery in cancer survivors are currently unknown.

Randomized trials have shown that intensive behavioral weight loss interventions can lead to weight loss in overweight/obese cancer survivors.[325-330] For example, the ENERGY trial used a group-based

behavioral intervention with telephone counseling and newsletters and achieved a 6.0% weight loss compared with a 1.5% weight loss in the control group at 12 months.[330] In general, however, these trials see some weight regained in survivors at the end of the intervention; maintenance of weight loss remains a challenge in this population.[325]

Recommendations for Underweight Survivors

Survivors with a BMI in the underweight range should be engaged in discussions about nutrition (see below), and contributing psychosocial factors should be assessed and addressed. In addition, advising underweight survivors to increase their frequency of eating and to avoid fluid intake with meals may help with weight gain. Furthermore, smoking status, dental health, swallowing and taste/smell disorders, and gastrointestinal motility should be assessed and addressed as appropriate. Foods that are both high in calories and nutrient-dense (eg, avocados, nuts) should be encouraged. Consideration can also be given to referral to a registered dietitian for individualized counseling.

Nutrition in Survivors

Systematic reviews and meta-analyses of observational studies have shown that healthy dietary patterns are associated with a decreased risk of primary cancer development and improved subsequent outcomes.[331-334] A population study in England with >65,000 participants found that consumption of ≥7 servings daily of fruit and vegetables reduced cancer incidence by 25% (HR, 0.75; 95% CI, 0.59–0.96).[335] A prospective cohort study that included >40,000 participants also found that a healthy diet is associated with a lower risk for cancer (12%; 95% CI, 8%–16%; $P <$ .0001).[336] In addition, results of randomized trials support the link between a healthful diet and reduced incidence of cancer. For instance, results of a randomized controlled trial, in which 4282 women were randomly assigned to a Mediterranean diet with olive oil, a Mediterranean diet with mixed nuts, or a control low-fat diet, suggest that the olive oil/Mediterranean diet reduced the risk of invasive breast cancer (HR, 0.32; 95% CI, 0.13–0.79).[337] In the Women's Health Initiative (WHI) Dietary Modification trial, nearly 49,000 postmenopausal individuals with a history of breast cancer and with a dietary fat intake of ≥32% of energy were randomized 3:2 to a usual diet group or a dietary intervention group.[338] After an average follow-up of 8.1 years, 655 (0.42%) individuals in the intervention group and 1072 individuals (0.45%) in the comparison group developed invasive breast cancer (HR, 0.91; 95% CI, 0.83–1.01). Furthermore, after a median cumulative follow-up of 19.6 years in the WHI Dietary Modification trial, a significant reduction in deaths after breast cancer that was seen after earlier follow-up persisted (HR, 0.85; 95% CI, 0.74–0.96; P = .01) and a significant reduction in deaths as a result of breast cancer emerged (HR, 0.79; 95% CI, 0.64–0.97; P = .02).[339]

Data also suggest that healthy dietary patterns (as characterized by plant-based diets that have ample amounts of fruits, vegetables, and whole grains, with limited quantities of red and processed meats and refined grains and sugars) are associated with a decrease in cancer recurrence and improved outcomes in survivors.[212,340-342] In survivors of stage III colon cancer, a diet consisting of more fruits, vegetables, whole grains, poultry, and fish, and less red meat, refined grains, and concentrated sweets was found to be associated with an improved outcome in terms of cancer recurrence and death, as well as overall survival.[343] Higher dietary glycemic load (associated with high intakes of refined starches and sugars) was associated with an increased risk of recurrence and mortality in this same population.[344] The link between red and processed meats and mortality in survivors of non-metastatic colorectal cancer has been further supported by recent data from the Cancer Prevention Study II Nutrition Cohort, in which survivors with consistently high intakes of red and processed meat had a higher risk of colorectal cancer-specific mortality than those with low intakes (RR, 1.79; 95% CI, 1.11–2.89).[345] For survivors of non-colorectal cancers, the evidence linking a healthy diet

with better outcomes is less robust. A study of 1901 survivors of early-stage breast cancer found that a diet higher in fruits, vegetables, whole grains, and poultry and lower in red and processed meats and refined grains resulted in a decreased risk of overall death and death from non-breast cancer causes, but was not associated with risk of breast cancer recurrence or death from breast cancer.[346]

Unfortunately, cancer survivors often do not follow recommendations for a healthy diet and, in some studies, show worse patterns than non-cancer controls.[347,348] For example, a national survey of 1533 adult cancer survivors and 3075 matched controls found that cancer survivors had worse dietary patterns.[348] Other studies show that survivors may make improvements to their diet quality post-diagnosis.[349-351]

Recommendations for Nutrition in Survivors

All survivors should be encouraged to make informed choices about food to ensure variety and an adequate nutrient intake. Recommendations for food sources in a healthy diet are included in the guidelines. In general, a healthy diet is rich in plant sources, such as vegetables, fruits, whole grains, legumes, olive or canola oil, avocados, seeds, and nuts. Fish and poultry are recommended, whereas red meats should be limited and processed meats avoided. Other processed foods and foods and beverages with high amounts of added sugars and/or fats should also be limited. Other nutrition recommendations for survivors include eating a diet that is at least 50% plant-based, with the majority of food being vegetables, fruit, and whole grains, and tracking calorie intake. Self-monitoring of caloric intake has been shown to be an effective strategy for weight management.[352,353]

In addition, survivors should be advised to avoid alcohol, or if partaking, limit alcohol intake to one drink per day for a 2000-calorie daily diet and two drinks per day for a 2000-calorie daily diet.[212] This is especially important for survivors of liver, esophageal, kidney, and head and neck cancers, who should refrain from alcohol due to an increased risk of mortality with alcohol consumption.[341,354,355] Survivors of breast cancer do not need to be advised to refrain completely from alcohol consumption, because it has no proven impact on outcomes, but should adhere to general population recommendations.[341,356,357]

Currently, no consensus regarding the role of soy foods in cancer control exists. Several large studies have found no adverse effects on breast cancer recurrence or total mortality related to the intake of soy food.[358-362] In fact, trends towards decreased recurrence and mortality were observed. The panel therefore considers moderate consumption of soy foods (≤3 servings a day) to be prudent.

For patients desiring further recommendations for dietary guidelines, a referral to a dietitian or nutritionist should be considered. The USDA approximate food plate volumes (www.choosemyplate.gov) are:

- Vegetables and fruits should comprise half the volume of food on the plate (30% vegetables; 20% fruit)
- Whole grains should comprise 30% of the plate
- Protein should comprise 20% of the plate

Sources of dietary components:

- Fat: plant sources such as olive or canola oil, avocados, seeds and nuts, and fatty fish
- Carbohydrates: vegetables, fruits, whole grains, and legumes
- Protein: poultry, fish, legumes, low-fat dairy foods, and nuts

The use of healthy recipes, such as those found in resources such as the ACS's "Find Healthy Recipes" website, http://www.cancer.org/healthy/eathealthygetactive/eathealthy/findhealthyrecipes/index, should be encouraged.

Supplement Use in Survivors

Numerous systematic reviews and meta-analyses and a few randomized controlled trials have assessed the role of various vitamins or other dietary supplements for the purposes of primary cancer prevention, cancer control, or preventing cancer recurrence.[363-377] No clear evidence supports an effect of dietary supplements for cancer prevention, control, or recurrence, although a few exceptions may warrant further studies.[378,379] In fact, a prospective cohort study of 2118 postmenopausal cancer survivors found that post-diagnosis dietary supplement use was associated with a trend towards higher mortality among those with a poor diet.[380]

Although the FDA regulates dietary supplement products under the Dietary Supplement Health and Education Act of 1994 (DSHEA),[381] analyses of dietary supplements from multiple manufacturers have found that many products do not contain the purported active ingredient and can contain unlisted ingredients such as cheap fillers (eg, rice, house plants) or banned pharmaceutical ingredients.[382,383] Furthermore, dietary supplements may remain available to consumers even following FDA class I drug recalls.[382]

Despite the lack of data supporting supplement use and the lack of assurance regarding supplement quality, as many as 70% to 85% of survivors take some vitamin or mineral dietary supplements, often without disclosing this information to their physicians.[380,384-386] Thus, the panel recommends that providers ask survivors about supplement use at regular intervals.

The panel notes that supplement use is not recommended for most survivors, except in instances of documented deficiencies (eg, survivors of gastric cancer), inadequate diet, or comorbid indications (eg, osteoporosis,[387] ophthalmologic disorders,[388] cirrhosis[389,390]). Survivors should be advised that taking vitamin supplements does not replace the need for adhering to a healthy diet. If deemed necessary (eg, for survivors taking multiple and/or or unfamiliar supplements), referral to a registered dietitian, especially a CSO, should be considered for guidance in supplement use.

Health Behavioral Change

Lifestyle behaviors are one area survivors can control if they are encouraged to change and are aware of resources to help them. Ambivalence about changing behavior is common in the general population, but among cancer survivors levels of motivation are often heightened, especially close to the time of diagnosis.[205,285,391]

Data suggest that recommendations from the oncologist can carry significant weight for patients with cancer, yet many providers do not discuss healthy lifestyle changes with survivors.[285-287,392] Print materials and telephone counseling are other strategies that may be effective for improving healthy behavior in the survivor population, and several trials show support for these strategies.[289,296,304-307,326,393] In fact, a recent trial showed that telephone-based health behavior coaching had a positive effect on physical activity, diet, and BMI in survivors of colorectal cancer.[305,394] Moreover, results of the recently completed Reach Out to Enhance Wellness (RENEW) trial showed that an intervention of telephone counseling and mailed materials in 641 older, obese, and overweight survivors of breast, prostate, and colorectal cancers not only resulted in improved diet quality, weight loss, and physical activity but also had a long-lasting effect that was sustained a year after the intervention was complete.[289] The Exercise and Nutrition Routine Improving Cancer Health (ENRICH) intervention, which includes 6 theory-based 2-hour sessions, has also shown a positive effect on physical activity, diet, weight, and BMI.[395]

Another strategy, motivational interviewing, may be an effective technique for increasing physical activity and other healthy behaviors in cancer survivors.[302,303] Motivational interviewing focuses on exploring the survivor's thoughts, wants, and feelings and is directed at moving ambivalence so survivors choose to change their behavior.[396] Other behavioral strategies may also be useful, such as improving self-efficacy (ie, the belief that one can perform the actions of new activity and maintain this practice by addressing barriers and planning for behavior change) and self-monitoring.[397,398] Clinicians can consider referral to a provider trained in the techniques of motivational interviewing.

Immunizations and Prevention of Infections

Cancer survivors are at elevated risk for infection because of immune suppression associated with previous cancer treatments, such as chemotherapy, radiation, corticosteroids, certain surgeries, and stem cell transplantation. In fact, antibody titers to vaccine-preventable diseases decrease after anti-cancer treatment.[399,400] In addition, survivors are at increased risk of complications from vaccine-preventable diseases, such as those caused by HPV and influenza viruses.[400,401]

Many infections in survivors can be prevented by the use of vaccines. However, data from the BRFSS found that 42% of survivors did not receive an influenza vaccination in 2009, and 52% reported never receiving a pneumococcal vaccination.[183] Analysis of the SEER-Medicare database showed that survivors of breast cancer, aged ≥65 years, were less likely to receive an influenza vaccination than matched non-cancer controls.[141] A separate analysis of the SEER-Medicare database by another group found similar results.[402]

Vaccines represent a unique challenge in cancer and transplant survivors, because they may or may not trigger the desired protective immune responses due to possible residual immune deficits.[403-405] In addition, certain vaccines, such as those that are live attenuated (eg, zoster [ZVL, MMRV, or VAR]; MMR), are contraindicated in actively immunosuppressed survivors because of an increased risk of developing the disease and/or prolonged shedding of the live organism given in the vaccine.

Risk Assessment and Screening for Immunizations and Prevention of Infections

Survivors are at elevated risk for infections if their cancer treatment included chemotherapy, monoclonal antibodies (eg, rituximab, alemtuzumab), radiation, corticosteroids, splenectomy, CAR T-cell therapy, and/or HCT (which includes peripheral blood stem cell transplantation, bone marrow transplantation, and cord blood transplantation). Risk is also elevated if the survivor has prior or current exposure to endemic infections or epidemics, or has a history of blood transfusion.

Interventions for Prevention of Infections

Infection in survivors can be prevented by education, antimicrobial prophylaxis, and the judicious use of vaccines. For information regarding antimicrobial prophylaxis, please see the NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections (available online at www.NCCN.org).

Education

Survivors should be educated about safe pet care, the avoidance of zoonosis, travel precautions, gardening precautions, proper hand hygiene, and avoidance of respiratory droplets during a respiratory virus pandemic.[406-413] Contact with pets did not increase the risk of fever, bacteremia, pneumonia, and gastroenteritis in children with acute myeloid leukemia (AML),[414] and the panel believes that contact with pets is generally safe for most survivors. However, survivors should wash hands with soap and running water after handling animal feces. If possible,

survivors at high risk for immune suppression should avoid direct contact with animal feces and other bodily secretions. Survivors with elevated risk of infection and those who are immunocompromised are at higher risk for zoonoses and should use extra caution and avoid contact with exotic animals (ie, snakes, turtles). Travel precautions include education on the need for pre-travel vaccines, prophylaxis against specific infections, and education on how to prevent waterborne, airborne, and zoonotic infections.[415] Travelers may find useful information at https://wwwnc.cdc.gov/travel/yellowbook/2018/advising-travelers-with-specific-needs/immunocompromised-travelers or by consulting a travel clinic. Gardening precautions include wearing gloves to avoid cuts and punctures that could be delayed in healing or become infected with fungus or staphylococcus/streptococcus that may be present on thorns, and wearing a protective mask to avoid inhalation of spores.

Immunizations

Vaccination, or "active immunization," involves administration of all or part of a microorganism or a modified product of a microorganism (eg, a toxoid, a purified antigen, an antigen produced by genetic engineering) to produce an immunologic response that mimics that of natural infection but usually presents little or no risk to the recipient. The use of vaccines that do not contain live organisms should be considered and encouraged in all cancer and transplant survivors who have completed immune-suppressive therapy (ie, chemotherapy or antibody-based therapy) at least 3 months prior to the planned vaccination. Patients receiving anti-estrogen or other hormone-modulating therapy do not have to delay vaccination for the completion of therapy. In general, the usual doses and schedules are recommended, as outlined by the Advisory Committee on Immunization Practices (ACIP).[416] The Infectious Diseases Society of America (IDSA) has outlined guidance for vaccination in immunocompromised patients, including those with cancer and those post-HCT.[417] The NCCN Survivorship Panel outlined immunization guidelines specific to survivors of hematologic malignancies and solid tumors, with separate guidelines for survivors who have received cellular therapies (ie, CAR T-cell therapy, HCT). In survivors who received anti–B-cell antibody therapy, vaccination should be delayed for at least 6 months after chemotherapy or the last dose of such therapy to allow for reconstitution of the B-cell population. More details are available in the guidelines.

Before vaccination, immune system viability and history of allergic reactions to vaccines should be assessed. Baseline white blood cell (WBC) counts should be in the normal range or within reasonable limits before starting vaccinations, unless they are elevated because of disease status. The survivor should not be on immunosuppressive drugs or chemotherapy, and ongoing infection should not be present.

The following vaccines should be considered and encouraged for all survivors, and administered according to the usual doses and schedules: influenza vaccine (only inactivated or recombinant); tetanus, diphtheria, pertussis; recombinant zoster vaccine (RZV) in all survivors ≥50 years; and HPV in previously unvaccinated survivors through age 45 years.[416] These vaccines do not contain live organisms; instead, they contain inactivated organisms, purified antigens, bacterial components, or genetically engineered recombinant antigens. Whereas the effectiveness of these vaccinations might be suboptimal because of lingering immune suppression,[405] their administration is likely worthwhile to achieve some protection in the absence of known harm.

Pneumococcal vaccine (PPSV-23/PCV-13) is recommended for all adults aged ≥65 years and those at any age with immunocompromising conditions.[418,419] Pneumococcal vaccination is also recommended for survivors of lung cancer and those who had lung resection. Data from a population-based matched cohort study in Taiwan found that administration of PPSV-23 to ≥5-year survivors of cancer reduced hospitalization for pneumonia.[420] Other vaccines, as listed in the

guidelines, should be considered in consultation with an infectious disease or travel medicine specialist if unique circumstances in the survivor's lifestyle, upcoming travel, functional or anatomic asplenia, or local epidemic/risks merit their use.

Live Viral Vaccines

Vaccines that contain live attenuated organisms (eg, live-attenuated influenza vaccine; MMR; ZVL; VAR; yellow fever vaccine) are contraindicated in actively immunocompromised survivors because of a proven or theoretical increased risk of disease and prolonged shedding of the live organism present in the vaccine. They should not be offered to actively immunocompromised survivors, unless cleared by a clinician experienced in vaccine use or by an infectious disease specialist.

Live viral vaccines can be administered, however, to immunocompetent survivors 3 or more months after chemotherapy or 6 or more months after anti–B-cell antibody therapy, although consultation with an infectious disease specialist or clinician familiar with vaccination in patients with cancer is strongly recommended. Live viral vaccines should not be administered to survivors who had cellular therapies (ie, CAR T-cell therapy, HCT) with active graft-versus-host disease (GVHD) or ongoing immunosuppression. They should only be administered to HCT survivors without active GVHD or ongoing immunosuppression following consultation with an infectious diseases specialist. For all survivors, when other vaccine options exist, they are preferred over live-attenuated vaccines (eg, RZV).

Healthy immunocompetent individuals who live in a household with immunocompromised survivors can receive the following live vaccines with caution: MMR, varicella zoster (VAR, MMRV, or ZVL), yellow fever, rotavirus, and oral typhoid vaccines.[417] Immunocompromised survivors should avoid contact with persons who develop skin lesions after receipt of varicella zoster vaccination until the lesions clear. In addition, immunocompromised survivors should avoid handling diapers of children who have been vaccinated with rotavirus vaccine for 4 weeks after vaccination.

Influenza Vaccines

Annual influenza vaccination is recommended for all cancer and transplant survivors.[421] Live attenuated influenza vaccines should be avoided in some survivors (see *Live Viral Vaccines*, above).[422,423] Therefore, preferred vaccines include inactivated influenza vaccines (ie, trivalent [IIV3] standard-dose, trivalent [IIV3] high-dose, and quadrivalent [IIV4] standard-dose) or recombinant influenza vaccine (ie, trivalent [RIV3] or quadrivalent [RIV4]).[416,422,423] Some evidence suggests that the high-dose IIV3 vaccine may provide better protection than standard-dose IIV3 in individuals 65 years or older.[424] No studies have addressed the superiority of any influenza vaccine in the cancer survivor population specifically. Administration of the influenza vaccine to survivors with egg allergy symptoms (other than hives) should be done at a center that can manage severe allergic reactions, as currently recommended for all individuals.[425]

Zoster (Shingles) Vaccine

A new recombinant zoster vaccine (RZV) has become available in the United States. The recombinant vaccine is the preferred zoster vaccine for cancer survivors, and is recommended for survivors aged ≥50 years.[426] Studies have shown it to be safe and effective in survivor populations.[427,428] In survivors who have previously received the live-attenuated zoster vaccine, immunization with RZV should be considered. The recombinant vaccine should not be given sooner than 2 months after administration of the live attenuated vaccine.

If RZV is unavailable or access to it is an issue, live zoster vaccine can be given as a single dose to survivors aged ≥60 years without active or

ongoing immunodeficiency, no history of cellular immunodeficiency or HCT, and who have not received chemotherapy or radiation within the past 3 months, or it can be given at least 4 weeks before initiation of chemotherapy or immunosuppressive drugs.[417,429] Live zoster vaccine can also be considered for survivors aged 50 to 59 years with a history of varicella zoster virus (VZV) infection or VZV seropositivity with no previous doses of VAR vaccine if the recombinant vaccine is unavailable. Live zoster vaccine should be avoided in immunocompromised survivors, but VAR can be considered in transplant survivors without active GVHD or enhanced immunosuppression 24 or more months after transplantation.

Recommendations for Specific Effects of Cancer and Its Treatment

Randomized controlled trials have provided evidence for the effectiveness of interventions for cancer survivors to lessen symptoms such as depression, fatigue, pain, sleep disorders, and sexual dysfunction.[179] The NCCN Survivorship Panel used such evidence as the basis for the recommendations in these guidelines. When evidence in survivorship populations was lacking, extrapolation from other populations was used as deemed appropriate. The panel also evaluated existing guidelines from other organizations as appropriate when making recommendations. Otherwise, expert opinion and panel consensus was used to form recommendations. These recommendations and their evidence base are discussed below. The panel also notes that referral to other health care disciplines/providers or community resources may be used to address several indications or identified issues with one intervention (eg, rehabilitation for fatigue, depression, and pain).

Cardiovascular Disease Risk Assessment

CVD and cancer are the two leading causes of death in the United States, together accounting for approximately 44% of deaths in 2017.[430] CVD is also a leading cause of death in cancer survivors; for survivors of most cancer types, it is the most common cause of non-cancer death.[431] In fact, survivors of most cancers have a markedly increased risk of developing CVD compared with non-cancer populations.[432-435] One reason for this increased CVD risk in cancer survivors is that cytotoxic, hormonal, and targeted systemic cancer therapies (eg, HER2-directed therapy, VEGF signaling pathway inhibitors, cisplatin, anthracyclines with or without taxanes, androgen deprivation therapy [ADT]) and radiation therapy are associated with cardiovascular toxicities and can result in diverse cardiovascular issues, including cardiomyopathy, hypertension, hyperlipidemia, cardiac arrhythmia, myocardial infarction, and cerebrovascular accidents.[436-444] In addition, shared risk factors for both cancer and CVD likely contribute to the development of CVD and structural heart disease or heart failure in cancer survivors. These risk factors include well-established and well-studied risk factors such as tobacco use, obesity, and poor health behaviors, as well as recently discovered ones. For example, somatic mutations in blood cells cause clonal hematopoiesis of indeterminate potential (CHIP) and increase the risk of hematologic malignancies; CHIP is also emerging to be an important causal risk factor for CVD.[445] Other well-defined CVD risk factors (eg, hypertension, hyperlipidemia, diabetes) are more common in cancer than non-cancer populations.[446,447] Most CVDs (eg, atherosclerosis) develop over time as a result of these and other risk factors. Thus, the risk of CVD-related death varies with years from cancer diagnosis, with most survivors being at greatest risk 5 or more years after diagnosis and completion of curative therapy.[448]

Control of CVD and shared CVD/cancer risk factors can decrease the risk of subsequent cardiovascular events.[448,449] Data show that attention to and counseling about CVD/cancer risk factors may improve cancer- and cardiovascular-related outcomes. [450] However, data also show that fewer than half of cancer survivors discuss diet, exercise, or smoking or other lifestyle changes with their physician.[287,446]

Tools exist to help quantify atherosclerotic CVD risk (eg, ASCVD risk score[451]), but these tools do not take into account cancer treatment history (eg, anthracycline or tyrosine kinase inhibitor [TKI] exposure) and thus may not accurately capture true CVD risk in a given survivor.

The panel recommends that physicians provide CVD risk assessment and counseling on CVD risk factor management to all cancer survivors throughout the survivorship continuum. The assessment should include: 1) pre-existing and emerging CVD including CAD, CHF, peripheral vascular disease, and arrhythmias including atrial fibrillation; 2) CVD risk factors including hypertension, dyslipidemia, obesity, cigarette/tobacco use, and diabetes mellitus; 3) cancer treatment history including systemic therapy regimen and radiation field, including cumulative doses received of applicable cardiotoxic therapies; and 4) diet and exercise habits and cigarette/tobacco use. The counseling should include discussions of any increased risk of CVD the survivor may have based on prior cancer treatment, comorbidity, or CVD risk factors and on the ABCDE's of CVD Prevention. Interventions for modifiable risk factors should be recommended as appropriate. Cooperation and shared care with primary care providers, and with cardiovascular specialists as needed, is key to optimizing cardiac and vascular outcomes in cancer survivors. Referral to cardio-oncology or a cardiology specialist should be considered for cancer survivors deemed to be at high risk for the development of CVD.

The *ABCDEs to Promote Cardiovascular Wellness in Cancer Survivors* table in the Guidelines above was adapted from a paradigm developed to address CVD risk factors in survivors of breast and prostate cancer.[452,453] The table includes items such as aspirin use for secondary prevention (with clinician-survivor discussion required for primary prevention with careful weighing of benefits and risks), blood pressure monitoring/management, cholesterol assessment/management, healthy lifestyle recommendations including diet/weight management and exercise, and an echocardiogram (ECHO) and/or electrocardiogram (ECG) based on individual risk.

Anthracycline-Induced Cardiac Toxicity

Many cancer treatments, including chemotherapeutics, targeted agents, hormonal therapies, and radiation, are associated with cardiovascular toxicities.[436-442] Cardiovascular sequelae can include arrhythmias, pericardial disease, hypertension, thrombosis, cardiomyopathy/heart failure, and vascular and metabolic issues. Survivors of some cancer types have a markedly increased risk of developing CVD compared with non-cancer populations.[432-434] As a result, a new field, called “Cardio-Oncology,” focused on the cardiovascular health of patients with cancer and survivors has become established.[448,454]

Anthracyclines (eg, doxorubicin, epirubicin, daunorubicin) are used to treat many cancer types, including lymphoma, sarcoma, and breast cancer, and are among the best-studied and most common causes of cancer treatment-induced cardiac injury.[455-457] The mechanism by which anthracyclines cause cardiomyopathy is not fully understood, but likely involves the formation of reactive oxygen species (ROS), oxidative injury, and the subsequent induction of apoptosis in cardiac cells.[458] A role for topoisomerase-IIβ in cardiomyocytes in the production of ROS in response to anthracyclines has been suggested.[459]

Studies suggest that the incidence of clinical CHF after anthracycline-based therapy for adult-onset cancer is <5%.[460-463] For instance, in the NSABP B-31 trial of patients with breast cancer, the rates of symptomatic heart failure after 7 years were 4% in patients treated with anthracycline-based chemotherapy and trastuzumab and 1.3% in those treated with anthracycline-based chemotherapy alone.[462] However, a significantly higher percentage of patients have evidence of subclinical heart failure

with reports of asymptomatic left ventricular ejection fraction (LVEF) decline being 9% to 50% in various studies.[460,464-466]

The panel has focused specifically on anthracycline-induced cardiac toxicity in these guidelines. Other systemic therapies (eg, HER2-targeted agents, angiogenesis inhibitors, immunotherapies) may cause cardiomyopathy or other myopathies like myocarditis,[437,467,468] and the panel acknowledges that some of the concepts presented in these recommendations may apply to these other cardiomyopathies. However, it is important to note that fewer data are available on the cardiomyopathies associated with non-anthracycline systemic therapies and that these cardiomyopathies may differ in nature from those induced by anthracyclines.[437] More research is needed to understand the specific mechanisms of cardiomyopathies associated with newer agents. In addition, the panel emphasizes that the approach to cardiomyopathy may be different than the approach to other cardiac diseases such as CAD, which could occur, for example, as a result of radiation therapy.[469]

Panel Considerations Regarding Anthracycline-Induced Cardiac Toxicity

Anthracycline-induced heart failure may take years or decades to manifest. Previous dogma has suggested that anthracycline-induced heart failure portends poor prognosis and is not responsive to therapy. However, emerging data in heart failure due to other types of cardiac injury suggest that signs of cardiac dysfunction can be seen early, prior to the development of symptoms.[470] Additionally, data from these other types of cardiac injury suggest that early intervention with cardioprotective medications results in better long-term cardiac function.[471,472] It is possible that if anthracycline-induced cardiac dysfunction is detected early, it may also be responsive to cardioprotective medications.[437,470-473] In fact, data from a prospective study that followed 2625 patients who received anthracycline-containing therapy through the survivorship phase suggest that early initiation of heart failure therapy may allow for at least partial recovery of LVEF in this population.[464] In this study, survivors were started on treatment when LVEF decreased by >10 absolute points and was <50%. A full recovery was observed in 11% of treated survivors (LVEF increased to the baseline value), and 71% had partial recovery (LVEF increased by >5 absolute points and reached >50%). In addition, a growing body of preclinical, observational, and pilot research suggests that lifestyle changes, such as weight control,[474-476] dietary modification (either through correcting dietary deficiencies or increasing intake of various nutrients),[477] and exercise,[220,221,478-480] may also be helpful at these early stages, prior to the onset of heart failure symptoms, although more research is necessary.[481,482]

These emerging issues in anthracycline-induced cardiomyopathy are consistent with the changes in the cardiology community's approach to heart failure at large. Clinical heart failure has established risk factors, and the earliest signs of heart failure begin with the accumulation of these risk factors over time, ultimately resulting in structural cardiac abnormalities and later symptomatic heart failure. As a result, more than a decade ago, this evolutionary and progressive nature of heart failure was recognized by cardiologists and incorporated into the American Heart Association (AHA)/American College of Cardiology (ACC) Guidelines for the Evaluation and Management of Heart Failure.[483] In 2001, the AHA/ACC guidelines proposed a new classification for heart failure.[483] Traditional classifications only recognized heart failure when patients presented with clinical signs and symptoms. The 2001 classification scheme, in contrast, introduced stages of heart failure beginning before the patient is symptomatic, and emphasized the importance of prevention in heart failure management.

The panel believes that this revised AHA/ACC classification is particularly relevant to cardio-oncology populations. Therefore, in formulating the present recommendations for screening, evaluation, and treatment of

cardiac dysfunction in survivors who received anthracyclines during their cancer treatment, the panel took into consideration the updated AHA/ACC classification and guidelines for management of heart failure. For these NCCN Guidelines for Survivorship, the panel emphasized early recognition of cardiac toxicity with the goal of preventing the development of clinical, symptomatic heart failure by addressing other known risk factors for heart failure. In particular, appropriate use of cardioprotective medications, such as neurohormonal antagonists (ie, angiotensin-converting enzyme [ACE] inhibitors, beta-blockers), can be considered with the goal of preventing cardiac remodeling over time in some patients. In this respect, the panel emphasizes a thorough clinical screen for heart failure for all survivors with exposure to anthracyclines after completion of therapy, with the additional consideration of an echocardiographic screen in high-risk survivors, as discussed in more detail below. The panel also believes that early involvement of a cardio-oncologist or cardiologist in the care of the cancer survivor is important. Therefore, there should be a low threshold for referral to a cardio-oncologist or cardiologist. In addition, symptoms of heart failure may mimic other conditions such as pulmonary issues and/or cardiac ischemia; therefore, a global approach may be necessary when assessing survivors with decreased cardiorespiratory fitness.[484]

Classification of the Stages of Heart Failure

The revised AHA/ACC classification identifies patients who do not have symptoms associated with heart failure but are either at risk for heart failure (Stage A) or have structural abnormalities of the heart (Stage B).[483] This revised classification has both diagnostic and therapeutic utility, because evidence suggests that treatments prescribed in the absence of structural heart abnormalities or symptoms can reduce the morbidity and mortality of heart failure in the general population.[437,464,470-473] Left untreated, however, the accumulation of cardiac risk factors leads to injury or stress on the myocardium and generates a cascade of signaling events in the heart. The subsequent change in the geometry and structure of the left ventricle, often referred to as cardiac remodeling (Stage B), may manifest as cardiac hypertrophy or chamber dilatation. In other cases, the result may be decreased cardiac contractility, which can result in decreased LVEF (also Stage B). Cardiac remodeling generally precedes the development of symptoms (by months or even years), continues after symptoms become evident, and contributes substantially to symptom progression and mortality despite treatment. Individuals are considered to have Stage C heart failure when clinical signs and symptoms accompany structural changes to the heart. Stage D is the most advanced stage, with patients showing advanced structural heart disease and significant heart failure symptoms at rest that are refractory to medical therapy; these patients require specialized interventions.

The panel also considered the New York Heart Association's (NYHA) functional classification of heart failure.[485] In this system, which is based on limitations to physical activity and the effect of physical activity on heart failure symptoms, NYHA Class I is similar to AHA/ACC Stage B, while NYHA Class II and III would be considered AHA/ACC Stage C and NYHA Class IV is similar to AHA/ACC Stage D.

Assessment for Anthracycline-Induced Cardiac Toxicity

The panel recognizes a lack of high-quality data to inform the benefits of screening for heart failure among patients treated with anthracyclines. However, the panel believes that all survivors who have completed anthracycline therapy should undergo a clinical evaluation to assess for signs and symptoms of heart failure. The lack of data is illustrated in a 2007 clinical evidence review by ASCO, which concluded that no studies had systematically addressed the benefits of screening adult cancer survivors with a history of anthracyclines for cardiotoxicity.[486] The review also found no direct evidence showing the effectiveness of cardiac treatment on outcomes of asymptomatic survivors.[486] A 2008

multidisciplinary task force from the Children's Oncology Group came to largely similar conclusions regarding screening for cardiotoxicity in survivors of pediatric cancers.[487] Some reasons for the lack of data on screening survivors for cardiotoxicity have been discussed,[488] and, unfortunately, high-quality data have not been forthcoming since ASCO's 2007 review.

In the absence of data, the Children's Oncology Group relied on the collective clinical experience of its panel members and recommended echocardiograms or comparable imaging to evaluate cardiac anatomy and function for survivors of pediatric cancer at the conclusion of treatment and then every 1 to 5 years for life depending on age at treatment, anthracycline dose, and chest irradiation (http://www.survivorshipguidelines.org). An international collaborative supports lifelong echocardiographic surveillance at least every 5 years in survivors of childhood cancer treated with anthracyclines.[489] Although the frequency of cardiac assessment using echocardiograms or multigated acquisition (MUGA) scans in this population has been a matter of debate, there is general support for at least one assessment in children who have completed anthracycline therapy.[490,491]

A 2014 joint expert consensus statement from the American Society of Echocardiography and the European Association of Cardiovascular Imaging recommends yearly cardiovascular assessment of adult survivors after the completion of potentially cardiotoxic therapy to look for early signs and symptoms of CVD, with cardiac imaging used at the discretion of the clinician.[492] The groups recommend echocardiogram as the preferred imaging modality, when imaging is performed. The report also acknowledged the limited data available to inform their recommendations.

In 2017, ASCO released a clinical practice guideline for the prevention and monitoring of cardiac dysfunction in survivors of adult cancers.[493] The ASCO panel gave a moderate-strength recommendation (as based on evidence and the balance between harms and benefits) that echocardiogram can be performed for asymptomatic survivors deemed to be at increased risk for cardiac dysfunction at 6 to 12 months after treatment, including survivors with a history of anthracycline therapy. Insufficient evidence prevented the ASCO panel from making a recommendation regarding the frequency and duration of additional surveillance of survivors who are asymptomatic and who showed no signs of cardiac dysfunction on initial assessment.

The NCCN Survivorship Panel defined its screening recommendations based largely on consensus and on the idea that early recognition and treatment of cardiotoxicity can allow for earlier interventions that may improve prognosis (discussed below).

Assessment for Symptoms of Heart Failure

According to the 2013 AHA/ACC guidelines, the cardinal manifestations of clinical heart failure (Stage C) include dyspnea and fatigue (which may lead to limited exercise tolerance) or fluid retention (which may lead to pulmonary and peripheral edema).[494] These symptoms can lead to decreased functional capacity and affect quality of life. Heart failure symptoms associated with fluid retention may also include orthopnea or paroxysmal nocturnal dyspnea. Therefore, the panel recommends a history and physical to look for these symptoms to help identify survivors who might already be symptomatic. These survivors should undergo evaluation with an echocardiogram. If no evidence of structural heart disease is seen, then a workup for other causes of the symptoms is warranted with referral to other specialties (eg, pulmonology or cardiology) as needed. Symptomatic survivors with evidence of structural heart disease require immediate referral to a cardio-oncologist or cardiologist.

Assessment of Comorbidities and Cardiovascular Risk Factors

The panel recommends assessment of comorbidities and other traditional risk factors for heart disease (see *Cardiovascular Disease Risk Assessment*, above). Furthermore, the oncologic history of the survivor should be reviewed. Chest radiation can increase the risk of ischemic cardiac disease, which can contribute to heart failure.[436,442,448,495] The addition of other cardiotoxic therapies (eg, HER2-targeted agents) to anthracyclines can further increase the risk of heart failure over that seen with the use of anthracyclines alone.[496] Older survivors, those with a higher cumulative anthracycline dose (cumulative doxorubicin dose of 250 mg/m^2 or equivalent[497]), those with underlying CVD or risk factors, and those who had a low-normal (50%–54%) baseline ejection fraction are also at increased risk for the development of heart failure. Recent data also showed that being overweight or obese and visceral and intramuscular adiposity are risk factors for cardiotoxicity from anthracyclines in breast cancer survivors.[498,499] In addition, the risk of cardiac events and death in survivors of breast cancer has been shown to increase as the number of cardiovascular risk factors increases.[500]

Imaging

When developing these imaging guidelines for screening for cardiac toxicity in survivors with a history of anthracycline exposure, the panel considered several questions: 1) Is the prevalence of structural heart disease high enough to warrant screening of anthracycline-treated survivors?; 2) Is an abnormal echocardiogram post-anthracycline therapy associated with an increased risk for the future development of symptomatic heart failure?; and 3) Does the recognition of cardiac abnormalities and treatment of cardiac risk factors post-anthracycline therapy affect outcomes?

As for the prevalence of structural heart disease in patients treated with anthracyclines, a study of 2625 patients with cancer (mostly breast cancer or non-Hodgkin lymphoma) assessed LVEF before, every 3 months during anthracycline chemotherapy and during the following year, every 6 months for the next 4 years, and annual after that.[464] Cardiotoxicity, defined as LVEF <50% and decreased by >10 absolute points, was observed in 9% of the study population. In the large randomized controlled NSABP B-31 trial, cardiac function was assessed by cardiac imaging in patients after initial anthracycline-based therapy as a requirement for further treatment with trastuzumab.[501] Over 7% of patients experienced cardiac symptoms and/or a decrease in LVEF of >15% after receiving anthracyclines, thus excluding them from being considered for trastuzumab. It is important to note that this was a clinical trial patient population without significant cardiac risk factors or history of cardiac disease. In a non-clinical trial population of patients with cancer, many may already have cardiac risk factors or actual cardiomyopathy prior to treatment, thus elevating the risk of developing heart failure. Together, these results indicate that a significant proportion of survivors with early-onset Stage B or greater heart failure can be identified with appropriate imaging after therapy. However, it is not clear that these declines in LVEF after anthracycline therapy were associated with an increased risk of developing subsequent heart failure.

Regarding the second question, little is known regarding the natural history of heart failure in survivors with Stage B heart failure post-anthracycline therapy, and the long-term prognosis of survivors with cardiac structural abnormalities following anthracycline exposure is not known. However, regarding the final question, limited evidence suggests that further remodeling of the heart may be able to be mitigated by initiation of cardioprotective medications. A number of observational and retrospective studies have suggested that early intervention with cardioprotective medication may decrease the rate of cardiac remodeling and progression to heart failure. A randomized controlled trial of 135 survivors of pediatric cancer with ≥1 cardiac abnormality found that the angiotensin-converting enzyme (ACE) inhibitor enalapril reduced left

ventricular end-systolic wall stress compared to placebo (P = .03).[473] The authors concluded that any theoretical benefit of reduced left ventricular end-systolic wall stress must be weighed against the side effects of treatment; dizziness or hypotension was observed in 22% of the treatment group versus 3% of those receiving placebo (P = .0003), and fatigue was observed in 10% versus 0% (P = .013) of participants. More recently, a review of 247 patients with cancer and declines in LVEF at the Stanford cardiology clinic found that mean LVEF increased after treatment (most often with ACE inhibitors and beta-blockers) and rose to ≥50% in 77% of patients.[472] In addition, a study of 201 adult patients with cancer, who were treated with anthracyclines and had an LVEF of ≤45%, found that earlier initiation of enalapril (and sometimes the beta-blocker carvedilol) was associated with a higher likelihood of LVEF recovery.[470] In addition, in the larger study by this group (2625 patients), heart failure therapy was initiated in all patients with LVEF <50% that had decreased by >10 absolute points, and 82% of patients experienced a full or partial recovery.[464] In the non-cancer setting, a randomized controlled trial of >4200 participants found that treatment of patients with asymptomatic left ventricular dysfunction (ejection fraction ≤35%) with enalapril reduced the incidence of heart failure compared with placebo (20.7% vs. 30.2%; P < .001).[471]

Considering these data, the panel believes that survivors with a high cumulative anthracycline dose (ie, cumulative doxorubicin dose ≥250 mg/m^2 or equivalent) or a low cumulative anthracycline dose and 1 or more heart failure risk factors (ie, hypertension, dyslipidemia, diabetes mellitus, family history of cardiomyopathy, age >65 years, low-normal baseline LVEF [50%–54%], history of other cardiovascular comorbidities [atrial fibrillation, known CAD, baseline evidence of structural heart disease], smoking, obesity) can be considered for assessment for structural heart disease with appropriate cardiac imaging within 12 months of the last anthracycline dose. In one study with a median follow-up of 5.2 years, 98% of cases of cardiotoxicity were observed within the first year after treatment.[464] The prevalence of late-onset cardiotoxicity has not been well studied beyond 5 years, but the panel acknowledges that longer-term cardiovascular surveillance may be needed for survivors of certain cancer types (see the NCCN Guidelines for Treatment of Cancer by Site, at www.NCCN.org, for specific monitoring recommendations).

The panel recommends two-dimensional echocardiogram, coupled with Doppler flow studies, as the cardiac imaging modality of choice when imaging is performed. This technique is widely available and inexpensive, gives no radiation exposure, and is the most useful diagnostic test in the evaluation of patients with possible heart failure.[502,503] It can recognize early stages of heart failure by revealing abnormalities of the pericardium, myocardium, and heart valves.[494] While radionuclide ventriculography (also called radionuclide angiography or MUGA scan) can provide accurate measurements of left ventricular size and function and assessment of ventricular enlargement, it cannot assess valvular abnormalities or cardiac hypertrophy and exposes patients to radiation. Other imaging modalities for the assessment of heart failure have been reviewed elsewhere.[502,504]

In agreement with these guidelines, ASCO's guidelines that address monitoring of cardiac toxicity after treatment in survivors of adult-onset cancer indicate that echocardiogram can be considered for asymptomatic survivors deemed to be at increased risk for cardiac dysfunction, including survivors with a history of anthracycline therapy.[493]

Biomarkers

The panel recognizes the growing body of literature suggesting the possible utility of cardiac biomarkers (specifically troponin) as a non-invasive marker of cardiotoxicity. The panel believes that more prospective, multi-institutional studies are needed, but that biomarker use can be considered in select patients at high risk for heart failure. The

optimal timing of troponin assessment in relation to completion of chemotherapy is currently unclear, the cut-off point for a positive test is undefined, and the optimal assay platform remains to be determined. In addition, the sensitivity and specificity of troponin I levels for predicting cardiotoxicity are fairly low, reported at 48% (95% CI, 0.27–0.69) and 73% (95% CI, 0.59–0.84), respectively.[505] A systematic review of the role of post-treatment cardiac troponins as predictive markers of anthracycline-induced left ventricular dysfunction revealed few studies and inconsistent data.[506] The utility of other potential cardiac biomarkers has been reviewed elsewhere.[504]

Treatment of Anthracycline-Induced Cardiac Toxicity

Progression of heart failure is accelerated with accumulation of risk factors. Injury or stress on the myocardium (such as during and after treatment with anthracyclines) can lead to activation of endogenous neurohormonal systems, which play a critical role in cardiac remodeling and therefore progression to Stage B heart failure.

The panel recommends that heart failure risk factors, including hypertension, obesity, metabolic syndrome, and diabetes, be addressed in all survivors who have completed anthracycline therapy. In addition, survivors with a history of anthracycline therapy should be advised to engage in regular physical activity, eat a healthy diet, and avoid behaviors that may increase the risk of heart failure or CVD (eg, cigarette/tobacco or illicit drug use). Physical activity has been shown to improve control of hypertension and to slow cardiac remodeling in breast cancer survivors with heart failure.[507] Involvement of the survivor's primary care provider in managing risk factors is encouraged.

The panel recommends that a low threshold be established for referral to a cardio-oncologist or cardiologist for all patients previously treated with an anthracycline. Additional recommendations for each stage of heart failure are discussed below.

Treatment of Stage A Heart Failure

Stage A heart failure recognizes several well-established risk factors, each of which contribute to early stages of heart failure. These include hypertension, CAD, diabetes mellitus, a family history of heart failure, or a history of cardiotoxins such as anthracyclines. Therefore, all survivors with exposure to anthracyclines have, by definition, at least one risk factor that predisposes them to cardiac disease and should be treated as appropriate. Other anti-cancer systemic therapies are potentially cardiotoxic and may increase the risk of cardiac disease.[439] Involvement of the survivor's PCP in the management of survivors with cardiac risk factors is encouraged. Management can include addressing underlying risk factors, recommending physical activity and healthy dietary habits, and referral to a cardiologist.

Treatment of Stages B, C, and D Heart Failure

The panel recommends referral to a cardiologist for all survivors with Stages B, C, or D heart failure. The sooner treatment is initiated, the more likely it is to be successful.[470]

Anxiety, Depression, Trauma, and Distress

Cancer survivors are at elevated risk for anxiety, depression, and other forms of psychosocial distress and mental health concerns. A large nationwide matched cohort study in Sweden found that mental health disorders can persist in survivors for as long as 10 years post-diagnosis.[508] Unfortunately, the majority of community-based physicians report insufficient psycho-oncology services and difficulty in the referral process, such that psycho-oncology needs often do not receive the attention they need.[509]

Many cancer survivors do not have psychiatric clinical diagnoses but still have symptoms that can have a negative impact on quality of life and require further evaluation and intervention. Such survivors have what the

NCCN Guidelines for Distress Management (available at www.NCCN.org) define as distress: "a multifactorial unpleasant experience of a psychological (ie, cognitive, behavioral, emotional), social, spiritual, and/or physical nature that may interfere with one's ability to cope effectively with cancer, its physical symptoms, and its treatment." Distress, often related to fear of recurrence, is common in survivors and can negatively impact quality of life.[19,69,510-512] Survivors with untreated, uncontrolled emotional distress are less likely to adhere to recommended surveillance and are less likely to engage in health-promoting activities, such as exercise and smoking cessation.[120] Sometimes these individuals develop thoughts of ending their lives; the incidence of completed suicide among patients with cancer and survivors in the United States is about twice that of the general population.[513-518]

Risk factors for psychosocial distress in cancer survivors include persistent problems with physical health; enduring physical signs of cancer/negative body image; a tendency towards self-criticism; non-white race; low educational, financial, or social support; financial concerns; being unmarried; and having survived multiple primary cancers.[519]

Fear of recurrence, with persisting worry and distress sometimes reaching levels of clinical anxiety, is common, occurring in up to 80% of cancer survivors.[519] This fear can increase at times of routine cancer surveillance testing or with physical symptoms that may or may not be related to the cancer diagnosis.[19,69,510-512,520] Anxiety and/or depression can also occur in survivors secondary to physical compromise, social isolation, or work and financial problems that result from cancer treatment.[66,69,73,512,521] These challenges are accentuated by the usual decreased medical and interpersonal support following completion of treatment and transition to the surveillance phase of care.[179]

Anxiety and/or depression affect up to 29% of survivors.[66,69,74-76,522,523] Studies also show that 17% to 38% of survivors have PTSD symptoms while 5% to 12% meet full criteria, and symptoms do not resolve with time for many survivors.[519] A meta-analysis determined the log odds ratio for a PTSD diagnosis in cancer survivors compared with non-cancer controls to be 1.66 (95% CI, 1.09–2.53).[524] In one longitudinal study, 12% of survivors reported that their PTSD symptoms resolved over 5 years, whereas 37% reported that their symptoms persisted or worsened during that time.[75] Another study found that 22% of survivors had PTSD symptoms at 6 months, and 6% had such symptoms at 4 years.[525] PTSD symptoms in survivors can fluctuate over time, because of other events or trauma occurring in the survivor's life.

The panel's recommendations for the management of anxiety, depression, and distress in survivors adhere to the following general structure: screen regularly, refer those with needs beyond the clinician's scope of expertise, and ensure the safety of the survivor. Referral to mental health services may include a psychiatrist, psychologist, advanced practice clinicians, and/or social worker, or management with oncology or primary care support and online, telephone-based, or community support resources. Therapists with psycho-oncology training are preferred if available; therefore, distance-based methods may be needed for those without resources in their communities.

For additional information regarding anxiety, depression, and distress in patients with cancer, please see the NCCN Guidelines for Distress Management (available at www.NCCN.org). The NCCN Guidelines for Survivorship complement the NCCN Guidelines for Distress Management. These guidelines may be modified to accommodate the individual circumstances of cancer survivors.

Screening for Anxiety, Depression, and Distress

Psychosocial problems are pervasive in survivors and many distressed survivors may not appear distressed. Therefore, all survivors should be screened for anxiety, depression, and distress, especially at times of

disease transition, surveillance, significant loss, major life events, and social isolation. Survivors who present with multiple or repeated somatic complaints should also be screened as part of their overall workup.

The panel lists questions that can be asked of survivors to determine if they have been feeling nervous/anxious or sad/depressed and whether these moods are impacting quality of life. The panel does not recommend use of the NCCN Distress Thermometer (DT) as an initial screening tool in survivors, because studies generally find that it lacks sufficient sensitivity and specificity in this population.[526-533] For example, a study of 120 survivors of adult-onset cancer found that the DT had a sensitivity of 47.6% and 51.7%, using cutoff values of 5 and 4, respectively.[531] The panel therefore recommends supplemental screening when the DT is used as an initial screening tool. Survivors with an elevated level of distress by the DT should still be asked the initial screening questions provided in these guidelines. These more specific questions allow the clinician to determine what particular psychological symptoms are affecting the survivor and may provide more sensitivity and specificity than the DT in identifying distressed survivors who need treatment or additional resources.

Diagnosis of Anxiety, Depression, and Distress

Oncologists and PCPs generally do not feel comfortable diagnosing major psychiatric disorders, nor should they be doing so. Therefore, these guidelines do not specify the full diagnostic criteria for depression, anxiety, PTSD, etc. Instead, the guidelines list the essential criteria for screening psychiatric diagnoses that are most common in survivors and some key symptoms from the Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM-5[534]). The panel's intent is to provide information to facilitate initial steps in providing care and decisions about referrals rather than to provide guidelines for psychiatric diagnosis and extended treatment.

Safety Evaluation

Cancer survivors with anxiety, depression, PTSD, or another psychiatric disorder that is impacting quality of life should undergo a safety evaluation to assess whether they are a danger to themselves or others.[535] Risk factors to assess include previous attempts at suicide or self-injury, a family history or other exposure to suicide, not having a spouse or live-in partner, social isolation, and other factors that suggest difficulty with severe stress. These include perceiving oneself as a burden, recent loss of an important person, a relationship breakdown, chronic illness or recent change in health status, alcohol or other substance abuse, loss of rational thinking, feeling hopelessness or loss of control, financial instability, and access to firearms/weapons or potentially lethal medications (eg, opioids, benzodiazepines [BZDs], antidepressants). Males and those in their late teens or age >55 years are also at elevated safety risk. Medical risk factors should also be assessed, including the presence of a sleep disorder, which has been shown to be associated with an increased risk of suicide.[536]

Protective factors also should be considered to balance against risk factors.[535] Survivors who are married, have child-rearing responsibilities, and/or are employed are less likely to pose a danger to themselves or others. In addition, survivors with strong interpersonal bonds to family or community, who identify reasons for living, or with cultural, spiritual, and religious beliefs about the meaning and value of life are at lower risk. The panel lists additional protective factors in the algorithm above.

Survivors with suicidal or homicidal thoughts or a plan and/or with multiple other risk factors are at an elevated risk of danger to themselves or others. In addition, the inability of the survivor to care for themself may also indicate an elevated safety risk. Survivors judged to be at elevated risk require an emergency intervention that includes arranging to have weapons secured, maintaining direct observation of the individual, and

possibly calling 911, along with following other state mental health emergency plans or referring the person to emergency psychiatric evaluation procedures onsite.

Survivors with intermittent suicidal ideation or thoughts that they might be better off dead, but no plan to harm themselves nor thoughts of endangering others, are at lower safety risk, as are those with fewer risk factors. A safety plan should be developed with these survivors and their families and should include immediate referral for mental health evaluation based on urgency, regular follow-up and monitoring until psychiatric care is in place, and having the survivor agree to contact a health care provider, call 911, or go to an emergency room if suicidal thoughts increase or change. Underlying conditions and risk factors that contribute to suicidal thoughts should be addressed whenever possible.

Management of Anxiety, Depression, and Distress

Survivors with suspected major psychiatric diagnoses, including mania or psychosis, those with an extensive psychiatric history, and those with a moderate to high safety risk should be referred for psychiatric evaluation and treatment. Survivors with substance abuse issues should be referred to a substance abuse specialist. Survivors with moderate- to severe-intensity major depression, generalized anxiety, panic, or PTSD also should be referred for evaluation and treatment by a mental health professional; however, pharmacologic and/or nonpharmacologic treatments, as described below, can also be considered for these survivors.

All treatable contributing factors (eg, pain, sleep disturbance, fatigue, metabolic/endocrine problems, other medical comorbidities) should be addressed. Reassurance can be offered that symptoms of worry, stress, anxiety, and depression are common problems among cancer survivors and that these symptoms can be treated. In addition, support and education should be provided to the survivor and family regarding normal recovery phases after treatment, common stresses, distress, and fears, and strategies for managing uncertainty and distress. Finally, resources need to be provided for social support networks and specific social, emotional, spiritual, intimacy, and practical needs. Additional treatment options are described below.

Nonpharmacologic Treatments

Treatment recommendations for managing depression, anxiety, and distress include a strong recommendation for regular physical activity, which has been shown in clinical trials and meta-analyses to have significant effects in reducing symptoms of anxiety and depression among survivors.[537-539] In fact, evidence suggests that exercise and antidepressants (discussed below) may be equally effective in the treatment of depression.[540]

Psychotherapy, and in particular cognitive behavioral therapy (CBT) and problem-solving therapy, have been shown to be effective at treating depression, anxiety, and PTSD in the general population.[541-546] Therapy, including CBT, has also been shown to be effective at reducing anxiety, depression, and distress in the survivorship population.[179,547-555] One study found that a psychoeducation program that included three telephone-based psychotherapy sessions reduced the severity of fear of recurrence in melanoma survivors.[556] Another study randomly assigned 222 participants to either an attention control or to five face-to-face sessions of a program called ConquerFear, which included attention training, metacognitions, acceptance/mindfulness, screening behavior, and values-based goal setting.[557] Those in the ConquerFear group experienced clinically and statistically greater improvements in total scores immediately post-therapy and 3 and 6 months later on the Fear of Cancer Recurrence Inventory than those in the control group. Greater improvements were also seen immediately post-therapy in symptoms including total cancer-specific distress and general anxiety.

Other alternative treatments (eg, yoga, tai chi, mindfulness) may also be helpful to survivors suffering from distress, although data showing their effectiveness are limited.[558-562] Mindfulness is possibly the best-studied alternative treatment for psychological problems in cancer survivors.[563-567] For example, a randomized controlled trial of 322 survivors of breast cancer found that a 6-week mindfulness-based stress reduction (MBSR) program reduced anxiety and fear of recurrence and also improved fatigue.[567] In non-cancer settings, weight loss interventions have improved depression in obese individuals,[568] although evidence in cancer or survivor populations is lacking.

Pharmacologic Treatments

Cancer survivors use medication for anxiety and depression at a rate about twice that of the general population.[569] A population-based study in Canada found that 44% of cancer survivors were using an anxiolytic, and 22% were using an antidepressant.[570] Antidepressants and antianxiety drugs have been shown to be beneficial for the treatment of depression and anxiety in patients with cancer.[571-578] Evidence of these effects is lacking in cancer survivors, although these drugs have been studied in this population for their effects on vasomotor symptoms (see *Hormone-Related Symptoms*). Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) can therefore be used in survivors with moderate- to severe-intensity major depression, generalized anxiety, panic, or PTSD. SNRIs should be considered for concomitant pain or concomitant hot flashes (also see *Hormone-Related Symptoms*). Psychotropics with cytochrome P450 interactions (ie, fluoxetine, paroxetine, sertraline, bupropion, fluvoxamine, nefazodone, duloxetine, clomipramine) should be used with caution in survivors taking tamoxifen. Pure SSRIs, and in particular paroxetine, block conversion of tamoxifen to active metabolites through CYP2D6 and should be used with caution for patients on tamoxifen (see *Hormone-Related Symptoms* for a discussion of psychotropics and cytochrome P450 interactions).[579-581]

Survivors should be counseled that it may take up to 2 to 6 weeks at a therapeutic dose for SSRIs and SNRIs to take effect, and that a trial of several different drugs may be needed to find the best option for an individual. BZDs (ie, clonazepam, lorazepam) can be used for acute anxiety relief or while waiting for antidepressants to take effect. The BZD dose should be adjusted once SSRIs or SNRIs are fully effective and symptoms are partially or completely abated. Survivors should also be counseled that symptoms of withdrawal may occur should any of the above-mentioned medications be abruptly discontinued. Referral to a mental health professional should be considered if the response to first-line treatment is inadequate.

Cognitive Dysfunction

Cognitive impairment is a common complaint among cancer survivors and may be a consequence of the tumors themselves or of the direct effects of cancer-related treatment (eg, chemotherapy, radiation therapy). This symptom may be especially prominent in survivors of primary central nervous system (CNS) cancers or those with brain metastases, but survivors who never had brain involvement may also report difficulties in cognition.[582] For some survivors, symptoms persist long-term.[583] When severe, the presence of cognitive dysfunction can impact quality of life and function. Cognitive dysfunction is most commonly connected with chemotherapy (sometimes referred to as “chemobrain”), but evidence suggests that therapies other than chemotherapy, such as endocrine therapy, radiation, and surgery may be associated with cognitive impairments.[584-594] A national cross-sectional study found that a history of cancer is independently associated with a 40% increase in the likelihood of self-reported memory problems.[595]

Cancer-related cognitive changes have primarily been studied in patients with CNS cancer, breast cancer, and lymphoma and in those who have undergone hematopoietic stem cell transplant (HSCT), with a reported

incidence ranging widely from 19% to 78%.[583,596-610] In the 2010 LIVESTRONG survey of 3108 post-treatment survivors of a variety of cancer types, approximately 46% of respondents perceived cognitive deficits.[611] In a prospective, longitudinal study of 581 patients with breast cancer treated at several U.S. community oncology clinics and 364 controls, patients reported significantly greater cognitive difficulties than controls before chemotherapy, post-chemotherapy, and after an additional 6 months, with 45% of patients reporting a decline in cognitive function over time compared with 10% of controls.[612]

Growing evidence supports the patient experience of cognitive dysfunction associated with cancer diagnoses and treatments, with deficits commonly occurring in the domains of executive function, learning and memory, attention, and processing speed.[583,609,613-615] In one meta-analysis of 17 studies, individuals previously treated with chemotherapy for breast cancer (n = 807) had lower functional abilities than those not treated with chemotherapy (n = 291).[600] These deficits were limited to verbal (eg, word-finding) and visuospatial (eg, copying complex images) abilities. However, when compared with their pre-chemotherapy baseline, no differences were noted among patients complaining of cognitive dysfunction. In another study, cognitive function was compared among 196 long-term survivors of breast cancer treated with cyclophosphamide, methotrexate, and fluorouracil (CMF) who were, on average, 21 years out from diagnosis, and 1509 control patients with no history of cancer.[616] The chemotherapy group did significantly worse on several neuropsychological tests (eg, immediate and delayed verbal memory, executive functioning, psychomotor speed). Another study compared 101 patients who underwent an HSCT with 82 patients treated with a non-myeloablative therapy; both groups showed mild cognitive impairments at baseline.[617] Although no significant differences in cognitive dysfunction were identified at 2-year follow-up, patients who underwent HSCT had poorer performances in several areas, including executive and psychomotor functions and attention. More recent prospective, longitudinal studies have seen declines in neurocognitive or neuropsychological test results in survivors of head and neck cancer (eg, in intellectual capacity, concentration/short-term attention, verbal memory, executive function) and survivors with a history of hematopoietic cell transplantation (HCT) (eg, in fine motor dexterity, verbal speed, processing speed, auditory memory, executive function).[618,619]

The correlation between patient reports of cognitive decline and results of neuropsychological testing has not been consistently demonstrated, possibly because of various definitions of cognitive dysfunction and differences in the statistical analyses across studies.[609] Other reasons for the weak correlation between perceived and objective cognitive decline have been proposed, including the fact that perceived cognitive decline is influenced by patient expectations whereas expectations do not affect objective assessments and that objective assessments assess cognitive performance under optimal rather than real-life conditions.[620] However, some studies have shown a strong correlation. For example, a study of 189 breast cancer survivors found that memory and executive function complaints, present in approximately 20% of the cohort, showed a statistically significant association with results of domain-specific neuropsychological tests.[621] A study that included 291 participants with stage I–III colorectal cancer before or after surgery and healthy controls found that 45% of patients with cancer had cognitive impairment versus 15% of the control group (odds ratio [OR], 4.51; $P < .001$), with the largest effects seen in complex processing speed, attention/working memory, and verbal learning efficiency.[589] Results of this study suggest that the cancer diagnosis itself and/or the surgical intervention contribute to cognitive dysfunction, because these patients had not received chemotherapy at the time of neurocognitive testing.

The underlying mechanisms that might increase the risk for cancer-related cognitive changes are not known. Studies have reported elevated levels of cytokines or DNA damage as some of the possible mechanisms.[622] Structural studies have supported the hypothesis that neurotoxicity resulting in damage to white matter of the brain may play an important role in cognitive deficits after chemotherapy treatment,[583,586,599,623,624] and functional MRI studies show that changes in brain activity accompany cognitive complaints or cognitive deficits in survivors.[624-626] In addition, insomnia, fatigue, and depression, common in cancer survivors, may negatively influence cognitive function, although several studies have found that cognitive dysfunction does not correlate with mood.[616,627,628] Psychosomatic effects can also contribute, as evidenced by a study of patients to be treated with chemotherapy that found that those who were informed of the possible cognitive side effects were more likely to report cognitive dysfunction and perform worse on neuropsychological testing than uninformed patients.[629] A better understanding of the mechanisms that cause cancer-related cognitive impairment is essential for the development of treatments to improve cognitive function and quality of life in patients with cancer and survivors.[582,630,631]

In October 2006, the International Cognition and Cancer Task Force (ICCTF) was formed, comprising a multidisciplinary group of health professionals and health advocates. The mission of ICCTF is to advance understanding of the impact of cancer and cancer-related treatment on cognitive and behavioral functioning in patients with CNS and non-CNS cancers.[632] The group published recommendations regarding neuropsychological testing, defining cognitive impairment/changes, neuroimaging, and future study design.[631,633]

These NCCN Guidelines address cognitive function of survivors with non-CNS malignancies who did not have CNS-directed therapies.

Assessment and Evaluation for Cognitive Dysfunction

Patients who report cognitive impairment should be screened for potentially reversible factors that may contribute to cognitive impairment, including depression, pain, fatigue, and sleep disturbance. Some medications can also contribute to cognitive impairment. Therefore, current medications, including over-the-counter medications and supplements, should be reviewed.

For those who present with concomitant focal neurologic deficits and those whose symptoms evolve to include these findings, imaging is indicated to rule out structural abnormalities (ie, brain or CNS disease). In addition, imaging in the absence of focal findings may be appropriate for patients deemed to be at high risk for recurrence or metastatic disease involving the CNS.

Unfortunately, no effective brief screening tool for cancer-associated cognitive dysfunction in the asymptomatic cancer survivor currently exists. The Mini-Mental State Examination (MMSE[634]) and similar screening tools lack adequate sensitivity to detect the subtle decline in cognitive performance seen in most cancer survivors. Instead, the panel listed several questions that can help clarify the nature of the impairment, including inquiries about the ability to pay attention, find words, remember things, think clearly, and perform functions. The time of onset of symptoms and the trajectory over time should also be assessed.

Management of Cognitive Dysfunction

Survivors benefit from validation of their symptom experience and should be reassured that, in most survivors, cognitive dysfunction does not worsen over time. In fact, data from breast cancer survivors suggest that symptoms may improve over time.[585] The panel recommends the use of nonpharmacologic interventions whenever possible, with pharmacologic interventions as a last line of therapy in survivors for whom other interventions have been insufficient, as discussed in the following

sections. Additional recommendations for cognitive dysfunction in older adults can be found in the cognitive function section of the NCCN Guidelines for Older Adult Oncology (available at www.NCCN.org).

Nonpharmacologic Interventions for Cognitive Dysfunction

Prospective data to inform the use or potential benefits of non-pharmacologic interventions for cancer survivors who complain of cognitive dysfunction are limited. Practical suggestions include instruction in self-management and coping strategies (eg, using planners, reminder notes, and/or smart phone technology; keeping items in the same place), which the panel believes can be very helpful to patients. Discontinuation or limitation of use of medications known to cause or contribute to cognitive impairment should be attempted. Management of depression/emotional distress, pain, sleep disturbances, and fatigue should be provided. In fact, a study showed that CBT for fatigue was effective at reducing self-reported cognitive disability and concentration problems in 98 severely fatigued cancer survivors randomized to CBT compared with those randomized to a wait list.[635] However, no difference in neuropsychological test performance was observed.

CBT for cognitive dysfunction may also help some survivors. In one small study, CBT was evaluated in 40 breast cancer survivors using a waitlist control trial design.[636] Although overall quality of life improved with the intervention, statistically significant improvement was noted only with verbal memory, not with self-reports of daily cognitive complaints. Another study of CBT delivered by video conference in 47 survivors of breast cancer found that CBT led to improvements in self-reported cognitive impairment and in neuropsychological processing speed compared with supportive therapy.[637]

Routine physical activity should be encouraged. Substantial evidence shows that physical activity enhances cognitive function in elderly people in general, although only few studies specific to cancer survivors have been reported.[638-642] A small randomized controlled trial of an exercise intervention versus control in breast cancer survivors evaluated objective and self-reported cognition.[642] The exercise intervention significantly improved processing speed among those who had been diagnosed within the past 2 years, but no other significant differences were observed.

Cognitive training (ie, brain games) can also be considered. Cognitive training has demonstrated benefits in self-reported and objectively assessed cognitive function, including memory, executive function, and verbal function.[639,643] One study randomized 157 breast cancer survivors to web-based cognitive training with telephone support or to wait-list control.[644] Verbal learning and results on a working memory test showed statistically significant improvement in the cognitive training group, but no improvements were seen for an objective measure of working memory and a measure of perceived cognitive functioning. Another study used a 5-session, small-group intervention of psychoeducation and cognitive exercises in 48 breast cancer survivors.[645] Compared to survivors randomized to a wait-list control group, survivors in the intervention arm experienced improvements in self-reported cognitive complaints and memory functioning on neurocognitive testing. A larger study of 242 survivors with self-reported, persistent cognitive symptoms after chemotherapy for non-CNS cancers found that survivors randomized to a web-based cognitive training program had statistically significant improvements in perceived cognitive impairment immediately and 6 months after the intervention.[646] Improvements in anxiety, depression, fatigue, and stress were also seen after the intervention, which used adaptive exercises that targeted cognitive domains, such as visual precision, working memory, and visual processing speed.

Relaxation, stress management, meditation, and yoga can also be considered. A small pilot randomized controlled trial of 71 fatigued survivors showed that MBSR improved some domains of cognitive

function.[647] A larger study also found improvements in cognitive symptoms after a mindfulness-based approach.[565] Two studies have assessed the effects of yoga on cognition in survivors.[648,649] Both reported improvements in patient-reported cognitive dysfunction.

Neuropsychological evaluation can be therapeutic and validating. Evaluation may also be necessary if an individual is pursuing disability benefits and cognitive impairment is a contributing factor to work limitation. Cognitive rehabilitation, including occupational therapy, speech therapy, and treatment by a neuropsychologist, may also be useful. Occupational therapy strategies focus on improvement of cognitive functioning and may be most effective for individuals who note the impact of specific functional limitations, such as word finding, comprehension, and task completion, on work performance, quality of life, or role expectations.[650] Psychotherapy is another option.

Pharmacologic Interventions for Cognitive Dysfunction

If nonpharmacologic interventions have been insufficient, consideration of a trial of medications such as methylphenidate, modafinil, or donepezil is reasonable in select survivors or certain clinical scenarios, although data informing the efficacy of these agents are lacking. Trials assessing the effects of the psychostimulant methylphenidate have reported mixed results.[651] For example, a randomized, placebo-controlled, double-blind trial found that d-methylphenidate had no effect on neuropsychological test scores.[652] In contrast, a randomized, double-blind, crossover trial of child survivors of acute lymphoblastic leukemia (ALL) or brain tumors showed that methylphenidate was more effective than placebo at improving attention, cognitive flexibility, and processing speed.[653]

Results of studies on modafinil, another psychostimulant, are more consistent. A randomized controlled trial assessing the efficacy of modafinil for fatigue and cognitive function in breast cancer survivors found significantly greater improvement in memory and attention among patients receiving modafinil than in the placebo group.[654] Similarly, a double-blind, randomized, crossover trial also in breast cancer survivors found that participants receiving modafinil performed significantly better on cognitive tests of attention and psychomotor speed.[655] Benefits with treatment were also noted among patients with primary brain tumors.[656]

Donepezil is an acetylcholinesterase inhibitor used to treat patients with Alzheimer's disease. It has been studied for its effects on cognitive impairments after the treatment of brain tumors, with modest improvements seen in attention/concentration, memory, and motor speed and dexterity.[657,658] Donepezil was also studied in a randomized trial of 62 breast cancer survivors who had received adjuvant chemotherapy.[659] Although there were no differences in subjective cognitive function, the donepezil group showed improved memory on objective tests. Further work is needed before concrete recommendations for pharmacologic therapy in survivor populations can be made.

Fatigue

Note: The Discussion text regarding fatigue in survivors has been adapted from the NCCN Guidelines for Cancer-Related Fatigue (available at www.NCCN.org).

NCCN defines cancer-related fatigue as "a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning."[660] Fatigue is a common symptom in patients with cancer and is nearly universal in those receiving cytotoxic chemotherapy, radiation therapy, bone marrow transplantation, or treatment with biological response modifiers.[661-663] According to a survey of 1569 patients with cancer, the symptom is experienced by 80% of individuals who receive chemotherapy and/or radiotherapy.[664,665] Cancer survivors report that fatigue continues to be a

disruptive symptom after treatment ends,[666-674] with studies showing that 17% to 29% of cancer survivors experience persistent fatigue for years after the completion of active therapy.[675-677] In fact, a study of 6011 long-term cancer survivors found that 39% to 51% (depending on tumor type) were classified as fatigued after completion of the Fatigue Assessment Scale compared with 21% of a representative normal population.[678]

Persistent cancer-related fatigue affects quality of life, because individuals become too tired to fully participate in the roles and activities that make life meaningful.[668,679] In fact, severe fatigue in survivors of Hodgkin lymphoma is associated with a decreased likelihood of employment.[680] Disability-related issues are also relevant for cancer survivors, because obtaining or retaining disability benefits from insurers is often difficult for patients with cancer-related fatigue. Identification and management of fatigue remain an unmet need for many cancer survivors.

The specific mechanisms involved in the pathophysiology of cancer-related fatigue are unknown. Proposed mechanisms include pro-inflammatory cytokines, hypothalamic-pituitary-adrenal (HPA) axis dysregulation, circadian rhythm desynchronization, skeletal muscle wasting, and genetic dysregulation.[681-686] Several studies have focused on the cause of fatigue, especially in cancer survivors with no evidence of active disease, and have suggested that persistent immune system activation and chronic inflammatory processes may be involved.[666,687-689] Evidence supporting these mechanisms is limited.

Screening for Fatigue

All survivors should be screened for fatigue to ensure that those with moderate to severe fatigue are identified and treated promptly and effectively. Because fatigue is a subjective experience, clinicians must rely on patients' descriptions of their fatigue level. The panel recommends the use of a severity scale, with survivors being asked, "How would you rate your fatigue on a scale of 0 to 10 over the past 7 days?" Alternatively, screening can be performed with patients asked to rate their fatigue as none, mild, moderate, or severe. Scores of 0 to 3 or none to mild fatigue require no further assessment or interventions; these patients should be rescreened at regular intervals. Patients with scores of 4 or greater or indicating moderate or severe fatigue should be evaluated further. Studies in patients with cancer have revealed a marked decrease in physical functioning at a reported fatigue level of 7 or higher on the 0 to 10 scale.[690,691]

Evaluation for Moderate to Severe Fatigue

When fatigue is rated as moderate to severe, with a score of 4 to 10, a more focused history and physical examination should be conducted. A thorough history is warranted, because the recommended workup for fatigue differs according to the timing of fatigue onset in relation to the completion of active therapy and the presence of predisposing factors and other symptoms. Fatigue has a variable natural history, with some patients complaining of only mild levels of fatigue even during active therapy and others experiencing severe fatigue for years after treatment completion.

In general, mild to moderate levels of fatigue that persist for 6 to 12 months after the completion of therapy do not warrant an extensive workup, unless other symptoms are present. Conversely, when moderate to severe fatigue begins after or worsens during this period, or when other symptoms are present, such as pain, pulmonary complaints, or unintentional weight loss, a more extensive workup is warranted to screen for the presence of metastatic disease or other comorbidities. Referral to a pulmonologist should be made for pulmonary complaints.

Regardless of fatigue onset, it is always relevant to screen for common contributing factors such as emotional distress, sleep disturbance, pain, and the use of prescriptions or over-the-counter medications or supplements. Possible medical causes of fatigue, including cardiac disease, gastrointestinal or hepatic dysfunction, and hypothyroidism,

should also be assessed. Disease and treatment considerations also affect recommendations for screening, such as the inclusion of echocardiograms for patients who received cardiotoxic treatments and thyroid screening for patients who received radiation to the neck or thorax or agents such as immunotherapies or small molecule TKIs.

Management of Fatigue

Several interventions and strategies have been shown to help alleviate fatigue and reduce distress caused by this symptom in patients with cancer and survivors; recommended strategies and interventions are described herein. For additional information about fatigue in survivors and patients with cancer, please see the NCCN Guidelines for Cancer-Related Fatigue (available at www.NCCN.org). These guidelines may be modified to fit the individual survivor's circumstances.

Treatment of Contributing Factors

Management of fatigue in survivors first includes the treatment of contributing factors such as pain, distress, anemia, and sleep disturbances (more information on the treatment of pain, anxiety/depression, and sleep disorders in survivors can be found throughout these guidelines). In a randomized controlled trial of 152 fatigued patients with advanced cancer, treatment of accompanying physical symptoms, including pain, nausea, vomiting, and shortness of breath, resulted in a significantly higher impact on general fatigue, activity, and motivation than usual care.[692]

Patient and Family Education and Counseling

Education and counseling can be beneficial in helping patients cope with fatigue. Understanding typical patterns of fatigue during and after treatment can help patients set reasonable expectations regarding improvements in energy after the completion of cancer therapy and can help allay concerns that persistent fatigue after the completion of therapy is evidence of disease recurrence. Counseling can help patients develop strategies for self-monitoring of fatigue and techniques such as energy conservation that may be helpful in the immediate post-treatment period.[693]

Physical Activity

Activity enhancement is a category 1 recommendation for the management of fatigue in survivors. Improving strength, energy, and fitness through regular exercise, even a moderate-intensity walking program, has been shown to facilitate the transition from patient to survivor, decrease anxiety and depression, improve body image, and increase tolerance for physical activity. Therefore, survivors with moderate to severe fatigue should be encouraged to maintain adequate levels of physical activity (category 1). Robust data support the efficacy of increased physical activity for reducing fatigue in patients with cancer and survivors.[204,210,215,217,219,560,694-700] Multiple meta-analyses of randomized controlled trials have found that cancer survivors who participate in exercise interventions, either during or after treatment for cancer, experience significant improvements in fatigue compared with patients randomized to the control group.[204,700-703] A randomized phase 3 trial that included 410 cancer survivors showed that a 4-week yoga therapy program led to improvements in fatigue and sleep quality and reductions in daytime dysfunction.[704]

Survivors at a higher risk of injury should be referred to a physical therapist or exercise specialist (also see *Healthy Lifestyles*, above).

Psychosocial and Other Interventions

Psychosocial interventions, such as CBT, MBSR, psycho-educational therapy, and supportive expressive therapy, including support groups, counseling, and journal writing (all category 1 recommendations), have also been shown to reduce fatigue in cancer survivors, although data are not entirely consistent.[567,705-710] Several meta-analyses have evaluated the role of psychosocial interventions in reducing fatigue.[700,705,709,711] For

example, Kangas et al[709] reported a weighted pooled mean effect of −0.31 for psychosocial interventions on fatigue in an analysis of 3620 patients with cancer from 41 studies. Jacobsen et al[711] analyzed 30 randomized controlled trials and found a significant effect size (dw) for psychological interventions (dw, 0.10; 95% CI, 0.02–0.18) but not for activity-based programs (dw, 0.05; 95% CI, −0.08–0.19). A meta-analysis by Duijts et al[705] reported that, like exercise programs, behavioral techniques, including CBT, relaxation techniques, counseling, social support, hypnosis, and biofeedback, are beneficial in improving fatigue among patients with breast cancer during and after treatment (standardized mean difference [SMD], −0.16).

Several published studies support the conclusion that CBT interventions designed to optimize sleep quality (CBT for insomnia; CBT-I) in patients with cancer may also improve fatigue.[712-716] Two randomized clinical trials of patients who reported chronic insomnia in the survivorship phase demonstrated improvements in both sleep and fatigue after 4 to 5 weekly behavioral therapy sessions.[706,707,717] Two smaller studies of patients with current complaints of insomnia in the survivorship phase reported improved sleep and fatigue.[712,715] Two other studies found positive benefits of a behavioral intervention on sleep and fatigue that were not sustained over time.[716,718] The American Academy of Sleep Medicine (AASM) has recommended three specific therapies for the initial approach to chronic insomnia in healthy individuals: relaxation therapy, CBT-I, and stimulus control therapy.[719]

Acupuncture and acupressure have been studied for the treatment of fatigue in patients with cancer and survivors.[720-727] A pilot study in 30 breast cancer survivors found that acupuncture resulted in a significant reduction in fatigue after 2 weeks.[725] In addition, a phase 3 randomized, single-blind clinical trial in 424 breast cancer survivors found that self-administered relaxing acupressure reduced persistent fatigue and improved sleep quality and quality of life.[727] Although results of studies are mixed and many compared acupuncture to usual care rather than sham acupuncture or another active comparator, the panel believes acupuncture is an acceptable option that may improve symptoms for survivors with moderate to severe fatigue.

Pharmacologic Interventions

Psychostimulants, such as methylphenidate, are also used to treat fatigue, although data regarding their use to treat fatigue in cancer survivors are very limited. A 54% response rate to methylphenidate was reported in a phase II trial of 37 breast cancer survivors.[728] A randomized trial in 154 patients post-chemotherapy also found an improvement in fatigue symptoms in the dexmethylphenidate arm.[729] A recent meta-analysis of five randomized controlled trials of patients with cancer found limited evidence for the efficacy of 4 or more weeks of methylphenidate treatment for cancer-related fatigue (mean difference, −3.70; 95% CI, −7.03 to −0.37; P = .03).[730] However, another meta-analysis identified seven trials of methylphenidate and concluded that it was superior to placebo for the treatment of cancer-related fatigue.[731] A Cochrane review found that methylphenidate was likely effective for cancer-related fatigue and warrants further study.[732] However, a second comprehensive meta-analysis did not support this finding, nor did it support the use of pharmacologic interventions for the treatment of cancer-related fatigue.[700]

Other drugs, including modafinil, have also been studied for post-treatment fatigue.[733,734] In particular, a large phase III trial of 631 patients receiving chemotherapy suggested that modafinil is beneficial in patients with severe fatigue.[734] However, a placebo-controlled, double-blind, randomized controlled trial in 208 patients with non-small cell lung cancer (NSCLC) showed no effect of modafinil on cancer-related fatigue.[735] In addition, a meta-analysis identified three studies evaluating modafinil for fatigue in patients with cancer and found that the drug was not better than

placebo.[731] Recommendations for modafinil have therefore been removed from both the NCCN Guidelines for Cancer-Related Fatigue and the NCCN Guidelines for Survivorship. Both guidelines continue to recommend that methylphenidate may be considered after ruling out other causes of fatigue and failure of other interventions, although they acknowledge the limited data supporting the use of this agent in this setting, especially in cancer survivors.

Small pilot studies and one recent randomized controlled trial have evaluated the impact of supplements, including ginseng and vitamin D, for cancer-related fatigue.[736] The evidence to date is inconsistent, and the panel currently does not recommend the use of supplements for the treatment of fatigue.

Lymphedema

Lymphedema is a common side effect of cancer treatment, occurring on the same side of the body as the cancer treatment, resulting from damage to the lymphatic system. It occurs when lymph fluid accumulates in the interstitial tissue, causing swelling of the limb or other areas such as the neck, trunk, or genitals. Lymphedema is most often diagnosed within 18 months of treatment; however, it can develop any time in the life of the survivor.

More than 20% of cancer survivors reported lymphedema as a physical concern in a survey of almost 14 million survivors in the United States in a 2010 LIVESTRONG study.[23] The incidence of lymphedema varies by disease site. In one study, 41% of almost 1000 breast cancer survivors developed lymphedema by 10-year follow-up.[737] In a study of survivors of gynecologic cancers, the incidence of lymphedema in one or both legs 2 years after surgery was 37%.[738] In one study of 431 survivors of melanoma who had been treated with complete lymph node dissection and/or wide local excision and axillary or inguinal sentinel lymph node surgery, the reported incidence of lymphedema was 25%.[739]

Lymphedema may cause or exacerbate psychological distress.[740,741] In a study that included 692 breast cancer survivors with lymphedema, almost half reported moderate to extreme distress related to their lymphedema.[742] Lymphedema can also affect social roles, employment, medical expenses, physical function, and quality of life and can cause disability.[743-746] Unfortunately, only 55% of cancer survivors with self-reported lymphedema in the LIVESTRONG study said that they received care for lymphedema.[23]

Risk Factors for Lymphedema

Survivors whose cancer treatment included surgery and/or radiation to the axillary, supraclavicular, cervical, or inguinal lymph node system are at risk for the development of lymphedema.[747-750] Sentinel lymph node biopsy also appears to increase the risk of lymphedema, although it poses less risk than complete dissection or radiation to the nodal group, and data are not completely consistent.[748,751-755] Other treatment-related factors that have been associated with an increased risk of lymphedema are receipt of chemotherapy or radiation and the extent of lymph node dissection.[737,738,747-750,753,755-757] Overweight (BMI ≥25 kg/m^2) and obesity (BMI ≥30 kg/m^2), localized infection, and higher initial stage of disease also raise the risk of lymphedema development.[737,738,747,748,750,755,757-759]

Assessment and Workup for Lymphedema

Survivors with a history of radiation or surgery to the lymph nodes should be asked about swelling or feelings of heaviness, fatigue, or fullness at each visit. Early detection and diagnosis are key for optimal lymphedema management, because stages 0 and 1 are reversible, whereas stages 2 and 3 are less responsive to treatment (see *Definition and Stages of Lymphedema* in the algorithm). Swelling on the same side as the cancer treatment is a universal symptom of lymphedema. Additional initial

symptoms may include pain or discomfort and/or sensations of heaviness, fatigue, fullness, and/or tightness in the skin. Symptoms including decreased range of motion or strength and thickening of the skin may occur in later stages. If symptoms are present, survivors should be asked about the frequency and severity of swelling, pain and/or discomfort, any issues with strength or range of motion and mobility (ie, bending, stretching, flexibility), and whether symptoms interfere with daily activities.

If lymphedema symptoms are present, a recurrence of cancer should be ruled out. The survivor should then be referred to a certified lymphedema therapist, if available, for additional assessments. These assessments can include subjective signs and symptoms of lymphedema and limb volume measurements. Ideally, pretreatment limb measurement of both sides should be performed as a baseline prior to initiation of any therapy for those with treatment-related or individual risk factors. If not, the contralateral limb can be used for comparison in the post-treatment setting. Clinical examination by a lymphedema therapist may include range of motion, muscle performance, circulation, sensation, hemodynamic monitoring, and functional mobility.

Survivors with lymphedema should also be assessed for distress (see *Anxiety, Depression, Trauma, and Distress*, above).

Treatment of Lymphedema

High-level evidence supporting treatments for lymphedema are lacking, and most studies have been performed in breast cancer survivors.[31,760-762] Most of the recommendations made by the panel are thus based on lower-level evidence, clinical experience, and expert consensus.

The oncology team should provide education regarding self-care management, including infection prevention measures, risk-reduction strategies, and maintenance of skin integrity on the affected side (see *Survivor Lymphedema Education*, below). Distress should be treated if present (see *Anxiety, Depression, Trauma, and Distress*, above). Referral should be made to a certified lymphedema therapist, if available, for prescription and fitting of compression garments, performance of manual lymphatic drainage, and direction of supervised progressive strength training. If a certified lymphedema therapist is not available, referral to an appropriate alternative provider for treatment should be considered.

Compression garments have been shown to reduce limb volume, and are often used with other modalities such as manual lymphatic drainage.[762-764] Manual lymphatic drainage is performed by a specific massage technique designed to encourage lymph fluid to drain from the affected area. Systematic reviews and meta-analyses have assessed the efficacy of manual lymphatic drainage in breast cancer survivors with lymphedema and found that it can provide additional benefit when added to standard therapy.[765,766] In particular, compression bandaging alone leads to limb volume reductions of 30% to 39%, and manual lymphatic drainage appears to increase that reduction by an additional 7%.

Progressive strength training and physical activity are not associated with exacerbation or development of lymphedema, and may improve lymphedema symptoms.[214,255-259,767-770] The WISER Survivor trial randomized 351 overweight breast cancer survivors with lymphedema to a control group that received hospital-based care, a home-based exercise intervention group, a home-based weight loss intervention group, or a combined home-based exercise/weight loss group.[771] Although the groups that included a weight-loss intervention experienced about a 7% to 8% weight loss, no group experienced improvements in breast cancer-related lymphedema outcomes. This result suggests that home-based interventions may not be effective for treatment of lymphedema in cancer survivors.

Progressive strength under supervision is recommended for survivors with lymphedema. However, caution is advised in this population,[260] and

survivors with or at risk for lymphedema should consider discussing physical activity plans with a lymphedema specialist before starting a program that involves strength training. Survivors with lymphedema should work with trained exercise professionals with knowledge of cancer-related physical activity principles and initiate strength training exercise involving the affected body part only if lymphedema is stable (eg, no need for lymphedema therapy within the past 3 months, no recent limb infections requiring antibiotics, no change in limb circumference >10%, no change in the ability to perform activities of daily living). Survivors should undergo baseline and periodic evaluation for development or exacerbation of lymphedema and should stop exercise and see a lymphedema specialist if exacerbation of lymphedema occurs. Weights should be slowly progressed as tolerated, and lymphedema should be evaluated periodically. Compression garments may be required during training sessions.

The National Lymphedema Network has published a position statement with additional guidance for exercise in individuals with lymphedema.[768]

Survivor Lymphedema Education

Early detection and diagnosis is key for optimal lymphedema management because earlier stages are reversible. Therefore, survivors should be educated about the signs and symptoms of lymphedema and the importance of rapid reporting to the treatment team. Survivors should be told to inform their medical provider if subtle swelling or any other symptoms (eg, fullness, tightness, heaviness, pain) on the treated side are noted.

Survivors at risk for lymphedema and those with lymphedema are at a higher risk of localized infection in the affected area. These infections can require hospitalization for IV antibiotics. Therefore, survivors with or at risk for lymphedema should be educated to inform their medical provider immediately of signs of infection in the affected area. Risk of infections can be reduced by safe pet care and gardening techniques (See *Immunizations and Prevention of Infections*, above). Survivors should also be educated on how to maintain skin integrity with meticulous skin care of the affected area that includes avoidance of cuts, burns, skin irritants and allergens, insect bites, and pet scratches.[772,773] The use of moisturizing soaps and over-the-counter, fragrance-free emollients may also be helpful.[773]

Observational studies have demonstrated that air travel, venipuncture, and blood pressure measurement (via arm cuff) are not associated with exacerbation or development of lymphedema, and precautionary measures are likely unnecessary.[747,749,758,759,774-777] For instance, in one study of 632 patients with breast cancer prospectively screened for lymphedema with 3041 arm volume measurements, no association was found between the development of lymphedema and blood draws, injections, or air travel.[759] In the absence of high-level data, however, the panel recommends that medical procedures such as venipuncture and blood pressure measurements be done on the non–at-risk arm/limb if possible.[778] If necessary, procedures may be done using the at-risk arm/limb. More research is needed to determine the effect of these procedures on the risk of lymphedema.

Survivors should be informed that lymphedema is not a contraindication for physical activity and that no special precautions are required for cardiovascular/aerobic exercise or strength training of unaffected limbs.[255-260] In addition, continued full use of the involved extremity and range-of-motion exercises should be encouraged to maintain strength and range of motion even in the presence of lymphedema. Progressive strength training under supervision is recommended for patients with lymphedema, as discussed above (see *Treatment of Lymphedema*). Exercise and physical therapy may also help prevent lymphedema symptoms. In the randomized controlled Lymphedema Education and Prevention study (CALGB 70305),

patients randomized to the education plus exercise arm self-reported greater range of motion at 12 months after lymph node dissection (a pre-specified secondary outcome) compared with patients in the education only arm (left, 91% vs. 84%; *P* = .16; right, 90% vs. 83%; *P* = .02).[779] Finally, survivors can be informed that water exercise under supervision may be an option to consider in the absence of any skin integrity and/or incision issues.[780] In a controlled clinical intervention study, 88 patients with lymphedema secondary to cancer participated in either a water-based or land-based exercise program.[780] A higher proportion of those who performed water exercises experienced a reduction in their secondary arm limb volume (*P* = .029) and self-reported frequency of swelling (*P* = .031).

Surveillance of Survivors with Lymphedema

Survivors with lymphedema should have follow-up with the treatment team as clinically indicated. Clinicians should check range of motion, inquire about the fit and age of compression garments, replace compression garments if needed, and inquire about the performance of prescribed exercises and self-care management. Assessment for distress should also be performed as part of routine surveillance.

Hormone-Related Symptoms

Sexual function and management of hormone-related symptoms are important aspects of quality of life for all cancer survivors. The recommendations here are intended for cisgender survivors based on the availability of data in this population, but should be followed for transgender and intersex survivors as applicable, with the involvement of the appropriate health care specialists.

Hormonal symptoms in cancer survivors have been most extensively studied in female survivors after treatment of breast cancer. Hot flashes are reported to occur in about 46% to 73% of breast cancer survivors.[781-784] In one study of breast cancer survivors diagnosed at age 40 years or younger, 46% of participants reported hot flashes, 51% reported vaginal dryness, and 39% reported dyspareunia.[784] Similarly, about 50% to 80% of patients on ADT experience hot flashes, which can persist after treatment.[785-790] The incidence of gynecomastia in patients on ADT varies with the method of ADT used and can be as high as 80% in those on estrogen therapy.[787,791]

The NCCN Guidelines for Survivorship define menopause as no menses for one year in the absence of prior chemotherapy or tamoxifen use or no menses after surgical removal of all ovarian tissue. Healthy individuals reach menopause at a mean age of 51 years, with 95% reaching menopause between 45 and 55 years of age.[792] Many cancer survivors experience menopausal symptoms without meeting the definition of menopause, including female survivors on tamoxifen or aromatase inhibitors or with a history of oophorectomy or chemotherapy and male survivors who received or are receiving androgen ablative therapies (ie, ADT). These symptoms can include hot flashes/night sweats, vaginal dryness, urinary complaints, sexual dysfunction, sleep disturbance, mood disturbance, depression, cognitive dysfunction, arthralgias/myalgias, and fatigue. Hormonal symptoms can occur in patients of all genders. Individuals assigned male at birth may experience many of the same symptoms as those assigned female at birth, as well as gynecomastia, decreased testicle size, and thinning of body hair. Hormonal symptoms can have a profound impact on quality of life.[783,793]

Premenopausal cancer survivors who have received chemotherapy may experience transient or permanent menopause, dependent on the age of the patient and the type of chemotherapy.[794-796] If appropriate and desired, referral for fertility preservation should be considered before chemotherapy, because studies report that 33% to 73% of premenopausal patients treated for breast cancer become peri- or postmenopausal after treatment.[783] Younger survivors with irregular menses may have primary

ovarian insufficiency and may develop menopausal symptoms.[797] These patients may or may not be fertile, and should be counseled about the possibility of pregnancy despite amenorrhea if they are sexually active and do not meet the definition of menopause. In non-cancer populations, primary ovarian insufficiency or early menopause may be associated with specific menopause-related health risks. However, there are limited data in cancer survivors.

Assessment and Evaluation for Hormonal Symptoms

Survivors with hormonal symptoms disruptive to quality of life should be assessed and treated for medical causes of hormonal symptoms such as thyroid disease and diabetes. Lab evaluation includes estradiol, follicle-stimulating hormone (FSH), luteinizing hormone (LH), and prolactin, as clinically indicated. For peri- or pre-menopausal female survivors who have become amenorrheic and later develop bleeding, serial estradiol levels can be useful to determine return of ovarian function. Other markers including FSH, anti-Müllerian hormone (AMH), and inhibin may provide additional information on ovarian status in female cancer survivors with prior chemotherapy or pelvic radiation exposure or those on tamoxifen, but alone are not reliable to ensure menopausal status.[798,799] In male survivors, morning total testosterone and free testosterone may also be checked if hypogonadism is suspected.[800] For survivors with complaints of vaginal dryness, a pelvic evaluation should be done to assess for vaginal atrophy and can be accomplished by referral to an appropriate specialist.

Management of Hormonal Symptoms in Female Survivors

Management of sexual dysfunction, lack of sexual desire, sleep disturbance, mood disturbance, depression, cognitive dysfunction, fatigue, and arthralgias/myalgias is described in other sections of these guidelines. Management of hot flashes, vaginal dryness, and urogenital complaints associated with menopause are described herein. The panel prefers the use of non-hormonal options as first-line therapy for female survivors with hormonal symptoms disruptive to quality of life, but hormonal therapies can also be used after consideration of the risks and benefits to an individual survivor.

Non-Hormonal Pharmacologic Treatment of Hot Flashes

For the management of hot flashes, non-hormonal pharmacologic options include antidepressants, anti-convulsants, neuropathic pain relievers, and certain anti-hypertensives.[801-804] When antidepressants are used, a lower dose than typically given for depression is often effective to treat hot flashes.

SSRIs and SNRIs have been shown to improve vasomotor symptoms in the general population, although the degree of symptom reduction may be smaller than with hormonal treatments.[805-807] A randomized clinical trial in healthy postmenopausal individuals showed that low-dose paroxetine reduces the frequency and severity of hot flashes.[807] Small studies have shown that SSRIs and SNRIs also reduce the severity and frequency of hot flashes in female cancer and survivor populations.[808-817] One of these studies was a randomized, double-blind, placebo-controlled study in 80 survivors of gynecologic cancers.[809] Results showed that 7.5 mg daily of paroxetine reduced the frequency and severity of vasomotor symptoms and the number of resultant nighttime awakenings. However, pure SSRIs, and in particular paroxetine, should be used with caution in survivors on tamoxifen, because these drugs block the conversion of tamoxifen to active metabolites through inhibition of cytochrome P450 2D6 (CYP2D6).[580,818] However, an analysis of a large database that included almost 17,000 breast cancer survivors found no evidence of an increase in cancer recurrence in those on concurrent tamoxifen and antidepressants, including SSRIs such as paroxetine.[579] In contrast, a study of 2430 breast cancer survivors found an increased risk of cancer death in those taking tamoxifen and an SSRI.[819] The panel recommends alternative therapy if available for survivors on tamoxifen, although no definitive conclusion

regarding the impact of the interaction between pure SSRIs and tamoxifen can be drawn. Doses of antidepressants required for improvements in vasomotor symptoms are typically much lower than those needed for depression, and the response is typically faster. Side effects include dry mouth, decreased appetite, fatigue, nausea, constipation, and possible sexual dysfunction. Upon discontinuation, SNRIs and SSRIs should be gradually tapered to minimize withdrawal symptoms. Venlafaxine has been the most well studied, and the panel lists venlafaxine as the preferred antidepressant for the treatment of vasomotor symptoms.

The anticonvulsants gabapentin and pregabalin have also been shown to improve hormone-related vasomotor symptoms in the general population and in female cancer survivors.[820-825] For example, one trial of 420 survivors of breast cancer experiencing ≥2 hot flashes/day found that 900 mg/day gabapentin decreased the hot flash severity score by 46% at 8 weeks compared with a 15% reduction in the placebo group.[824] The panel lists gabapentin as the preferred anticonvulsant for the treatment of vasomotor symptoms. As with antidepressants, the doses of anticonvulsants used in this setting are lower than in other settings. Side effects of anticonvulsants include somnolence, so they may be particularly useful when given at bedtime in patients with hot flashes disturbing sleep.

Small studies provide evidence that the alpha agonist antihypertensive clonidine can reduce hot flashes in some healthy postmenopausal individuals.[826,827] Randomized controlled trials in breast cancer survivors also show that clonidine can reduce hot flash frequency and severity in postmenopausal survivors taking tamoxifen.[828,829] Side effects include sleep difficulties, dry mouth, fatigue, dizziness, and nausea.

Several studies have compared non-hormonal pharmacologic treatments. For example, venlafaxine has been compared with clonidine in breast cancer survivors.[830-832] Results of these studies have varied, but it appears that venlafaxine may have a faster effect but is less well tolerated than clonidine. A randomized, crossover study compared venlafaxine with gabapentin in breast cancer survivors.[825] Whereas both treatments resulted in similar reductions in hot flash severity, 68% of participants indicated a preference for venlafaxine compared with 32% who preferred gabapentin.

Non-Pharmacologic Treatment of Hot Flashes

Non-pharmacologic treatments, including acupuncture, exercise/physical activity, yoga, lifestyle modifications, weight loss if overweight or obese, hypnosis, and CBT may help survivors manage hot flashes.[309,801,803,804,833-837] Phytoestrogens, botanicals, and dietary supplements are often used for treatment of vasomotor symptoms; however, data are limited on the effectiveness and safety of these particular treatments in the general menopausal population and in survivors.[802,838-845] Vitamin E has been thought to have marginal improvement in vasomotor symptoms in both general menopause and in patients with breast cancer, but data are limited and have shown mixed results.[846] Limited data show a possible benefit of black cohosh for vasomotor symptoms in the general population.[847-849] However, randomized data in breast cancer survivors show no benefit.[850] Furthermore, there is concern about potential liver toxicity with long-term use of black cohosh. The panel consensus is that the efficacy and safety data for these treatments are too limited to make a recommendation for use.

Acupuncture is used as a treatment for hot flashes in the general population, although evidence supporting its benefit is limited in the non-cancer setting.[851,852] Several studies in women with cancer or female survivors have shown acupuncture to be a safe and effective option for managing vasomotor symptoms.[853-856] In fact, three of these studies compared acupuncture with either venlafaxine or gabapentin and found acupuncture to be equivalent to or better than drug treatment.[853,855,856]

Yoga may also help survivors manage hot flashes. A randomized trial in 355 healthy peri- and postmenopausal women found that yoga improved quality of life associated with menopause, including an improvement in the vasomotor symptom domain.[857] Another randomized controlled trial showed that yoga improved sleep but did not affect the frequency of symptomatic burden of vasomotor symptoms.[858]

Evidence that exercise/physical activity helps manage hot flashes in postmenopausal individuals is inconclusive.[801,857,859-865] In fact, a randomized controlled trial of 261 peri-menopausal and postmenopausal individuals found no difference in the frequency of hot flashes between those randomized to an exercise intervention and the control group.[860] A similar trial involving 248 participants also found that physical activity did not improve vasomotor symptoms.[863] Studies in the survivorship and cancer populations are limited and also do not support a role for the use of physical activity specifically to improve hot flash symptoms.[866] Despite the lack of data suggesting a benefit for vasomotor symptoms, the panel believes that physical activity should be recommended in menopausal cancer survivors given the many beneficial effects on overall health.

Other lifestyle modifications may also help minimize vasomotor symptoms. In the WHI Dietary Modification trial of 17,473 postmenopausal individuals who were not taking menopausal hormone therapy (MHT), those who lost ≥10% of their body weight were more likely to eliminate hot flash symptoms than those who maintained their body weight.[835] Data in breast cancer survivors also suggest that weight loss may help alleviate hot flashes in this population.[309,837] A longitudinal study in 761 women showed that those who quit smoking saw improvements in the frequency and severity of hot flashes compared to women who continued to smoke.[867] Although studies of this sort have not been done in survivor populations, data suggest that survivors who are current smokers are more likely to experience hot flashes.[868] Individual vasomotor responses to alcohol vary.[869] If alcohol triggers hot flashes in an individual survivor, limiting intake should be recommended.

Evidence suggests that CBT may reduce vasomotor symptoms in the general population.[870,871] CBT has also been studied for the management of vasomotor symptoms in cancer and survivor populations. In one trial, patients with breast cancer were randomized to receive CBT, CBT plus an exercise intervention, or to a control group.[866] Results suggested that CBT lessened the perceived burden of hot flashes. Another study randomized 96 survivors with hormonal symptoms after breast cancer treatment to a group CBT intervention or a usual care group.[872] The hot flashes and night sweats problem rating was significantly reduced in the CBT arm. Another trial randomized 254 breast cancer survivors to three groups: therapist-guided CBT, self-managed internet-based CBT (iCBT), or wait-list control.[873] Both of the CBT groups reported a significant decrease in the perceived impact of hot flashes compared to the control group. Improvements were also seen in sleep quality and the overall levels of menopausal symptoms.

Hormonal Treatment of Hot Flashes

MHT is the most effective treatment for the management of vasomotor symptoms in postmenopausal individuals.[792,874-879] However, the use of long-term MHT is controversial because, for many, the health risks associated with MHT are thought to outweigh the potential benefits. In the past, MHT was typically given to postmenopausal individuals not only to treat vasomotor symptoms, but with the thought that MHT was effective at preventing heart disease. The best data looking at health benefits and risks came from the large WHI study that showed that estrogen alone in older postmenopausal individuals with prior hysterectomy was associated with an increased risk of stroke and decreased risk of hip fracture, and had no effect on coronary heart disease or breast cancer incidence.[880] In the WHI, estrogen plus progestin in older postmenopausal individuals with a

uterus was associated with a decreased risk of colorectal cancer and hip fracture, and an increased risk of stroke, pulmonary embolism, and invasive breast cancer.[881] The participants in these trials also had a higher rate of death from lung cancer during the intervention and were diagnosed with more advanced stages of colorectal cancer during the intervention and follow-up than those who received placebo.[882-884] MHT was also associated with an increase in breast cancer incidence and the cancers were more likely to be lymph node positive.[885,886] However, the absolute numbers of trial participants diagnosed with breast cancer were small, and the absolute risk was low. After longer follow-up, all-cause, cardiovascular, and cancer-specific mortality were not affected by MHT.[887] A systematic review of randomized double-blind studies of MHT versus placebo found no evidence that MHT affects the incidence of colorectal cancer, but found that MHT increases the risk of breast cancer and death from lung cancer in postmenopausal individuals taking estrogen and progestins combined.[888]

Data from retrospective studies and an incomplete randomized controlled trial suggest that MHT is safe to use in survivors of early-stage endometrial cancer.[889-893] In survivors of breast cancer, the data are inconclusive, because the only two randomized controlled trials of MHT in breast cancer survivors had conflicting results. The HABITS trial found an increased risk of breast cancer recurrence with the use of MHT; the cumulative incidence at 5 years was 22.2% in the MHT arm and 8.0% in the control arm.[894] In the Stockholm trial, no difference was seen in breast cancer recurrence after 10.8 years of follow-up.[895]

Overall, based on these data, the panel believes that MHT can be used in appropriate female cancer survivors. Alternatives to MHT should typically be tried first and patients should be referred to an appropriate specialist for dosing and management of MHT. MHT is contraindicated in survivors with a history of hormonally mediated cancers, although as noted above MHT is likely safe in survivors of early-stage endometrial cancer. Other contraindications for survivors mirror those for the general population, and include a history of abnormal vaginal bleeding, active or recent history of a thromboembolic event, pregnancy, and active liver disease. In addition, MHT should be used with caution in survivors with coronary heart disease or hypertension, in current smokers, and in those with increased genetic cancer risk. In general, the lowest dose possible to control symptoms should be used, and treatment should be individualized based on risks.

Hormonal treatments for the relief of hot flashes include combination estrogen and progestins (for survivors with an intact uterus) or estrogen alone (for survivors assigned female at birth without a uterus). There are different local and systemic formulations of hormones including oral, transdermal, vaginal ring, and an intrauterine device. Estrogen transdermal formulations may be preferred over other formulations due to lower rates of venous thromboembolism (VTE) and stroke.[896] Micronized progestin may be preferred over medroxyprogesterone acetate (MPA) due to lower rates of VTE and breast cancer risk. Other hormonal options for treating hot flashes include novel therapies that combine a selective estrogen receptor modulator (SERM) with estrogen, creating a tissue-selective estrogen complex (TSEC). One of these TSECs contains a conjugated estrogen and the SERM bazedoxifene,[897] and is FDA-approved for treating menopausal symptoms in healthy postmenopausal individuals. Custom compounded bioidentical hormones are not recommended, because data supporting claims that they are safer and more effective than standard hormones are lacking and they may be harmful.[898,899] Furthermore, these compounds are contraindicated in survivors of hormonally mediated cancers, and should only be used with caution in those with increased genetic cancer risk. Young cancer survivors experiencing menopause at an early age can consider oral contraceptives or MHT for symptom relief and potential cardiac and bone benefits as long as not contraindicated.

Treatment of Vaginal Dryness

Vaginal dryness can be treated with over-the-counter vaginal moisturizers, gels, oils, and topicals for comfort (category 2B).[900,901] Lubricants can be used for sexual activity.[902,903] In one study of breast cancer survivors, the control group used a non-hormonal moisturizer and saw a transient improvement in vaginal symptoms.[900] Survivors should be cautioned that some lubricants may be irritating to the area of application.

Local hormonal treatments can also be used (category 2B), although some data suggest that they may not be more effective than vaginal gels or moisturizers.[881,904-910] Furthermore, some controversy exists regarding their safety in survivors of hormone-dependent cancers.[911] However, evidence suggests that local estrogen does not increase the risk of breast cancer recurrence.[912] Vaginal estrogen preparations include rings, suppositories, and creams and have been shown to be effective for managing symptoms of vaginal dryness in menopausal individuals.[910,913] Limited data in breast cancer survivors suggest minimal systemic absorption with rings and suppositories, and they are therefore preferred for survivors with hormonally sensitive tumors if estrogen-based treatment is warranted.[911,914] Other topical hormones (ie, testosterone, DHEA) can also be considered, but data regarding their safety or effectiveness are limited. One randomized controlled trial of 464 survivors of breast or gynecologic cancer showed that vaginal DHEA led to significant improvements in sexual desire, arousal, pain, and overall sexual function, although a plain moisturizer also improved symptoms.[905] In this trial, clinically important systemic estrogenic activity was not evident, and the treatment was safe and well tolerated. Overall, the decision to use local hormones should be individualized with a discussion of the possible risks and benefits. Referral to an appropriate specialist for management can also be considered. DHEA should be used with caution in survivors with a history of estrogen-dependent cancers.

The use of a fractional microablative CO_2 laser has been studied for the treatment of vaginal dryness and other genitourinary symptoms in postmenopausal individuals. Significant improvements in symptoms were observed in as many as 84% of participants, although sample sizes are small.[915-917] Limited data also suggest that the laser treatment is effective in breast cancer survivors.[918-921] Studies suggest that adverse events are infrequent and include pelvic pain, vaginal infections, genital herpes reactivation, and postmenopausal bleeding.[915,918,920] However, the FDA issued a safety communication in July 2018 warning that energy-based devices such as lasers used for vaginal procedures including the treatment of menopausal symptoms may be associated with serious adverse events.[922] The FDA has not cleared or approved for marketing any energy-based devices for the treatment of menopausal symptoms and notes that the safety and effectiveness of these devices for these types of treatments have not been established. The panel believes that larger trials are needed before this technique can be recommended.

Treatment of Urogenital Complaints

Patients sometimes present with urogenital complaints associated with menopause, such as urogenital atrophy and urinary incontinence. The panel recommends treatment with local vaginal estrogen and referral to an appropriate specialist.[913,923] See *Treatment of Vaginal Dryness*, above, for a discussion on the safety of vaginal estrogen.

Management of ADT-Related Symptoms in Male Survivors

Survivors of prostate cancer may be on ADT (see the NCCN Guidelines for Prostate Cancer, available at www.NCCN.org), and may experience many symptoms, including hot flashes, gynecomastia, and anemia.

Vasomotor Symptoms

For vasomotor symptoms disruptive to quality of life, alternative ADT options, such as intermittent ADT, can be tried if deemed appropriate by

the oncologist (see the NCCN Guidelines for Prostate Cancer, available at www.NCCN.org).

Androgens (eg, testosterone) are used for the relief of hot flashes in those who have hypogonadism from chemotherapy or radiation for other malignancies. Hormonal options for the relief of hot flashes in survivors on ADT include MPA, estrogen, and cyproterone acetate.[924-927] Individuals with vasomotor symptoms should be offered medication for symptomatic improvements. Options include venlafaxine, MPA, cyproterone acetate, and gabapentin.[928]

The non-hormonal options include the SSRIs venlafaxine and the anti-convulsant gabapentin. Gabapentin has been shown to be safe and moderately effective at controlling hot flashes in patients with prostate cancer in two randomized controlled trials.[929-931] Case reports and small pilot studies have shown that venlafaxine may improve hot flash symptoms in patients with prostate cancer undergoing ADT.[932] The panel lists venlafaxine as the preferred antidepressant and gabapentin as the preferred anticonvulsant for hormone-related symptoms.

Survivors with ADT-related symptoms can try non-pharmacologic treatments, including acupuncture, exercise/physical activity, yoga, lifestyle modifications, weight loss if overweight or obese, hypnosis, and CBT.[928] Small studies in prostate cancer survivors with a history of ADT have also found that acupuncture is effective at controlling hot flashes in this population.[933,934] A study of 68 patients with prostate cancer on ADT also found that CBT reduced the perceived burden of hot flashes compared with usual care.[935]

Phytoestrogens, botanicals, and dietary supplements are often used. However, data are limited on the effectiveness and safety of these nonpharmacologic treatments in survivors on ADT.[936] Furthermore, there are concerns that supplemental vitamin E may increase the risk for prostate cancer.[937,938] The panel consensus is that the efficacy and safety data for these treatments are too limited to make a recommendation for use.

Hypogonadism

Clinicians should consider measuring free and total testosterone, LH, and prolactin in individuals with anemia, bone density loss, diabetes, exposure to chemotherapy or testicle radiation, HIV/AIDS, chronic narcotic use, infertility, pituitary dysfunction, and chronic corticosteroid use.[939] Clinicians should check testosterone levels, even if the patient has a history of cancer not typically associated with hormonal changes. Diagnosis of hypogonadism requires two total testosterone measurements taken on separate, early-morning blood draws. Testosterone therapy should be discussed when testosterone levels are low (<300 ng/dL) or low normal and the patient is symptomatic.[928] When to initiate or resume treatment for low testosterone in survivors of prostate cancer who have no evidence of recurrent disease and are not on ADT is controversial and should be coordinated with the patient's primary cancer physician (ie, surgeon, oncologist, radiation oncologist). Patients still receiving ADT should not receive androgens (eg, testosterone).

Androgens are contraindicated in patients with prostate cancer on active surveillance or observation, in patients actively being treated for prostate cancer, and in those with advanced prostate malignancy on ADT. The 2018 AUA Guidelines Committee found insufficient evidence to quantify the risk-benefit ratio of testosterone therapy in survivors with prior history of prostate cancer.[939] After curative-intent therapies for prostate cancer, patients should discuss with their surgeon or radiation oncologist when to resume testosterone (if they had a history of hypogonadism prior to treatment of prostate cancer) or when to initiate testosterone therapy for hypogonadism.

Gynecomastia

Gynecomastia and breast pain can be treated in patients on ADT by prophylactic radiation (must be delivered prior to development of breast tissue), tamoxifen, or reduction mammoplasty.[791,940,941]

Anemia

Anemia in patients on ADT is generally responsive to erythropoietin (EPO) or blood transfusion. These individuals can be treated as per the NCCN Guidelines for Cancer- and Chemotherapy-Induced Anemia (available at www.NCCN.org).

Pain

More than one-third of post-treatment cancer survivors experience chronic pain, which often leads to psychological distress; decreased activity, motivation, and personal interactions; and an overall poor quality of life.[942-946] Pain in survivors is often ineffectively managed. Barriers to optimal pain management in cancer survivors include health care providers' lack of training, fear of side effects and addiction, and reimbursement issues.[947]

Pain has two predominant mechanisms: nociceptive and neuropathic.[948,949] Injury to somatic and visceral structures and the resulting activation of nociceptors present in skin, viscera, muscles, and connective tissues cause nociceptive pain. Somatic nociceptive pain is often described as sharp, throbbing, or pressure-like, and often occurs after surgical procedures. Visceral nociceptive pain is often diffuse and described as aching or cramping. Neuropathic pain is caused by injury to the peripheral nervous system or CNS and might be described as numbness or as burning, sharp, tingling, prickling, electrical, or shooting pain. Neuropathic pain often occurs as a side effect of chemotherapy or radiation therapy or is caused by surgical injury to the nerves.

The incidence of chronic pain after surgical treatment varies with the type of procedure and is as high as 60% in patients treated with breast surgery and 50% in those treated with lung surgery.[942] Arthralgias, characterized by joint pain and stiffness, occur in roughly half of patients taking aromatase inhibitors as adjuvant therapy for breast cancer.[950] Pelvic pain often occurs after pelvic radiation, resulting from fractures, fistulae, proctitis, cystitis, dyspareunia, or enteritis.[942]

These NCCN Guidelines for Survivorship make recommendations for the management of seven categories of cancer pain syndromes: neuropathic pain, chronic pain syndromes (ie, pain syndromes after amputation, neck dissection, mastectomy, thoracotomy), myalgias/arthralgias, skeletal pain, myofascial pain, gastrointestinal/urinary/pelvic pain, and postradiation pain. Recommendations for the prevention and management of chemotherapy-induced peripheral neuropathy (CIPN) in survivors can be found in ASCO's clinical practice guideline.[951] ASCO also has a clinical practice guideline for the management of chronic pain in survivors of adult cancers.[952]

Screening for and Assessment of Pain

All cancer survivors should be screened for pain at regular intervals. If pain is present, the intensity should be quantified by the survivor. Because pain is inherently subjective, self-report of pain is the current standard of care for assessment. Intensity of pain should be quantified using a 0 to 10 numeric rating scale, a categorical scale, or a pictorial scale (eg, Wong-Baker FACES Pain Rating Scale).[953-956] In addition, the survivor should be asked to describe the characteristics of the pain (eg, aching, burning). Severe uncontrolled pain is a medical emergency and should be addressed promptly. In addition, an oncologic emergency should also be ruled out in these cases.

A comprehensive evaluation, as outlined in the NCCN Guidelines for Adult Cancer Pain (available at www.NCCN.org), is essential to ensure proper

pain management. The survivor's goals for comfort and function and the cause and pathophysiology of the pain should be identified to determine the optimal therapeutic strategy. If the pain is new and acute, the possibility of pain due to cancer recurrence should be considered. If the pain is chronic, a specific cancer pain syndrome should be identified if possible. Referral to a PCP can be made for non-cancer or non-cancer-treatment–related workup and pain management (ie, rheumatoid arthritis).

Management of Pain

The goals of pain management are to increase comfort, maximize function, and improve quality of life. A multidisciplinary approach, which may include a combination of pharmacologic treatments, psychosocial and behavioral interventions, physical therapy and physical activity, occupational therapy, local therapies, and interventional procedures, is recommended.[943,957,958] These approaches are discussed in more detail below. For survivors with refractory pain and/or those who might benefit from further pain interventions, referral to a specialist (ie, pain management services, interventional specialist, physical therapy, physical medicine, palliative care, rehabilitation, interventional pain, urology, gynecology, orthopedic surgery, gastroenterology, other appropriate consultants) can also be considered. Finally, psychological support for survivors with chronic pain is necessary, and referral to psychosocial services should be considered for survivors in distress.

The panel acknowledges the legalization of medical marijuana for various conditions in multiple states. However, there are presently not enough data to make any guideline recommendations regarding use in cancer survivors.

For more information about the management of cancer-related pain, please see the NCCN Guidelines for Adult Cancer Pain (available at www.NCCN.org). These guidelines include information on opioid use and controlled substance agreements for patients at risk for medication misuse or diversion; adjuvant analgesics; and psychosocial support and behavioral interventions that may be modified to fit the individual survivor's circumstances.

Pharmacologic Interventions

Pharmacologic measures are the foundation of treatment of many of the common pain syndromes in survivors. Pharmacologic recommendations in these guidelines vary depending on the pain syndrome and include opioids, adjuvant analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), and muscle relaxants.[943,959-961] Topical medications are discussed in *Local Therapies*, below.

Opioids: Opioids may be recommended for the treatment of neuropathic pain, skeletal pain, and chronic pain syndromes in survivors.[962] An opioid analgesic with a dual mechanism of action as both a mu-opioid agonist and a noradrenaline reuptake inhibitor is also a recommended option for the treatment of neuropathic pain in survivors based on the available data. Tapentadol is a dual-action mu-opioid agonist/noradrenaline reuptake inhibitors.[963]Two separate randomized controlled trials in patients with painful diabetic peripheral neuropathy (n = 588 and n = 358) showed that tapentadol improved pain intensity compared with placebo.[964,965] Two other randomized trials in patients with chronic malignant tumor-related pain (n = 325 and n = 236) also showed improvements in pain intensity with tapentadol compared with placebo.[966,967] No studies in cancer survivors or in chemotherapy-induced neuropathy were identified by the panel. Data on the long-term use of opioids in survivors are lacking.[958,960,968] In fact, data on the long-term safety and effectiveness of opioids in the non-cancer setting are scarce as well.[969]

Opioid prescribing rates among cancer survivors are substantially higher compared to controls, even long after attaining cancer survivorship.[970,971] In a retrospective, population-wide cohort study, cancer survivors in Ontario, Canada, diagnosed ≥5 years prior were found to have an

adjusted relative rate of opioid prescriptions of 1.22 (95% CI, 1.11–1.34).[970] The 3-year mean cumulative number of filled opioid prescriptions was 7.7 in survivors compared with 6.3 in matched controls ($P < .0001$). Furthermore, a study of national insurance claims data showed that approximately 10% of opioid-naïve patients prescribed opioids for curative-intent cancer surgery continued to fill their prescriptions for 90 to 180 days after surgery, suggesting that aberrant opioid use or diversion of pain medication may be an issue in the survivor population.[972]

The NCCN Guidelines for Adult Cancer Pain (available at www.NCCN.org) recommend screening for risk factors of aberrant opioid use or diversion of pain medication, using a detailed patient evaluation and/or tools such as the Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R) or Opioid Risk Tool (ORT) before prescribing.[973-977] Patients and caregivers should be educated on the potential risks and benefits of opioid therapy, including the potential for diversion or misuse of opioids and safe storage and disposal of opioid medications. Various strategies may be employed to support patients determined to be at high risk for opioid misuse; behavioral/cognitive-behavioral interventions, education on naloxone, pain medication diaries/pill counts, and urine drug testing represent just a few of these strategies. Furthermore, the FDA has established Risk Evaluation and Mitigation Strategy (REMS) programs for opioid products to reduce addiction, misuse, abuse, overdose, and death through provider, patient, and family/caregiver education.[978-980] In addition, if opioids are deemed necessary for any survivor (regardless of aberrant use risk level), the NCCN Survivorship Panel recommends using the lowest dose possible for the shortest period of time possible and reevaluating the effectiveness and necessity of opioids on a regular basis. Pain treatment agreements can also be considered.[981]

In March 2016, the CDC released guidelines for prescribing opioids for chronic pain.[982] In May 2016, ASCO released a policy statement, describing principles to help balance concerns for the abuse and misuse of opioids with concerns for appropriate access of opioids for pain management in patients with cancer and survivors.[983] The NCCN Survivorship Panel shares these concerns and supports ASCO's statement. Overall, the panel believes that the concerns for the abuse and misuse of opioids must be balanced with concerns for appropriate access of opioids for pain management in patients with cancer and survivors.[983-985]

Adjuvant Analgesics: Adjuvant analgesics include antidepressants (eg, SNRIs, tricyclic antidepressants) and anticonvulsants (eg, gabapentin, pregabalin).[962] These are recommended for the treatment of survivors with neuropathic pain, post-radiation pain, chronic pain syndromes, myalgias, and arthralgias. The term adjuvant refers to the fact that they are often co-administered with an opioid to enhance analgesia or reduce the opioid requirement, but they may also be used as the sole pain treatment. A systematic review found that antidepressants, anticonvulsants, other adjuvant analgesics, and opioids were all effective at reducing neuropathic pain in patients with cancer.[960] Another review found that antidepressants and anticonvulsants may provide additional neuropathic pain relief when added to opioids in patients with cancer.[986]

Tricyclic antidepressants have been shown to relieve neuropathic pain in the non-cancer setting.[987,988] In addition, the SNRI duloxetine was shown to effectively reduce pain in a multi-institutional, randomized, double-blind, placebo-controlled, crossover trial of 231 patients with painful CIPN.[989] The ASCO clinical practice guidelines for the prevention and management of CIPN in survivors of adult cancers recommend duloxetine in this setting.[951] Duloxetine can also improve aromatase inhibitor-associated arthralgia. A randomized, double-blind, placebo-controlled, phase III trial, which included 299 postmenopausal survivors of early-stage breast cancer with joint pain, showed that duloxetine improved average joint pain score, worst pain, joint stiffness, pain interference, and functioning at 12

weeks.[990] SNRIs are therefore listed as a category 1 recommendation for survivors with aromatase inhibitor-induced arthralgia.

The most commonly used anticonvulsant drugs for the treatment of cancer-related pain are gabapentin and pregabalin. They are recommended in these guidelines for the treatment of myalgias and arthralgias.[991] Both drugs have also demonstrated efficacy in diabetic and postherpetic neuropathy,[992-994] but have not been well-studied in the cancer or survivorship settings.[951] One randomized, placebo-controlled, crossover trial in 115 survivors found that gabapentin did not effectively treat CIPN.[995] However, because high-level evidence is limited to this one trial, the panel concurs with ASCO's CIPN panel and believes that extrapolation from other neuropathic pain conditions is reasonable and that gabapentin can be offered to select survivors with CIPN after informing them about the inconclusiveness of the evidence and of potential harms, benefits, and costs.[951] A randomized, double-blind trial of pregabalin compared with placebo in 128 patients with neuropathic pain following radiation therapy for head and neck cancer found that pregabalin reduced pain scores to a greater extent than placebo.[996] A ≥30% pain relief was achieved by 59% versus 33% of participants (P = .006), and a ≥50% pain relief was achieved by 30% versus 8% (P = .003).

Corticosteroids are not recommended for the management of pain in cancer survivors. A randomized, placebo-controlled, double-blind trial of adult patients with advanced cancer receiving opioids found that methylprednisolone did not provide additional analgesia over that provided by the opioids.[997]

Nonsteroidal Anti-Inflammatory Drugs: NSAIDs, including COX-2 inhibitors, and acetaminophen are recommended for the treatment of myofascial, skeletal, and post-radiation pain, and for myalgias and arthralgias. NSAIDs are non-opioid analgesics that block the biosynthesis of prostaglandins, which are inflammatory mediators that can initiate, cause, intensify, or maintain pain. A systematic review found that data supporting the use of NSAIDs for control of pain in patients with advanced cancer are limited and weak, but suggest some efficacy at reducing pain and opioid dose requirement.[998]

A discussion of contraindications and safety precautions that should be considered before prescribing NSAIDs is provided in the NCCN Guidelines for Adult Cancer Pain (available at www.NCCN.org).

Muscle Relaxants: Muscle relaxants (eg, diazepam, lorazepam, metaxalone) reduce muscle spasms and are recommended for the treatment of skeletal pain, myalgias, and arthralgias. Evidence for their efficacy in providing pain relief in the non-cancer setting is limited.[999,1000] No data could be found in the setting of cancer-related pain.

Psychosocial Support and Behavioral Interventions

Cognitive interventions are aimed at enhancing a sense of control over the pain or its underlying cause. Breathing exercises, relaxation, imagery or hypnosis, and other behavioral therapies can be very useful.[944,1001-1006] A randomized controlled trial of 129 breast cancer survivors with pain found that an 8-week mindfulness-based cognitive therapy program reduced pain intensity and nonprescription pain medication use compared with a waitlist control group.[1007] Quality of life was also improved in the intervention arm, but distress was not reduced.

Psychosocial support and education should also be provided.[1008] Some studies in patients with cancer suggest that psychosocial and behavioral interventions such as skills training, education, relaxation training, supportive–expressive therapy, and CBT may be effective at reducing pain.[1003,1009] Hypnosis can also be considered for treatment of neuropathic pain. Overall, data support the benefit of hypnosis for controlling pain in cancer and other settings, but are lacking in the survivorship population.[1010]

Mirror therapy, if available, can be considered for the treatment of chronic "phantom limb" pain after amputation. In mirror therapy the survivor views a reflected image of their intact limb in a mirror while trying to move the amputated limb. In a small randomized trial, mirror therapy reduced pain in 6 of 6 patients and in 8 of 9 patients who switched to mirror therapy from the control conditions (covered mirror or mental visualization).[1011] One case report suggests that this therapy can be effective in survivors.[1012]

In general, studies regarding psychosocial support and behavioral interventions for reducing pain in survivors are limited. A systematic review and meta-analysis assessed the efficacy of psychosocial interventions for treating pain in patients with breast cancer and survivors.[1013] Although results suggest an effect, more studies are clearly needed in the survivorship population.

Physical Therapy and Physical Activity

Physical therapy and general physical activity may also be effective for the treatment of pain in survivors, with the main goal of increasing mobility.[210,944,957,1014] Several randomized controlled trials have reported a reduction of neck and shoulder pain associated with exercise or therapy programs.[1015-1019] In one study, 52 survivors of head and neck cancer were randomized to a progressive resistance exercise training (PRET) program or standard therapeutic exercise for 12 weeks.[1017] Pain scores decreased more dramatically in the PRET group (P = .001). In another study of 66 survivors of breast cancer, those randomized to an 8-week water exercise program experienced a greater reduction of neck and shoulder pain than those randomized to usual care.[1015] A more recent randomized trial showed that breast cancer survivors with aromatase-inhibitor–induced arthralgia randomized to an exercise arm (150 min/wk of aerobic exercise plus supervised strength training twice per week) experienced greater improvements in worst joint pain scores, pain severity, and pain interference than those in the usual care arm (all P < .001).[1018] Physical activity is thus listed as a category 1 recommendation for survivors with aromatase inhibitor-induced arthralgia.

In addition, group exercise in the community with trainers specifically trained to work with cancer survivors has been shown to reduce pain and other symptoms.[291] Yoga may also be helpful for pain management in cancer survivors. In a randomized controlled trial of 167 breast cancer survivors on aromatase inhibitors or tamoxifen, yoga reduced musculoskeletal pain symptoms.[1020]

Local Therapies

Local therapies, including heat, cold packs, massage, and medicated creams, ointments, and patches, are recommended for the treatment of myalgias, arthralgias, and neuropathic pain.[944] Specifically, topical ointments (ketamine) and patches (ie, lidocaine, capsaicin) are recommended for myofascial pain. Compounded creams containing agents such as lidocaine, capsaicin, baclofen, ketamine, and amitriptyline are recommended for treatment of neuropathic pain. Use of transcutaneous electrical nerve stimulation (TENS) can be used for neuropathic pain and for chronic post-mastectomy and post-thoracotomy pain.

Data are limited on the effectiveness of ketamine and amitriptyline,[1021-1026] but the evidence for the effectiveness of lidocaine and capsaicin is stronger.[1021,1023-1025] In a randomized trial of 208 participants with CIPN, the group that received a compounded topical gel containing baclofen, amitriptyline, and ketamine showed a trend towards improvements in the sensory and motor subscales of the EORTC QLQ-CIPN20 compared with the placebo group.[1027] The greatest improvements were seen in tingling, cramping, shooting/burning pain in the hands, and difficulty holding a pen. Lidocaine has been shown to reduce the severity of postherpetic neuropathy and cancer-related pain.[1028,1029] In a randomized trial of 35 patients with non–cancer-related postherpetic, postoperative, or diabetes-

related neuropathic pain, pain intensity was reduced with topical lidocaine but not with topical amitriptyline when compared with placebo.[1024] A larger trial with a similar population of 92 patients found no effect of topical amitriptyline, ketamine, or a combination of the two.[1030] Another study found that a higher dose of amitriptyline had some efficacy in reducing peripheral neuropathy, but also showed systemic effects.[1031] More recently, results of a multicenter, phase III, randomized, double-blind, placebo-controlled trial of 462 survivors with CIPN found that ketamine/amitriptyline cream had no effect.[1032] Similarly, a randomized trial that included 133 patients with non-cancer neuropathic pain found that compounded cream containing ketamine, gabapentin, clonidine, and lidocaine was no more effective than placebo at reducing the average pain score 1 month after treatment.[1033]

TENS is a noninvasive procedure in which electrodes are placed on or around the painful area.[944] A systematic review demonstrated that data supporting the efficacy of TENS for reducing cancer-related pain are inconclusive.[1034] The goal of invasive interventions, such as an intercostal nerve block, is to interrupt nerve conduction by either destroying nerves or interfering with their function.[944] The data on these interventions are also limited.[944]

Acupuncture

Acupuncture is recommended as a possible option for the treatment of myofascial or neuropathic pain in survivors. Evidence supporting the efficacy of this technique for reducing cancer-related pain is evolving.[1035-1037] A small randomized controlled trial compared electro-acupuncture (EA) to white light cystoscopy (WLC) and sham acupuncture in 67 postmenopausal patients with breast cancer and aromatase inhibitor-associated arthralgia.[1038] Pain severity was improved in both the EA and sham acupuncture arms compared with the control arm (mean reduction in pain severity in the EA vs. WLC groups at week 8, -2.2 vs. -0.2; P = .0004). Another trial randomized 226 postmenopausal patients with early-stage breast cancer and AI-induced joint pain 2:1:1 to acupuncture, sham acupuncture, or waitlist.[1039] The acupuncture group experienced a small but statistically significant reduction in joint pain at 6 weeks. Acupuncture is thus listed as a category 1 recommendation for survivors with aromatase inhibitor-induced arthralgia. Neuropathic pain was also reduced with acupuncture in a small randomized trial of 40 breast cancer survivors with CIPN.[1040]

Management of Refractory Pain

For refractory pain, referral to pain management services, an interventional specialist, physical therapy, physical medicine and rehabilitation, and/or palliative care should be considered. Intercostal nerve blocks, neurotomy with radiofrequency ablation, and dorsal column stimulation are some of the options that can be considered.

Sexual Dysfunction

Sexual function and management of hormone-related symptoms are important aspects of quality of life for all cancer survivors. The recommendations here are intended for cisgender survivors based on the availability of data in this population, but should be followed for transgender and intersex survivors as applicable, with the involvement of the appropriate health care specialists.

Cancer treatment, especially hormonal therapy and surgical and/or radiation therapy directed towards the pelvis, can often impair sexual function. In addition, depression and anxiety, which are common in survivors, can contribute to sexual problems. Thus, sexual dysfunction is common in survivors and can cause increased distress and have a significant negative impact on quality of life.[1041-1046] Nonetheless, sexual function is often not discussed with survivors.[1047-1051] Reasons for this include a lack of training of health care professionals, discomfort of

providers and/or survivors with the topic, survivors' perception of discomfort from the provider, and insufficient time during visits for discussion.[1041] However, effective strategies for treating both female and male sexual dysfunction exist, making these discussions a critical part of survivorship care.

Panel recommendations for the management of sexual dysfunction in survivors are described herein. Cancer Care Ontario has developed recommendations for the management of sexual problems in patients with cancer that ASCO has endorsed.[928,1052] Most of their recommendations are consistent with those put forth by the NCCN Survivorship Panel.

NCCN is aware that many regenerative, restorative, or rejuvenation therapies are being marketed to patients with sexual dysfunction. Survivors should be aware that the FDA has not approved injections of autologous platelet-rich plasma or stem cells for treatment of male sexual dysfunction. The FDA has not cleared energy-based devices (ie, vaginal rejuvenation by lasers or erectile dysfunction [ED] by shock waves, also discussed in *Treatment of Vaginal Dryness,* above and *Interventions for Male Sexual Dysfunction,* below) for treatment of menopausal changes, ED, or incontinence. Cancer survivors with sexual dysfunction should be referred to specialists for discussions of non–FDA-approved therapeutics and special consideration should be given to their primary diagnosis of cancer prior to enrollment in clinical trials for sexual dysfunction or incontinence.

Female Sexual Dysfunction

Female sexual problems relate to issues with sexual desire, arousal, orgasm, and pain.[1053-1055] Sexual dysfunction after cancer treatment is common in female survivors.[30,1045,1056-1061] A survey of 221 survivors of vaginal and cervical cancer found that the prevalence of sexual problems was significantly higher among survivors than among age- and race-matched controls from the National Health and Social Life Survey (mean number of problems 2.6 vs. 1.1; $P < .001$).[1060] A survey of survivors of ovarian germ cell tumors and age- and race- and education-matched controls found that survivors reported a significant decrease in sexual pleasure.[1062]

Female sexual dysfunction varies with cancer site and treatment modalities.[1057,1058] For example, survivors of cervical cancer who were treated with radiotherapy had worse sexual functioning scores (for arousal, lubrication, orgasm, pain, and satisfaction) than those treated with surgery, whose sexual functioning was similar to that of age- and race-matched non-cancer controls.[1057] A systematic review of sexual functioning in cervical cancer survivors found similar results, except that no differences in orgasm/satisfaction were observed.[1063] Chemotherapy seems to be linked to female sexual dysfunction in breast cancer survivors,[1058] possibly related to the prevalence of chemotherapy-induced menopause in this population.[1054] Furthermore, body image changes related to breast cancer surgery and reconstruction can affect sexual health and well-being.[1064] In addition, survivors with a history of HSCT may have multiple types of sexual dysfunction even 5 to 10 years after diagnosis.[1065-1067] Some of the sexual dysfunction associated with HSCT is related to GVHD, which can result in vaginal fibrosis, stenosis, mucosal changes, vaginal irritation, bleeding, and increased sensitivity of genital tissues.[1066,1068] In addition, high-dose corticosteroids used for chronic GVHD can increase emotional lability and depression, affecting feelings of attractiveness, sexual activity, and quality of sexual life.

Male Sexual Dysfunction

The NIH Consensus Conference on Impotence defined impotence as "male erectile dysfunction, that is, the inability to achieve or maintain an erection sufficient for satisfactory sexual performance."[1069] In fact, impotence and ED are not synonymous. Impotence can involve problems

of sexual desire, orgasm, or ejaculation, which are not necessarily linked with achieving or maintaining an erection.[1070]

ED associated with a cancer diagnosis and cancer therapy may have a psychologic component, but is most often physiologic and iatrogenic. In the case of surgery, ED may be immediately evident; in the case of radiation treatments, presentations can be delayed. ED occurs frequently in the general population and increases with age.[1071] In one community-based study, 33% of participants aged ≥75 years reported moderate or worse ED.[1072] ED is also very common in cancer survivors. Anticancer treatment modalities used in a variety of cancers have the potential to damage blood vessels, leading to a reduction in blood circulation to the penis and/or damage to the autonomic nervous system. Thus, higher rates of ED are seen in cancer survivors than in the general population. The prevalence of ED in male survivors of colorectal cancer has been reported to range from 45% to 75%,[1042,1073,1074] and it has been reported in up to 90% of survivors of prostate cancer.[1075-1079]

Male cancer survivors exposed to radiation or chemotherapy often experience hypogonadism—usually primary hypogonadism. Hypogonadism refers to a decrease in the production of sperm and/or testosterone. Primary hypogonadism is the result of testicular failure; testosterone levels and sperm counts are below normal, and serum LH and FSH are above normal. Secondary hypogonadism is a disease of the pituitary or hypothalamus. In survivors with secondary hypogonadism, serum testosterone levels and sperm counts are subnormal, and the serum LH and FSH levels are normal or reduced. Adult-onset hypogonadism is characterized by a deficiency of testosterone and a failure of the body to produce an adequate compensatory response. In these individuals, low testosterone levels are associated with normal or low levels of gonadotropins, suggesting physiologic failure of both the testicles and hypothalamic-pituitary system.[1080]

Evaluation and Assessment for Sexual Function

All adult cancer survivors, regardless of gender identity and sexual orientation, should be asked about their sexual function at regular intervals, by inquiring about any concerns or distress regarding sexual function, sexual activity, sexual relationships, or sex life. Cancer survivors who report distress should be evaluated further. Inquiries into treatment-related infertility should be made if indicated, with referrals as appropriate. ASCO's recently updated clinical practice guidelines on fertility preservation for patients with cancer have more information on the topic.[1081] It is important for providers to be aware that fertility issues should be addressed in the survivorship phase, whether or not they were addressed prior to treatment.[1082-1084] A discussion regarding the need for contraception may also be helpful in some cases, because the incidence of unplanned pregnancies is approximately three times higher in cancer survivors than in the general population.[1085]

Survivors for whom screening does not indicate an issue with sexual function should be rescreened at subsequent visits. For survivors with sexual function concerns who do not wish to discuss them at the current visit, referral can be made to a sexual health specialist if the survivor is interested. These survivors should also be re-evaluated and engaged in discussions about the potential impact of treatment on sexual function at future visits.

For survivors who want to discuss their sexual function further, screening tools can be considered. Several screening tools are available for both men and women. For women, options include the Brief Sexual Symptom Checklist for Women, the Arizona Sexual Experience Scale (ASEX), the Female Sexual Function Index (FSFI), and a breast cancer-specific adaptation of the FSFI (FSFI-BC).[1086-1089] For men, the Sexual Health Inventory for Men (SHIM), the Sexual Quality of Life Questionnaire-Men, and the PROMIS Brief Function Profile-Male are examples.[1071,1090,1091] The

FSFI has been validated in patients with cancer and cancer survivors.[1092,1093] The FSFI and ASEX were also identified in a systematic review as tools that have acceptable psychometric properties in patients with breast cancer.[1094] The other tools have not been validated in cancer or survivor populations.

Survivors with concerns about their sexual function should undergo a more thorough evaluation, including screening for possible psychosocial problems or mental health issues (ie, anxiety, depression, relationship issues, body image concerns, drug or alcohol use) that can contribute to sexual dysfunction. It is also important to identify prescription and over-the-counter medications (especially hormone therapy, narcotics, beta-blockers, and SSRIs) that could be a contributing factor. Traditional risk factors for sexual dysfunction, such as CVD, diabetes, obesity, smoking, and alcohol abuse, should also be assessed, as should the patient's oncologic and treatment history. In addition, the impact of cancer and cancer treatment on sexual function should be explored further. Finally, total morning testosterone should be measured if indicated by concerns regarding hypogonadism.[800]

Interventions for Female Sexual Dysfunction

Female sexual dysfunction is often multifactorial in nature. Therefore, treatment of sexual dysfunction often requires a multidimensional treatment plan that addresses the underlying issues, which can be physiologic (eg, menopause, illness), disease-induced, medication-induced, psychologic (eg, anxiety, depression), and interpersonal. Informed patient and physician decision-making is the standard for guiding treatment decisions for treatment of female sexual dysfunction. Referrals to specialists (ie, psychotherapy, sexual/couples counseling, gynecologic care, sexual health specialist) should be made if appropriate and available.

Overall, the evidence base for interventions to treat female sexual dysfunction in survivors is weak and high-quality studies are needed.[1095,1096] Based on evidence from other populations, evidence from survivors when available, recommendations from the American College of Obstetricians and Gynecologists (ACOG),[1053] and consensus among NCCN Survivorship Panel Members, the panel made recommendations for treatment of female sexual dysfunction in survivors. The panel recommends that treatment be guided by the specific type of problem. Treatments depend on the type of sexual dysfunction and may include both over-the-counter and prescription options, as well as pelvic physical therapy and integrative therapies. When prescription medications are being considered, the risks and benefits should be discussed, or the survivor should be referred to an appropriate health care provider (eg, sexual health specialist) for prescription and/or treatment. The evidence base for each recommendation is described herein.

Integrative therapies, including yoga and meditation, may be helpful for female survivors with sexual dysfunction.[857,1097] In addition, CBT has been shown to be effective at improving sexual functioning in breast cancer survivors.[1098]

Vaginal moisturizers, vaginal gels, oils, and topical vitamin D or E can help alleviate symptoms such as vaginal dryness and sexual pain,[901,1099] although data on these over-the-counter products are limited in the general population (also see *Treatment of Vaginal Dryness*, under *Hormone-Related Symptoms* above). Topical anesthetics may help with vaginal pain as shown in a study in 46 breast cancer survivors that found that application of lidocaine to the vulvar vestibule before vaginal penetration improved dyspareunia.[1100]

Pelvic physical therapy (ie, pelvic floor muscle training) may improve sexual pain, arousal, lubrication, orgasm, and satisfaction. A small study of

34 survivors of gynecologic cancers found that pelvic floor training significantly improved sexual function.[1101]

Vaginal dilators are an option for survivors with pain during sexual activity. In addition, vaginal dilators are used for survivors with vaginal stenosis from pelvic radiation. However, evidence for the effectiveness of dilators is limited.[1102]

Several topical prescription medications can also be considered for female survivors with sexual dysfunction (also see *Treatment of Vaginal Dryness*, under *Hormone-Related Symptoms* above). For example, vaginal estrogen (pills, rings, or creams) has been shown to be effective in treating vaginal dryness, itching, discomfort, and painful intercourse in postmenopausal individuals.[881,906-910] A study in 76 postmenopausal breast cancer survivors on aromatase inhibitor therapy found that intravaginal testosterone cream or an estradiol-releasing vaginal ring were safe and improved vaginal atrophy and sexual function.[1103] The panel notes that focal application of creams applied to external vulvar regions are absorbed to a lesser degree than creams placed inside the vagina.

Vaginal androgens (ie, DHEA; also known as prasterone) can be considered for vaginal dryness or pain with sexual activity (also see *Treatment of Vaginal Dryness*, under *Hormone-Related Symptoms* above). Vaginal DHEA received FDA approval in 2016. Several studies have shown it to be effective at reducing dyspareunia in postmenopausal individuals.[1104-1108] However, a systematic review and meta-analysis published in 2015 concluded that it is uncertain whether vaginal DHEA improves vasomotor symptoms and vaginal dryness.[1109] A randomized controlled trial of 464 survivors of breast or gynecologic cancer showed that vaginal DHEA led to significant improvements in sexual desire, arousal, pain, and overall sexual function, although a plain moisturizer also improved symptoms.[905] In this trial, clinically important systemic estrogenic activity was not evident, and the treatment was safe and well tolerated.

Overall, safety data for the use of androgen-based therapy in survivors of hormonally mediated cancers are limited. The FDA label for vaginal DHEA warns that exogenous estrogens are contraindicated in those with a history of breast cancer.[1110] The panel cautions that DHEA should be used with caution in survivors with a history of estrogen-dependent cancers.

In 2013, the FDA approved the SERM ospemifene for treating moderate to severe dyspareunia in postmenopausal individuals without known or suspected breast cancer and without a history of breast cancer.[1111] Ospemifene has been studied in several large trials of individuals with postmenopausal vulvar and vaginal atrophy and was found to effectively treat vaginal dryness and dyspareunia.[1112-1114] Data in the survivor population are very limited. One prospective study, in which 52 survivors of stage I–IIa cervical cancer with vulvovaginal atrophy were treated with ospemifene, found improvements in vaginal health and function, sexual activity, body image, sexual enjoyment, global health status, and emotional and social functioning.[1115] The panel recommends consideration of ospemifene for dyspareunia in survivors of cancers that are not hormonally sensitive.

In August 2015, the FDA approved flibanserin to treat acquired, generalized hypoactive sexual desire disorder (HSDD) in premenopausal women.[1116] Meta-analyses have shown that flibanserin resulted in approximately 1 additional satisfying sexual event every 2 months in premenopausal individuals.[1117,1118] This drug has not been studied in patients with cancer or survivors, but it is a reasonable option to discuss with premenopausal survivors with low or lack of desire, libido, or intimacy.

In June 2019, the FDA approved bremelanotide for the treatment of premenopausal women with acquired, generalized HSDD as characterized by low sexual desire that causes marked distress or interpersonal difficulty and is not due to 1) a coexisting medical or psychiatric condition; 2) problems with the relationship; or 3) the effects of a medication or drug

substance.[1119] The safety and efficacy of bremelanotide in premenopausal individuals with HSDD was evaluated in two phase 3, randomized, double-blind, placebo-controlled, multicenter clinical trials (RECONNECT; BMT-301, and BMT-302).[1120] Bremelanotide administered subcutaneously as needed was generally well tolerated, with nausea, flushing, and headache (mild-to-moderate in most participants) reported more frequently than in patients taking placebo. Participants in the bremelanotide group experienced a statistically significant increase in sexual desire (BMT-301: 0.30, $P < .001$; BMT-302: 0.42, $P < .001$) and a statistically significant reduction in distress related to low sexual desire (BMT-301: -0.37, $P < .001$; BMT-302: -0.29, $P = .005$) compared with placebo. Bremelanotide has not been studied in cancer survivors, but the panel believes it may be an appropriate option for some survivors with HSDD.

Other options for female survivors with low or lack of desire, libido, or intimacy include bupropion and buspirone.[1121] These drugs have been studied in a few trials involving non-cancer populations.[1122-1124] Despite limited safety and efficacy data, these drugs may be considered as options for HSDD.

Currently, the panel does not recommend the use of oral phosphodiesterase type 5 inhibitors (PDE5i) for female sexual dysfunction because of the lack of data regarding their effectiveness in this setting. Although thought to increase pelvic blood flow to the clitoris and vagina,[1125,1126] PDE5i showed contradictory results in randomized clinical trials of various non-cancer populations of women being treated for sexual arousal disorder.[1127-1132] More research is needed before a recommendation can be made regarding the use of sildenafil for the treatment of female sexual dysfunction.

Interventions for Male Sexual Dysfunction

Using a consensus-based approach, the NCCN Survivorship Panel concluded that: 1) informed patient and physician decision-making is the standard for guiding treatment decisions for treatment of male sexual dysfunction; and 2) a psychological overlay frequently exists in patients with sexual dysfunction and may be even more pronounced in the face of cancer survivorship. Thus, treatment of male sexual dysfunction may require a multidimensional treatment plan that addresses the underlying issues. Referrals to specialists (ie, psychotherapy, sexual/couples counseling, urology, sexual health specialist) should be made if appropriate and available. Treatment of sexual dysfunction in male survivors should be guided by the specific type of problem.

Treatment for male sexual dysfunction should include modification of risk factors, such as smoking cessation, weight loss, increasing physical activity, and avoiding excess alcohol consumption. Several trials have shown that such lifestyle modifications can improve sexual function in this population.[1133-1136] In fact, one study found that PDE5i treatment with an aerobic activity program was more effective than PDE5i treatment alone in 60 patients with ED.[1137] Evidence for these effects in patients with cancer and survivors is lacking.

In addition, treatment of psychosocial problems, with referral to sex and couples therapy as appropriate, can often alleviate symptoms of male sexual dysfunction.[1138-1142] Small studies in survivors of prostate cancer suggest that these approaches can be helpful in the survivorship population as well.[1143,1144] Therapy is often offered in conjunction with medical therapy.

PDE5i treatment has been shown to improve the symptoms of ED and be well tolerated.[1145,1146] The 2017 ASCO Practice on Interventions to Address Sexual Problems in People with Cancer recommends PDE5i medications be used to help patients with ED.[928] Many studies have also shown the efficacy and tolerability of PDE5i for treating ED in patients with cancer and survivors.[1147,1148] Importantly, PDE5i are contraindicated in patients taking oral nitrates, because together they can lead to a

dangerous decrease in blood pressure.[1149,1150] The timing and dose of on-demand PDE5i should be started conservatively, and it should be titrated to the maximum dose as needed.[1070] Survivors on PDE5is should be monitored periodically for efficacy, side effects, and any significant change in health status. In addition to on-demand PDE5i treatment, studies have shown that daily, low-dose treatment with these drugs can be effective.[1151-1154]

If total morning testosterone is <300 ng/dL, then hypogonadism is diagnosed and testosterone therapy may relieve symptoms of ED, problems with ejaculation, or problems with orgasm.[1155] A randomized controlled trial in 470 patients older than 65 years of age with testosterone levels <275 ng/dL found that testosterone gel led to improvements in sexual function, desire, and activity.[1156,1157] Other studies have shown that the addition of testosterone to PDE5i therapy in individuals with low serum testosterone levels helps improve ED.[1158-1163] Testosterone therapy should not be used if contraindicated by the primary oncologic diagnosis (eg, prostate cancer on active surveillance, prostate cancer on ADT).

Other treatments may help with ED and with ejaculation and orgasm issues. Although evidence in the general population is lacking,[1164] studies in prostate cancer survivors suggest that pelvic physical therapy (ie, pelvic floor muscle training) may improve sexual function in this population.[1165,1166] Vibratory therapy may reduce problems with premature ejaculation.[1167] Cancer therapies can result in a variety of ejaculatory dysfunctions (premature, absent, delayed, or climacturia), and these are best addressed with urology specialist consultation.[1168-1171]

Survivorship caregivers should be aware that “restorative or regenerative” therapies for ED are being widely advertised in the United States, but, as of the publication of these NCCN Guidelines, none of these treatments has been approved or cleared by the FDA for the treatment of ED. Survivors should be made aware that regenerative therapies for ED are being administered in cash-only practices. The Sexual Medicine Society of North America position statement on regenerative therapies for ED concludes: “given the current lack of regulatory agency approval for any restorative (regenerative) therapies for the treatment of ED and until such time as approval is granted, SMSNA believes that the use of shock waves or stem cells or platelet rich plasma is experimental and should be conducted under research protocols in compliance with Institutional Review Board approval. Patients considering such therapies should be fully informed and consented regarding the potential benefits and risks. Finally, the SMSNA advocates that patients involved in these clinical trials should not incur more than basic research costs for their participation.”[1172]

Sleep Disorders

Sleep disturbances include insomnia (trouble falling or staying asleep resulting in daytime dysfunction), excessive sleepiness (which can result from insufficient sleep opportunity, insomnia, or other sleep disorders), and sleep-related movement or breathing disorders.[1173] Sleep disturbances are common, affecting 30% to 50% of patients with cancer and survivors, often in combination with pain, fatigue, anxiety, and/or depression.[1173-1184] In fact, sleep disorders have been shown to be a risk factor for suicide.[536] Improvements in sleep quality lead to improvements in fatigue, mood, and overall quality of life.[717] Most clinicians, however, do not know how best to evaluate and treat sleep disorders.[1173]

Sleep disorders are common in patients with cancer as a result of multiple factors, including disease- or treatment-related biologic changes in sleep and wake regulation, the stress of diagnosis and treatment, and side effects of therapy (eg, pain, fatigue).[1185] In addition, evidence suggests that changes in inflammatory processes from cancer and its treatment play a role in sleep disorders. These sleep disturbances can be perpetuated in the survivorship phase by chronic side effects, anxiety, depression,

medications, and maladaptive behaviors such as shifting sleep times, excessive time in bed because of fatigue, and unplanned naps.[1185]

Additional information about sleep disorders in patients with cancer can be found in the NCCN Guidelines for Palliative Care and the NCCN Guidelines for Cancer-Related Fatigue (available at www.NCCN.org). These guidelines may be modified to fit the individual survivor's circumstances.

Screening for and Assessment of Sleep Disorders

Survivors should be screened for possible sleep disorders at regular intervals, especially when they experience a change in clinical status or treatment. The panel lists screening questions that can help determine whether concerns about sleep disorders or disturbances warrant further assessment. Other tools to screen for sleep problems have also been validated and may be used for individual intensive screening to assess sleep quality.[1186-1189] It is important to note that survivors may have more than 1 sleep disorder simultaneously.

The panel recommends that sleep/wake timing and/or sleep logs or diaries be reviewed. Many survivors may be using wearable devices to track sleep. However, studies have shown that these devices do not accurately measure sleep when compared to results of polysomnography.[1190-1195] Results from wearable devices may be useful for tracking sleep patterns, but should not be used for diagnosis or clinical decision-making.

If concerns regarding sleep quality are significant, the panel recommends that treatable or modifiable contributing factors be assessed and managed. Comorbidities that can contribute to sleep problems include alcohol and substance abuse, obesity, cardiac dysfunction, endocrine dysfunction, respiratory disorders, anemia, neurologic disorders (including CIPN), pain, fatigue, and emotional distress. Screening for common sleep disorders such as obstructive sleep apnea (OSA), restless legs syndrome (RLS, also known as Willis-Ekbom disease), and circadian rhythm sleep wake disorders (such as shift work) can help identify specific therapies for these conditions that may be helpful. In addition, some medications, both prescription and over-the-counter, can contribute to sleep issues. For instance, pain medication, antiemetics, antihistamines, antidepressants, and antipsychotics can all contribute to sleep disturbance, as can the persistent use of sleep aids.

Diagnosis of Sleep Disorders

The panel divided sleep disorders into two general categories: 1) insomnia; and 2) sleep disturbance and/or excessive sleepiness. Insomnia is diagnosed when patients have difficulty falling asleep, staying asleep, or waking up too early at least 3 times per week for at least 4 weeks. These categories were based on the most common types of symptoms that patients with sleep disturbances are likely to report.

Diagnosing patients with excessive sleepiness can be challenging, because it can be caused by a variety of factors. When excessive sleepiness is associated with observed apneas or snoring, the STOP questionnaire can be used as a screening tool to determine the risk of OSA.[1196] Other screening tools for OSA risk have also been validated.[1197,1198] Sleep studies can confirm the diagnosis of OSA; alternatively, referral can be made to a sleep specialist or PCP for further evaluation. Narcolepsy should be considered when excessive sleepiness is accompanied by cataplexy. Parasomnias (eg, sleep walking, sleep paralysis, periodic limb movement disorder) and circadian rhythm disorders (eg, shift work sleep disorder, advanced or delayed sleep phase disorders) should also be considered; survivors with these types of sleep disturbances may also present with symptoms of insomnia.

Excessive sleepiness can also be associated with uncomfortable sensations or an urge to move the legs (and sometimes the arms or other body parts). These symptoms are usually worse at night and with

inactivity, may be improved or relieved with movement such as walking or stretching, and indicate RLS. In these individuals, a history and physical exam should be performed, with evaluation for iron deficiency if RLS is diagnosed.[1199,1200] Alternatively, referral can be made to a sleep specialist or PCP for further evaluation.

Evaluation for Insomnia

If insomnia is diagnosed, details should be obtained regarding the course of insomnia, including the duration of symptoms. Insomnia is considered to be chronic if symptoms have been ongoing for ≥3 months. It should also be determined whether or not the insomnia symptoms are causing distress, impacting daytime functioning, or affecting the survivor's quality of life.

Management of Sleep Disorders

In all cases, comorbidities that may be contributing to the sleep disorder should be addressed. Survivors should also be advised that sleepiness can increase the risk of accidents, including while operating a motor vehicle. In addition, several types of interventions are recommended, as described below.[1173,1201,1202] Referral to a sleep specialist can be considered in most cases, especially for OSA, RLS, parasomnias, circadian rhythm disorders, narcolepsy, and chronic or refractory insomnia. Referral to a PCP can also be considered, except in cases of circadian rhythm disorder, prolonged wakefulness or awakenings, prolonged nocturnal sleep (ie, >9 hours for adults), cataplexy, frequent short naps, vivid dreams, disrupted sleep, or sleep paralysis, in which cases a sleep specialist is recommended.

Sleep Hygiene Education

Educating survivors about general sleep hygiene is recommended, especially for the treatment of circadian rhythm disorders, insomnia, and excessive sleepiness associated with insufficient sleep time.[1203-1205] Key points are listed in the guidelines and include regular morning or afternoon physical activity; daytime exposure to bright light; keeping the sleep environment dark, quiet, and comfortable; and avoiding heavy meals, moderate to strenuous physical activity, alcohol, and nicotine near bedtime. However, sleep hygiene alone is insufficient for the effective management of sleep disorders.

Physical Activity

Physical activity can improve sleep in middle-aged and older individuals in non-cancer settings.[1206-1208] Physical activity may also improve sleep in patients with cancer and survivors.[210,1209-1214] One randomized controlled trial compared a standardized yoga intervention plus standard care with standard care alone in 410 survivors (75% breast cancer; 96% women) with moderate to severe sleep disruption.[1211] Participants in the yoga arm experienced greater improvements in global and subjective sleep quality, daytime functioning, and sleep efficiency (all $P \leq .05$). In addition, the use of sleep medication declined in the intervention arm ($P \leq .05$). However, a 2013 systematic review concluded that the evidence that yoga programs aimed at cancer survivors improve insomnia or sleep quality is very limited.[1215] Another randomized controlled trial assessed the effects of a 3-month physical activity behavior change intervention on 222 breast cancer survivors.[1216] Participants in the intervention arm experienced significant improvement in self-reported global sleep quality at 3 and 6 months. However, actigraphy results showed no differences between the intervention and usual care arms. Overall, data supporting improvement in sleep with physical activity are limited in the survivorship population.

Psychosocial Interventions

Cognitive behavior treatments such as CBT-I, iCBT, relaxation therapy, stimulus control, and sleep restriction are recommended to treat sleep disturbances in survivors.[1217-1219] These approaches are preferred over pharmacologic interventions as first-line therapy.

Several randomized controlled trials have shown that CBT improves sleep in the survivor population.[706-708,716,1220-1222] For example, a randomized controlled trial in 150 survivors (58% breast cancer; 23% prostate cancer; 16% bowel cancer; 69% women) found that a series of 5 weekly group CBT sessions was associated with a reduction in mean wakefulness of almost 1 hour per night, whereas usual care (in which physicians could treat insomnia as they would in normal clinical practice) had no effect on wakefulness.[706] Another trial randomized 96 survivors (68% breast cancer; 87% female) to a 7-week intervention of CBT, armodafinil, CBT plus armodafinil, or placebo.[1222] CBT resulted in significant improvements in insomnia symptoms and sleep quality at 0 and 3 months after the intervention, but armodafinil had no effect. A recent meta-analysis identified 8 studies, including 752 cancer survivors, and found large effect sizes for self-reported insomnia severity (d = .77) following CBT.[1223] Further, a meta-analysis of randomized controlled trials in cancer survivors found strong evidence that CBT-I can produce large and durable effects on insomnia severity.[1223] In fact, the American College of Physicians recommends that CBT be the initial treatment for all adults with chronic insomnia disorder.[1217]

A small randomized controlled trial of 57 survivors (54% breast cancer; 75% women) found that mind–body interventions (mindfulness meditation or mind-body bridging) decreased sleep disturbance more than sleep hygiene education did.[1224] A preliminary report of a subset of participants in a larger randomized controlled trial of breast cancer survivors showed that MBSR improved objective sleep parameters, including sleep efficiency and percent of sleep time.[1225]

A randomized, partially blinded, noninferiority trial compared CBT with MBSR in 111 patients with cancer.[1226] Both groups experienced improvements in sleep diary-measured sleep onset latency, wake after sleep onset, total sleep time, stress, and mood disturbance. MBSR was inferior to CBT for improving insomnia severity immediately following the intervention, but was noninferior at 5 months. These results have not been replicated in survivors, and the relative efficacy of these strategies is not established in this population. Another randomized study compared Tai Chi Chih, a mindful movement meditation, with CBT-I in 90 breast cancer survivors and found it to be non-inferior for improving insomnia symptoms at 3, 6, and 15 months after the intervention.[1227]

Pharmacologic Interventions

Many pharmacologic treatments for sleep disturbances are available, including hypnotics for insomnia (eg, zolpidem, ramelteon).[1228,1229] Many of the FDA-approved hypnotics are BZD receptor agonists and can be associated with dependence, abuse, and withdrawal. The panel therefore recommends that survivors taking these medications be assessed every 1 to 3 months to determine if they are still needed. In addition, survivors should be informed that hypnotic medications may cause complex sleep-related behaviors (eg, sleep driving, sleep eating).

In addition, antidepressants, antihistamines, atypical antipsychotics, other BZD receptor agonists, and nutritional/herbal supplements (eg, melatonin) are often used off-label for the treatment of insomnia, even though limited to no efficacy or effectiveness data are available for this use. The panel noted that these medications are associated with significant risks and should be used with caution. One small, open-label study found that the antidepressant mirtazapine increased the total amount of nighttime sleep in patients with cancer.[1230] A recent randomized, double-blind, placebo-controlled study of 95 postmenopausal breast cancer survivors found that melatonin subjectively improved sleep quality after 4 months of treatment (mean change in Pittsburgh Sleep Quality Index [PSQI] score, -0.1 for placebo and -1.9 for melatonin; $P < .001$).[845] Overall, however, data on pharmacologic interventions aimed at improving sleep in patients with cancer and survivors are lacking.[1183]

Treatment of Obstructive Sleep Apnea

Weight loss should be recommended to survivors with OSA, because studies have shown weight loss to be associated with reduced hypoxia and excessive sleepiness in patients with OSA.[1231] Small randomized studies have also shown that physical activity can improve OSA symptoms independent of weight loss.[1232,1233] In addition, survivors with OSA should be referred to a sleep specialist or PCP. The most common medical treatment for OSA is continuous positive airway pressure (CPAP).[1234]

Treatment of Restless Legs Syndrome

For RLS associated with iron deficiency, iron replacement can improve symptoms. In addition, preferred first-line treatments for RLS are dopamine agonists, gabapentin, and enacarbil.[1235-1243] Two separate recent meta-analyses found dopamine agonists and calcium channel alpha-2-delta ligands (eg, gabapentin) to be helpful for reducing RLS symptoms and improving sleep in the non-cancer setting.[1243,1244]

Additional treatment options include opioids, clonazepam, and sleep hygiene education. Referral to a sleep specialist or PCP is also an appropriate option for survivors with RLS. In addition, certain mind-body interventions and dietary supplementation may benefit some patients with RLS, although data are limited.[1245] The American Academy of Neurology also has clinical practice guidelines for the treatment of adults with RLS.[1246]

Summary

With improved diagnostic and treatment modalities, the population of cancer survivors is rapidly growing. Many survivors will experience late and/or long-term effects of cancer and its treatment that can include physical and/or psychosocial problems. These issues need to be addressed in a regular and systematic manner. Unfortunately, many of these effects are not addressed until discharge from the oncologist, and interventions may be left to health care providers who may not have much experience treating the concerns of cancer survivors. The NCCN Survivorship Panel hopes that these guidelines can help both oncologic and primary health care professionals lessen the burden left on survivors by their cancer experience so they can transition back to a rewarding life.

References

1. Bluethmann SM, Mariotto AB, Rowland JH. Anticipating the "silver tsunami": prevalence trajectories and comorbidity burden among older cancer survivors in the United States. Cancer Epidemiol Biomarkers Prev 2016;25:1029-1036. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27371756.

2. Cancer survivors--United States, 2007. MMWR Morb Mortal Wkly Rep 2011;60:269-272. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21389929.

3. Miller KD, Nogueira L, Mariotto AB, et al. Cancer treatment and survivorship statistics, 2019. CA Cancer J Clin 2019. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31184787.

4. DeSantis CE, Lin CC, Mariotto AB, et al. Cancer treatment and survivorship statistics, 2014. CA Cancer J Clin 2014;64:252-271. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24890451.

5. Mariotto AB, Rowland JH, Yabroff KR, et al. Long-term survivors of childhood cancers in the United States. Cancer Epidemiol Biomarkers Prev 2009;18:1033-1040. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19336557.

6. Nekhlyudov L, Aziz NM, Lerro C, Virgo KS. Oncologists' and primary care physicians' awareness of late and long-term effects of chemotherapy: implications for care of the growing population of survivors. J Oncol Pract 2014;10:e29-36. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24222054.

7. McCabe MS, Bhatia S, Oeffinger KC, et al. American Society of Clinical Oncology statement: achieving high-quality cancer survivorship care. J Clin Oncol 2013;31:631-640. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23295805.

8. El-Shami K, Oeffinger KC, Erb NL, et al. American Cancer Society colorectal cancer survivorship care guidelines. CA Cancer J Clin 2015;65:428-455. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26348643.

9. Resnick MJ, Lacchetti C, Penson DF, American Society of Clinical O. Prostate cancer survivorship care guidelines: American Society of Clinical Oncology practice guideline endorsement. J Oncol Pract 2015;11:e445-449. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25829527.

10. Runowicz CD, Leach CR, Henry NL, et al. American Cancer Society/American Society of Clinical Oncology breast cancer survivorship care guideline. J Clin Oncol 2016;34:611-635. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26644543.

11. Cohen EE, LaMonte SJ, Erb NL, et al. American Cancer Society head and neck cancer survivorship care guideline. CA Cancer J Clin 2016;66:203-239. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27002678.

12. Nekhlyudov L, Lacchetti C, Siu LL. Head and neck cancer survivorship care guideline: American Society of Clinical Oncology clinical practice guideline endorsement summary. J Oncol Pract 2018;14:167-171. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29257719.

13. Ligibel JA, Denlinger CS. New NCCN guidelines for survivorship care. J Natl Compr Canc Netw 2013;11:640-644. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23704233.

14. U.S. National Library of Medicine-Key MEDLINE® Indicators. Available at: http://www.nlm.nih.gov/bsd/bsd_key.html. Accessed June 5, 2020.

15. Langbaum T, Smith TJ. Time to study metastatic-cancer survivorship. N Engl J Med 2019;380:1300-1302. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30943335.

16. Statistics, Graphs and Definitions. Office of Cancer Survivorship, The National Cancer Institute; 2019. Available at: https://cancercontrol.cancer.gov/ocs/statistics/index.html#definition-survivorship. Accessed June 5, 2020.

17. Bloom JR, Petersen DM, Kang SH. Multi-dimensional quality of life among long-term (5+ years) adult cancer survivors. Psychooncology 2007;16:691-706. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17628036.

18. Stein KD, Syrjala KL, Andrykowski MA. Physical and psychological long-term and late effects of cancer. Cancer 2008;112:2577-2592. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18428205.

19. Harrison SE, Watson EK, Ward AM, et al. Primary health and supportive care needs of long-term cancer survivors: a questionnaire survey. J Clin Oncol 2011;29:2091-2098. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21519023.

20. de Rooij BH, Park ER, Perez GK, et al. Cluster analysis demonstrates the need to individualize care for cancer survivors. Oncologist 2018;23:1474-1481. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29739897.

21. Hsu T, Ennis M, Hood N, et al. Quality of life in long-term breast cancer survivors. J Clin Oncol 2013;31:3540-3548. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23980087.

22. Zucca AC, Boyes AW, Linden W, Girgis A. All's well that ends well? Quality of life and physical symptom clusters in long-term cancer survivors across cancer types. J Pain Symptom Manage 2012;43:720-731. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22277904.

23. Beckjord EB, Reynolds KA, van Londen GJ, et al. Population-level trends in posttreatment cancer survivors' concerns and associated receipt of care: results from the 2006 and 2010 LIVESTRONG surveys. J Psychosoc Oncol 2014;32:125-151. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24364920.

24. Burg MA, Adorno G, Lopez ED, et al. Current unmet needs of cancer survivors: analysis of open-ended responses to the American Cancer Society Study of Cancer Survivors II. Cancer 2015;121:623-630. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25581252.

25. Weaver KE, Forsythe LP, Reeve BB, et al. Mental and physical health-related quality of life among U.S. cancer survivors: population estimates from the 2010 National Health Interview Survey. Cancer Epidemiol Biomarkers Prev 2012;21:2108-2117. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23112268.

26. Valdivieso M, Kujawa AM, Jones T, Baker LH. Cancer survivors in the United States: a review of the literature and a call to action. Int J Med Sci 2012;9:163-173. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22275855.

27. Harrington CB, Hansen JA, Moskowitz M, et al. It's not over when it's over: long-term symptoms in cancer survivors--a systematic review. Int J Psychiatry Med 2010;40:163-181. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20848873.

28. Hewitt M, Greenfield S, Stovall E. From Cancer Patient to Cancer Survivor: Lost in Transition. Committee on Cancer Survivorship: Improving Care and Quality of Life, Institute of Medicine and National Research Council 2005. Available at: http://www.nap.edu/catalog/11468.html.

29. Hwangbo Y, Kang D, Kang M, et al. Incidence of diabetes after cancer development: A Korean national cohort study. JAMA Oncol 2018. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29879271.

30. Park SY, Bae D-S, Nam JH, et al. Quality of life and sexual problems in disease-free survivors of cervical cancer compared with the general population. Cancer 2007;110:2716-2725. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17960806.

31. Paskett ED, Dean JA, Oliveri JM, Harrop JP. Cancer-related lymphedema risk factors, diagnosis, treatment, and impact: a review. J Clin Oncol 2012;30:3726-3733. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23008299.

32. Ruddy KJ, Partridge AH. Fertility (male and female) and menopause. J Clin Oncol 2012;30:3705-3711. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23008319.

33. Brana I, Tabernero J. Cardiotoxicity. Ann Oncol 2010;21 Suppl 7:vii173-179. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20943611.

34. Ewer MS, Ewer SM. Cardiotoxicity of anticancer treatments: what the cardiologist needs to know. Nat Rev Cardiol 2010;7:564-575. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20842180.

35. Lenihan DJ, Cardinale DM. Late cardiac effects of cancer treatment. J Clin Oncol 2012;30:3657-3664. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23008297.

36. Lustberg MB, Reinbolt RE, Shapiro CL. Bone health in adult cancer survivorship. J Clin Oncol 2012;30:3665-3674. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23008309.

37. Adams E, Boulton MG, Horne A, et al. The effects of pelvic radiotherapy on cancer survivors: symptom profile, psychological morbidity and quality of life. Clin Oncol (R Coll Radiol) 2014;26:10-17. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23992740.

38. Nam RK, Cheung P, Herschorn S, et al. Incidence of complications other than urinary incontinence or erectile dysfunction after radical prostatectomy or radiotherapy for prostate cancer: a population-based cohort study. Lancet Oncol 2014;15:223-231. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24440474.

39. Chen T, Fallah M, Jansen L, et al. Distribution and risk of the second discordant primary cancers combined after a specific first primary cancer in German and Swedish cancer registries. Cancer Lett 2015;369:152-166. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26319898.

40. Gibson TM, Park Y, Robien K, et al. Body mass index and risk of second obesity-associated cancers after colorectal cancer: a pooled analysis of prospective cohort studies. J Clin Oncol 2014;32:4004-4011. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25267739.

41. Lam CJ, Curtis RE, Dores GM, et al. Risk factors for melanoma among survivors of non-Hodgkin lymphoma. J Clin Oncol 2015;33:3096-3104. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26240221.

42. Park SM, Yun YH, Kim YA, et al. Prediagnosis body mass index and risk of secondary primary cancer in male cancer survivors: a large cohort study. J Clin Oncol 2016;34:4116-4124. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27863195.

43. Ricceri F, Fasanelli F, Giraudo MT, et al. Risk of second primary malignancies in women with breast cancer: Results from the European prospective investigation into cancer and nutrition (EPIC). Int J Cancer 2015;137:940-948. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25650288.

44. Schaapveld M, Aleman BM, van Eggermond AM, et al. Second cancer risk up to 40 years after treatment for Hodgkin's lymphoma. N Engl J Med 2015;373:2499-2511. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26699166.

45. Shiels MS, Gibson T, Sampson J, et al. Cigarette smoking prior to first cancer and risk of second smoking-associated cancers among survivors of bladder, kidney, head and neck, and stage I lung cancers. J Clin Oncol 2014;32:3989-3995. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25385740.

46. Travis LB, Rabkin CS, Brown LM, et al. Cancer survivorship--genetic susceptibility and second primary cancers: research strategies and recommendations. J Natl Cancer Inst 2006;98:15-25. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16391368.

47. Wallis CJ, Mahar AL, Choo R, et al. Second malignancies after radiotherapy for prostate cancer: systematic review and meta-analysis. BMJ 2016;352:i851. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26936410.

48. Wood ME, Vogel V, Ng A, et al. Second malignant neoplasms: assessment and strategies for risk reduction. J Clin Oncol 2012;30:3734-3745. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23008293.

49. Adjei Boakye E, Buchanan P, Hinyard L, et al. Trends in the risk and burden of second primary malignancy among survivors of smoking-related

cancers in the United States. Int J Cancer 2019;145:143-153. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30613963.

50. Suk R, Mahale P, Sonawane K, et al. Trends in risks for second primary cancers associated with index human papillomavirus-associated cancers. JAMA Netw Open 2018;1:e181999. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30646145.

51. Murphy CC, Gerber DE, Pruitt SL. Prevalence of prior cancer among persons newly diagnosed with cancer: An initial report from the Surveillance, Epidemiology, and End Results program. JAMA Oncol 2018;4:832-836. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29167866.

52. Berrington de Gonzalez A, Curtis RE, Kry SF, et al. Proportion of second cancers attributable to radiotherapy treatment in adults: a cohort study in the US SEER cancer registries. Lancet Oncol 2011;12:353-360. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21454129.

53. Davis EJ, Beebe-Dimmer JL, Yee CL, Cooney KA. Risk of second primary tumors in men diagnosed with prostate cancer: a population-based cohort study. Cancer 2014;120:2735-2741. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24842808.

54. Dores GM, Curtis RE, van Leeuwen FE, et al. Pancreatic cancer risk after treatment of Hodgkin lymphoma. Ann Oncol 2014;25:2073-2079. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25185241.

55. Palumbo A, Bringhen S, Kumar SK, et al. Second primary malignancies with lenalidomide therapy for newly diagnosed myeloma: a meta-analysis of individual patient data. Lancet Oncol 2014;15:333-342. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24525202.

56. Rodriguez AM, Kuo YF, Goodwin JS. Risk of colorectal cancer among long-term cervical cancer survivors. Med Oncol 2014;31:943. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24696219.

57. Wolff AC, Blackford AL, Visvanathan K, et al. Risk of marrow neoplasms after adjuvant breast cancer therapy: the National Comprehensive Cancer Network experience. J Clin Oncol 2014;33:340-348. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25534386.

58. Wong JR, Morton LM, Tucker MA, et al. Risk of subsequent malignant neoplasms in long-term hereditary retinoblastoma survivors after chemotherapy and radiotherapy. J Clin Oncol 2014;32:3284-3290. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25185089.

59. Friedman DL, Whitton J, Leisenring W, et al. Subsequent neoplasms in 5-year survivors of childhood cancer: the Childhood Cancer Survivor Study. J Natl Cancer Inst 2010;102:1083-1095. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20634481.

60. Henderson TO, Oeffinger KC, Whitton J, et al. Secondary gastrointestinal cancer in childhood cancer survivors: a cohort study. Ann Intern Med 2012;156:757-766, W-260. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22665813.

61. Nottage K, McFarlane J, Krasin MJ, et al. Secondary colorectal carcinoma after childhood cancer. J Clin Oncol 2012;30:2552-2558. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22665546.

62. Reulen RC, Winter DL, Frobisher C, et al. Long-term cause-specific mortality among survivors of childhood cancer. JAMA 2010;304:172-179. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20628130.

63. Donin N, Filson C, Drakaki A, et al. Risk of second primary malignancies among cancer survivors in the United States, 1992 through 2008. Cancer 2016;122:3075-3086. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27377470.

64. Travis LB, Demark Wahnefried W, Allan JM, et al. Aetiology, genetics and prevention of secondary neoplasms in adult cancer survivors. Nat Rev Clin Oncol 2013;10:289-301. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23529000.

65. Ruddy KJ, Risendal BC, Garber JE, Partridge AH. Cancer survivorship care: an opportunity to revisit cancer genetics. J Clin Oncol 2016;34:539-541. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26712228.

66. Bellizzi KM, Miller MF, Arora NK, Rowland JH. Positive and negative life changes experienced by survivors of non-Hodgkin's lymphoma. Ann Behav Med 2007;34:188-199. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17927557.

67. Bower JE, Meyerowitz BE, Desmond KA, et al. Perceptions of positive meaning and vulnerability following breast cancer: predictors and outcomes among long-term breast cancer survivors. Ann Behav Med 2005;29:236-245. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15946118.

68. Crespi CM, Ganz PA, Petersen L, et al. Refinement and psychometric evaluation of the impact of cancer scale. J Natl Cancer Inst 2008;100:1530-1541. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18957678.

69. Hodgkinson K, Butow P, Fuchs A, et al. Long-term survival from gynecologic cancer: psychosocial outcomes, supportive care needs and positive outcomes. Gynecol Oncol 2007;104:381-389. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17027072.

70. Wakefield CE, McLoone J, Goodenough B, et al. The psychosocial impact of completing childhood cancer treatment: a systematic review of the literature. J Pediatr Psychol 2010;35:262-274. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19578137.

71. Zebrack BJ, Stuber ML, Meeske KA, et al. Perceived positive impact of cancer among long-term survivors of childhood cancer: a report from the childhood cancer survivor study. Psychooncology 2012;21:630-639. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21425388.

72. Adorno G, Lopez E, Burg MA, et al. Positive aspects of having had cancer: A mixed-methods analysis of responses from the American Cancer Society Study of Cancer Survivors-II (SCS-II). Psychooncology 2018;27:1412-1425. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28637082.

73. Hoffman KE, McCarthy EP, Recklitis CJ, Ng AK. Psychological distress in long-term survivors of adult-onset cancer: results from a national survey. Arch Intern Med 2009;169:1274-1281. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19636028.

74. Smith SK, Zimmerman S, Williams CS, et al. Post-traumatic stress outcomes in non-Hodgkin's lymphoma survivors. J Clin Oncol 2008;26:934-941. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18281667.

75. Smith SK, Zimmerman S, Williams CS, et al. Post-traumatic stress symptoms in long-term non-Hodgkin's lymphoma survivors: does time heal? J Clin Oncol 2011;29:4526-4533. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21990412.

76. Wiener L, Battles H, Bernstein D, et al. Persistent psychological distress in long-term survivors of pediatric sarcoma: the experience at a single institution. Psychooncology 2006;15:898-910. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16402373.

77. Bradley CJ. Financial hardship: a consequence of survivorship? J Clin Oncol 2012;30:1579-1580. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22412150.

78. McGrath PD, Hartigan B, Holewa H, Skarparis M. Returning to work after treatment for haematological cancer: findings from Australia. Support Care Cancer 2012;20:1957-1964. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22033835.

79. Mols F, Aaronson NK, Vingerhoets AJJM, et al. Quality of life among long-term non-Hodgkin lymphoma survivors: a population-based study. Cancer 2007;109:1659-1667. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17330853.

80. Short PF, Vargo MM. Responding to employment concerns of cancer survivors. J Clin Oncol 2006;24:5138-5141. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17093276.

81. Boyes AW, Girgis A, D'Este C, Zucca AC. Prevalence and correlates of cancer survivors' supportive care needs 6 months after diagnosis: a

population-based cross-sectional study. BMC Cancer 2012;12:150. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22510387.

82. Koch L, Jansen L, Brenner H, Arndt V. Fear of recurrence and disease progression in long-term (≥ 5 years) cancer survivors--a systematic review of quantitative studies. Psychooncology 2013;22:1-11. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22232030.

83. Savard J, Ivers H. The evolution of fear of cancer recurrence during the cancer care trajectory and its relationship with cancer characteristics. J Psychosom Res 2013;74:354-360. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23497839.

84. Thewes B, Butow P, Bell ML, et al. Fear of cancer recurrence in young women with a history of early-stage breast cancer: a cross-sectional study of prevalence and association with health behaviours. Support Care Cancer 2012;20:2651-2659. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22328003.

85. Hodges LJ, Humphris GM. Fear of recurrence and psychological distress in head and neck cancer patients and their carers. Psychooncology 2009;18:841-848. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19101920.

86. Koch L, Bertram H, Eberle A, et al. Fear of recurrence in long-term breast cancer survivors-still an issue. Results on prevalence, determinants, and the association with quality of life and depression from the Cancer Survivorship--a multi-regional population-based study. Psychooncology 2014;23:547-554. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24293081.

87. Mehnert A, de Boer A, Feuerstein M. Employment challenges for cancer survivors. Cancer 2013;119 Suppl 11:2151-2159. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23695927.

88. Moran JR, Short PF. Does cancer reduce labor market entry? Evidence for prime-age females. Med Care Res Rev 2014;71:224-242. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24243912.

89. Zajacova A, Dowd JB, Schoeni RF, Wallace RB. Employment and income losses among cancer survivors: Estimates from a national longitudinal survey of American families. Cancer 2015;121:4425-4432. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26501494.

90. Kim YA, Yun YH, Chang YJ, et al. Employment status and work-related difficulties in lung cancer survivors compared with the general population. Ann Surg 2014;259:569-575. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23657081.

91. Duijts SF, van Egmond MP, Spelten E, et al. Physical and psychosocial problems in cancer survivors beyond return to work: a systematic review. Psychooncology 2014;23:481-492. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24375630.

92. Moskowitz MC, Todd BL, Chen R, Feuerstein M. Function and friction at work: a multidimensional analysis of work outcomes in cancer survivors. J Cancer Surviv 2014;8:173-182. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24464639.

93. Islam T, Dahlui M, Majid H, et al. Factors associated with return to work of breast cancer survivors: a systematic review. BMC Public Health 2014;14 Suppl 3:S8. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25437351.

94. Jagsi R, Hawley ST, Abrahamse P, et al. Impact of adjuvant chemotherapy on long-term employment of survivors of early-stage breast cancer. Cancer 2014;120:1854-1862. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24777606.

95. Koch R, Wittekindt C, Altendorf-Hofmann A, et al. Employment pathways and work-related issues in head and neck cancer survivors. Head Neck 2015;37:585-593. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24677561.

96. Noeres D, Park-Simon TW, Grabow J, et al. Return to work after treatment for primary breast cancer over a 6-year period: results from a prospective study comparing patients with the general population. Support

Care Cancer 2013;21:1901-1909. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23417517.

97. Marino P, Luis Sagaon T, Laetitia M, Anne-Gaelle le CS. Sex differences in the return-to-work process of cancer survivors 2 years after diagnosis: results from a large French population-based sample. J Clin Oncol 2013;31:1277-1284. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23358985.

98. van Muijen P, Weevers NL, Snels IA, et al. Predictors of return to work and employment in cancer survivors: a systematic review. Eur J Cancer Care (Engl) 2013;22:144-160. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23279195.

99. Dumas A, Vaz Luis I, Bovagnet T, et al. Impact of breast cancer treatment on employment: Results of a multicenter prospective cohort study (CANTO). J Clin Oncol 2020;38:734-743. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31834818.

100. Stergiou-Kita M, Grigorovich A, Tseung V, et al. Qualitative meta-synthesis of survivors' work experiences and the development of strategies to facilitate return to work. J Cancer Surviv 2014;8:657-670. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24993807.

101. de Boer AG, Taskila TK, Tamminga SJ, et al. Interventions to enhance return-to-work for cancer patients. Cochrane Database Syst Rev 2015:CD007569. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26405010.

102. de Moor JS, Alfano CM, Kent EE, et al. Recommendations for research and practice to improve work outcomes among cancer survivors. J Natl Cancer Inst 2018;110:1041-1047. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30252079.

103. Lamore K, Dubois T, Rothe U, et al. Return to work interventions for cancer survivors: A systematic review and a methodological critique. Int J Environ Res Public Health 2019;16. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31014004.

104. Butow P, Laidsaar-Powell R, Konings S, et al. Return to work after a cancer diagnosis: a meta-review of reviews and a meta-synthesis of recent qualitative studies. J Cancer Surviv 2020;14:114-134. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31858379.

105. Banegas MP, Guy GP, Jr., de Moor JS, et al. For working-age cancer survivors, medical debt and bankruptcy create financial hardships. Health Aff (Millwood) 2016;35:54-61. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26733701.

106. Ramsey S, Blough D, Kirchhoff A, et al. Washington State cancer patients found to be at greater risk for bankruptcy than people without a cancer diagnosis. Health Aff (Millwood) 2013;32:1143-1152. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23676531.

107. Shankaran V, Jolly S, Blough D, Ramsey SD. Risk factors for financial hardship in patients receiving adjuvant chemotherapy for colon cancer: a population-based exploratory analysis. J Clin Oncol 2012;30:1608-1614. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22412136.

108. Guy GP, Jr., Ekwueme DU, Yabroff KR, et al. Economic burden of cancer survivorship among adults in the United States. J Clin Oncol 2013;31:3749-3757. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24043731.

109. Rubens M, Ramamoorthy V, Saxena A, et al. Recent health care expenditure trends among adult cancer survivors in United States, 2009-2016. Am J Clin Oncol 2020;43:349-355. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31990757.

110. Ekwueme DU, Zhao J, Rim SH, et al. Annual out-of-pocket expenditures and financial hardship among cancer survivors aged 18-64 years - United States, 2011-2016. MMWR Morb Mortal Wkly Rep 2019;68:494-499. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31170127.

111. Zheng Z, Jemal A, Han X, et al. Medical financial hardship among cancer survivors in the United States. Cancer 2019;125:1737-1747. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30663039.

112. Zheng Z, Jemal A, Tucker-Seeley R, et al. Worry about daily financial needs and food insecurity among cancer survivors in the United States. J Natl Compr Canc Netw 2020;18:315-327. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32135509.

113. Han X, Zhao J, Zheng Z, et al. Medical financial hardship intensity and financial sacrifice associated with cancer in the United States. Cancer Epidemiol Biomarkers Prev 2020;29:308-317. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31941708.

114. Jagsi R, Pottow JA, Griffith KA, et al. Long-term financial burden of breast cancer: experiences of a diverse cohort of survivors identified through population-based registries. J Clin Oncol 2014;32:1269-1276. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24663041.

115. Wheeler SB, Spencer JC, Pinheiro LC, et al. Financial impact of breast cancer in black versus white women. J Clin Oncol 2018;36:1695-1701. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29668368.

116. Bestvina CM, Zullig LL, Rushing C, et al. Patient-oncologist cost communication, financial distress, and medication adherence. J Oncol Pract 2014;10:162-167. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24839274.

117. Kale HP, Carroll NV. Self-reported financial burden of cancer care and its effect on physical and mental health-related quality of life among US cancer survivors. Cancer 2016;122:283-289. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26991528.

118. Zheng Z, Han X, Guy GP, Jr., et al. Do cancer survivors change their prescription drug use for financial reasons? Findings from a nationally representative sample in the United States. Cancer 2017;123:1453-1463. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28218801.

119. Knight TG, Deal AM, Dusetzina SB, et al. Financial toxicity in adults with cancer: Adverse outcomes and noncompliance. J Oncol Pract 2018:JOP1800120. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30355027.

120. Carmack CL, Basen-Engquist K, Gritz ER. Survivors at higher risk for adverse late outcomes due to psychosocial and behavioral risk factors. Cancer Epidemiol Biomarkers Prev 2011;20:2068-2077. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21980014.

121. Adler NE, Page NEK. Institute of Medicine (IOM). 2008. Cancer Care for the Whole Patient: Meeting Psychosocial Health Needs. 2008. Available at: https://www.nap.edu/catalog/11993/cancer-care-for-the-whole-patient-meeting-psychosocial-health-needs.

122. Earle CC, Ganz PA. Cancer survivorship care: don't let the perfect be the enemy of the good. J Clin Oncol 2012;30:3764-3768. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23008287.

123. Alfano CM, Mayer DK, Bhatia S, et al. Implementing personalized pathways for cancer follow-up care in the United States: Proceedings from an American Cancer Society-American Society of Clinical Oncology summit. CA Cancer J Clin 2019;69:234-247. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30849190.

124. Kline RM, Arora NK, Bradley CJ, et al. Long-term survivorship care after cancer treatment - summary of a 2017 National Cancer Policy Forum Workshop. J Natl Cancer Inst 2018;110:1300-1310. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30496448.

125. Downs-Holmes C, Dracon A, Svarovsky T, Sustin M. Development of a survivorship program. Clin J Oncol Nurs 2014;18 Suppl:53-56. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25252995.

126. Halpern MT, Viswanathan M, Evans TS, et al. Models of cancer survivorship care: overview and summary of current evidence. J Oncol Pract 2015;11:e19-27. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25205779.

127. Nekhlyudov L. Integrating primary care in cancer survivorship programs: models of care for a growing patient population. Oncologist 2014;19:579-582. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24794157.

128. Oeffinger KC, Argenbright KE, Levitt GA, et al. Models of cancer survivorship health care: moving forward. Am Soc Clin Oncol Educ Book 2014:205-213. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24857078.

129. Glaser KM, McDaniel DC, Hess SM, et al. Implementing an integrative survivorship program at a comprehensive cancer center: A multimodal approach to life after cancer. J Altern Complement Med 2019;25:S106-s111. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30870027.

130. Choi Y, Radhakrishnan A, Mahabare D, et al. The Johns Hopkins Primary Care for Cancer Survivor Clinic: lessons learned in our first 4 years. J Cancer Surviv 2020;14:19-25. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31650473.

131. Spears JA, Craft M, White S. Outcomes of cancer survivorship care provided by advanced practice RNs compared to other models of care: a systematic review. Oncol Nurs Forum 2017;44:E34-E41. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28067032.

132. Hoekstra RA, Heins MJ, Korevaar JC. Health care needs of cancer survivors in general practice: a systematic review. BMC Fam Pract 2014;15:94. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24885266.

133. Luctkar-Flude M, Aiken A, McColl MA, et al. Are primary care providers implementing evidence-based care for breast cancer survivors? Can Fam Physician 2015;61:978-984. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26889509.

134. Potosky AL, Han PK, Rowland J, et al. Differences between primary care physicians' and oncologists' knowledge, attitudes and practices regarding the care of cancer survivors. J Gen Intern Med 2011;26:1403-1410. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21785923.

135. Virgo KS, Lerro CC, Klabunde CN, et al. Barriers to breast and colorectal cancer survivorship care: perceptions of primary care physicians and medical oncologists in the United States. J Clin Oncol 2013;31:2322-2336. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23690429.

136. Walter FM, Usher-Smith JA, Yadlapalli S, Watson E. Caring for people living with, and beyond, cancer: an online survey of GPs in England. Br J Gen Pract 2015;65:e761-768. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26500324.

137. Geramita EM, Parker IR, Brufsky JW, et al. Primary care providers' knowledge, attitudes, beliefs, and practices regarding their preparedness to provide cancer survivorship care. J Cancer Educ 2019. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31388974.

138. McDonough AL, Rabin J, Horick N, et al. Practice, preferences, and practical tips from primary care physicians to improve the care of cancer survivors. J Oncol Pract 2019;15:e600-e606. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31150311.

139. Rubinstein EB, Miller WL, Hudson SV, et al. Cancer survivorship care in advanced primary care practices: A qualitative study of challenges and opportunities. JAMA Intern Med 2017;177:1726-1732. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28973067.

140. Heins M, Schellevis F, Rijken M, et al. Determinants of increased primary health care use in cancer survivors. J Clin Oncol 2012;30:4155-4160. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23071230.

141. Snyder CF, Frick KD, Peairs KS, et al. Comparing care for breast cancer survivors to non-cancer controls: a five-year longitudinal study. J Gen Intern Med 2009;24:469-474. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19156470.

142. Klabunde CN, Han PK, Earle CC, et al. Physician roles in the cancer-related follow-up care of cancer survivors. Fam Med 2013;45:463-474. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23846965.

143. Hudson SV, Miller SM, Hemler J, et al. Adult cancer survivors discuss follow-up in primary care: 'not what i want, but maybe what i need'. Ann Fam Med 2012;10:418-427. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22966105.

144. Mayer EL, Gropper AB, Neville BA, et al. Breast cancer survivors' perceptions of survivorship care options. J Clin Oncol 2012;30:158-163. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22162585.

145. Khan NF, Evans J, Rose PW. A qualitative study of unmet needs and interactions with primary care among cancer survivors. Br J Cancer 2011;105 Suppl 1:S46-51. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22048032.

146. Grunfeld E, Levine MN, Julian JA, et al. Randomized trial of long-term follow-up for early-stage breast cancer: a comparison of family physician versus specialist care. J Clin Oncol 2006;24:848-855. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16418496.

147. Wattchow DA, Weller DP, Esterman A, et al. General practice vs surgical-based follow-up for patients with colon cancer: randomised controlled trial. Br J Cancer 2006;94:1116-1121. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16622437.

148. Rechis R, Beckjord EB, Nutt S. Potential benefits of treatment summaries for survivors' health and information needs: results from a LIVESTRONG survey. J Oncol Pract 2014;10:75-78. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24003173.

149. Majhail NS, Murphy E, Laud P, et al. Randomized controlled trial of individualized treatment summary and survivorship care plans for hematopoietic cell transplantation survivors. Haematologica 2019;104:1084-1092. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30514795.

150. Grunfeld E, Julian JA, Pond G, et al. Evaluating survivorship care plans: results of a randomized, clinical trial of patients with breast cancer. J Clin Oncol 2011;29:4755-4762. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22042959.

151. Boekhout AH, Maunsell E, Pond GR, et al. A survivorship care plan for breast cancer survivors: extended results of a randomized clinical trial. J Cancer Surviv 2015;9:683-691. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25896265.

152. Jefford M, Schofield P, Emery J. Improving survivorship care. J Clin Oncol 2012;30:1391-1392; author reply 1393-1394. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22291077.

153. Smith TJ, Snyder C. Is it time for (survivorship care) plan B? J Clin Oncol 2011;29:4740-4742. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22042961.

154. Stricker CT, Jacobs LA, Palmer SC. Survivorship care plans: an argument for evidence over common sense. J Clin Oncol 2012;30:1392-1393; author reply 1393-1395. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22291072.

155. Jefford M, Gough K, Drosdowsky A, et al. A randomized controlled trial of a nurse-led supportive care package (SurvivorCare) for survivors of colorectal cancer. Oncologist 2016;21:1014-1023. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27306909.

156. Nicolaije KA, Ezendam NP, Vos MC, et al. Impact of an automatically generated cancer survivorship care plan on patient-reported outcomes in routine clinical practice: longitudinal outcomes of a pragmatic, cluster randomized trial. J Clin Oncol 2015;33:3550-3559. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26304900.

157. Maly RC, Liang LJ, Liu Y, et al. Randomized controlled trial of survivorship care plans among low-income, predominantly Latina breast cancer survivors. J Clin Oncol 2017:JCO2016689497. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28418767.

158. Parker PA, Banerjee SC, Matasar MJ, et al. Efficacy of a survivorship-focused consultation versus a time-controlled rehabilitation consultation in patients with lymphoma: A cluster randomized controlled trial. Cancer 2018;124:4567-4576. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30335188.

159. Tevaarwerk AJ, Hocking WG, Buhr KA, et al. A randomized trial of immediate versus delayed survivorship care plan receipt on patient satisfaction and knowledge of diagnosis and treatment. Cancer 2019;125:1000-1007. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30690714.

160. Jacobsen PB, DeRosa AP, Henderson TO, et al. Systematic review of the impact of cancer survivorship care plans on health outcomes and health care delivery. J Clin Oncol 2018:JCO2018777482. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29775389.

161. Blanch-Hartigan D, Forsythe LP, Alfano CM, et al. Provision and discussion of survivorship care plans among cancer survivors: results of a nationally representative survey of oncologists and primary care physicians. J Clin Oncol 2014;32:1578-1585. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24752057.

162. Kenzik KM, Kvale EA, Rocque GB, et al. Treatment summaries and follow-up care instructions for cancer survivors: improving survivor self-efficacy and health care utilization. Oncologist 2016;21:817-824. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27245567.

163. Swoboda CM, Fareed N, Walker DM, Huerta TR. The effect of cancer treatment summaries on patient-centered communication and quality of care for cancer survivors: A pooled cross-sectional HINTS analysis. Patient Educ Couns 2019. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31477514.

164. Mayer DK, Nekhlyudov L, Snyder CF, et al. American society of clinical oncology clinical expert statement on cancer survivorship care planning. J Oncol Pract 2014;10:345-351. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25316025.

165. Tevaarwerk AJ, Wisinski KB, Buhr KA, et al. Leveraging electronic health record systems to create and provide electronic cancer survivorship care plans: a pilot study. J Oncol Pract 2014;10:e150-159. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24520142.

166. Garcia SF, Kircher SM, Oden M, et al. Survivorship care planning in a comprehensive cancer center using an implementation framework. J Community Support Oncol 2016;14:192-199. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27258051.

167. Tevaarwerk AJ, Hocking WG, Zeal JL, et al. Accuracy and thoroughness of treatment summaries provided as part of survivorship care plans prepared by two cancer centers. J Oncol Pract 2017:JOP2016018648. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28221896.

168. Mayer DK, Gerstel A, Walton AL, et al. Implementing survivorship care plans for colon cancer survivors. Oncol Nurs Forum 2014;41:266-273. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24769591.

169. Brenner DJ, Hall EJ. Computed tomography--an increasing source of radiation exposure. N Engl J Med 2007;357:2277-2284. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18046031.

170. Chien SH, Liu CJ, Hu YW, et al. Frequency of surveillance computed tomography in non-Hodgkin lymphoma and the risk of secondary primary malignancies: A nationwide population-based study. Int J Cancer 2015;137:658-665. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25630766.

171. Avis NE, Smith KW, McGraw S, et al. Assessing quality of life in adult cancer survivors (QLACS). Qual Life Res 2005;14:1007-1023. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16041897.

172. Campbell HS, Hall AE, Sanson-Fisher RW, et al. Development and validation of the Short-Form Survivor Unmet Needs Survey (SF-SUNS). Support Care Cancer 2014;22:1071-1079. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24292016.

173. Chopra I, Kamal KM. A systematic review of quality of life instruments in long-term breast cancer survivors. Health Qual Life Outcomes 2012;10:14. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22289425.

174. Ferrell BR, Dow KH, Grant M. Measurement of the quality of life in cancer survivors. Qual Life Res 1995;4:523-531. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8556012.

175. Ganz PA. Cancer Rehabilitation Evaluation System (CARES) and CARES-SF now publicly available. J Clin Oncol 2012;30:4046-4047. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23008314.

176. Pearce NJ, Sanson-Fisher R, Campbell HS. Measuring quality of life in cancer survivors: a methodological review of existing scales. Psychooncology 2008;17:629-640. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17973235.

177. Richardson A, Addington-Hall J, Amir Z, et al. Knowledge, ignorance and priorities for research in key areas of cancer survivorship: findings from a scoping review. Br J Cancer 2011;105 Suppl 1:S82-94. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22048036.

178. Palesh O, Demark-Wahnefried W, Mustian K, et al. Conducting cancer control and survivorship research via cooperative groups: a report from the American Society of Preventive Oncology. Cancer Epidemiol Biomarkers Prev 2011;20:1050-1055. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21502540.

179. Stanton AL. What happens now? Psychosocial care for cancer survivors after medical treatment completion. J Clin Oncol 2012;30:1215-1220. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22412133.

180. Jacobsen PB, Rowland JH, Paskett ED, et al. Identification of key gaps in cancer survivorship research: findings from the American Society of Clinical Oncology survey. J Oncol Pract 2016;12:190-193. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26907451.

181. Rowland JH, Gallicchio L, Mollica M, et al. Survivorship science at the NIH: Lessons learned from grants funded in fiscal year 2016. J Natl Cancer Inst 2019;111:109-117. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30657942.

182. Alfano CM, Smith T, de Moor JS, et al. An action plan for translating cancer survivorship research into care. J Natl Cancer Inst 2014;106. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25249551.

183. Underwood JM, Townsend JS, Stewart SL, et al. Surveillance of demographic characteristics and health behaviors among adult cancer survivors--Behavioral Risk Factor Surveillance System, United States, 2009. MMWR Surveill Summ 2012;61:1-23. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22258477.

184. Harding M. Health-promotion behaviors and psychological distress in cancer survivors. Oncol Nurs Forum 2012;39:E132-140. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22374501.

185. Rausch SM, Millay S, Scott C, et al. Health behaviors among cancer survivors receiving screening mammography. Am J Clin Oncol 2012;35:22-31. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21293247.

186. Shoemaker ML, White MC, Hawkins NA, Hayes NS. Prevalence of smoking and obesity among U.S. cancer survivors: estimates from the National Health Interview Survey, 2008-2012. Oncol Nurs Forum 2016;43:436-441. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27314186.

187. Hyland KA, Jacobs JM, Lennes IT, et al. Are cancer survivors following the National Comprehensive Cancer Network health behavior guidelines? An assessment of patients attending a cancer survivorship clinic. J Psychosoc Oncol 2018;36:64-81. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29303476.

188. Westmaas JL, Alcaraz KI, Berg CJ, Stein KD. Prevalence and correlates of smoking and cessation-related behavior among survivors of ten cancers: findings from a nationwide survey nine years after diagnosis. Cancer Epidemiol Biomarkers Prev 2014;23:1783-1792. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25100826.

189. Carpentier MY, Vernon SW, Bartholomew LK, et al. Receipt of recommended surveillance among colorectal cancer survivors: a

systematic review. J Cancer Surviv 2013;7:464-483. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23677524.

190. Grunfeld E, Moineddin R, Gunraj N, et al. Cancer screening practices of cancer survivors: population-based, longitudinal study. Can Fam Physician 2012;58:980-986. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22972732.

191. Wirtz HS, Boudreau DM, Gralow JR, et al. Factors associated with long-term adherence to annual surveillance mammography among breast cancer survivors. Breast Cancer Res Treat 2014;143:541-550. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24407530.

192. Campbell PT, Patel AV, Newton CC, et al. Associations of recreational physical activity and leisure time spent sitting with colorectal cancer survival. J Clin Oncol 2013;31:876-885. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23341510.

193. Dignam JJ, Polite BN, Yothers G, et al. Body mass index and outcomes in patients who receive adjuvant chemotherapy for colon cancer. J Natl Cancer Inst 2006;98:1647-1654. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17105987.

194. Kabat GC, Matthews CE, Kamensky V, et al. Adherence to cancer prevention guidelines and cancer incidence, cancer mortality, and total mortality: a prospective cohort study. Am J Clin Nutr 2015;101:558-569. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25733641.

195. Inoue-Choi M, Lazovich D, Prizment AE, Robien K. Adherence to the World Cancer Research Fund/American Institute for Cancer Research recommendations for cancer prevention is associated with better health-related quality of life among elderly female cancer survivors. J Clin Oncol 2013;31:1758-1766. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23569318.

196. Lee IM, Wolin KY, Freeman SE, et al. Physical activity and survival after cancer diagnosis in men. J Phys Act Health 2014;11:85-90. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23250326.

197. Sinicrope FA, Foster NR, Yoon HH, et al. Association of obesity with DNA mismatch repair status and clinical outcome in patients with stage II or III colon carcinoma participating in NCCTG and NSABP adjuvant chemotherapy trials. J Clin Oncol 2012;30:406-412. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22203756.

198. Van Blarigan EL, Fuchs CS, Niedzwiecki D, et al. Association of survival with adherence to the American Cancer Society nutrition and physical activity guidelines for cancer survivors after colon cancer diagnosis: The CALGB 89803/Alliance trial. JAMA Oncol 2018;4:783-790. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29710284.

199. Wyszynski A, Tanyos SA, Rees JR, et al. Body mass and smoking are modifiable risk factors for recurrent bladder cancer. Cancer 2014;120:408-414. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24122218.

200. Karavasiloglou N, Pestoni G, Wanner M, et al. Healthy lifestyle is inversely associated with mortality in cancer survivors: Results from the Third National Health and Nutrition Examination Survey (NHANES III). PLoS One 2019;14:e0218048. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31242220.

201. Yang B, Jacobs EJ, Gapstur SM, et al. Active smoking and mortality among colorectal cancer survivors: the Cancer Prevention Study II nutrition cohort. J Clin Oncol 2015;33:885-893. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25646196.

202. Hudis CA, Jones L. Promoting exercise after a cancer diagnosis: easier said than done. Br J Cancer 2014;110:829-830. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24548883.

203. Lakoski SG, Eves ND, Douglas PS, Jones LW. Exercise rehabilitation in patients with cancer. Nat Rev Clin Oncol 2012;9:288-296. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22392097.

204. Brown JC, Huedo-Medina TB, Pescatello LS, et al. Efficacy of exercise interventions in modulating cancer-related fatigue among adult cancer survivors: a meta-analysis. Cancer Epidemiol Biomarkers Prev

2011;20:123-133. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21051654.

205. Demark-Wahnefried W, Jones LW. Promoting a healthy lifestyle among cancer survivors. Hematol Oncol Clin North Am 2008;22:319-342. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18395153.

206. Ferrer RA, Huedo-Medina TB, Johnson BT, et al. Exercise interventions for cancer survivors: a meta-analysis of quality of life outcomes. Ann Behav Med 2011;41:32-47. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20931309.

207. Fong DY, Ho JW, Hui BP, et al. Physical activity for cancer survivors: meta-analysis of randomised controlled trials. BMJ 2012;344:e70. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22294757.

208. Gardner JR, Livingston PM, Fraser SF. Effects of exercise on treatment-related adverse effects for patients with prostate cancer receiving androgen-deprivation therapy: a systematic review. J Clin Oncol 2014;32:335-346. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24344218.

209. Jones LW, Alfano CM. Exercise-oncology research: Past, present, and future. Acta Oncol 2013;52:195-215. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23244677.

210. Mishra SI, Scherer RW, Geigle PM, et al. Exercise interventions on health-related quality of life for cancer survivors. Cochrane Database Syst Rev 2012;8:CD007566. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22895961.

211. Mishra SI, Scherer RW, Snyder C, et al. Are exercise programs effective for improving health-related quality of life among cancer survivors? A systematic review and meta-analysis. Oncol Nurs Forum 2014;41:E326-342. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25355029.

212. Rock CL, Doyle C, Demark-Wahnefried W, et al. Nutrition and physical activity guidelines for cancer survivors. CA Cancer J Clin 2012;62:242-274. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22539238.

213. Schmitt J, Lindner N, Reuss-Borst M, et al. A 3-week multimodal intervention involving high-intensity interval training in female cancer survivors: a randomized controlled trial. Physiol Rep 2016;4. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26869680.

214. Schmitz KH, Courneya KS, Matthews C, et al. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. Med Sci Sports Exerc 2010;42:1409-1426. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20559064.

215. Speck RM, Courneya KS, Masse LC, et al. An update of controlled physical activity trials in cancer survivors: a systematic review and meta-analysis. J Cancer Surviv 2010;4:87-100. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20052559.

216. Dieli-Conwright CM, Courneya KS, Demark-Wahnefried W, et al. Aerobic and resistance exercise improves physical fitness, bone health, and quality of life in overweight and obese breast cancer survivors: a randomized controlled trial. Breast Cancer Res 2018;20:124. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30340503.

217. Courneya KS, Mackey JR, Bell GJ, et al. Randomized controlled trial of exercise training in postmenopausal breast cancer survivors: cardiopulmonary and quality of life outcomes. J Clin Oncol 2003;21:1660-1668. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12721239.

218. Markes M, Brockow T, Resch KL. Exercise for women receiving adjuvant therapy for breast cancer. Cochrane Database Syst Rev 2006:CD005001. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17054230.

219. McNeely ML, Campbell KL, Rowe BH, et al. Effects of exercise on breast cancer patients and survivors: a systematic review and meta-analysis. CMAJ 2006;175:34-41. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16818906.

220. Jones LW, Liu Q, Armstrong GT, et al. Exercise and risk of major cardiovascular events in adult survivors of childhood hodgkin lymphoma: a report from the childhood cancer survivor study. J Clin Oncol 2014;32:3643-3650. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25311213.

221. Jones LW, Habel LA, Weltzien E, et al. Exercise and risk of cardiovascular events in women with nonmetastatic breast cancer. J Clin Oncol 2016;34:2743-2749. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27217451.

222. Arem H, Pfeiffer RM, Engels EA, et al. Pre- and postdiagnosis physical activity, television viewing, and mortality among patients with colorectal cancer in the National Institutes of Health-AARP Diet and Health study. J Clin Oncol 2014;33:180-188. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25488967.

223. Arem H, Moore SC, Patel A, et al. Leisure time physical activity and mortality: a detailed pooled analysis of the dose-response relationship. JAMA Intern Med 2015;175:959-967. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25844730.

224. Betof AS, Dewhirst MW, Jones LW. Effects and potential mechanisms of exercise training on cancer progression: A translational perspective. Brain Behav Immun 2013;30:S75-S87. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22610066.

225. Courneya KS, Sellar CM, Stevinson C, et al. Randomized controlled trial of the effects of aerobic exercise on physical functioning and quality of life in lymphoma patients. J Clin Oncol 2009;27:4605-4612. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19687337.

226. Ibrahim EM, Al-Homaidh A. Physical activity and survival after breast cancer diagnosis: meta-analysis of published studies. Med Oncol 2011;28:753-765. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20411366.

227. Kenfield SA, Stampfer MJ, Giovannucci E, Chan JM. Physical activity and survival after prostate cancer diagnosis in the health professionals follow-up study. J Clin Oncol 2011;29:726-732. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21205749.

228. Kohler LN, Garcia DO, Harris RB, et al. Adherence to diet and physical activity cancer prevention guidelines and cancer outcomes: a systematic review. Cancer Epidemiol Biomarkers Prev 2016;25:1018-1028. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27340121.

229. Kyu HH, Bachman VF, Alexander LT, et al. Physical activity and risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and ischemic stroke events: systematic review and dose-response meta-analysis for the Global Burden of Disease Study 2013. BMJ 2016;354:i3857. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27510511.

230. Lahart IM, Metsios GS, Nevill AM, Carmichael AR. Physical activity, risk of death and recurrence in breast cancer survivors: A systematic review and meta-analysis of epidemiological studies. Acta Oncol 2015;54:635-654. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25752971.

231. Ligibel J. Lifestyle factors in cancer survivorship. J Clin Oncol 2012;30:3697-3704. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23008316.

232. McTiernan A, Friedenreich CM, Katzmarzyk PT, et al. Physical activity in cancer prevention and survival: A systematic review. Med Sci Sports Exerc 2019;51:1252-1261. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31095082.

233. Meyerhardt JA, Heseltine D, Niedzwiecki D, et al. Impact of physical activity on cancer recurrence and survival in patients with stage III colon cancer: findings from CALGB 89803. J Clin Oncol 2006;24:3535-3541. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16822843.

234. Meyerhardt JA, Ma J, Courneya KS. Energetics in colorectal and prostate cancer. J Clin Oncol 2010;28:4066-4073. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20644082.

235. Moore SC, Lee IM, Weiderpass E, et al. Association of leisure-time physical activity with risk of 26 types of cancer in 1.44 million adults. JAMA Intern Med 2016;176:816-825. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27183032.

236. Schmid D, Leitzmann MF. Association between physical activity and mortality among breast cancer and colorectal cancer survivors: a systematic review and meta-analysis. Ann Oncol 2014;25:1293-1311. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24644304.

237. Williams PT. Significantly greater reduction in breast cancer mortality from post-diagnosis running than walking. Int J Cancer 2014;135:1195-1202. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24470442.

238. Wu W, Guo F, Ye J, et al. Pre- and post-diagnosis physical activity is associated with survival benefits of colorectal cancer patients: a systematic review and meta-analysis. Oncotarget 2016;7:52095-52103. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27437765.

239. Patel AV, Friedenreich CM, Moore SC, et al. American College of Sports Medicine roundtable report on physical activity, sedentary behavior, and cancer prevention and control. Med Sci Sports Exerc 2019;51:2391-2402. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31626056.

240. Ballard-Barbash R, Friedenreich CM, Courneya KS, et al. Physical activity, biomarkers, and disease outcomes in cancer survivors: a systematic review. J Natl Cancer Inst 2012;104:815-840. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22570317.

241. Ariza-Garcia A, Galiano-Castillo N, Cantarero-Villanueva I, et al. Influence of physical inactivity in psychophysiological state of breast cancer survivors. Eur J Cancer Care (Engl) 2013;22:738-745. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23889104.

242. Biswas A, Oh PI, Faulkner GE, et al. Sedentary time and its association with risk for disease incidence, mortality, and hospitalization in adults: a systematic review and meta-analysis. Ann Intern Med 2015;162:123-132. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25599350.

243. Cannioto R, LaMonte MJ, Risch HA, et al. Chronic recreational physical inactivity and epithelial ovarian cancer risk: evidence from the Ovarian Cancer Association Consortium. Cancer Epidemiol Biomarkers Prev 2016;25:1114-1124. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27197285.

244. George SM, Alfano CM, Groves J, et al. Objectively measured sedentary time is related to quality of life among cancer survivors. PLoS One 2014;9:e87937. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24505335.

245. Patel AV, Hildebrand JS, Campbell PT, et al. Leisure-time spent sitting and site-specific cancer incidence in a large U.S. cohort. Cancer Epidemiol Biomarkers Prev 2015;24:1350-1359. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26126627.

246. Schmid D, Leitzmann MF. Television viewing and time spent sedentary in relation to cancer risk: a meta-analysis. J Natl Cancer Inst 2014;106. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24935969.

247. Shen D, Mao W, Liu T, et al. Sedentary behavior and incident cancer: a meta-analysis of prospective studies. PLoS One 2014;9:e105709. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25153314.

248. Godin G, Shephard RJ. Godin Leisure-Time Exercise Questionnaire. Medicine and Science in Sports and Exercise 1997;29 June Supplement:S36-S38. Available at: http://journals.lww.com/acsm-msse/Citation/1997/06001/Godin_Leisure_Time_Exercise_Questionnaire.9.aspx.

249. Amireault S, Godin G, Lacombe J, Sabiston CM. Validation of the Godin-Shephard Leisure-Time Physical Activity Questionnaire classification coding system using accelerometer assessment among breast cancer survivors. J Cancer Surviv 2015;9:532-540. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25666749.

250. Blaney JM, Lowe-Strong A, Rankin-Watt J, et al. Cancer survivors' exercise barriers, facilitators and preferences in the context of fatigue, quality of life and physical activity participation: a questionnaire-survey.

Psychooncology 2013;22:186-194. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23296635.

251. Jones LW. Evidence-based risk assessment and recommendations for physical activity clearance: cancer. Appl Physiol Nutr Metab 2011;36 Suppl 1:S101-112. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21800938.

252. Brown JC, Schmitz KH. The prescription or proscription of exercise in colorectal cancer care. Med Sci Sports Exerc 2014;46:2202-2209. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24781887.

253. Wolin KY, Schwartz AL, Matthews CE, et al. Implementing the exercise guidelines for cancer survivors. J Support Oncol 2012;10:171-177. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22579268.

254. Bredin SS, Gledhill N, Jamnik VK, Warburton DE. PAR-Q+ and ePARmed-X+: new risk stratification and physical activity clearance strategy for physicians and patients alike. Can Fam Physician 2013;59:273-277. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23486800.

255. Brown JC, John GM, Segal S, et al. Physical activity and lower limb lymphedema among uterine cancer survivors. Med Sci Sports Exerc 2013;45:2091-2097. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23657171.

256. Courneya KS, Segal RJ, Mackey JR, et al. Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant chemotherapy: a multicenter randomized controlled trial. J Clin Oncol 2007;25:4396-4404. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17785708.

257. Hayes SC, Speck RM, Reimet E, et al. Does the effect of weight lifting on lymphedema following breast cancer differ by diagnostic method: results from a randomized controlled trial. Breast Cancer Res Treat 2011;130:227-234. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21562712.

258. Schmitz KH, Ahmed RL, Troxel A, et al. Weight lifting in women with breast-cancer-related lymphedema. N Engl J Med 2009;361:664-673. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19675330.

259. Schmitz KH, Ahmed RL, Troxel AB, et al. Weight lifting for women at risk for breast cancer-related lymphedema: a randomized trial. JAMA 2010;304:2699-2705. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21148134.

260. Brown JC, Troxel AB, Schmitz KH. Safety of weightlifting among women with or at risk for breast cancer-related lymphedema: musculoskeletal injuries and health care use in a weightlifting rehabilitation trial. Oncologist 2012;17:1120-1128. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22752068.

261. Campbell KL, Winters-Stone KM, Wiskemann J, et al. Exercise guidelines for cancer survivors: Consensus statement from international multidisciplinary roundtable. Med Sci Sports Exerc 2019;51:2375-2390. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31626055.

262. Piercy KL, Troiano RP, Ballard RM, et al. The physical activity guidelines for Americans. JAMA 2018;320:2020-2028. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30418471.

263. Rock CL, Thomson C, Gansler T, et al. American Cancer Society guideline for diet and physical activity for cancer prevention. CA Cancer J Clin 2020. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32515498.

264. Blanchard CM, Courneya KS, Stein K. Cancer survivors' adherence to lifestyle behavior recommendations and associations with health-related quality of life: results from the American Cancer Society's SCS-II. J Clin Oncol 2008;26:2198-2204. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18445845.

265. Blair CK, Morey MC, Desmond RA, et al. Light-intensity activity attenuates functional decline in older cancer survivors. Med Sci Sports Exerc 2014;46:1375-1383. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24389524.

266. Jones LW, Eves ND, Peppercorn J. Pre-exercise screening and prescription guidelines for cancer patients. Lancet Oncol 2010;11:914-916. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20708967.

267. Scharhag-Rosenberger F, Kuehl R, Klassen O, et al. Exercise training intensity prescription in breast cancer survivors: validity of current practice and specific recommendations. J Cancer Surviv 2015;9:612-619. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25711667.

268. Battaglini CL, Mills RC, Phillips BL, et al. Twenty-five years of research on the effects of exercise training in breast cancer survivors: A systematic review of the literature. World J Clin Oncol 2014;5:177-190. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24829866.

269. Brown JC, Schmitz KH. Weight lifting and physical function among survivors of breast cancer: a post hoc analysis of a randomized controlled trial. J Clin Oncol 2015;33:2184-2189. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25964257.

270. Focht BC, Clinton SK, Devor ST, et al. Resistance exercise interventions during and following cancer treatment: a systematic review. J Support Oncol 2013;11:45-60. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23967493.

271. Hanson ED, Wagoner CW, Anderson T, Battaglini CL. The independent effects of strength training in cancer survivors: a systematic review. Curr Oncol Rep 2016;18:31. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27025505.

272. Lonbro S. The effect of progressive resistance training on lean body mass in post-treatment cancer patients - a systematic review. Radiother Oncol 2014;110:71-80. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24060169.

273. Strasser B, Steindorf K, Wiskemann J, Ulrich CM. Impact of resistance training in cancer survivors: a meta-analysis. Med Sci Sports Exerc 2013;45:2080-2090. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23669878.

274. Hardee JP, Porter RR, Sui X, et al. The effect of resistance exercise on all-cause mortality in cancer survivors. Mayo Clin Proc 2014;89:1108-1115. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24958698.

275. Bluethmann SM, Vernon SW, Gabriel KP, et al. Taking the next step: a systematic review and meta-analysis of physical activity and behavior change interventions in recent post-treatment breast cancer survivors. Breast Cancer Res Treat 2015;149:331-342. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25555831.

276. Shuval K, Leonard T, Drope J, et al. Physical activity counseling in primary care: Insights from public health and behavioral economics. CA Cancer J Clin 2017;67:233-244. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28198998.

277. Swartz MC, Lewis ZH, Lyons EJ, et al. Effect of home and community-based physical activity interventions on physical function among cancer survivors: a systematic review and meta-analysis. Arch Phys Med Rehabil 2017;98:1652-1665. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28427925.

278. Bourke L, Homer KE, Thaha MA, et al. Interventions to improve exercise behaviour in sedentary people living with and beyond cancer: a systematic review. Br J Cancer 2014;110:831-841. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24335923.

279. Pinto BM, Ciccolo JT. Physical activity motivation and cancer survivorship. Recent Results Cancer Res 2011;186:367-387. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21113773.

280. White SM, McAuley E, Estabrooks PA, Courneya KS. Translating physical activity interventions for breast cancer survivors into practice: an evaluation of randomized controlled trials. Ann Behav Med 2009;37:10-19. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19255819.

281. Turner RR, Steed L, Quirk H, et al. Interventions for promoting habitual exercise in people living with and beyond cancer. Cochrane Database Syst Rev 2018;9:CD010192. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30229557.

282. Belanger LJ, Plotnikoff RC, Clark A, Courneya KS. A survey of physical activity programming and counseling preferences in young-adult cancer survivors. Cancer Nurs 2012;35:48-54. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21558852.

283. Jones LW, Courneya KS. Exercise counseling and programming preferences of cancer survivors. Cancer Pract 2002;10:208-215. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12100105.

284. Stevinson C, Capstick V, Schepansky A, et al. Physical activity preferences of ovarian cancer survivors. Psychooncology 2009;18:422-428. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19243089.

285. Demark-Wahnefried W, Aziz NM, Rowland JH, Pinto BM. Riding the crest of the teachable moment: promoting long-term health after the diagnosis of cancer. J Clin Oncol 2005;23:5814-5830. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16043830.

286. Jones LW, Courneya KS, Fairey AS, Mackey JR. Effects of an oncologist's recommendation to exercise on self-reported exercise behavior in newly diagnosed breast cancer survivors: a single-blind, randomized controlled trial. Ann Behav Med 2004;28:105-113. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15454357.

287. Sabatino SA, Coates RJ, Uhler RJ, et al. Provider counseling about health behaviors among cancer survivors in the United States. J Clin Oncol 2007;25:2100-2106. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17513816.

288. Demark-Wahnefried W, Clipp EC, Lipkus IM, et al. Main outcomes of the FRESH START trial: a sequentially tailored, diet and exercise mailed print intervention among breast and prostate cancer survivors. J Clin Oncol 2007;25:2709-2718. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17602076.

289. Demark-Wahnefried W, Morey MC, Sloane R, et al. Reach out to enhance wellness home-based diet-exercise intervention promotes reproducible and sustainable long-term improvements in health behaviors, body weight, and physical functioning in older, overweight/obese cancer survivors. J Clin Oncol 2012;30:2354-2361. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22614994.

290. Heston AH, Schwartz AL, Justice-Gardiner H, Hohman KH. Addressing physical activity needs of survivors by developing a community-based exercise program: LIVESTRONG(R) at the YMCA. Clin J Oncol Nurs 2015;19:213-217. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25840387.

291. Rajotte EJ, Yi JC, Baker KS, et al. Community-based exercise program effectiveness and safety for cancer survivors. J Cancer Surviv 2012;6:219-228. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22246463.

292. Martin SS, Feldman DI, Blumenthal RS, et al. mActive: a randomized clinical trial of an automated mHealth intervention for physical activity promotion. J Am Heart Assoc 2015;4. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26553211.

293. Morgan AL, Tobar DA, Snyder L. Walking toward a new me: the impact of prescribed walking 10,000 steps/day on physical and psychological well-being. J Phys Act Health 2010;7:299-307. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20551485.

294. Schneider PL, Bassett DR, Jr., Thompson DL, et al. Effects of a 10,000 steps per day goal in overweight adults. Am J Health Promot 2006;21:85-89. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17152246.

295. Shuger SL, Barry VW, Sui X, et al. Electronic feedback in a diet- and physical activity-based lifestyle intervention for weight loss: a randomized controlled trial. Int J Behav Nutr Phys Act 2011;8:41. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21592351.

296. Vallance JKH, Courneya KS, Plotnikoff RC, et al. Randomized controlled trial of the effects of print materials and step pedometers on physical activity and quality of life in breast cancer survivors. J Clin Oncol 2007;25:2352-2359. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17557948.

297. Wang JB, Cadmus-Bertram LA, Natarajan L, et al. Wearable sensor/device (Fitbit One) and SMS text-messaging prompts to increase physical activity in overweight and obese adults: a randomized controlled trial. Telemed J E Health 2015;21:782-792. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26431257.

298. Yuenyongchaiwat K. Effects of 10,000 steps a day on physical and mental health in overweight participants in a community setting: a preliminary study. Braz J Phys Ther 2016;0. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27333480.

299. Lynch BM, Nguyen NH, Moore MM, et al. Maintenance of physical activity and sedentary behavior change, and physical activity and sedentary behavior change after an abridged intervention: Secondary outcomes from the ACTIVATE Trial. Cancer 2019;125:2856-2860. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31012968.

300. Lynch BM, Nguyen NH, Moore MM, et al. A randomized controlled trial of a wearable technology-based intervention for increasing moderate to vigorous physical activity and reducing sedentary behavior in breast cancer survivors: The ACTIVATE Trial. Cancer 2019;125:2846-2855. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31012970.

301. Schaffer K, Panneerselvam N, Loh KP, et al. Systematic review of randomized controlled trials of exercise interventions using digital activity trackers in patients with cancer. J Natl Compr Canc Netw 2019;17:57-63. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30659130.

302. Bennett JA, Lyons KS, Winters-Stone K, et al. Motivational interviewing to increase physical activity in long-term cancer survivors: a randomized controlled trial. Nurs Res 2007;56:18-27. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17179870.

303. Britt E, Hudson SM, Blampied NM. Motivational interviewing in health settings: a review. Patient Educ Couns 2004;53:147-155. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15140454.

304. Goode AD, Lawler SP, Brakenridge CL, et al. Telephone, print, and Web-based interventions for physical activity, diet, and weight control among cancer survivors: a systematic review. J Cancer Surviv 2015;9:660-682. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25757733.

305. Hawkes AL, Chambers SK, Pakenham KI, et al. Effects of a telephone-delivered multiple health behavior change intervention (CanChange) on health and behavioral outcomes in survivors of colorectal cancer: a randomized controlled trial. J Clin Oncol 2013;31:2313-2321. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23690410.

306. Pinto BM, Frierson GM, Rabin C, et al. Home-based physical activity intervention for breast cancer patients. J Clin Oncol 2005;23:3577-3587. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15908668.

307. Short CE, James EL, Girgis A, et al. Main outcomes of the Move More for Life Trial: a randomised controlled trial examining the effects of tailored-print and targeted-print materials for promoting physical activity among post-treatment breast cancer survivors. Psychooncology 2015;24:771-778. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25060288.

308. Park JH, Lee J, Oh M, et al. The effect of oncologists' exercise recommendations on the level of exercise and quality of life in survivors of breast and colorectal cancer: A randomized controlled trial. Cancer 2015;121:2740-2748. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25965782.

309. Caan BJ, Emond JA, Su HI, et al. Effect of postdiagnosis weight change on hot flash status among early-stage breast cancer survivors. J Clin Oncol 2012;30:1492-1497. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22430275.

310. Chen X, Lu W, Gu K, et al. Weight change and its correlates among breast cancer survivors. Nutr Cancer 2011;63:538-548. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21541900.

311. Greenlee H, Shi Z, Sardo Molmenti CL, et al. Trends in obesity prevalence in adults with a history of cancer: results from the US National

Health Interview Survey, 1997 to 2014. J Clin Oncol 2016;34:3133-3140. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27458295.

312. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila) 2011;4:486-501. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21233290.

313. Chalfin HJ, Lee SB, Jeong BC, et al. Obesity and long-term survival after radical prostatectomy. J Urol 2014;192:1100-1104. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24769031.

314. Chan DS, Vieira AR, Aune D, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol 2014;25:1901-1914. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24769692.

315. Forsythe LP, Alfano CM, George SM, et al. Pain in long-term breast cancer survivors: the role of body mass index, physical activity, and sedentary behavior. Breast Cancer Res Treat 2013;137:617-630. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23242613.

316. Ho T, Gerber L, Aronson WJ, et al. Obesity, prostate-specific antigen nadir, and biochemical recurrence after radical prostatectomy: biology or technique? Results from the SEARCH database. Eur Urol 2012;62:910-916. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22921964.

317. Imayama I, Alfano CM, Neuhouser ML, et al. Weight, inflammation, cancer-related symptoms and health related quality of life among breast cancer survivors. Breast Cancer Res Treat 2013;140:159-176. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23797178.

318. Joshu CE, Mondul AM, Menke A, et al. Weight gain is associated with an increased risk of prostate cancer recurrence after prostatectomy in the PSA era. Cancer Prev Res (Phila) 2011;4:544-551. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21325564.

319. Young A, Weltzien E, Kwan M, et al. Pre- to post-diagnosis weight change and associations with physical functional limitations in breast cancer survivors. J Cancer Surviv 2014;8:539-547. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24806261.

320. Maliniak ML, Patel AV, McCullough ML, et al. Obesity, physical activity, and breast cancer survival among older breast cancer survivors in the Cancer Prevention Study-II Nutrition Cohort. Breast Cancer Res Treat 2018;167:133-145. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28856470.

321. Pan H, Gray RG, on behalf of the Early Breast Cancer Trialists' Collaborative Group. Effect of obesity in premenopausal ER+ early breast cancer: EBCTCG data on 80,000 patients in 70 trials [abstract]. ASCO Meeting Abstracts 2014;32:503. Available at: http://meetinglibrary.asco.org/content/133648-144.

322. Caan BJ, Kwan ML, Shu XO, et al. Weight change and survival after breast cancer in the after breast cancer pooling project. Cancer Epidemiol Biomarkers Prev 2012;21:1260-1271. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22695738.

323. Ligibel JA, Alfano CM, Courneya KS, et al. American Society of Clinical Oncology position statement on obesity and cancer. J Clin Oncol 2014;32:3568-3574. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25273035.

324. Assessing Your Weight and Health Risk. Available at: http://www.nhlbi.nih.gov/health/educational/lose_wt/risk.htm. Accessed June 5, 2020.

325. Chlebowski RT, Reeves MM. Weight loss randomized intervention trials in female cancer survivors. J Clin Oncol 2016;34:4238-4248. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27903147.

326. Goodwin PJ, Segal RJ, Vallis M, et al. Randomized trial of a telephone-based weight loss intervention in postmenopausal women with breast cancer receiving letrozole: the LISA trial. J Clin Oncol 2014;32:2231-2239. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24934783.

327. Harrigan M, Cartmel B, Loftfield E, et al. Randomized trial comparing telephone versus in-person weight loss counseling on body composition and circulating biomarkers in women treated for breast cancer: the Lifestyle, Exercise, and Nutrition (LEAN) study. J Clin Oncol 2016;34:669-676. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26598750.

328. Hoedjes M, van Stralen MM, Joe ST, et al. Toward the optimal strategy for sustained weight loss in overweight cancer survivors: a systematic review of the literature. J Cancer Surviv 2017;11:360-385. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28097452.

329. Morey MC, Snyder DC, Sloane R, et al. Effects of home-based diet and exercise on functional outcomes among older, overweight long-term cancer survivors: RENEW: a randomized controlled trial. JAMA 2009;301:1883-1891. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19436015.

330. Rock CL, Flatt SW, Byers TE, et al. Results of the Exercise and Nutrition to Enhance Recovery and Good Health for You (ENERGY) Trial: A Behavioral Weight Loss Intervention in Overweight or Obese Breast Cancer Survivors. J Clin Oncol 2015;33:3169-3176. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26282657.

331. Albuquerque RC, Baltar VT, Marchioni DM. Breast cancer and dietary patterns: a systematic review. Nutr Rev 2014;72:1-17. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24330083.

332. Bertuccio P, Rosato V, Andreano A, et al. Dietary patterns and gastric cancer risk: a systematic review and meta-analysis. Ann Oncol 2013;24:1450-1458. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23524862.

333. Yusof AS, Isa ZM, Shah SA. Dietary patterns and risk of colorectal cancer: a systematic review of cohort studies (2000-2011). Asian Pac J Cancer Prev 2012;13:4713-4717. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23167408.

334. Schwingshackl L, Schwedhelm C, Galbete C, Hoffmann G. Adherence to Mediterranean diet and risk of cancer: An updated systematic review and meta-analysis. Nutrients 2017;9. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28954418.

335. Oyebode O, Gordon-Dseagu V, Walker A, Mindell JS. Fruit and vegetable consumption and all-cause, cancer and CVD mortality: analysis of Health Survey for England data. J Epidemiol Community Health 2014;68:856-862. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24687909.

336. Lavalette C, Adjibade M, Srour B, et al. Cancer-specific and general nutritional scores and cancer risk: Results from the prospective nutrinet-sante cohort. Cancer Res 2018;78:4427-4435. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30049821.

337. Toledo E, Salas-Salvado J, Donat-Vargas C, et al. Mediterranean diet and invasive breast cancer risk among women at high cardiovascular risk in the PREDIMED trial: a randomized clinical trial. JAMA Intern Med 2015;175:1752-1760. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26365989.

338. Prentice RL, Caan B, Chlebowski RT, et al. Low-fat dietary pattern and risk of invasive breast cancer: the Women's Health Initiative Randomized Controlled Dietary Modification Trial. JAMA 2006;295:629-642. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16467232.

339. Chlebowski RT, Aragaki AK, Anderson GL, et al. Dietary modification and breast cancer mortality: Long-term follow-up of the Women's Health Initiative randomized trial. J Clin Oncol 2020;38:1419-1428. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32031879.

340. Davies NJ, Batehup L, Thomas R. The role of diet and physical activity in breast, colorectal, and prostate cancer survivorship: a review of the literature. Br J Cancer 2011;105 Suppl 1:S52-73. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22048034.

341. Schwedhelm C, Boeing H, Hoffmann G, et al. Effect of diet on mortality and cancer recurrence among cancer survivors: a systematic review and meta-analysis of cohort studies. Nutr Rev 2016;74:737-748. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27864535.

342. Deshmukh AA, Shirvani SM, Likhacheva A, et al. The association between dietary quality and overall and cancer-specific mortality among cancer survivors, NHANES III. JNCI Cancer Spectr 2018;2:pky022. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29905226.

343. Meyerhardt JA, Niedzwiecki D, Hollis D, et al. Association of dietary patterns with cancer recurrence and survival in patients with stage III colon cancer. JAMA 2007;298:754-764. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17699009.

344. Meyerhardt JA, Sato K, Niedzwiecki D, et al. Dietary glycemic load and cancer recurrence and survival in patients with stage III colon cancer: findings from CALGB 89803. J Natl Cancer Inst 2012;104:1702-1711. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23136358.

345. McCullough ML, Gapstur SM, Shah R, et al. Association between red and processed meat intake and mortality among colorectal cancer survivors. J Clin Oncol 2013;31:2773-2782. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23816965.

346. Kwan ML, Weltzien E, Kushi LH, et al. Dietary patterns and breast cancer recurrence and survival among women with early-stage breast cancer. J Clin Oncol 2009;27:919-926. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19114692.

347. Springfield S, Odoms-Young A, Tussing-Humphreys L, et al. Adherence to American Cancer Society and American Institute of Cancer Research dietary guidelines in overweight African American breast cancer survivors. J Cancer Surviv 2019;13:257-268. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30982113.

348. Zhang FF, Liu S, John EM, et al. Diet quality of cancer survivors and noncancer individuals: Results from a national survey. Cancer 2015;121:4212-4221. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26624564.

349. Shi Z, Rundle A, Genkinger JM, et al. Distinct trajectories of fruits and vegetables, dietary fat, and alcohol intake following a breast cancer diagnosis: the Pathways Study. Breast Cancer Res Treat 2020;179:229-240. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31599394.

350. Affret A, His M, Severi G, et al. Influence of a cancer diagnosis on changes in fruit and vegetable consumption according to cancer site, stage at diagnosis and socioeconomic factors: Results from the large E3N-EPIC study. Int J Cancer 2018;143:1678-1687. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29717489.

351. Gu Q, Dummer TBJ, Spinelli JJ, Murphy RA. Diet quality among cancer survivors and participants without cancer: A population-based, cross-sectional study in the Atlantic Partnership for Tomorrow's Health Project. Nutrients 2019;11. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31835839.

352. Patel ML, Hopkins CM, Brooks TL, Bennett GG. Comparing self-monitoring strategies for weight loss in a smartphone app: Randomized controlled trial. JMIR Mhealth Uhealth 2019;7:e12209. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30816851.

353. Dunn CG, Turner-McGrievy GM, Wilcox S, Hutto B. Dietary self-monitoring through calorie tracking but not through a digital photography app is associated with significant weight loss: The 2SMART pilot study-a 6-month randomized trial. J Acad Nutr Diet 2019;119:1525-1532. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31155474.

354. Fortin A, Wang CS, Vigneault E. Influence of smoking and alcohol drinking behaviors on treatment outcomes of patients with squamous cell carcinomas of the head and neck. Int J Radiat Oncol Biol Phys 2009;74:1062-1069. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19036528.

355. Thrift AP, Nagle CM, Fahey PP, et al. The influence of prediagnostic demographic and lifestyle factors on esophageal squamous cell carcinoma survival. Int J Cancer 2012;131:E759-768. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22213172.

356. Flatt SW, Thomson CA, Gold EB, et al. Low to moderate alcohol intake is not associated with increased mortality after breast cancer.

Cancer Epidemiol Biomarkers Prev 2010;19:681-688. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20160253.

357. Newcomb PA, Kampman E, Trentham-Dietz A, et al. Alcohol consumption before and after breast cancer diagnosis: associations with survival from breast cancer, cardiovascular disease, and other causes. J Clin Oncol 2013;31:1939-1946. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23569314.

358. Caan BJ, Natarajan L, Parker B, et al. Soy food consumption and breast cancer prognosis. Cancer Epidemiol Biomarkers Prev 2011;20:854-858. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21357380.

359. Fritz H, Seely D, Flower G, et al. Soy, red clover, and isoflavones and breast cancer: a systematic review. PLoS One 2013;8:e81968. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24312387.

360. Guha N, Kwan ML, Quesenberry CP, Jr., et al. Soy isoflavones and risk of cancer recurrence in a cohort of breast cancer survivors: the Life After Cancer Epidemiology study. Breast Cancer Res Treat 2009;118:395-405. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19221874.

361. Shu XO, Zheng Y, Cai H, et al. Soy food intake and breast cancer survival. Jama 2009;302:2437-2443. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19996398.

362. Zhang FF, Haslam DE, Terry MB, et al. Dietary isoflavone intake and all-cause mortality in breast cancer survivors: The Breast Cancer Family Registry. Cancer 2017;123:2070-2079. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28263368.

363. Arain MA, Abdul Qadeer A. Systematic review on "vitamin E and prevention of colorectal cancer". Pak J Pharm Sci 2010;23:125-130. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20363687.

364. Bjelakovic G, Nikolova D, Simonetti RG, Gluud C. Antioxidant supplements for preventing gastrointestinal cancers. Cochrane Database Syst Rev 2008:Cd004183. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18677777.

365. Chang YJ, Myung SK, Chung ST, et al. Effects of vitamin treatment or supplements with purported antioxidant properties on skin cancer prevention: a meta-analysis of randomized controlled trials. Dermatology 2011;223:36-44. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21846961.

366. Cortes-Jofre M, Rueda JR, Corsini-Munoz G, et al. Drugs for preventing lung cancer in healthy people. Cochrane Database Syst Rev 2012;10:Cd002141. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23076895.

367. Fife J, Raniga S, Hider PN, Frizelle FA. Folic acid supplementation and colorectal cancer risk: a meta-analysis. Colorectal Dis 2011;13:132-137. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19863600.

368. Fortmann SP, Burda BU, Senger CA, et al. Vitamin and mineral supplements in the primary prevention of cardiovascular disease and cancer: An updated systematic evidence review for the U.S. Preventive Services Task Force. Ann Intern Med 2013;159:824-834. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24217421.

369. Greenlee H, Hershman DL, Jacobson JS. Use of antioxidant supplements during breast cancer treatment: a comprehensive review. Breast Cancer Res Treat 2009;115:437-452. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18839308.

370. Jeon YJ, Myung SK, Lee EH, et al. Effects of beta-carotene supplements on cancer prevention: meta-analysis of randomized controlled trials. Nutr Cancer 2011;63:1196-1207. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21981610.

371. Mayne ST, Ferrucci LM, Cartmel B. Lessons learned from randomized clinical trials of micronutrient supplementation for cancer prevention. Annu Rev Nutr 2012;32:369-390. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22524186.

372. Misotti AM, Gnagnarella P. Vitamin supplement consumption and breast cancer risk: a review. Ecancermedicalscience 2013;7:365. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24171049.

373. Pais R, Dumitrascu DL. Do antioxidants prevent colorectal cancer? A meta-analysis. Rom J Intern Med 2013;51:152-163. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24620628.

374. Singal M, Banh HL, Allan GM. Daily multivitamins to reduce mortality, cardiovascular disease, and cancer. Can Fam Physician 2013;59:847. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23946027.

375. Vinceti M, Dennert G, Crespi CM, et al. Selenium for preventing cancer. Cochrane Database Syst Rev 2014;3:CD005195. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24683040.

376. Manson JE, Cook NR, Lee IM, et al. Vitamin D supplements and prevention of cancer and cardiovascular disease. N Engl J Med 2019;380:33-44. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30415629.

377. Scragg R, Khaw KT, Toop L, et al. Monthly high-dose vitamin D supplementation and cancer risk: A post hoc analysis of the vitamin D assessment randomized clinical trial. JAMA Oncol 2018;4:e182178. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30027269.

378. Carroll C, Cooper K, Papaioannou D, et al. Supplemental calcium in the chemoprevention of colorectal cancer: a systematic review and meta-analysis. Clin Ther 2010;32:789-803. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20685491.

379. Harris HR, Orsini N, Wolk A. Vitamin C and survival among women with breast cancer: a meta-analysis. Eur J Cancer 2014;50:1223-1231. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24613622.

380. Inoue-Choi M, Greenlee H, Oppeneer SJ, Robien K. The association between postdiagnosis dietary supplement use and total mortality differs by diet quality among older female cancer survivors. Cancer Epidemiol Biomarkers Prev 2014;23:865-875. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24621441.

381. Dietary Supplements. FDA; Available at: http://www.fda.gov/Food/DietarySupplements/. Accessed June 5, 2020.

382. Cohen PA, Maller G, DeSouza R, Neal-Kababick J. Presence of banned drugs in dietary supplements following FDA recalls. JAMA 2014;312:1691-1693. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25335153.

383. O'Connor A. What's in Those Supplements? New York Times; 2015. Available at: http://well.blogs.nytimes.com/2015/02/03/sidebar-whats-in-those-supplements/?_r=0.

384. Velicer CM, Ulrich CM. Vitamin and mineral supplement use among US adults after cancer diagnosis: a systematic review. J Clin Oncol 2008;26:665-673. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18235127.

385. John GM, Hershman DL, Falci L, et al. Complementary and alternative medicine use among US cancer survivors. J Cancer Surviv 2016;10:850-864. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26920872.

386. Du M, Luo H, Blumberg JB, et al. Dietary supplement use among adult cancer survivors in the United States. J Nutr 2020. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32101612.

387. Avenell A, Mak JC, O'Connell D. Vitamin D and vitamin D analogues for preventing fractures in post-menopausal women and older men. Cochrane Database Syst Rev 2014;4:Cd000227. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24729336.

388. Evans JR, Lawrenson JG. Antioxidant vitamin and mineral supplements for slowing the progression of age-related macular degeneration. Cochrane Database Syst Rev 2012;11:Cd000254. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23152201.

389. Saller R, Brignoli R, Melzer J, Meier R. An updated systematic review with meta-analysis for the clinical evidence of silymarin. Forsch Komplementmed 2008;15:9-20. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18334810.

390. Rambaldi A, Jacobs BP, Gluud C. Milk thistle for alcoholic and/or hepatitis B or C virus liver diseases. Cochrane Database Syst Rev 2007:CD003620. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17943794.

391. Satia JA, Campbell MK, Galanko JA, et al. Longitudinal changes in lifestyle behaviors and health status in colon cancer survivors. Cancer Epidemiol Biomarkers Prev 2004;13:1022-1031. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15184259.

392. Stump TK, Robinson JK, Yanez B, et al. Physicians' perspectives on medication adherence and health promotion among cancer survivors. Cancer 2019. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31448414.

393. Stacey FG, James EL, Chapman K, et al. A systematic review and meta-analysis of social cognitive theory-based physical activity and/or nutrition behavior change interventions for cancer survivors. J Cancer Surviv 2014;9:305-338. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25432633.

394. Lynch BM, Courneya KS, Sethi P, et al. A randomized controlled trial of a multiple health behavior change intervention delivered to colorectal cancer survivors: effects on sedentary behavior. Cancer 2014;120:2665-2672. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24816611.

395. James EL, Stacey FG, Chapman K, et al. Impact of a nutrition and physical activity intervention (ENRICH: Exercise and Nutrition Routine Improving Cancer Health) on health behaviors of cancer survivors and carers: a pragmatic randomized controlled trial. BMC Cancer 2015;15:710. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26471791.

396. Burke BL, Arkowitz H, Menchola M. The efficacy of motivational interviewing: a meta-analysis of controlled clinical trials. J Consult Clin Psychol 2003;71:843-861. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14516234.

397. Bandura A. Health promotion by social cognitive means. Health Educ Behav 2004;31:143-164. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15090118.

398. Short CE, James EL, Plotnikoff RC. How social cognitive theory can help oncology-based health professionals promote physical activity among breast cancer survivors. Eur J Oncol Nurs 2012;17:482-489. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23177321.

399. Kwon HJ, Lee JW, Chung NG, et al. Assessment of serologic immunity to diphtheria-tetanus-pertussis after treatment of Korean pediatric hematology and oncology patients. J Korean Med Sci 2012;27:78-83. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22219618.

400. Ljungman P, Cordonnier C, Einsele H, et al. Vaccination of hematopoietic cell transplant recipients. Bone Marrow Transplant 2009;44:521-526. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19861986.

401. Klosky JL, Gamble HL, Spunt SL, et al. Human papillomavirus vaccination in survivors of childhood cancer. Cancer 2009;115:5627-5636. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19813272.

402. Locher JL, Rucks AC, Spencer SA, et al. Influenza immunization in older adults with and without cancer. J Am Geriatr Soc 2012;60:2099-2103. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23126598.

403. Kawano Y, Suzuki M, Kawada J, et al. Effectiveness and safety of immunization with live-attenuated and inactivated vaccines for pediatric liver transplantation recipients. Vaccine 2015;33:1440-1445. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25665961.

404. Shah GL, Shune L, Purtill D, et al. Robust vaccine responses in adult and pediatric cord blood transplantation recipients treated for hematologic malignancies. Biol Blood Marrow Transplant 2015;21:2160-2166. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26271191.

405. Small TN, Zelenetz AD, Noy A, et al. Pertussis immunity and response to tetanus-reduced diphtheria-reduced pertussis vaccine (Tdap) after autologous peripheral blood stem cell transplantation. Biol Blood Marrow Transplant 2009;15:1538-1542. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19896077.

406. Committee to Advise on Tropical Medicine and Travel (CATMAT). The immunocompromised traveller. An Advisory Committee Statement (ACS). Can Commun Dis Rep 2007;33:1-24. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17520776.

407. Gradel KO, Norgaard M, Dethlefsen C, et al. Increased risk of zoonotic Salmonella and Campylobacter gastroenteritis in patients with haematological malignancies: a population-based study. Ann Hematol 2009;88:761-767. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19083236.

408. Lortholary O, Charlier C, Lebeaux D, et al. Fungal infections in immunocompromised travelers. Clin Infect Dis 2013;56:861-869. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23175562.

409. Mani I, Maguire JH. Small animal zoonoses and immuncompromised pet owners. Top Companion Anim Med 2009;24:164-174. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19945084.

410. Partridge-Hinckley K, Liddell GM, Almyroudis NG, Segal BH. Infection control measures to prevent invasive mould diseases in hematopoietic stem cell transplant recipients. Mycopathologia 2009;168:329-337. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19859825.

411. Visser LG. The immunosuppressed traveler. Infect Dis Clin North Am 2012;26:609-624. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22963773.

412. Handwashing: Clean hands save lives. Centers for Disease Control and Prevention; 2020. Available at: https://www.cdc.gov/handwashing/. Accessed June 30, 2020.

413. How to protect yourself & others. Centers for Disease Control and Prevention; 2020. Available at: https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html. Accessed June 30, 2020.

414. Tramsen L, Salzmann-Manrique E, Bochennek K, et al. Lack of effectiveness of neutropenic diet and social restrictions as anti-infective measures in children with acute myeloid leukemia: an analysis of the AML-BFM 2004 trial. J Clin Oncol 2016;34:2776-2783. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27269945.

415. Shah MK. The immunocompromised traveler. Oncology (Williston Park) 2016;30:142, 145-146, 159. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26888792.

416. Freedman MS, Hunter P, Ault K, Kroger A. Advisory Committee on Immunization Practices recommended immunization schedule for adults aged 19 years or older - United States, 2020. MMWR Morb Mortal Wkly Rep 2020;69:133-135. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32027627.

417. Rubin LG, Levin MJ, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clin Infect Dis 2014;58:309-318. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24421306.

418. Matanock A, Lee G, Gierke R, et al. Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine among adults aged >/=65 years: Updated recommendations of the Advisory Committee on Immunization Practices. MMWR Morb Mortal Wkly Rep 2019;68:1069-1075. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31751323.

419. Centers for Disease C, Prevention. Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine for adults with immunocompromising conditions: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep 2012;61:816-819. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23051612.

420. Chiou WY, Lee MS, Hung SK, et al. Effectiveness of 23-valent pneumococcal polysaccharide vaccine on elderly long-term cancer survivors: a population-based propensity score matched cohort study. BMJ Open 2018;8:e019364. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29769253.

421. Garten R, Blanton L, Elal AIA, et al. Update: Influenza activity in the United States during the 2017-18 season and composition of the 2018-19 influenza vaccine. MMWR Morb Mortal Wkly Rep 2018;67:634-642. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29879098.

422. Grohskopf LA, Sokolow LZ, Fry AM, et al. Update: ACIP recommendations for the use of quadrivalent live attenuated influenza vaccine (LAIV4) - United States, 2018-19 influenza season. MMWR Morb Mortal Wkly Rep 2018;67:643-645. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29879095.

423. Grohskopf LA, Sokolow LZ, Broder KR, et al. Prevention and control of seasonal influenza with vaccines: Recommendations of the Advisory Committee on Immunization Practices-United States, 2018-19 influenza season. MMWR Recomm Rep 2018;67:1-20. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30141464.

424. DiazGranados CA, Dunning AJ, Kimmel M, et al. Efficacy of high-dose versus standard-dose influenza vaccine in older adults. N Engl J Med 2014;371:635-645. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25119609.

425. Grohskopf LA, Alyanak E, Broder KR, et al. Prevention and control of seasonal influenza with vaccines: Recommendations of the Advisory Committee on Immunization Practices - United States, 2019-20 influenza season. MMWR Recomm Rep 2019;68:1-21. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31441906.

426. Dooling KL, Guo A, Patel M, et al. Recommendations of the Advisory Committee on Immunization Practices for use of herpes zoster vaccines. MMWR Morb Mortal Wkly Rep 2018;67:103-108. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29370152.

427. Bastidas A, de la Serna J, El Idrissi M, et al. Effect of recombinant zoster vaccine on incidence of herpes zoster after autologous stem cell transplantation: A randomized clinical trial. JAMA 2019;322:123-133. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31287523.

428. Vink P, Delgado Mingorance I, Maximiano Alonso C, et al. Immunogenicity and safety of the adjuvanted recombinant zoster vaccine in patients with solid tumors, vaccinated before or during chemotherapy: A randomized trial. Cancer 2019;125:1301-1312. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30707761.

429. Hales CM, Harpaz R, Ortega-Sanchez I, et al. Update on recommendations for use of herpes zoster vaccine. MMWR Morb Mortal Wkly Rep 2014;63:729-731. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25144544.

430. Heron M. Deaths: Leading causes for 2017. National Vital Statistics Reports 2019;68. Available at: https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68_06-508.pdf.

431. Zaorsky NG, Churilla TM, Egleston BL, et al. Causes of death among cancer patients. Ann Oncol 2017;28:400-407. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27831506.

432. Armenian SH, Xu L, Ky B, et al. Cardiovascular disease among survivors of adult-onset cancer: a community-based retrospective cohort study. J Clin Oncol 2016;34:1122-1130. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26834065.

433. Strongman H, Gadd S, Matthews A, et al. Medium and long-term risks of specific cardiovascular diseases in survivors of 20 adult cancers: a population-based cohort study using multiple linked UK electronic health records databases. Lancet 2019. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31443926.

434. Schoormans D, Vissers PAJ, van Herk-Sukel MPP, et al. Incidence of cardiovascular disease up to 13 year after cancer diagnosis: A matched cohort study among 32 757 cancer survivors. Cancer Med 2018;7:4952-4963. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30220107.

435. Sturgeon KM, Deng L, Bluethmann SM, et al. A population-based study of cardiovascular disease mortality risk in US cancer patients. Eur Heart J 2019;40:3889-3897. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31761945.

436. Darby SC, Ewertz M, McGale P, et al. Risk of ischemic heart disease in women after radiotherapy for breast cancer. N Engl J Med 2013;368:987-998. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23484825.

437. Ky B, Vejpongsa P, Yeh ET, et al. Emerging paradigms in cardiomyopathies associated with cancer therapies. Circ Res 2013;113:754-764. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23989717.

438. Li W, Croce K, Steensma DP, et al. Vascular and metabolic implications of novel targeted cancer therapies: focus on kinase inhibitors. J Am Coll Cardiol 2015;66:1160-1178. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26337996.

439. Moslehi JJ. Cardiovascular toxic effects of targeted cancer therapies. N Engl J Med 2016;375:1457-1467. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27732808.

440. O'Farrell S, Garmo H, Holmberg L, et al. Risk and timing of cardiovascular disease after androgen-deprivation therapy in men with prostate cancer. J Clin Oncol 2015;33:1243-1251. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25732167.

441. Schmid M, Sammon JD, Reznor G, et al. Dose-dependent effect of androgen deprivation therapy for localized prostate cancer on adverse cardiac events. BJU Int 2015;118:221-229. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26074405.

442. Dess RT, Sun Y, Matuszak MM, et al. Cardiac events after radiation therapy: combined analysis of prospective multicenter trials for locally advanced non-small-cell lung cancer. J Clin Oncol 2017;35:1395-1402. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28301264.

443. Lauritsen J, Hansen MK, Bandak M, et al. Cardiovascular risk factors and disease after male germ cell cancer. J Clin Oncol 2020;38:584-592. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31821065.

444. Abdel-Qadir H, Thavendiranathan P, Fung K, et al. Association of early-stage breast cancer and subsequent chemotherapy with risk of atrial fibrillation. JAMA Netw Open 2019;2:e1911838. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31539076.

445. Jaiswal S, Fontanillas P, Flannick J, et al. Age-related clonal hematopoiesis associated with adverse outcomes. N Engl J Med 2014;371:2488-2498. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25426837.

446. Weaver KE, Foraker RE, Alfano CM, et al. Cardiovascular risk factors among long-term survivors of breast, prostate, colorectal, and gynecologic cancers: a gap in survivorship care? J Cancer Surviv 2013;7:253-261. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23417882.

447. Meacham LR, Chow EJ, Ness KK, et al. Cardiovascular risk factors in adult survivors of pediatric cancer--a report from the childhood cancer survivor study. Cancer Epidemiol Biomarkers Prev 2010;19:170-181. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20056636.

448. Moslehi J. The cardiovascular perils of cancer survivorship. N Engl J Med 2013;368:1055-1056. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23484833.

449. Gilchrist SC, Barac A, Ades PA, et al. Cardio-oncology rehabilitation to manage cardiovascular outcomes in cancer patients and survivors: A scientific statement from the American Heart Association. Circulation 2019;139:e997-e1012. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30955352.

450. Rasmussen-Torvik LJ, Shay CM, Abramson JG, et al. Ideal cardiovascular health is inversely associated with incident cancer: the Atherosclerosis Risk In Communities study. Circulation 2013;127:1270-1275. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23509058.

451. ASCVD Risk Estimator Plus. American College of Cardiology; Available at: http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/. Accessed March 5, 2020.

452. Montazeri K, Unitt C, Foody JM, et al. ABCDE steps to prevent heart disease in breast cancer survivors. Circulation 2014;130:e157-159. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25462826.

453. Guan J, Khambhati J, Jones LW, et al. Cardiology patient page. ABCDE steps for heart and vascular wellness following a prostate cancer diagnosis. Circulation 2015;132:e218-220. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26527696.

454. Moslehi J, Cheng S. Cardio-oncology: it takes two to translate. Sci Transl Med 2013;5:187fs120. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23720578.

455. Lipshultz SE, Colan SD, Gelber RD, et al. Late cardiac effects of doxorubicin therapy for acute lymphoblastic leukemia in childhood. N Engl J Med 1991;324:808-815. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1997853.

456. Lipshultz SE, Lipsitz SR, Mone SM, et al. Female sex and drug dose as risk factors for late cardiotoxic effects of doxorubicin therapy for childhood cancer. N Engl J Med 1995;332:1738-1743. Available at: http://www.ncbi.nlm.nih.gov/pubmed/7760889.

457. Smith LA, Cornelius VR, Plummer CJ, et al. Cardiotoxicity of anthracycline agents for the treatment of cancer: systematic review and meta-analysis of randomised controlled trials. BMC Cancer 2010;10:337. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20587042.

458. Minotti G, Menna P, Salvatorelli E, et al. Anthracyclines: molecular advances and pharmacologic developments in antitumor activity and cardiotoxicity. Pharmacol Rev 2004;56:185-229. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15169927.

459. Zhang S, Liu X, Bawa-Khalfe T, et al. Identification of the molecular basis of doxorubicin-induced cardiotoxicity. Nat Med 2012;18:1639-1642. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23104132.

460. Koelwyn GJ, Khouri M, Mackey JR, et al. Running on empty: cardiovascular reserve capacity and late effects of therapy in cancer survivorship. J Clin Oncol 2012;30:4458-4461. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23045598.

461. Lotrionte M, Biondi-Zoccai G, Abbate A, et al. Review and meta-analysis of incidence and clinical predictors of anthracycline cardiotoxicity. Am J Cardiol 2013;112:1980-1984. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24075281.

462. Romond EH, Jeong JH, Rastogi P, et al. Seven-year follow-up assessment of cardiac function in NSABP B-31, a randomized trial comparing doxorubicin and cyclophosphamide followed by paclitaxel (ACP) with ACP plus trastuzumab as adjuvant therapy for patients with node-positive, human epidermal growth factor receptor 2-positive breast cancer. J Clin Oncol 2012;30:3792-3799. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22987084.

463. Russell SD, Blackwell KL, Lawrence J, et al. Independent adjudication of symptomatic heart failure with the use of doxorubicin and cyclophosphamide followed by trastuzumab adjuvant therapy: a combined review of cardiac data from the National Surgical Adjuvant breast and Bowel Project B-31 and the North Central Cancer Treatment Group N9831 clinical trials. J Clin Oncol 2010;28:3416-3421. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20530275.

464. Cardinale D, Colombo A, Bacchiani G, et al. Early detection of anthracycline cardiotoxicity and improvement with heart failure therapy. Circulation 2015;131:1981-1988. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25948538.

465. Drafts BC, Twomley KM, D'Agostino R, Jr., et al. Low to moderate dose anthracycline-based chemotherapy is associated with early noninvasive imaging evidence of subclinical cardiovascular disease. JACC

Cardiovasc Imaging 2013;6:877-885. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23643285.

466. Groarke J, Tong D, Khambhati J, et al. Breast Cancer therapies and cardiomyopathy. Medical Clinics of North America 2012;96:1001-1019. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22980061.

467. Johnson DB, Balko JM, Compton ML, et al. Fulminant myocarditis with combination immune checkpoint blockade. N Engl J Med 2016;375:1749-1755. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27806233.

468. Moslehi JJ, Salem JE, Sosman JA, et al. Increased reporting of fatal immune checkpoint inhibitor-associated myocarditis. Lancet 2018;391:933. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29536852.

469. Daniels LA, Krol AD, de Graaf MA, et al. Screening for coronary artery disease after mediastinal irradiation in Hodgkin lymphoma survivors: phase II study of indication and acceptancedagger. Ann Oncol 2014;25:1198-1203. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24692582.

470. Cardinale D, Colombo A, Lamantia G, et al. Anthracycline-induced cardiomyopathy: clinical relevance and response to pharmacologic therapy. J Am Coll Cardiol 2010;55:213-220. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20117401.

471. Effect of enalapril on mortality and the development of heart failure in asymptomatic patients with reduced left ventricular ejection fractions. The SOLVD Investigattors. N Engl J Med 1992;327:685-691. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1463530.

472. Thakur A, Witteles RM. Cancer therapy-induced left ventricular dysfunction: interventions and prognosis. J Card Fail 2014;20:155-158. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24378722.

473. Silber JH, Cnaan A, Clark BJ, et al. Enalapril to prevent cardiac function decline in long-term survivors of pediatric cancer exposed to anthracyclines. J Clin Oncol 2004;22:820-828. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14990637.

474. Adamo V, Ricciardi GR, Adamo B, et al. The risk of toxicities from trastuzumab, alone or in combination, in an elderly breast cancer population. Oncology 2014;86:16-21. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24335608.

475. Mitra MS, Donthamsetty S, White B, Mehendale HM. High fat diet-fed obese rats are highly sensitive to doxorubicin-induced cardiotoxicity. Toxicol Appl Pharmacol 2008;231:413-422. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18674790.

476. Scott E, Daley AJ, Doll H, et al. Effects of an exercise and hypocaloric healthy eating program on biomarkers associated with long-term prognosis after early-stage breast cancer: a randomized controlled trial. Cancer Causes Control 2013;24:181-191. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23184120.

477. Ferrari N, Tosetti F, De Flora S, et al. Diet-derived phytochemicals: from cancer chemoprevention to cardio-oncological prevention. Curr Drug Targets 2011;12:1909-1924. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21158708.

478. Dolinsky VW, Rogan KJ, Sung MM, et al. Both aerobic exercise and resveratrol supplementation attenuate doxorubicin-induced cardiac injury in mice. Am J Physiol Endocrinol Metab 2013;305:E243-253. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23695218.

479. Emter CA, Bowles DK. Curing the cure: utilizing exercise to limit cardiotoxicity. Med Sci Sports Exerc 2008;40:806-807. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18408620.

480. Hydock DS, Lien CY, Jensen BT, et al. Exercise preconditioning provides long-term protection against early chronic doxorubicin cardiotoxicity. Integr Cancer Ther 2011;10:47-57. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21382960.

481. Rock E, DeMichele A. Nutritional approaches to late toxicities of adjuvant chemotherapy in breast cancer survivors. J Nutr 2003;133:3785S-3793S. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14608115.

482. Sturgeon KM, Ky B, Libonati JR, Schmitz KH. The effects of exercise on cardiovascular outcomes before, during, and after treatment for breast cancer. Breast Cancer Res Treat 2014;143:219-226. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24337598.

483. Hunt SA, Baker DW, Chin MH, et al. ACC/AHA guidelines for the evaluation and management of chronic heart failure in the adult: executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to revise the 1995 Guidelines for the Evaluation and Management of Heart Failure). J Am Coll Cardiol 2001;38:2101-2113. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11738322.

484. Jones LW, Eves ND, Haykowsky M, et al. Exercise intolerance in cancer and the role of exercise therapy to reverse dysfunction. Lancet Oncol 2009;10:598-605. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19482248.

485. The Criteria Committee of the New York Heart Association. Nomenclature and criteria for diagnosis of diseases of the heart and great vessels (ed 9th). Boston, MA: Little & Brown; 1994.

486. Carver JR, Shapiro CL, Ng A, et al. American Society of Clinical Oncology clinical evidence review on the ongoing care of adult cancer survivors: cardiac and pulmonary late effects. J Clin Oncol 2007;25:3991-4008. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17577017.

487. Shankar SM, Marina N, Hudson MM, et al. Monitoring for cardiovascular disease in survivors of childhood cancer: report from the Cardiovascular Disease Task Force of the Children's Oncology Group. Pediatrics 2008;121:e387-396. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18187811.

488. Earle CC. Cancer survivorship research and guidelines: maybe the cart should be beside the horse. J Clin Oncol 2007;25:3800-3801. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17646665.

489. Armenian SH, Hudson MM, Mulder RL, et al. Recommendations for cardiomyopathy surveillance for survivors of childhood cancer: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group. Lancet Oncol 2015;16:e123-136. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25752563.

490. Yeh JM, Nohria A, Diller L. Routine echocardiography screening for asymptomatic left ventricular dysfunction in childhood cancer survivors: a model-based estimation of the clinical and economic effects. Ann Intern Med 2014;160:661-671. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24842413.

491. Steingart RM, Liu JE, Oeffinger KC. Cost-effectiveness of screening for asymptomatic left ventricular dysfunction in childhood cancer survivors. Ann Intern Med 2014;160:731-732. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24842420.

492. Plana JC, Galderisi M, Barac A, et al. Expert consensus for multimodality imaging evaluation of adult patients during and after cancer therapy: a report from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2014;27:911-939. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25172399.

493. Armenian SH, Lacchetti C, Barac A, et al. Prevention and monitoring of cardiac dysfunction in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol 2017;35:893-911. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27918725.

494. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013;62:e147-239. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23747642.

495. Wang K, Eblan MJ, Deal AM, et al. Cardiac toxicity after radiotherapy for stage III non-small-cell lung cancer: pooled analysis of dose-escalation trials delivering 70 to 90 Gy. J Clin Oncol 2017;35:1387-1394. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28113017.

496. Bowles EJ, Wellman R, Feigelson HS, et al. Risk of heart failure in breast cancer patients after anthracycline and trastuzumab treatment: a retrospective cohort study. J Natl Cancer Inst 2012;104:1293-1305. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22949432.

497. Feijen EAM, Leisenring WM, Stratton KL, et al. Derivation of anthracycline and anthraquinone equivalence ratios to doxorubicin for late-onset cardiotoxicity. JAMA Oncol 2019;5:864-871. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30703192.

498. Guenancia C, Lefebvre A, Cardinale D, et al. Obesity as a risk factor for anthracyclines and trastuzumab cardiotoxicity in breast cancer: a systematic review and meta-analysis. J Clin Oncol 2016;34:3157-3165. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27458291.

499. Cespedes Feliciano EM, Chen WY, Bradshaw PT, et al. Adipose tissue distribution and cardiovascular disease risk among breast cancer survivors. J Clin Oncol 2019:JCO1900286. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31369302.

500. Hershman DL, Till C, Shen S, et al. Association of cardiovascular risk factors with cardiac events and survival outcomes among patients with breast cancer enrolled in SWOG clinical trials. J Clin Oncol 2018:JCO2017774414. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29584550.

501. Tan-Chiu E, Yothers G, Romond E, et al. Assessment of cardiac dysfunction in a randomized trial comparing doxorubicin and cyclophosphamide followed by paclitaxel, with or without trastuzumab as adjuvant therapy in node-positive, human epidermal growth factor receptor 2-overexpressing breast cancer: NSABP B-31. J Clin Oncol 2005;23:7811-7819. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16258083.

502. Groarke JD, Nguyen PL, Nohria A, et al. Cardiovascular complications of radiation therapy for thoracic malignancies: the role for non-invasive imaging for detection of cardiovascular disease. Eur Heart J 2014;35:612-623. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23666251.

503. Thavendiranathan P, Poulin F, Lim KD, et al. Use of myocardial strain imaging by echocardiography for the early detection of cardiotoxicity in patients during and after cancer chemotherapy: a systematic review. J Am Coll Cardiol 2014;63:2751-2768. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24703918.

504. Monsuez JJ. Detection and prevention of cardiac complications of cancer chemotherapy. Arch Cardiovasc Dis 2012;105:593-604. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23177488.

505. Sawaya H, Sebag IA, Plana JC, et al. Assessment of echocardiography and biomarkers for the extended prediction of cardiotoxicity in patients treated with anthracyclines, taxanes, and trastuzumab. Circ Cardiovasc Imaging 2012;5:596-603. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22744937.

506. Thigpen SC, Geraci SA. Prediction of anthracycline-induced left ventricular dysfunction by cardiac troponins. South Med J 2012;105:659-664. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23211501.

507. Scott JM, Khakoo A, Mackey JR, et al. Modulation of anthracycline-induced cardiotoxicity by aerobic exercise in breast cancer: current evidence and underlying mechanisms. Circulation 2011;124:642-650. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21810673.

508. Lu D, Andersson TM, Fall K, et al. Clinical diagnosis of mental disorders immediately before and after cancer diagnosis: a nationwide matched cohort study in Sweden. JAMA Oncol 2016;2:1188-1196. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27124325.

509. Zimmermann-Schlegel V, Hartmann M, Sklenarova H, et al. Accessibility, availability, and potential benefits of psycho-oncology services: the perspective of communitybBased physicians providing

cancer survivorship care. Oncologist 2017;22:719-727. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28438888.

510. Mehnert A, Koch U, Sundermann C, Dinkel A. Predictors of fear of recurrence in patients one year after cancer rehabilitation: a prospective study. Acta Oncol 2013;52:1102-1109. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23384721.

511. Ploos van Amstel FK, van den Berg SW, van Laarhoven HW, et al. Distress screening remains important during follow-up after primary breast cancer treatment. Support Care Cancer 2013;21:2107-2115. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23455455.

512. Roerink SH, de Ridder M, Prins J, et al. High level of distress in long-term survivors of thyroid carcinoma: results of rapid screening using the distress thermometer. Acta Oncol 2013;52:128-137. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23101467.

513. Kendal W. Suicide and cancer: a gender-comparative study. Annals of Oncology 2007;18:381-387. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17053045.

514. Miller M, Mogun H, Azrael D, et al. Cancer and the risk of suicide in older Americans. J Clin Oncol 2008;26:4720-4724. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18695256.

515. Misono S, Weiss NS, Fann JR, et al. Incidence of suicide in persons with cancer. J Clin Oncol 2008;26:4731-4738. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18695257.

516. Recklitis CJ, Diller LR, Li X, et al. Suicide ideation in adult survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. J Clin Oncol 2010;28:655-661. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19841325.

517. Recklitis CJ, Zhou ES, Zwemer EK, et al. Suicidal ideation in prostate cancer survivors: understanding the role of physical and psychological health outcomes. Cancer 2014;120:3393-3400. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24962506.

518. Walker J, Waters RA, Murray G, et al. Better off dead: suicidal thoughts in cancer patients. J Clin Oncol 2008;26:4725-4730. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18695258.

519. Syrjala KL, Yi J. Overview of psychosocial issues in the adult cancer survivor. In: Ganz PA, ed: UpToDate; 2017.

520. Ozga M, Aghajanian C, Myers-Virtue S, et al. A systematic review of ovarian cancer and fear of recurrence. Palliat Support Care 2015;13:1771-1780. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25728373.

521. Mitchell AJ, Ferguson DW, Gill J, et al. Depression and anxiety in long-term cancer survivors compared with spouses and healthy controls: a systematic review and meta-analysis. Lancet Oncol 2013;14:721-732. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23759376.

522. Watts S, Prescott P, Mason J, et al. Depression and anxiety in ovarian cancer: a systematic review and meta-analysis of prevalence rates. BMJ Open 2015;5:e007618. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26621509.

523. Zhao G, Okoro CA, Li J, et al. Current depression among adult cancer survivors: findings from the 2010 Behavioral Risk Factor Surveillance System. Cancer Epidemiol 2014;38:757-764. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25455653.

524. Swartzman S, Booth JN, Munro A, Sani F. Posttraumatic stress disorder after cancer diagnosis in adults: a meta-analysis. Depress Anxiety 2017;34:327-339. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27466972.

525. Chan CMH, Ng CG, Taib NA, et al. Course and predictors of post-traumatic stress disorder in a cohort of psychologically distressed patients with cancer: A 4-year follow-up study. Cancer 2018;124:406-416. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29152719.

526. Boyes A, D'Este C, Carey M, et al. How does the Distress Thermometer compare to the Hospital Anxiety and Depression Scale for detecting possible cases of psychological morbidity among cancer

survivors? Support Care Cancer 2013;21:119-127. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22618735.

527. Craike MJ, Livingston PM, Warne C. Sensitivity and specificity of the Distress Impact Thermometer for the detection of psychological distress among CRC survivors. J Psychosoc Oncol 2011;29:231-241. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21590570.

528. Ghazali N, Roe B, Lowe D, et al. Screening for distress using the distress thermometer and the University of Washington Quality of Life in post-treatment head and neck cancer survivors. Eur Arch Otorhinolaryngol 2017;274:2253-2260. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28168421.

529. Hong JS, Tian J. Sensitivity and specificity of the Distress Thermometer in screening for distress in long-term nasopharyngeal cancer survivors. Curr Oncol 2013;20:e570-576. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24311958.

530. Livingston PM, Craike MJ, White VM, et al. A nurse-assisted screening and referral program for depression among survivors of colorectal cancer: feasibility study. Med J Aust 2010;193:S83-87. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21542453.

531. Merport A, Bober SL, Grose A, Recklitis CJ. Can the distress thermometer (DT) identify significant psychological distress in long-term cancer survivors? A comparison with the Brief Symptom Inventory-18 (BSI-18). Support Care Cancer 2012;20:195-198. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21928051.

532. Recklitis CJ, Licht I, Ford J, et al. Screening adult survivors of childhood cancer with the distress thermometer: a comparison with the SCL-90-R. Psychooncology 2007;16:1046-1049. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17506074.

533. Recklitis CJ, Blackmon JE, Chang G. Screening young adult cancer survivors for distress with the Distress Thermometer: Comparisons with a structured clinical diagnostic interview. Cancer 2016;122:296-303. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26457669.

534. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (ed 5). Arlington, VA: American Psychiatric Publishing; 2013.

535. U.S. Department of Veteran Affairs. Assessment and Management of Patients at Risk for Suicide. 2013. Available at: https://www.healthquality.va.gov/guidelines/mh/srb/index.asp. Accessed June 5, 2020.

536. Ahmedani BK, Peterson EL, Hu Y, et al. Major physical health conditions and risk of suicide. Am J Prev Med 2017;53:308-315. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28619532.

537. Brown JC, Huedo-Medina TB, Pescatello LS, et al. The efficacy of exercise in reducing depressive symptoms among cancer survivors: a meta-analysis. PLoS One 2012;7:e30955. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22303474.

538. Zhu G, Zhang X, Wang Y, et al. Effects of exercise intervention in breast cancer survivors: a meta-analysis of 33 randomized controlled trails. Onco Targets Ther 2016;9:2153-2168. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27110131.

539. Patsou ED, Alexias GD, Anagnostopoulos FG, Karamouzis MV. Effects of physical activity on depressive symptoms during breast cancer survivorship: a meta-analysis of randomised control trials. ESMO Open 2017;2:e000271. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29259819.

540. Park SC, Oh HS, Oh DH, et al. Evidence-based, non-pharmacological treatment guideline for depression in Korea. J Korean Med Sci 2014;29:12-22. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24431900.

541. Hunot V, Churchill R, Silva de Lima M, Teixeira V. Psychological therapies for generalised anxiety disorder. Cochrane Database Syst Rev 2007:CD001848. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17253466.

542. Mendes DD, Mello MF, Ventura P, et al. A systematic review on the effectiveness of cognitive behavioral therapy for posttraumatic stress disorder. Int J Psychiatry Med 2008;38:241-259. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19069570.

543. Nieuwsma JA, Trivedi RB, McDuffie J, et al. Brief psychotherapy for depression: a systematic review and meta-analysis. Int J Psychiatry Med 2012;43:129-151. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22849036.

544. Ponniah K, Hollon SD. Empirically supported psychological treatments for adult acute stress disorder and posttraumatic stress disorder: a review. Depress Anxiety 2009;26:1086-1109. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19957280.

545. Roberts NP, Kitchiner NJ, Kenardy J, Bisson JI. Systematic review and meta-analysis of multiple-session early interventions following traumatic events. Am J Psychiatry 2009;166:293-301. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19188285.

546. Tauber NM, O'Toole MS, Dinkel A, et al. Effect of psychological intervention on fear of cancer recurrence: A systematic review and meta-analysis. J Clin Oncol 2019;37:2899-2915. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31532725.

547. Lengacher CA, Shelton MM, Reich RR, et al. Mindfulness based stress reduction (MBSR(BC)) in breast cancer: evaluating fear of recurrence (FOR) as a mediator of psychological and physical symptoms in a randomized control trial (RCT). J Behav Med 2014;37:185-195. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23184061.

548. Lerman R, Jarski R, Rea H, et al. Improving symptoms and quality of life of female cancer survivors: a randomized controlled study. Ann Surg Oncol 2012;19:373-378. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21913014.

549. Matthews HJ, Grunfeld EA, Turner A. The efficacy of interventions to improve psychosocial outcomes following surgical treatment for breast cancer: a systematic review and meta-analysis. Psychooncology 2016;26:593-607. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27333194.

550. Osborn RL, Demoncada AC, Feuerstein M. Psychosocial interventions for depression, anxiety, and quality of life in cancer survivors: meta-analyses. Int J Psychiatry Med 2006;36:13-34. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16927576.

551. Piet J, Wurtzen H, Zachariae R. The effect of mindfulness-based therapy on symptoms of anxiety and depression in adult cancer patients and survivors: a systematic review and meta-analysis. J Consult Clin Psychol 2012;80:1007-1020. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22563637.

552. Simpson JS, Carlson LE, Trew ME. Effect of group therapy for breast cancer on healthcare utilization. Cancer Pract 2001;9:19-26. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11879269.

553. van de Wal M, Thewes B, Gielissen M, et al. Efficacy of blended cognitive behavior therapy for high fear of recurrence in breast, prostate, and colorectal cancer survivors: the SWORD study, a randomized controlled trial. J Clin Oncol 2017:JCO2016705301. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28471726.

554. Burm R, Thewes B, Rodwell L, et al. Long-term efficacy and cost-effectiveness of blended cognitive behavior therapy for high fear of recurrence in breast, prostate and colorectal Cancer survivors: follow-up of the SWORD randomized controlled trial. BMC Cancer 2019;19:462. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31096934.

555. Hall DL, Luberto CM, Philpotts LL, et al. Mind-body interventions for fear of cancer recurrence: A systematic review and meta-analysis. Psychooncology 2018;27:2546-2558. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29744965.

556. Dieng M, Butow PN, Costa DS, et al. Psychoeducational intervention to reduce fear of cancer recurrence in people at high risk of developing another primary melanoma: results of a randomized controlled trial. J Clin

Oncol 2016;34:4405-4414. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27998215.

557. Butow PN, Turner J, Gilchrist J, et al. Randomized trial of ConquerFear: A novel, theoretically based psychosocial intervention for fear of cancer recurrence. J Clin Oncol 2017;35:4066-4077. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29095681.

558. Cramer H, Lange S, Klose P, et al. Yoga for breast cancer patients and survivors: a systematic review and meta-analysis. BMC Cancer 2012;12:412. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22988934.

559. Greenlee H, DuPont-Reyes MJ, Balneaves LG, et al. Clinical practice guidelines on the evidence-based use of integrative therapies during and after breast cancer treatment. CA Cancer J Clin 2017;67:194-232. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28436999.

560. Hunter EG, Gibson RW, Arbesman M, D'Amico M. Systematic review of occupational therapy and adult cancer rehabilitation: part 1. Impact of physical activity and symptom management interventions. Am J Occup Ther 2017;71:7102100030p7102100031-7102100030p7102100011. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28218585.

561. Salhofer I, Will A, Monsef I, Skoetz N. Meditation for adults with haematological malignancies. Cochrane Database Syst Rev 2016;2:CD011157. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26840029.

562. Stan DL, Collins NM, Olsen MM, et al. The evolution of mindfulness-based physical interventions in breast cancer survivors. Evid Based Complement Alternat Med 2012;2012:758641. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22997532.

563. Bower JE, Crosswell AD, Stanton AL, et al. Mindfulness meditation for younger breast cancer survivors: a randomized controlled trial. Cancer 2015;121:1231-1240. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25537522.

564. Carlson LE, Doll R, Stephen J, et al. Randomized controlled trial of Mindfulness-based cancer recovery versus supportive expressive group therapy for distressed survivors of breast cancer. J Clin Oncol 2013;31:3119-3126. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23918953.

565. Carlson LE, Tamagawa R, Stephen J, et al. Randomized-controlled trial of mindfulness-based cancer recovery versus supportive expressive group therapy among distressed breast cancer survivors (MINDSET): long-term follow-up results. Psychooncology 2016;25:750-759. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27193737.

566. Huang HP, He M, Wang HY, Zhou M. A meta-analysis of the benefits of mindfulness-based stress reduction (MBSR) on psychological function among breast cancer (BC) survivors. Breast Cancer 2016;23:568-576. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25820148.

567. Lengacher CA, Reich RR, Paterson CL, et al. Examination of broad symptom improvement resulting from mindfulness-based stress reduction in breast cancer survivors: a randomized controlled trial. J Clin Oncol 2016;34:2827-2834. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27247219.

568. Fabricatore AN, Wadden TA, Higginbotham AJ, et al. Intentional weight loss and changes in symptoms of depression: a systematic review and meta-analysis. Int J Obes (Lond) 2011;35:1363-1376. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21343903.

569. Hawkins NA, Soman A, Buchanan Lunsford N, et al. Use of medications for treating anxiety and depression in cancer survivors in the United States. J Clin Oncol 2017;35:78-85. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28034075.

570. Syrowatka A, Chang SL, Tamblyn R, et al. Psychotropic and opioid medication use in older patients with breast cancer across the care trajectory: A population-based cohort study. J Natl Compr Canc Netw 2016;14:1412-1419. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27799512.

571. Fisch MJ, Loehrer PJ, Kristeller J, et al. Fluoxetine versus placebo in advanced cancer outpatients: a double-blinded trial of the Hoosier Oncology Group. J Clin Oncol 2003;21:1937-1943. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12743146.

572. Holland JC, Morrow GR, Schmale A, et al. A randomized clinical trial of alprazolam versus progressive muscle relaxation in cancer patients with anxiety and depressive symptoms. J Clin Oncol 1991;9:1004-1011. Available at: http://www.ncbi.nlm.nih.gov/pubmed/2033413.

573. Holland JC, Romano SJ, Heiligenstein JH, et al. A controlled trial of fluoxetine and desipramine in depressed women with advanced cancer. Psychooncology 1998;7:291-300. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9741068.

574. Pirl WF. Evidence report on the occurrence, assessment, and treatment of depression in cancer patients. J Natl Cancer Inst Monogr 2004:32-39. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15263039.

575. Rayner L, Price A, Evans A, et al. Antidepressants for depression in physically ill people. Cochrane Database Syst Rev 2010;3:CD007503. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20238354.

576. Rayner L, Price A, Evans A, et al. Antidepressants for the treatment of depression in palliative care: systematic review and meta-analysis. Palliat Med 2010;25:36-51. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20935027.

577. Wald TG, Kathol RG, Noyes R, Jr., et al. Rapid relief of anxiety in cancer patients with both alprazolam and placebo. Psychosomatics 1993;34:324-332. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8351307.

578. Williams S, Dale J. The effectiveness of treatment for depression/depressive symptoms in adults with cancer: a systematic review. Br J Cancer 2006;94:372-390. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16465173.

579. Haque R, Shi J, Schottinger JE, et al. Tamoxifen and antidepressant drug interaction in a cohort of 16,887 breast cancer survivors. J Natl Cancer Inst 2016;108. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26631176.

580. Binkhorst L, Bannink M, de Bruijn P, et al. Augmentation of endoxifen exposure in tamoxifen-treated women following SSRI switch. Clin Pharmacokinet 2016;55:249-255. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26446141.

581. Wedret JJ, Tu TG, Paul D, et al. Interactions between antidepressants, sleep aids and selected breast cancer therapy. Ment Illn 2019;11:8115. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31281608.

582. Janelsins MC, Kohli S, Mohile SG, et al. An update on cancer- and chemotherapy-related cognitive dysfunction: current status. Semin Oncol 2011;38:431-438. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21600374.

583. Wefel JS, Schagen SB. Chemotherapy-related cognitive dysfunction. Curr Neurol Neurosci Rep 2012;12:267-275. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22453825.

584. Ahles TA, Saykin AJ, McDonald BC, et al. Cognitive function in breast cancer patients prior to adjuvant treatment. Breast Cancer Res Treat 2008;110:143-152. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17674194.

585. Ahles TA, Saykin AJ, McDonald BC, et al. Longitudinal assessment of cognitive changes associated with adjuvant treatment for breast cancer: impact of age and cognitive reserve. J Clin Oncol 2010;28:4434-4440. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20837957.

586. Ahles TA, Root JC, Ryan EL. Cancer- and cancer treatment-associated cognitive change: an update on the state of the science. J Clin Oncol 2012;30:3675-3686. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23008308.

587. Hodgson KD, Hutchinson AD, Wilson CJ, Nettelbeck T. A meta-analysis of the effects of chemotherapy on cognition in patients with cancer. Cancer Treat Rev 2012;39:297-304. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23219452.

588. Phillips KM, Jim HS, Small BJ, et al. Cognitive functioning after cancer treatment: a 3-year longitudinal comparison of breast cancer survivors treated with chemotherapy or radiation and noncancer controls. Cancer 2012;118:1925-1932. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22161750.

589. Vardy J, Dhillon HM, Pond GR, et al. Cognitive function and fatigue after diagnosis of colorectal cancer. Ann Oncol 2014;25:2404-2412. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25214544.

590. Wefel JS, Lenzi R, Theriault RL, et al. The cognitive sequelae of standard-dose adjuvant chemotherapy in women with breast carcinoma: results of a prospective, randomized, longitudinal trial. Cancer 2004;100:2292-2299. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15160331.

591. Wefel JS, Lenzi R, Theriault R, et al. 'Chemobrain' in breast carcinoma?: a prologue. Cancer 2004;101:466-475. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15274059.

592. Mandelblatt JS, Small BJ, Luta G, et al. Cancer-related cognitive outcomes among older breast cancer survivors in the thinking and living with cancer study. J Clin Oncol 2018:JCO1800140. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30281396.

593. Janelsins MC, Heckler CE, Peppone LJ, et al. Longitudinal trajectory and characterization of cancer-related cognitive impairment in a nationwide cohort study. J Clin Oncol 2018:JCO2018786624. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30240328.

594. Wagner LI, Gray RJ, Sparano JA, et al. Patient-reported cognitive impairment among women with early breast cancer randomly assigned to endocrine therapy alone versus chemoendocrine therapy: Results from TAILORx. J Clin Oncol 2020:JCO1901866. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32271671.

595. Jean-Pierre P, Winters PC, Ahles TA, et al. Prevalence of self-reported memory problems in adult cancer survivors: a national cross-sectional study. J Oncol Pract 2012;8:30-34. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22548008.

596. Ahles TA, Saykin AJ, Furstenberg CT, et al. Neuropsychologic impact of standard-dose systemic chemotherapy in long-term survivors of breast cancer and lymphoma. J Clin Oncol 2002;20:485-493. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11786578.

597. Anderson-Hanley C, Sherman ML, Riggs R, et al. Neuropsychological effects of treatments for adults with cancer: A meta-analysis and review of the literature. Journal of the International Neuropsychological Society 2003;9:967-982. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14738279.

598. Buchanan ND, Dasari S, Rodriguez JL, et al. Post-treatment neurocognition and psychosocial care among breast cancer survivors. Am J Prev Med 2015;49:S498-508. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26590645.

599. Deprez S, Amant F, Smeets A, et al. Longitudinal assessment of chemotherapy-induced structural changes in cerebral white matter and its correlation with impaired cognitive functioning. J Clin Oncol 2012;30:274-281. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22184379.

600. Jim HS, Phillips KM, Chait S, et al. Meta-analysis of cognitive functioning in breast cancer survivors previously treated with standard-dose chemotherapy. J Clin Oncol 2012;30:3578-3587. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22927526.

601. Jim HS, Small B, Hartman S, et al. Clinical predictors of cognitive function in adults treated with hematopoietic cell transplantation. Cancer 2012;118:3407-3416. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22139882.

602. Meadows ME, Chang G, Jones JA, et al. Predictors of neuropsychological change in patients with chronic myelogenous leukemia and myelodysplastic syndrome. Arch Clin Neuropsychol 2013;28:363-374. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23391504.

603. Santini B, Talacchi A, Squintani G, et al. Cognitive outcome after awake surgery for tumors in language areas. J Neurooncol 2012;108:319-326. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22350433.

604. Satoer D, Vork J, Visch-Brink E, et al. Cognitive functioning early after surgery of gliomas in eloquent areas. J Neurosurg 2012;117:831-838. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22937930.

605. Scherwath A, Schirmer L, Kruse M, et al. Cognitive functioning in allogeneic hematopoietic stem cell transplantation recipients and its medical correlates: a prospective multicenter study. Psychooncology 2013;22:1509-1516. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22945857.

606. Scoccianti S, Detti B, Cipressi S, et al. Changes in neurocognitive functioning and quality of life in adult patients with brain tumors treated with radiotherapy. J Neurooncol 2012;108:291-308. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22354791.

607. Stewart A, Bielajew C, Collins B, et al. A meta-analysis of the neuropsychological effects of adjuvant chemotherapy treatment in women treated for breast cancer. Clin Neuropsychol 2006;20:76-89. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16410227.

608. Syrjala KL, Artherholt SB, Kurland BF, et al. Prospective neurocognitive function over 5 years after allogeneic hematopoietic cell transplantation for cancer survivors compared with matched controls at 5 years. J Clin Oncol 2011;29:2397-2404. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21537032.

609. Vardy J, Rourke S, Tannock IF. Evaluation of cognitive function associated with chemotherapy: a review of published studies and recommendations for future research. J Clin Oncol 2007;25:2455-2463. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17485710.

610. Zucchella C, Bartolo M, Di Lorenzo C, et al. Cognitive impairment in primary brain tumors outpatients: a prospective cross-sectional survey. J Neurooncol 2013;112:455-460. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23417320.

611. Schmidt JE, Beckjord E, Bovbjerg DH, et al. Prevalence of perceived cognitive dysfunction in survivors of a wide range of cancers: results from the 2010 LIVESTRONG survey. J Cancer Surviv 2016;10:302-311. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26238504.

612. Janelsins MC, Heckler CE, Peppone LJ, et al. Cognitive complaints in survivors of breast cancer after chemotherapy compared with age-matched controls: An analysis from a nationwide, multicenter, prospective longitudinal study. J Clin Oncol 2017;35:506-514. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28029304.

613. Janelsins MC, Heckler CE, Peppone LJ, et al. Cognitive complaints in survivors of breast cancer after chemotherapy compared with age-matched controls: an analysis from a nationwide, multicenter, prospective longitudinal study. J Clin Oncol 2016:JCO2016685856. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28029304.

614. Vardy JL, Dhillon HM, Pond GR, et al. Cognitive function in patients with colorectal cancer who do and do not receive chemotherapy: a prospective, longitudinal, controlled study. J Clin Oncol 2015;33:4085-4092. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26527785.

615. Williams AM, Janelsins MC, van Wijngaarden E. Cognitive function in cancer survivors: analysis of the 1999-2002 National Health and Nutrition Examination Survey. Support Care Cancer 2016;24:2155-2162. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26559193.

616. Koppelmans V, Breteler MM, Boogerd W, et al. Neuropsychological performance in survivors of breast cancer more than 20 years after adjuvant chemotherapy. J Clin Oncol 2012;30:1080-1086. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22370315.

617. Harder H, Van Gool AR, Duivenvoorden HJ, et al. Case-referent comparison of cognitive functions in patients receiving haematopoietic

stem-cell transplantation for haematological malignancies: two-year follow-up results. Eur J Cancer 2007;43:2052-2059. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17719220.

618. Sharafeldin N, Bosworth A, Patel SK, et al. Cognitive functioning after hematopoietic cell transplantation for hematologic malignancy: Results from a prospective longitudinal study. J Clin Oncol 2018;36:463-475. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29252122.

619. Zer A, Pond GR, Razak ARA, et al. Association of neurocognitive deficits with radiotherapy or chemoradiotherapy for patients with head and neck cancer. JAMA Otolaryngol Head Neck Surg 2017. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29167901.

620. Costa DSJ, Fardell JE. Why are objective and perceived cognitive function weakly correlated in patients with cancer? J Clin Oncol 2019;37:1154-1158. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30920881.

621. Ganz PA, Kwan L, Castellon SA, et al. Cognitive complaints after breast cancer treatments: examining the relationship with neuropsychological test performance. J Natl Cancer Inst 2013;105:791-801. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23606729.

622. Ahles TA, Saykin AJ. Candidate mechanisms for chemotherapy-induced cognitive changes. Nat Rev Cancer 2007;7:192-201. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17318212.

623. Deprez S, Billiet T, Sunaert S, Leemans A. Diffusion tensor MRI of chemotherapy-induced cognitive impairment in non-CNS cancer patients: a review. Brain Imaging Behav 2013;7:409-435. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23329357.

624. Simo M, Rifa-Ros X, Rodriguez-Fornells A, Bruna J. Chemobrain: a systematic review of structural and functional neuroimaging studies. Neurosci Biobehav Rev 2013;37:1311-1321. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23660455.

625. Deprez S, Vandenbulcke M, Peeters R, et al. Longitudinal assessment of chemotherapy-induced alterations in brain activation during multitasking and its relation with cognitive complaints. J Clin Oncol 2014;32:2031-2038. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24868029.

626. de Ruiter MB, Schagen SB. Functional MRI studies in non-CNS cancers. Brain Imaging Behav 2013;7:388-408. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23934234.

627. Wefel JS, Saleeba AK, Buzdar AU, Meyers CA. Acute and late onset cognitive dysfunction associated with chemotherapy in women with breast cancer. Cancer 2010;116:3348-3356. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20564075.

628. Liou KT, Ahles TA, Garland SN, et al. The relationship between insomnia and cognitive impairment in breast cancer survivors. JNCI Cancer Spectr 2019;3:pkz041. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31355357.

629. Schagen SB, Das E, Vermeulen I. Information about chemotherapy-associated cognitive problems contributes to cognitive problems in cancer patients. Psychooncology 2012;21:1132-1135. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21769988.

630. Nelson CJ, Nandy N, Roth AJ. Chemotherapy and cognitive deficits: mechanisms, findings, and potential interventions. Palliat Support Care 2007;5:273-280. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17969831.

631. Wefel JS, Vardy J, Ahles T, Schagen SB. International Cognition and Cancer Task Force recommendations to harmonise studies of cognitive function in patients with cancer. Lancet Oncol 2011;12:703-708. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21354373.

632. International Cognition and Cancer Task Force: Mission. Available at: https://www.icctf.com/mission-1/. Accessed June 5, 2020.

633. Deprez S, Kesler SR, Saykin AJ, et al. International Cognition and Cancer Task Force recommendations for neuroimaging methods in the study of cognitive impairment in non-CNS cancer patients. J Natl Cancer Inst 2018;110:223-231. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29365201.

634. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-198. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1202204.

635. Goedendorp MM, Knoop H, Gielissen MF, et al. The effects of cognitive behavioral therapy for postcancer fatigue on perceived cognitive disabilities and neuropsychological test performance. J Pain Symptom Manage 2014;47:35-44. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23707383.

636. Ferguson RJ, McDonald BC, Rocque MA, et al. Development of CBT for chemotherapy-related cognitive change: results of a waitlist control trial. Psychooncology 2012;21:176-186. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22271538.

637. Ferguson RJ, Sigmon ST, Pritchard AJ, et al. A randomized trial of videoconference-delivered cognitive behavioral therapy for survivors of breast cancer with self-reported cognitive dysfunction. Cancer 2016;122:1782-1791. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27135464.

638. Angevaren M, Aufdemkampe G, Verhaar HJ, et al. Physical activity and enhanced fitness to improve cognitive function in older people without known cognitive impairment. Cochrane Database Syst Rev 2008:CD005381. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18646126.

639. Chan RJ, McCarthy AL, Devenish J, et al. Systematic review of pharmacologic and non-pharmacologic interventions to manage cognitive alterations after chemotherapy for breast cancer. Eur J Cancer 2015;51:437-450. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25623439.

640. Fitzpatrick TR, Edgar L, Holcroft C. Assessing the relationship between physical fitness activities, cognitive health, and quality of life among older cancer survivors. J Psychosoc Oncol 2012;30:556-572. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22963183.

641. Kramer AF, Erickson KI. Capitalizing on cortical plasticity: influence of physical activity on cognition and brain function. Trends Cogn Sci 2007;11:342-348. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17629545.

642. Hartman SJ, Nelson SH, Myers E, et al. Randomized controlled trial of increasing physical activity on objectively measured and self-reported cognitive functioning among breast cancer survivors: The memory & motion study. Cancer 2018;124:192-202. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28926676.

643. Treanor CJ, McMenamin UC, O'Neill RF, et al. Non-pharmacological interventions for cognitive impairment due to systemic cancer treatment. Cochrane Database Syst Rev 2016:CD011325. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27529826.

644. Damholdt MF, Mehlsen M, O'Toole MS, et al. Web-based cognitive training for breast cancer survivors with cognitive complaints-a randomized controlled trial. Psychooncology 2016;25:1293-1300. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26763774.

645. Ercoli LM, Petersen L, Hunter AM, et al. Cognitive rehabilitation group intervention for breast cancer survivors: results of a randomized clinical trial. Psychooncology 2015;24:1360-1367. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25759235.

646. Bray VJ, Dhillon HM, Bell ML, et al. Evaluation of a web-based cognitive rehabilitation program in cancer survivors reporting cognitive symptoms after chemotherapy. J Clin Oncol 2017;35:217-225. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28056205.

647. Johns SA, Von Ah D, Brown LF, et al. Randomized controlled pilot trial of mindfulness-based stress reduction for breast and colorectal cancer survivors: effects on cancer-related cognitive impairment. J Cancer Surviv

2016;10:437-448. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26586494.

648. Derry HM, Jaremka LM, Bennett JM, et al. Yoga and self-reported cognitive problems in breast cancer survivors: a randomized controlled trial. Psychooncology 2015;24:958-966. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25336068.

649. Janelsins MC, Peppone LJ, Heckler CE, et al. YOCAS(c)(R) yoga reduces self-reported memory difficulty in cancer survivors in a nationwide randomized clinical trial: investigating relationships between memory and sleep. Integr Cancer Ther 2016;15:263-271. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26621521.

650. Player L, Mackenzie L, Willis K, Loh SY. Women's experiences of cognitive changes or 'chemobrain' following treatment for breast cancer: A role for occupational therapy? Aust Occup Ther J 2014;61:230-240. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24499127.

651. Gehring K, Roukema JA, Sitskoorn MM. Review of recent studies on interventions for cognitive deficits in patients with cancer. Expert Rev Anticancer Ther 2012;12:255-269. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22316373.

652. Mar Fan HG, Clemons M, Xu W, et al. A randomised, placebo-controlled, double-blind trial of the effects of d-methylphenidate on fatigue and cognitive dysfunction in women undergoing adjuvant chemotherapy for breast cancer. Support Care Cancer 2008;16:577-583. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17972110.

653. Conklin HM, Khan RB, Reddick WE, et al. Acute neurocognitive response to methylphenidate among survivors of childhood cancer: a randomized, double-blind, cross-over trial. J Pediatr Psychol 2007;32:1127-1139. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17569711.

654. Kohli S, Fisher SG, Tra Y, et al. The effect of modafinil on cognitive function in breast cancer survivors. Cancer 2009;115:2605-2616. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19309747.

655. Lundorff LE, Jonsson BH, Sjogren P. Modafinil for attentional and psychomotor dysfunction in advanced cancer: a double-blind, randomised, cross-over trial. Palliat Med 2009;23:731-738. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19648224.

656. Gehring K, Patwardhan SY, Collins R, et al. A randomized trial on the efficacy of methylphenidate and modafinil for improving cognitive functioning and symptoms in patients with a primary brain tumor. J Neurooncol 2012;107:165-174. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21964738.

657. Rapp SR, Case LD, Peiffer A, et al. Donepezil for irradiated brain tumor survivors: A phase III randomized placebo-controlled clinical trial. J Clin Oncol 2015;33:1653-1659. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25897156.

658. Shaw EG, Rosdhal R, D'Agostino RB, Jr., et al. Phase II study of donepezil in irradiated brain tumor patients: effect on cognitive function, mood, and quality of life. J Clin Oncol 2006;24:1415-1420. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16549835.

659. Lawrence JA, Griffin L, Balcueva EP, et al. A study of donepezil in female breast cancer survivors with self-reported cognitive dysfunction 1 to 5 years following adjuvant chemotherapy. J Cancer Surviv 2016;10:176-184. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26130292.

660. Berger AM, Mooney K, Alvarez-Perez A, et al. Cancer-Related Fatigue, Version 2.2015. J Natl Compr Canc Netw 2015;13:1012-1039. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26285247.

661. Ahlberg K, Ekman T, Gaston-Johansson F, Mock V. Assessment and management of cancer-related fatigue in adults. Lancet 2003;362:640-650. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12944066.

662. Collins JJ, Devine TD, Dick GS, et al. The measurement of symptoms in young children with cancer: the validation of the Memorial Symptom Assessment Scale in children aged 7-12. J Pain Symptom Manage 2002;23:10-16. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11779663.

663. Wagner LI, Cella D. Fatigue and cancer: causes, prevalence and treatment approaches. Br J Cancer 2004;91:822-828. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15238987.

664. Henry DH, Viswanathan HN, Elkin EP, et al. Symptoms and treatment burden associated with cancer treatment: results from a cross-sectional national survey in the U.S. Support Care Cancer 2008;16:791-801. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18204940.

665. Hofman M, Ryan JL, Figueroa-Moseley CD, et al. Cancer-related fatigue: the scale of the problem. Oncologist 2007;12 Suppl 1:4-10. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17573451.

666. Bower JE, Ganz PA, Aziz N, et al. T-cell homeostasis in breast cancer survivors with persistent fatigue. J Natl Cancer Inst 2003;95:1165-1168. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12902446.

667. Bower JE, Ganz PA, Desmond KA, et al. Fatigue in breast cancer survivors: occurrence, correlates, and impact on quality of life. J Clin Oncol 2000;18:743-753. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10673515.

668. Crom DB, Hinds PS, Gattuso JS, et al. Creating the basis for a breast health program for female survivors of Hodgkin disease using a participatory research approach. Oncol Nurs Forum 2005;32:1131-1141. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16270109.

669. Fossa SD, Dahl AA, Loge JH. Fatigue, anxiety, and depression in long-term survivors of testicular cancer. J Clin Oncol 2003;21:1249-1254. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12663711.

670. Haghighat S, Akbari ME, Holakouei K, et al. Factors predicting fatigue in breast cancer patients. Support Care Cancer 2003;11:533-538. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12730728.

671. Kreissl S, Mueller H, Goergen H, et al. Cancer-related fatigue in patients with and survivors of Hodgkin's lymphoma: a longitudinal study of the German Hodgkin Study Group. Lancet Oncol 2016;17:1453-1462. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27612583.

672. Ruffer JU, Flechtner H, Tralls P, et al. Fatigue in long-term survivors of Hodgkin's lymphoma; a report from the German Hodgkin Lymphoma Study Group (GHSG). Eur J Cancer 2003;39:2179-2186. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14522376.

673. Servaes P, Verhagen S, Bleijenberg G. Determinants of chronic fatigue in disease-free breast cancer patients: a cross-sectional study. Ann Oncol 2002;13:589-598. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12056710.

674. Servaes P, Verhagen S, Schreuder HW, et al. Fatigue after treatment for malignant and benign bone and soft tissue tumors. J Pain Symptom Manage 2003;26:1113-1122. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14654263.

675. Abrahams HJ, Gielissen MF, Schmits IC, et al. Risk factors, prevalence, and course of severe fatigue after breast cancer treatment: a meta-analysis involving 12 327 breast cancer survivors. Ann Oncol 2016;27:965-974. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26940687.

676. Siegel R, DeSantis C, Virgo K, et al. Cancer treatment and survivorship statistics, 2012. CA Cancer J Clin 2012;62:220-241. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22700443.

677. Wang XS, Zhao F, Fisch MJ, et al. Prevalence and characteristics of moderate to severe fatigue: a multicenter study in cancer patients and survivors. Cancer 2014;120:425-432. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24436136.

678. Husson O, Mols F, van de Poll-Franse L, et al. Variation in fatigue among 6011 (long-term) cancer survivors and a normative population: a study from the population-based PROFILES registry. Support Care Cancer 2015;23:2165-2174. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25556703.

679. Janda M, Gerstner N, Obermair A, et al. Quality of life changes during conformal radiation therapy for prostate carcinoma. Cancer

2000;89:1322-1328. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11002229.

680. Behringer K, Goergen H, Muller H, et al. Cancer-related fatigue in patients with and survivors of Hodgkin lymphoma: the impact on treatment outcome and social reintegration. J Clin Oncol 2016;34:4329-4337. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27998235.

681. al-Majid S, McCarthy DO. Cancer-induced fatigue and skeletal muscle wasting: the role of exercise. Biol Res Nurs 2001;2:186-197. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11547540.

682. Berger AM, Wielgus K, Hertzog M, et al. Patterns of circadian activity rhythms and their relationships with fatigue and anxiety/depression in women treated with breast cancer adjuvant chemotherapy. Support Care Cancer 2009;18:105-114. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19381692.

683. Bower JE. Cancer-related fatigue: links with inflammation in cancer patients and survivors. Brain Behav Immun 2007;21:863-871. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17543499.

684. Miller AH, Ancoli-Israel S, Bower JE, et al. Neuroendocrine-immune mechanisms of behavioral comorbidities in patients with cancer. J Clin Oncol 2008;26:971-982. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18281672.

685. Rich TA. Symptom clusters in cancer patients and their relation to EGFR ligand modulation of the circadian axis. J Support Oncol 2007;5:167-174; discussion 176-167. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17500504.

686. Schubert C, Hong S, Natarajan L, et al. The association between fatigue and inflammatory marker levels in cancer patients: a quantitative review. Brain Behav Immun 2007;21:413-427. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17178209.

687. Alfano CM, Imayama I, Neuhouser ML, et al. Fatigue, inflammation, and omega-3 and omega-6 fatty acid intake among breast cancer survivors. J Clin Oncol 2012;30:1280-1287. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22412148.

688. Bower JE, Ganz PA, Irwin MR, et al. Inflammation and behavioral symptoms after breast cancer treatment: do fatigue, depression, and sleep disturbance share a common underlying mechanism? J Clin Oncol 2011;29:3517-3522. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21825266.

689. Bower JE, Ganz PA, Aziz N, Fahey JL. Fatigue and proinflammatory cytokine activity in breast cancer survivors. Psychosom Med 2002;64:604-611. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12140350.

690. Mendoza TR, Wang XS, Cleeland CS, et al. The rapid assessment of fatigue severity in cancer patients: use of the Brief Fatigue Inventory. Cancer 1999;85:1186-1196. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10091805.

691. Piper BF, Dodd MJ, Ream E. Improving the clinical measurement of cancer treatment-related fatigue. Better health through nursing research: International state of the science. Vol. 99. Washington, DC: American Nurses Association; 1999.

692. de Raaf PJ, de Klerk C, Timman R, et al. Systematic monitoring and treatment of physical symptoms to alleviate fatigue in patients with advanced cancer: a randomized controlled trial. J Clin Oncol 2013;31:716-723. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23284036.

693. Barsevick AM, Dudley W, Beck S, et al. A randomized clinical trial of energy conservation for patients with cancer-related fatigue. Cancer 2004;100:1302-1310. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15022300.

694. Baruth M, Wilcox S, Der Ananian C, Heiney S. Effects of home-based walking on quality of life and fatigue outcomes in early stage breast cancer survivors: a 12-week pilot study. J Phys Act Health 2015;12 Suppl 1:S110-118. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23963636.

695. Kampshoff CS, Chinapaw MJ, Brug J, et al. Randomized controlled trial of the effects of high intensity and low-to-moderate intensity exercise on physical fitness and fatigue in cancer survivors: results of the Resistance and Endurance exercise After ChemoTherapy (REACT) study. BMC Med 2015;13:275. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26515383.

696. Larkey LK, Roe DJ, Weihs KL, et al. Randomized controlled trial of Qigong/Tai Chi Easy on cancer-related fatigue in breast cancer survivors. Ann Behav Med 2015;49:165-176. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25124456.

697. Meneses-Echavez JF, Gonzalez-Jimenez E, Ramirez-Velez R. Effects of supervised exercise on cancer-related fatigue in breast cancer survivors: a systematic review and meta-analysis. BMC Cancer 2015;15:77. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25885168.

698. McMillan EM, Newhouse IJ. Exercise is an effective treatment modality for reducing cancer-related fatigue and improving physical capacity in cancer patients and survivors: a meta-analysis. Appl Physiol Nutr Metab 2011;36:892-903. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22067010.

699. McNeely ML, Courneya KS. Exercise programs for cancer-related fatigue: evidence and clinical guidelines. J Natl Compr Canc Netw 2010;8:945-953. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20870638.

700. Mustian KM, Alfano CM, Heckler C, et al. Comparison of pharmaceutical, psychological, and exercise treatments for cancer-related fatigue: a meta-analysis. JAMA Oncol 2017;3:961-968. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28253393.

701. Cramp F, Byron-Daniel J. Exercise for the management of cancer-related fatigue in adults. Cochrane Database Syst Rev 2012;11:CD006145. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23152233.

702. Dennett AM, Peiris CL, Shields N, et al. Moderate-intensity exercise reduces fatigue and improves mobility in cancer survivors: a systematic review and meta-regression. J Physiother 2016;62:68-82. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26996098.

703. Kessels E, Husson O, van der Feltz-Cornelis CM. The effect of exercise on cancer-related fatigue in cancer survivors: a systematic review and meta-analysis. Neuropsychiatr Dis Treat 2018;14:479-494. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29445285.

704. Lin PJ, Kleckner IR, Loh KP, et al. Influence of yoga on cancer-related fatigue and on mediational relationships between changes in sleep and cancer-related fatigue: A nationwide, multicenter randomized controlled trial of yoga in cancer survivors. Integr Cancer Ther 2019;18:1534735419855134. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31165647.

705. Duijts SF, Faber MM, Oldenburg HS, et al. Effectiveness of behavioral techniques and physical exercise on psychosocial functioning and health-related quality of life in breast cancer patients and survivors--a meta-analysis. Psychooncology 2011;20:115-126. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20336645.

706. Espie CA, Fleming L, Cassidy J, et al. Randomized controlled clinical effectiveness trial of cognitive behavior therapy compared with treatment as usual for persistent insomnia in patients with cancer. J Clin Oncol 2008;26:4651-4658. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18591549.

707. Epstein DR, Dirksen SR. Randomized trial of a cognitive-behavioral intervention for insomnia in breast cancer survivors. Oncol Nurs Forum 2007;34:E51-59. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17878117.

708. Gielissen MFM, Verhagen S, Witjes F, Bleijenberg G. Effects of cognitive behavior therapy in severely fatigued disease-free cancer patients compared with patients waiting for cognitive behavior therapy: a randomized controlled trial. J Clin Oncol 2006;24:4882-4887. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17050873.

709. Kangas M, Bovbjerg DH, Montgomery GH. Cancer-related fatigue: a systematic and meta-analytic review of non-pharmacological therapies for cancer patients. Psychol Bull 2008;134:700-741. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18729569.

710. Mustian KM, Morrow GR, Carroll JK, et al. Integrative nonpharmacologic behavioral interventions for the management of cancer-related fatigue. Oncologist 2007;12 Suppl 1:52-67. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17573456.

711. Jacobsen PB, Donovan KA, Vadaparampil ST, Small BJ. Systematic review and meta-analysis of psychological and activity-based interventions for cancer-related fatigue. Health Psychol 2007;26:660-667. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18020836.

712. Davidson JR, Waisberg JL, Brundage MD, MacLean AW. Nonpharmacologic group treatment of insomnia: a preliminary study with cancer survivors. Psychooncology 2001;10:389-397. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11536417.

713. Fleming L, Randell K, Harvey CJ, Espie CA. Does cognitive behaviour therapy for insomnia reduce clinical levels of fatigue, anxiety and depression in cancer patients? Psychooncology 2014;23:679-684. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24458543.

714. Heckler CE, Garland SN, Peoples AR, et al. Cognitive behavioral therapy for insomnia, but not armodafinil, improves fatigue in cancer survivors with insomnia: a randomized placebo-controlled trial. Support Care Cancer 2016;24:2059-2066. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26542272.

715. Quesnel C, Savard J, Simard S, et al. Efficacy of cognitive-behavioral therapy for insomnia in women treated for nonmetastatic breast cancer. J Consult Clin Psychol 2003;71:189-200. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12602439.

716. Savard J, Simard S, Ivers H, Morin CM. Randomized study on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer, part I: Sleep and psychological effects. J Clin Oncol 2005;23:6083-6096. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16135475.

717. Dirksen SR, Epstein DR. Efficacy of an insomnia intervention on fatigue, mood and quality of life in breast cancer survivors. J Adv Nurs 2008;61:664-675. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18302607.

718. Berger AM, VonEssen S, Khun BR, et al. Feasibilty of a sleep intervention during adjuvant breast cancer chemotherapy. Oncol Nurs Forum 2002;29:1431-1441. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12432414.

719. Schutte-Rodin S, Broch L, Buysse D, et al. Clinical guideline for the evaluation and management of chronic insomnia in adults. J Clin Sleep Med 2008;4:487-504. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18853708.

720. Deng G, Chan Y, Sjoberg D, et al. Acupuncture for the treatment of post-chemotherapy chronic fatigue: a randomized, blinded, sham-controlled trial. Support Care Cancer 2013;21:1735-1741. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23334562.

721. Ling WM, Lui LY, So WK, Chan K. Effects of acupuncture and acupressure on cancer-related fatigue: a systematic review. Oncol Nurs Forum 2014;41:581-592. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25355016.

722. Mao JJ, Farrar JT, Bruner D, et al. Electroacupuncture for fatigue, sleep, and psychological distress in breast cancer patients with aromatase inhibitor-related arthralgia: a randomized trial. Cancer 2014;120:3744-3751. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25077452.

723. Molassiotis A, Bardy J, Finnegan-John J, et al. Acupuncture for cancer-related fatigue in patients with breast cancer: a pragmatic randomized controlled trial. J Clin Oncol 2012;30:4470-4476. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23109700.

724. Posadzki P, Moon TW, Choi TY, et al. Acupuncture for cancer-related fatigue: a systematic review of randomized clinical trials. Support Care Cancer 2013;21:2067-2073. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23435597.

725. Smith C, Carmady B, Thornton C, et al. The effect of acupuncture on post-cancer fatigue and well-being for women recovering from breast cancer: a pilot randomised controlled trial. Acupunct Med 2013;31:9-15. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23196311.

726. Zeng Y, Luo T, Finnegan-John J, Cheng AS. Meta-analysis of randomized controlled trials of acupuncture for cancer-related fatigue. Integr Cancer Ther 2014;13:193-200. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24282102.

727. Zick SM, Sen A, Wyatt GK, et al. Investigation of 2 types of self-administered acupressure for persistent cancer-related fatigue in breast cancer survivors: a randomized clinical trial. JAMA Oncol 2016;2:1470-1476. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27388752.

728. Hanna A, Sledge G, Mayer ML, et al. A phase II study of methylphenidate for the treatment of fatigue. Support Care Cancer 2006;14:210-215. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16096772.

729. Lower EE, Fleishman S, Cooper A, et al. Efficacy of dexmethylphenidate for the treatment of fatigue after cancer chemotherapy: a randomized clinical trial. J Pain Symptom Manage 2009;38:650-662. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19896571.

730. Gong S, Sheng P, Jin H, et al. Effect of methylphenidate in patients with cancer-related fatigue: a systematic review and meta-analysis. PLoS One 2014;9:e84391. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24416225.

731. Qu D, Zhang Z, Yu X, et al. Psychotropic drugs for the management of cancer-related fatigue: a systematic review and meta-analysis. Eur J Cancer Care (Engl) 2016;25:970-979. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26490083.

732. Mucke M, Mochamat, Cuhls H, et al. Pharmacological treatments for fatigue associated with palliative care. Cochrane Database Syst Rev 2015:CD006788. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26026155.

733. Blackhall L, Petroni G, Shu J, et al. A pilot study evaluating the safety and efficacy of modafinal for cancer-related fatigue. J Palliat Med 2009;12:433-439. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19416039.

734. Jean-Pierre P, Morrow GR, Roscoe JA, et al. A phase 3 randomized, placebo-controlled, double-blind, clinical trial of the effect of modafinil on cancer-related fatigue among 631 patients receiving chemotherapy: a University of Rochester Cancer Center Community Clinical Oncology Program Research base study. Cancer 2010;116:3513-3520. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20564068.

735. Spathis A, Fife K, Blackhall F, et al. Modafinil for the treatment of fatigue in lung cancer: results of a placebo-controlled, double-blind, randomized trial. J Clin Oncol 2014;32:1882-1888. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24778393.

736. Barton DL, Liu H, Dakhil SR, et al. Wisconsin Ginseng (Panax quinquefolius) to improve cancer-related fatigue: a randomized, double-blind trial, N07C2. J Natl Cancer Inst 2013;105:1230-1238. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23853057.

737. Ribeiro Pereira ACP, Koifman RJ, Bergmann A. Incidence and risk factors of lymphedema after breast cancer treatment: 10 years of follow-up. Breast 2017;36:67-73. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28992556.

738. Hayes SC, Janda M, Ward LC, et al. Lymphedema following gynecological cancer: Results from a prospective, longitudinal cohort study on prevalence, incidence and risk factors. Gynecol Oncol

2017;146:623-629. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28624154.

739. Gjorup CA, Groenvold M, Hendel HW, et al. Health-related quality of life in melanoma patients: Impact of melanoma-related limb lymphoedema. Eur J Cancer 2017;85:122-132. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28918186.

740. Vassard D, Olsen MH, Zinckernagel L, et al. Psychological consequences of lymphoedema associated with breast cancer: a prospective cohort study. Eur J Cancer 2010;46:3211-3218. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20797846.

741. Syrowatka A, Motulsky A, Kurteva S, et al. Predictors of distress in female breast cancer survivors: a systematic review. Breast Cancer Res Treat 2017;165:229-245. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28553684.

742. Dominick SA, Natarajan L, Pierce JP, et al. The psychosocial impact of lymphedema-related distress among breast cancer survivors in the WHEL Study. Psychooncology 2014;23:1049-1056. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24615880.

743. Hormes JM, Bryan C, Lytle LA, et al. Impact of lymphedema and arm symptoms on quality of life in breast cancer survivors. Lymphology 2010;43:1-13. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20552814.

744. McWayne J, Heiney SP. Psychologic and social sequelae of secondary lymphedema: a review. Cancer 2005;104:457-466. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15968692.

745. Boyages J, Kalfa S, Xu Y, et al. Worse and worse off: the impact of lymphedema on work and career after breast cancer. Springerplus 2016;5:657. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27330922.

746. Dean LT, Moss SL, Ransome Y, et al. "It still affects our economic situation": long-term economic burden of breast cancer and lymphedema. Support Care Cancer 2019;27:1697-1708. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30121786.

747. Asdourian MS, Swaroop MN, Sayegh HE, et al. Association between precautionary behaviors and breast cancer-related lymphedema in patients undergoing bilateral surgery. J Clin Oncol 2017;35:3934-3941. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28976793.

748. DiSipio T, Rye S, Newman B, Hayes S. Incidence of unilateral arm lymphoedema after breast cancer: a systematic review and meta-analysis. Lancet Oncol 2013;14:500-515. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23540561.

749. Kilbreath SL, Refshauge KM, Beith JM, et al. Risk factors for lymphoedema in women with breast cancer: A large prospective cohort. Breast 2016;28:29-36. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27183497.

750. Kuroda K, Yamamoto Y, Yanagisawa M, et al. Risk factors and a prediction model for lower limb lymphedema following lymphadenectomy in gynecologic cancer: a hospital-based retrospective cohort study. BMC Womens Health 2017;17:50. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28743274.

751. Black DM, Jiang J, Kuerer HM, et al. Racial disparities in adoption of axillary sentinel lymph node biopsy and lymphedema risk in women with breast cancer. JAMA Surg 2014;149:788-796. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25073831.

752. Li CZ, Zhang P, Li RW, et al. Axillary lymph node dissection versus sentinel lymph node biopsy alone for early breast cancer with sentinel node metastasis: A meta-analysis. Eur J Surg Oncol 2015;41:958-966. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26054706.

753. Norman SA, Localio AR, Kallan MJ, et al. Risk factors for lymphedema after breast cancer treatment. Cancer Epidemiol Biomarkers Prev 2010;19:2734-2746. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20978176.

754. de Vries M, Hoekstra HJ, Hoekstra-Weebers JE. Quality of life after axillary or groin sentinel lymph node biopsy, with or without completion lymph node dissection, in patients with cutaneous melanoma. Ann Surg Oncol 2009;16:2840-2847. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19639366.

755. Huang J, Yu N, Wang X, Long X. Incidence of lower limb lymphedema after vulvar cancer: A systematic review and meta-analysis. Medicine (Baltimore) 2017;96:e8722. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29145314.

756. Ahmed RL, Schmitz KH, Prizment AE, Folsom AR. Risk factors for lymphedema in breast cancer survivors, the Iowa Women's Health Study. Breast Cancer Res Treat 2011;130:981-991. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21761159.

757. Dominick SA, Madlensky L, Natarajan L, Pierce JP. Risk factors associated with breast cancer-related lymphedema in the WHEL Study. J Cancer Surviv 2013;7:115-123. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23212606.

758. Asdourian MS, Skolny MN, Brunelle C, et al. Precautions for breast cancer-related lymphoedema: risk from air travel, ipsilateral arm blood pressure measurements, skin puncture, extreme temperatures, and cellulitis. Lancet Oncol 2016;17:e392-405. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27599144.

759. Ferguson CM, Swaroop MN, Horick N, et al. Impact of ipsilateral blood draws, injections, blood pressure measurements, and air travel on the risk of lymphedema for patients treated for breast cancer. J Clin Oncol 2016;34:691-698. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26644530.

760. Li L, Yuan L, Chen X, et al. Current treatments for breast cancer-related lymphoedema: A systematic review. Asian Pac J Cancer Prev 2016;17:4875-4883. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28030915.

761. Lymphology ISo. The diagnosis and treatment of peripheral lymphedema: 2013 Consensus Document of the International Society of Lymphology. Lymphology 2013;46:1-11. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23930436.

762. Smile TD, Tendulkar R, Schwarz G, et al. A review of treatment for breast cancer-related lymphedema: Paradigms for clinical practice. Am J Clin Oncol 2018;41:178-190. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28009597.

763. Stout Gergich NL, Pfalzer LA, McGarvey C, et al. Preoperative assessment enables the early diagnosis and successful treatment of lymphedema. Cancer 2008;112:2809-2819. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18428212.

764. Ochalek K, Partsch H, Gradalski T, Szygula Z. Do compression sleeves reduce the incidence of arm lymphedema and improve quality of life? Two-year results from a prospective randomized trial in breast cancer survivors. Lymphat Res Biol 2019;17:70-77. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30339481.

765. Ezzo J, Manheimer E, McNeely ML, et al. Manual lymphatic drainage for lymphedema following breast cancer treatment. Cochrane Database Syst Rev 2015:CD003475. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25994425.

766. Shao Y, Zhong DS. Manual lymphatic drainage for breast cancer-related lymphoedema. Eur J Cancer Care (Engl) 2017;26. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27167238.

767. Nelson NL. Breast cancer-related lymphedema and resistance exercise: a systematic review. J Strength Cond Res 2016;30:2656-2665. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26840439.

768. Position Statement of the National Lymphedema Network: Exercise. NLN Medical Advisory Committee; 2011. Available at: https://issuu.com/lymphnet/docs/exercise. Accessed June 5, 2020.

769. Irwin M, ed ACSM's Guide to Exercise and Cancer Survivorship. Champaign, IL: The American College of Sports Medicine; 2012.

770. Ammitzboll G, Johansen C, Lanng C, et al. Progressive resistance training to prevent arm lymphedema in the first year after breast cancer surgery: Results of a randomized controlled trial. Cancer 2019;125:1683-1692. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30633334.

771. Schmitz KH, Troxel AB, Dean LT, et al. Effect of home-based exercise and weight loss programs on breast cancer-related lymphedema outcomes among overweight breast cancer survivors: The WISER Survivor randomized clinical trial. JAMA Oncol 2019;5:1605-1613. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31415063.

772. Harris SR, Hugi MR, Olivotto IA, et al. Clinical practice guidelines for the care and treatment of breast cancer: 11. Lymphedema. CMAJ 2001;164:191-199. Available at: https://www.ncbi.nlm.nih.gov/pubmed/11332311.

773. Fife CE, Farrow W, Hebert AA, et al. Skin and wound care in lymphedema patients. Advances in Skin & Wound Care 2017;30:305-318. Available at:

774. Ahn S, Port ER. Lymphedema precautions: Time to abandon old practices? J Clin Oncol 2016;34:655-658. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26712226.

775. Cheng CT, Deitch JM, Haines IE, et al. Do medical procedures in the arm increase the risk of lymphoedema after axillary surgery? A review. ANZ J Surg 2014;84:510-514. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24274353.

776. Jakes AD, Twelves C. Breast cancer-related lymphoedema and venepuncture: a review and evidence-based recommendations. Breast Cancer Res Treat 2015;154:455-461. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26589315.

777. McLaughlin SA. Lymphedema: separating fact from fiction. Oncology (Williston Park) 2012;26:242-249. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22545305.

778. Position Statement of the National Lymphedema Network: Lymphedema Risk Reduction Practices. NLN Medical Advisory Committee; 2012. Available at: https://issuu.com/lymphnet/docs/risk_reduction. Accessed June 5, 2020.

779. Paskett ED, Liu H, Oliveri J, et al. Effects of a lymphedema prevention intervention on range of motion among women receiving lymph node dissection for breast cancer treatment (Alliance) CALGB 70305 [abstract]. J Clin Oncol 2018;36 (suppl 7S; abstr 123). Available at: https://meetinglibrary.asco.org/record/157859/abstract.

780. Lindquist H, Enblom A, Dunberger G, et al. Water exercise compared to land exercise or standard care in female cancer survivors with secondary lymphedema. Lymphology 2015;48:64-79. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26714371.

781. Chandwani KD, Heckler CE, Mohile SG, et al. Hot flashes severity, complementary and alternative medicine use, and self-rated health in women with breast cancer. Explore (NY) 2014;10:241-247. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25037667.

782. Chang HY, Jotwani AC, Lai YH, et al. Hot flashes in breast cancer survivors: Frequency, severity and impact. Breast 2016;27:116-121. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27065357.

783. Howard-Anderson J, Ganz PA, Bower JE, Stanton AL. Quality of life, fertility concerns, and behavioral health outcomes in younger breast cancer survivors: a systematic review. J Natl Cancer Inst 2012;104:386-405. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22271773.

784. Leining MG, Gelber S, Rosenberg R, et al. Menopausal-type symptoms in young breast cancer survivors. Ann Oncol 2006;17:1777-1782. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16971671.

785. Charig CR, Rundle JS. Flushing. Long-term side effect of orchiectomy in treatment of prostatic carcinoma. Urology 1989;33:175-178. Available at: http://www.ncbi.nlm.nih.gov/pubmed/2465644.

786. Freedland SJ, Eastham J, Shore N. Androgen deprivation therapy and estrogen deficiency induced adverse effects in the treatment of prostate cancer. Prostate Cancer Prostatic Dis 2009;12:333-338. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19901933.

787. Guise TA, Oefelein MG, Eastham JA, et al. Estrogenic side effects of androgen deprivation therapy. Rev Urol 2007;9:163-180. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18231613.

788. Sarosdy MF, Schellhammer PF, Soloway MS, et al. Endocrine effects, efficacy and tolerability of a 10.8-mg depot formulation of goserelin acetate administered every 13 weeks to patients with advanced prostate cancer. BJU Int 1999;83:801-806. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10368200.

789. Schow DA, Renfer LG, Rozanski TA, Thompson IM. Prevalence of hot flushes during and after neoadjuvant hormonal therapy for localized prostate cancer. South Med J 1998;91:855-857. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9743058.

790. Walker LM, Tran S, Robinson JW. Luteinizing hormone--releasing hormone agonists: a quick reference for prevalence rates of potential adverse effects. Clin Genitourin Cancer 2013;11:375-384. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23891497.

791. Autorino R, Perdona S, D'Armiento M, et al. Gynecomastia in patients with prostate cancer: update on treatment options. Prostate Cancer Prostatic Dis 2006;9:109-114. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16432533.

792. Martin K, Barbieri R. Treatment of menopausal symptoms with hormone therapy In: Crowley W, Jr, Martin K eds. UpToDate; 2016. Available at: http://www.uptodate.com/.

793. Nishiyama T, Kanazawa S, Watanabe R, et al. Influence of hot flashes on quality of life in patients with prostate cancer treated with androgen deprivation therapy. Int J Urol 2004;11:735-741. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15379937.

794. Bines J, Oleske DM, Cobleigh MA. Ovarian function in premenopausal women treated with adjuvant chemotherapy for breast cancer. J Clin Oncol 1996;14:1718-1729. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8622093.

795. De Bruin ML, Huisbrink J, Hauptmann M, et al. Treatment-related risk factors for premature menopause following Hodgkin lymphoma. Blood 2008;111:101-108. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17890454.

796. Goodwin PJ, Ennis M, Pritchard KI, et al. Risk of menopause during the first year after breast cancer diagnosis. J Clin Oncol 1999;17:2365-2370. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10561298.

797. Nelson LM. Clinical practice. Primary ovarian insufficiency. N Engl J Med 2009;360:606-614. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19196677.

798. Krekow LK, Hellerstedt BA, Collea RP, et al. Incidence and predictive factors for recovery of ovarian function in amenorrheic women in their 40s treated with letrozole. J Clin Oncol 2016;34:1594-1600. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26884554.

799. Su HI, Sammel MD, Green J, et al. Antimullerian hormone and inhibin B are hormone measures of ovarian function in late reproductive-aged breast cancer survivors. Cancer 2010;116:592-599. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19918920.

800. Skinner R, Mulder RL, Kremer LC, et al. Recommendations for gonadotoxicity surveillance in male childhood, adolescent, and young adult cancer survivors: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group in collaboration with the PanCareSurFup Consortium. Lancet Oncol 2017;18:e75-e90. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28214419.

801. Nonhormonal management of menopause-associated vasomotor symptoms: 2015 position statement of The North American Menopause Society. Menopause 2015;22:1155-1172; quiz 1173-1154. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26382310.

802. Drewe J, Bucher KA, Zahner C. A systematic review of non-hormonal treatments of vasomotor symptoms in climacteric and cancer patients. Springerplus 2015;4:65. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25713759.

803. Johns C, Seav SM, Dominick SA, et al. Informing hot flash treatment decisions for breast cancer survivors: a systematic review of randomized trials comparing active interventions. Breast Cancer Res Treat 2016;156:415-426. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27015968.

804. Rada G, Capurro D, Pantoja T, et al. Non-hormonal interventions for hot flushes in women with a history of breast cancer. Cochrane Database Syst Rev 2010:CD004923. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20824841.

805. Joffe H, Guthrie KA, LaCroix AZ, et al. Low-dose estradiol and the serotonin-norepinephrine reuptake inhibitor venlafaxine for vasomotor symptoms: a randomized clinical trial. JAMA Intern Med 2014;174:1058-1066. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24861828.

806. Kelsberg G, Maragh L, Safranek S. Clinical Inquiry: Which nonhormonal treatments are effective for hot flashes? J Fam Pract 2016;65:E1-3. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27275942.

807. Simon JA, Portman DJ, Kaunitz AM, et al. Low-dose paroxetine 7.5 mg for menopausal vasomotor symptoms: two randomized controlled trials. Menopause 2013;20:1027-1035. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24045678.

808. Barton DL, Loprinzi CL, Novotny P, et al. Pilot evaluation of citalopram for the relief of hot flashes. J Support Oncol 2003;1:47-51. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15352642.

809. Capriglione S, Plotti F, Montera R, et al. Role of paroxetine in the management of hot flashes in gynecological cancer survivors: Results of the first randomized single-center controlled trial. Gynecol Oncol 2016;143:584-588. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27751589.

810. Carpenter JS, Storniolo AM, Johns S, et al. Randomized, double-blind, placebo-controlled crossover trials of venlafaxine for hot flashes after breast cancer. Oncologist 2007;12:124-135. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17227907.

811. Biglia N, Bounous VE, Susini T, et al. Duloxetine and escitalopram for hot flushes: efficacy and compliance in breast cancer survivors. Eur J Cancer Care (Engl) 2016. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26936232.

812. Kimmick GG, Lovato J, McQuellon R, et al. Randomized, double-blind, placebo-controlled, crossover study of sertraline (Zoloft) for the treatment of hot flashes in women with early stage breast cancer taking tamoxifen. Breast J 2006;12:114-122. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16509835.

813. Loprinzi CL, Pisansky TM, Fonseca R, et al. Pilot evaluation of venlafaxine hydrochloride for the therapy of hot flashes in cancer survivors. J Clin Oncol 1998;16:2377-2381. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9667254.

814. Loprinzi CL, Sloan JA, Perez EA, et al. Phase III evaluation of fluoxetine for treatment of hot flashes. J Clin Oncol 2002;20:1578-1583. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11896107.

815. Wu MF, Hilsenbeck SG, Tham YL, et al. The efficacy of sertraline for controlling hot flashes in women with or at high risk of developing breast cancer. Breast Cancer Res Treat 2009;118:369-375. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19495957.

816. Ramaswami R, Villarreal MD, Pitta DM, et al. Venlafaxine in management of hot flashes in women with breast cancer: a systematic

review and meta-analysis. Breast Cancer Res Treat 2015;152:231-237. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26067931.

817. Shams T, Firwana B, Habib F, et al. SSRIs for hot flashes: a systematic review and meta-analysis of randomized trials. J Gen Intern Med 2014;29:204-213. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23888328.

818. Brauch H, Murdter TE, Eichelbaum M, Schwab M. Pharmacogenomics of tamoxifen therapy. Clin Chem 2009;55:1770-1782. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19574470.

819. Kelly CM, Juurlink DN, Gomes T, et al. Selective serotonin reuptake inhibitors and breast cancer mortality in women receiving tamoxifen: a population based cohort study. BMJ 2010;340:c693. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20142325.

820. Butt DA, Lock M, Lewis JE, et al. Gabapentin for the treatment of menopausal hot flashes: a randomized controlled trial. Menopause 2008;15:310-318. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17917611.

821. Yurcheshen ME, Guttuso T, Jr., McDermott M, et al. Effects of gabapentin on sleep in menopausal women with hot flashes as measured by a Pittsburgh Sleep Quality Index factor scoring model. J Womens Health (Larchmt) 2009;18:1355-1360. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19708803.

822. Reddy SY, Warner H, Guttuso T, Jr., et al. Gabapentin, estrogen, and placebo for treating hot flushes: a randomized controlled trial. Obstet Gynecol 2006;108:41-48. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16816054.

823. Loprinzi CL, Qin R, Balcueva EP, et al. Phase III, randomized, double-blind, placebo-controlled evaluation of pregabalin for alleviating hot flashes, N07C1. J Clin Oncol 2010;28:641-647. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19901102.

824. Pandya KJ, Morrow GR, Roscoe JA, et al. Gabapentin for hot flashes in 420 women with breast cancer: a randomised double-blind placebo-controlled trial. Lancet 2005;366:818-824. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16139656.

825. Bordeleau L, Pritchard KI, Loprinzi CL, et al. Multicenter, randomized, cross-over clinical trial of venlafaxine versus gabapentin for the management of hot flashes in breast cancer survivors. J Clin Oncol 2010;28:5147-5152. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21060031.

826. Laufer LR, Erlik Y, Meldrum DR, Judd HL. Effect of clonidine on hot flashes in postmenopausal women. Obstet Gynecol 1982;60:583-586. Available at: http://www.ncbi.nlm.nih.gov/pubmed/7145250.

827. Nagamani M, Kelver ME, Smith ER. Treatment of menopausal hot flashes with transdermal administration of clonidine. Am J Obstet Gynecol 1987;156:561-565. Available at: http://www.ncbi.nlm.nih.gov/pubmed/3826200.

828. Pandya KJ, Raubertas RF, Flynn PJ, et al. Oral clonidine in postmenopausal patients with breast cancer experiencing tamoxifen-induced hot flashes: a University of Rochester Cancer Center Community Clinical Oncology Program study. Ann Intern Med 2000;132:788-793. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10819701.

829. Goldberg RM, Loprinzi CL, O'Fallon JR, et al. Transdermal clonidine for ameliorating tamoxifen-induced hot flashes. J Clin Oncol 1994;12:155-158. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8270972.

830. Loibl S, Schwedler K, von Minckwitz G, et al. Venlafaxine is superior to clonidine as treatment of hot flashes in breast cancer patients--a double-blind, randomized study. Ann Oncol 2007;18:689-693. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17229772.

831. Buijs C, Mom CH, Willemse PH, et al. Venlafaxine versus clonidine for the treatment of hot flashes in breast cancer patients: a double-blind, randomized cross-over study. Breast Cancer Res Treat 2009;115:573-580. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18670875.

832. Boekhout AH, Vincent AD, Dalesio OB, et al. Management of hot flashes in patients who have breast cancer with venlafaxine and clonidine: a randomized, double-blind, placebo-controlled trial. J Clin Oncol 2011;29:3862-3868. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21911720.

833. Cramer H, Rabsilber S, Lauche R, et al. Yoga and meditation for menopausal symptoms in breast cancer survivors-A randomized controlled trial. Cancer 2015;121:2175-2184. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25739642.

834. Elkins G, Marcus J, Stearns V, et al. Randomized trial of a hypnosis intervention for treatment of hot flashes among breast cancer survivors. J Clin Oncol 2008;26:5022-5026. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18809612.

835. Kroenke CH, Caan BJ, Stefanick ML, et al. Effects of a dietary intervention and weight change on vasomotor symptoms in the Women's Health Initiative. Menopause 2012;19:980-988. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22781782.

836. Stefanopoulou E, Grunfeld EA. Mind-body interventions for vasomotor symptoms in healthy menopausal women and breast cancer survivors. A systematic review. J Psychosom Obstet Gynaecol 2016:1-16. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27832718.

837. Su HI, Sammel MD, Springer E, et al. Weight gain is associated with increased risk of hot flashes in breast cancer survivors on aromatase inhibitors. Breast Cancer Res Treat 2010;124:205-211. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20182796.

838. Franco OH, Chowdhury R, Troup J, et al. Use of plant-based therapies and menopausal symptoms: a systematic review and meta-analysis. JAMA 2016;315:2554-2563. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27327802.

839. Quella SK, Loprinzi CL, Barton DL, et al. Evaluation of soy phytoestrogens for the treatment of hot flashes in breast cancer survivors: A North Central Cancer Treatment Group Trial. J Clin Oncol 2000;18:1068-1074. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10694559.

840. Taku K, Melby MK, Kronenberg F, et al. Extracted or synthesized soybean isoflavones reduce menopausal hot flash frequency and severity: systematic review and meta-analysis of randomized controlled trials. Menopause 2012;19:776-790. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22433977.

841. Thomas AJ, Ismail R, Taylor-Swanson L, et al. Effects of isoflavones and amino acid therapies for hot flashes and co-occurring symptoms during the menopausal transition and early postmenopause: a systematic review. Maturitas 2014;78:263-276. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24951101.

842. Van Patten CL, Olivotto IA, Chambers GK, et al. Effect of soy phytoestrogens on hot flashes in postmenopausal women with breast cancer: a randomized, controlled clinical trial. J Clin Oncol 2002;20:1449-1455. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11896091.

843. MacGregor CA, Canney PA, Patterson G, et al. A randomised double-blind controlled trial of oral soy supplements versus placebo for treatment of menopausal symptoms in patients with early breast cancer. Eur J Cancer 2005;41:708-714. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15763646.

844. Sharma P, Wisniewski A, Braga-Basaria M, et al. Lack of an effect of high dose isoflavones in men with prostate cancer undergoing androgen deprivation therapy. J Urol 2009;182:2265-2272. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19758646.

845. Chen WY, Giobbie-Hurder A, Gantman K, et al. A randomized, placebo-controlled trial of melatonin on breast cancer survivors: impact on sleep, mood, and hot flashes. Breast Cancer Res Treat 2014;145:381-388. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24718775.

846. Dennehy C, Tsourounis C. A review of select vitamins and minerals used by postmenopausal women. Maturitas 2010;66:370-380. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20580500.

847. Laakmann E, Grajecki D, Doege K, et al. Efficacy of Cimicifuga racemosa, Hypericum perforatum and Agnus castus in the treatment of climacteric complaints: a systematic review. Gynecol Endocrinol 2012;28:703-709. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22385322.

848. Leach MJ, Moore V. Black cohosh (Cimicifuga spp.) for menopausal symptoms. Cochrane Database Syst Rev 2012;9:CD007244. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22972105.

849. Jacobson JS, Troxel AB, Evans J, et al. Randomized trial of black cohosh for the treatment of hot flashes among women with a history of breast cancer. J Clin Oncol 2001;19:2739-2745. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11352967.

850. Pockaj BA, Gallagher JG, Loprinzi CL, et al. Phase III double-blind, randomized, placebo-controlled crossover trial of black cohosh in the management of hot flashes: NCCTG Trial N01CC1. J Clin Oncol 2006;24:2836-2841. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16782922.

851. Cho SH, Whang WW. Acupuncture for vasomotor menopausal symptoms: a systematic review. Menopause 2009;16:1065-1073. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19424092.

852. Dodin S, Blanchet C, Marc I, et al. Acupuncture for menopausal hot flushes. Cochrane Database Syst Rev 2013;7:CD007410. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23897589.

853. Garland SN, Xie SX, Li Q, et al. Comparative effectiveness of electro-acupuncture versus gabapentin for sleep disturbances in breast cancer survivors with hot flashes: a randomized trial. Menopause 2017;24:517-523. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27875389.

854. Lesi G, Razzini G, Musti MA, et al. Acupuncture as an integrative approach for the treatment of hot flashes in women with breast cancer: A prospective multicenter randomized controlled trial (AcCliMaT). J Clin Oncol 2016;34:1795-1802. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27022113.

855. Walker EM, Rodriguez AI, Kohn B, et al. Acupuncture versus venlafaxine for the management of vasomotor symptoms in patients with hormone receptor-positive breast cancer: a randomized controlled trial. J Clin Oncol 2010;28:634-640. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20038728.

856. Mao JJ, Bowman MA, Xie SX, et al. Electroacupuncture versus gabapentin for hot flashes among breast cancer survivors: a randomized placebo-controlled trial. J Clin Oncol 2015;33:3615-3620. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26304905.

857. Reed SD, Guthrie KA, Newton KM, et al. Menopausal quality of life: RCT of yoga, exercise, and omega-3 supplements. Am J Obstet Gynecol 2014;210:244 e241-211. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24215858.

858. Newton KM, Reed SD, Guthrie KA, et al. Efficacy of yoga for vasomotor symptoms: a randomized controlled trial. Menopause 2014;21:339-346. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24045673.

859. Aiello EJ, Yasui Y, Tworoger SS, et al. Effect of a yearlong, moderate-intensity exercise intervention on the occurrence and severity of menopause symptoms in postmenopausal women. Menopause 2004;11:382-388. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15243275.

860. Daley AJ, Thomas A, Roalfe AK, et al. The effectiveness of exercise as treatment for vasomotor menopausal symptoms: randomised controlled trial. BJOG 2015;122:565-575. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25516405.

861. Daley A, Stokes-Lampard H, Thomas A, MacArthur C. Exercise for vasomotor menopausal symptoms. Cochrane Database Syst Rev 2014;11:CD006108. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25431132.

862. Lindh-Astrand L, Nedstrand E, Wyon Y, Hammar M. Vasomotor symptoms and quality of life in previously sedentary postmenopausal

women randomised to physical activity or estrogen therapy. Maturitas 2004;48:97-105. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15172083.

863. Sternfeld B, Guthrie KA, Ensrud KE, et al. Efficacy of exercise for menopausal symptoms: a randomized controlled trial. Menopause 2014;21:330-338. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23899828.

864. Sternfeld B, Dugan S. Physical activity and health during the menopausal transition. Obstet Gynecol Clin North Am 2011;38:537-566. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21961719.

865. Ueda M. A 12-week structured education and exercise program improved climacteric symptoms in middle-aged women. J Physiol Anthropol Appl Human Sci 2004;23:143-148. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15472458.

866. Duijts SF, van Beurden M, Oldenburg HS, et al. Efficacy of cognitive behavioral therapy and physical exercise in alleviating treatment-induced menopausal symptoms in patients with breast cancer: results of a randomized, controlled, multicenter trial. J Clin Oncol 2012;30:4124-4133. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23045575.

867. Smith RL, Flaws JA, Gallicchio L. Does quitting smoking decrease the risk of midlife hot flashes? A longitudinal analysis. Maturitas 2015;82:123-127. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26149340.

868. Peppone LJ, Mustian KM, Morrow GR, et al. The effect of cigarette smoking on cancer treatment-related side effects. Oncologist 2011;16:1784-1792. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22135122.

869. Gallicchio L, Miller SR, Kiefer J, et al. Risk factors for hot flashes among women undergoing the menopausal transition: baseline results from the Midlife Women's Health Study. Menopause 2015;22:1098-1107. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25783472.

870. Ayers B, Smith M, Hellier J, et al. Effectiveness of group and self-help cognitive behavior therapy in reducing problematic menopausal hot flushes and night sweats (MENOS 2): a randomized controlled trial. Menopause 2012;19:749-759. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22336748.

871. Alder J, Eymann Besken K, Armbruster U, et al. Cognitive-behavioural group intervention for climacteric syndrome. Psychother Psychosom 2006;75:298-303. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16899966.

872. Mann E, Smith MJ, Hellier J, et al. Cognitive behavioural treatment for women who have menopausal symptoms after breast cancer treatment (MENOS 1): a randomised controlled trial. Lancet Oncol 2012;13:309-318. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22340966.

873. Atema V, van Leeuwen M, Kieffer JM, et al. Efficacy of internet-based cognitive behavioral therapy for treatment-induced menopausal symptoms in breast cancer survivors: Results of a randomized controlled trial. J Clin Oncol 2019;37:809-822. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30763176.

874. Baber RJ, Panay N, Fenton A, Group IMSW. 2016 IMS recommendations on women's midlife health and menopause hormone therapy. Climacteric 2016;19:109-150. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26872610.

875. Barnabei VM, Grady D, Stovall DW, et al. Menopausal symptoms in older women and the effects of treatment with hormone therapy. Obstet Gynecol 2002;100:1209-1218. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12468165.

876. Brunner RL, Aragaki A, Barnabei V, et al. Menopausal symptom experience before and after stopping estrogen therapy in the Women's Health Initiative randomized, placebo-controlled trial. Menopause 2010;17:946-954. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20505547.

877. de Villiers TJ, Hall JE, Pinkerton JV, et al. Revised global consensus statement on menopausal hormone therapy. Climacteric 2016;19:313-315. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27322027.

878. Greendale GA, Reboussin BA, Hogan P, et al. Symptom relief and side effects of postmenopausal hormones: results from the Postmenopausal Estrogen/Progestin Interventions Trial. Obstet Gynecol 1998;92:982-988. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9840563.

879. The 2017 hormone therapy position statement of The North American Menopause Society. Menopause 2017;24:728-753. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28650869.

880. Anderson GL, Limacher M, Assaf AR, et al. Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial. JAMA 2004;291:1701-1712. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15082697.

881. Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. JAMA 2002;288:321-333. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12117397.

882. Chlebowski RT, Wactawski-Wende J, Ritenbaugh C, et al. Estrogen plus progestin and colorectal cancer in postmenopausal women. N Engl J Med 2004;350:991-1004. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14999111.

883. Chlebowski RT, Schwartz AG, Wakelee H, et al. Oestrogen plus progestin and lung cancer in postmenopausal women (Women's Health Initiative trial): a post-hoc analysis of a randomised controlled trial. Lancet 2009;374:1243-1251. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19767090.

884. Simon MS, Chlebowski RT, Wactawski-Wende J, et al. Estrogen plus progestin and colorectal cancer incidence and mortality. J Clin Oncol 2012;30:3983-3990. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23008295.

885. Chlebowski RT, Anderson GL, Gass M, et al. Estrogen plus progestin and breast cancer incidence and mortality in postmenopausal women. JAMA 2010;304:1684-1692. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20959578.

886. Chlebowski RT, Rohan TE, Manson JE, et al. Breast Cancer After Use of Estrogen Plus Progestin and Estrogen Alone: Analyses of Data From 2 Women's Health Initiative Randomized Clinical Trials. JAMA Oncol 2015;1:296-305. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26181174.

887. Manson JE, Aragaki AK, Rossouw JE, et al. Menopausal hormone therapy and long-term all-cause and cause-specific mortality: The Women's Health Initiative randomized trials. JAMA 2017;318:927-938. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28898378.

888. Marjoribanks J, Farquhar C, Roberts H, et al. Long-term hormone therapy for perimenopausal and postmenopausal women. Cochrane Database Syst Rev 2017;1:CD004143. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28093732.

889. Barakat RR, Bundy BN, Spirtos NM, et al. Randomized double-blind trial of estrogen replacement therapy versus placebo in stage I or II endometrial cancer: a Gynecologic Oncology Group Study. J Clin Oncol 2006;24:587-592. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16446331.

890. Chapman JA, DiSaia PJ, Osann K, et al. Estrogen replacement in surgical stage I and II endometrial cancer survivors. Am J Obstet Gynecol 1996;175:1195-1200. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8942487.

891. Creasman WT, Henderson D, Hinshaw W, Clarke-Pearson DL. Estrogen replacement therapy in the patient treated for endometrial cancer. Obstet Gynecol 1986;67:326-330. Available at: http://www.ncbi.nlm.nih.gov/pubmed/3003636.

892. Lee RB, Burke TW, Park RC. Estrogen replacement therapy following treatment for stage I endometrial carcinoma. Gynecol Oncol 1990;36:189-191. Available at: http://www.ncbi.nlm.nih.gov/pubmed/2298408.

893. Suriano KA, McHale M, McLaren CE, et al. Estrogen replacement therapy in endometrial cancer patients: a matched control study. Obstet Gynecol 2001;97:555-560. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11275027.

894. Holmberg L, Iversen OE, Rudenstam CM, et al. Increased risk of recurrence after hormone replacement therapy in breast cancer survivors. J Natl Cancer Inst 2008;100:475-482. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18364505.

895. Fahlen M, Fornander T, Johansson H, et al. Hormone replacement therapy after breast cancer: 10 year follow up of the Stockholm randomised trial. Eur J Cancer 2013;49:52-59. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22892060.

896. Bergendal A, Kieler H, Sundstrom A, et al. Risk of venous thromboembolism associated with local and systemic use of hormone therapy in peri- and postmenopausal women and in relation to type and route of administration. Menopause 2016;23:593-599. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27023862.

897. Kagan R, Williams RS, Pan K, et al. A randomized, placebo- and active-controlled trial of bazedoxifene/conjugated estrogens for treatment of moderate to severe vulvar/vaginal atrophy in postmenopausal women. Menopause 2010;17:281-289. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19779382.

898. American College of Obstetricians and Gynecologists Committee on Gynecologic Practice; American Society for Reproductive Medicine Practice Committee. Compounded bioidentical menopausal hormone therapy. Fertil Steril 2012;98:308-312. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22831824.

899. Whelan AM, Jurgens TM, Trinacty M. Bioidentical progesterone cream for menopause-related vasomotor symptoms: is it effective? Ann Pharmacother 2013;47:112-116. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23249728.

900. Biglia N, Peano E, Sgandurra P, et al. Low-dose vaginal estrogens or vaginal moisturizer in breast cancer survivors with urogenital atrophy: a preliminary study. Gynecol Endocrinol 2010;26:404-412. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20196634.

901. Sutton KS, Boyer SC, Goldfinger C, et al. To lube or not to lube: experiences and perceptions of lubricant use in women with and without dyspareunia. J Sex Med 2012;9:240-250. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22082320.

902. Loprinzi CL, Abu-Ghazaleh S, Sloan JA, et al. Phase III randomized double-blind study to evaluate the efficacy of a polycarbophil-based vaginal moisturizer in women with breast cancer. J Clin Oncol 1997;15:969-973. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9060535.

903. Nachtigall LE. Comparative study: Replens versus local estrogen in menopausal women. Fertil Steril 1994;61:178-180. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8293835.

904. Mitchell CM, Reed SD, Diem S, et al. Efficacy of vaginal estradiol or vaginal moisturizer vs placebo for treating postmenopausal vulvovaginal symptoms: A randomized clinical trial. JAMA Intern Med 2018;178:681-690. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29554173.

905. Barton DL, Sloan JA, Shuster LT, et al. Evaluating the efficacy of vaginal dehydroepiandosterone for vaginal symptoms in postmenopausal cancer survivors: NCCTG N10C1 (Alliance). Support Care Cancer 2018;26:643-650. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28921241.

906. Ayton RA, Darling GM, Murkies AL, et al. A comparative study of safety and efficacy of continuous low dose oestradiol released from a vaginal ring compared with conjugated equine oestrogen vaginal cream in the treatment of postmenopausal urogenital atrophy. Br J Obstet Gynaecol

1996;103:351-358. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8605133.

907. Fooladi E, Davis SR. An update on the pharmacological management of female sexual dysfunction. Expert Opin Pharmacother 2012;13:2131-2142. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22984935.

908. Krychman ML. Vaginal estrogens for the treatment of dyspareunia. J Sex Med 2011;8:666-674. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21091878.

909. Raghunandan C, Agrawal S, Dubey P, et al. A comparative study of the effects of local estrogen with or without local testosterone on vulvovaginal and sexual dysfunction in postmenopausal women. J Sex Med 2010;7:1284-1290. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20102444.

910. Suckling J, Lethaby A, Kennedy R. Local oestrogen for vaginal atrophy in postmenopausal women. Cochrane Database Syst Rev 2006:CD001500. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17054136.

911. Committee Opinion No. 659 Summary: The Use of Vaginal Estrogen in Women With a History of Estrogen-Dependent Breast Cancer. Obstet Gynecol 2016;127:618-619. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26901332.

912. Le Ray I, Dell'Aniello S, Bonnetain F, et al. Local estrogen therapy and risk of breast cancer recurrence among hormone-treated patients: a nested case-control study. Breast Cancer Res Treat 2012;135:603-609. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22903687.

913. Trinkaus M, Chin S, Wolfman W, et al. Should urogenital atrophy in breast cancer survivors be treated with topical estrogens? Oncologist 2008;13:222-231. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18378532.

914. Wills S, Ravipati A, Venuturumilli P, et al. Effects of vaginal estrogens on serum estradiol levels in postmenopausal breast cancer survivors and women at risk of breast cancer taking an aromatase inhibitor or a selective estrogen receptor modulator. J Oncol Pract 2012;8:144-148. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22942807.

915. Behnia-Willison F, Sarraf S, Miller J, et al. Safety and long-term efficacy of fractional CO2 laser treatment in women suffering from genitourinary syndrome of menopause. Eur J Obstet Gynecol Reprod Biol 2017;213:39-44. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28419911.

916. Pitsouni E, Grigoriadis T, Tsiveleka A, et al. Microablative fractional CO2-laser therapy and the genitourinary syndrome of menopause: An observational study. Maturitas 2016;94:131-136. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27823733.

917. Salvatore S, Nappi RE, Parma M, et al. Sexual function after fractional microablative CO(2) laser in women with vulvovaginal atrophy. Climacteric 2015;18:219-225. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25333211.

918. Pagano T, De Rosa P, Vallone R, et al. Fractional microablative CO2 laser for vulvovaginal atrophy in women treated with chemotherapy and/or hormonal therapy for breast cancer: a retrospective study. Menopause 2016;23:1108-1113. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27648595.

919. Pagano T, De Rosa P, Vallone R, et al. Fractional microablative CO2 laser in breast cancer survivors affected by iatrogenic vulvovaginal atrophy after failure of nonestrogenic local treatments: a retrospective study. Menopause 2018;25:657-662. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29286986.

920. Pieralli A, Fallani MG, Becorpi A, et al. Fractional CO2 laser for vulvovaginal atrophy (VVA) dyspareunia relief in breast cancer survivors. Arch Gynecol Obstet 2016;294:841-846. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27170261.

921. Quick AM, Zvinovski F, Hudson C, et al. Fractional CO2 laser therapy for genitourinary syndrome of menopause for breast cancer survivors.

Support Care Cancer 2019. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31811486.

922. FDA Warns Against Use of Energy-Based Devices to Perform Vaginal 'Rejuvenation' or Vaginal Cosmetic Procedures: FDA Safety Communication. U.S. Food & Drug Administration; Available at: https://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm615013.htm. Accessed June 5, 2020.

923. Mazzarello S, Hutton B, Ibrahim MF, et al. Management of urogenital atrophy in breast cancer patients: a systematic review of available evidence from randomized trials. Breast Cancer Res Treat 2015;152:1-8. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26003182.

924. Frisk J. Managing hot flushes in men after prostate cancer--a systematic review. Maturitas 2010;65:15-22. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19962840.

925. Gerber GS, Zagaja GP, Ray PS, Rukstalis DB. Transdermal estrogen in the treatment of hot flushes in men with prostate cancer. Urology 2000;55:97-101. Available at: https://www.ncbi.nlm.nih.gov/pubmed/10654902.

926. Irani J, Salomon L, Oba R, et al. Efficacy of venlafaxine, medroxyprogesterone acetate, and cyproterone acetate for the treatment of vasomotor hot flushes in men taking gonadotropin-releasing hormone analogues for prostate cancer: a double-blind, randomised trial. Lancet Oncol 2010;11:147-154. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19963436.

927. Loprinzi CL, Michalak JC, Quella SK, et al. Megestrol acetate for the prevention of hot flashes. N Engl J Med 1994;331:347-352. Available at: https://www.ncbi.nlm.nih.gov/pubmed/8028614.

928. Carter J, Lacchetti C, Andersen BL, et al. Interventions to address sexual problems in people with cancer: American Society of Clinical Oncology clinical practice guideline adaptation of Cancer Care Ontario guideline. J Clin Oncol 2018;36:492-511. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29227723.

929. Ahmadi H, Daneshmand S. Androgen deprivation therapy: evidence-based management of side effects. BJU Int 2013;111:543-548. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23351025.

930. Moraska AR, Atherton PJ, Szydlo DW, et al. Gabapentin for the management of hot flashes in prostate cancer survivors: a longitudinal continuation Study-NCCTG Trial N00CB. J Support Oncol 2010;8:128-132. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20552926.

931. Loprinzi CL, Dueck AC, Khoyratty BS, et al. A phase III randomized, double-blind, placebo-controlled trial of gabapentin in the management of hot flashes in men (N00CB). Ann Oncol 2009;20:542-549. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19129205.

932. Quella SK, Loprinzi CL, Sloan J, et al. Pilot evaluation of venlafaxine for the treatment of hot flashes in men undergoing androgen ablation therapy for prostate cancer. J Urol 1999;162:98-102. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10379749.

933. Ashamalla H, Jiang ML, Guirguis A, et al. Acupuncture for the alleviation of hot flashes in men treated with androgen ablation therapy. Int J Radiat Oncol Biol Phys 2011;79:1358-1363. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20605360.

934. Frisk J, Spetz AC, Hjertberg H, et al. Two modes of acupuncture as a treatment for hot flushes in men with prostate cancer--a prospective multicenter study with long-term follow-up. Eur Urol 2009;55:156-163. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18294761.

935. Stefanopoulou E, Yousaf O, Grunfeld EA, Hunter MS. A randomised controlled trial of a brief cognitive behavioural intervention for men who have hot flushes following prostate cancer treatment (MANCAN). Psychooncology 2015;24:1159-1166. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25753889.

936. Dueregger A, Heidegger I, Ofer P, et al. The use of dietary supplements to alleviate androgen deprivation therapy side effects during prostate cancer treatment. Nutrients 2014;6:4491-4519. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25338271.

937. Klein EA, Thompson IM, Jr., Tangen CM, et al. Vitamin E and the risk of prostate cancer: the Selenium and Vitamin E Cancer Prevention Trial (SELECT). JAMA 2011;306:1549-1556. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21990298.

938. Peters U, Littman AJ, Kristal AR, et al. Vitamin E and selenium supplementation and risk of prostate cancer in the Vitamins and lifestyle (VITAL) study cohort. Cancer Causes Control 2008;19:75-87. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17943452.

939. Evaluation and Management of Testosterone Deficiency. American Urological Association 2018. Available at: https://www.auanet.org/guidelines/testosterone-deficiency-(2018). Accessed June 5, 2020.

940. Bautista-Vidal C, Barnoiu O, Garcia-Galisteo E, et al. Treatment of gynecomastia in patients with prostate cancer and androgen deprivation. Actas Urol Esp 2014;38:34-40. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23850393.

941. Viani GA, Bernardes da Silva LG, Stefano EJ. Prevention of gynecomastia and breast pain caused by androgen deprivation therapy in prostate cancer: tamoxifen or radiotherapy? Int J Radiat Oncol Biol Phys 2012;83:e519-524. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22704706.

942. Pachman DR, Barton DL, Swetz KM, Loprinzi CL. Troublesome symptoms in cancer survivors: fatigue, insomnia, neuropathy, and pain. J Clin Oncol 2012;30:3687-3696. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23008320.

943. Paice JA, Ferrell B. The management of cancer pain. CA Cancer J Clin 2011;61:157-182. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21543825.

944. Raphael J, Hester J, Ahmedzai S, et al. Cancer pain: part 2: physical, interventional and complimentary therapies; management in the community; acute, treatment-related and complex cancer pain: a perspective from the British Pain Society endorsed by the UK Association of Palliative Medicine and the Royal College of General Practitioners. Pain Med 2010;11:872-896. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20456069.

945. van den Beuken-van Everdingen MH, de Rijke JM, Kessels AG, et al. Prevalence of pain in patients with cancer: a systematic review of the past 40 years. Ann Oncol 2007;18:1437-1449. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17355955.

946. Meretoja TJ, Leidenius MH, Tasmuth T, et al. Pain at 12 months after surgery for breast cancer. JAMA 2014;311:90-92. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24381969.

947. Sun V, Borneman T, Piper B, et al. Barriers to pain assessment and management in cancer survivorship. J Cancer Surviv 2008;2:65-71. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18648988.

948. Caraceni A, Weinstein SM. Classification of cancer pain syndromes. Oncology (Williston Park) 2001;15:1627-1640. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11780704.

949. Hewitt DJ. The management of pain in the oncology patient. Obstet Gynecol Clin North Am 2001;28:819-846. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11766154.

950. Crew KD, Greenlee H, Capodice J, et al. Prevalence of joint symptoms in postmenopausal women taking aromatase inhibitors for early-stage breast cancer. J Clin Oncol 2007;25:3877-3883. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17761973.

951. Hershman DL, Lacchetti C, Dworkin RH, et al. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol 2014;32:1941-1967. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24733808.

952. Paice JA, Portenoy R, Lacchetti C, et al. Management of chronic pain in survivors of adult cancers: American Society of Clinical Oncology

clinical practice guideline. J Clin Oncol 2016;34:3325-3345. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27458286.

953. Hicks CL, von Baeyer CL, Spafford PA, et al. The Faces Pain Scale-Revised: toward a common metric in pediatric pain measurement. Pain 2001;93:173-183. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11427329.

954. Serlin RC, Mendoza TR, Nakamura Y, et al. When is cancer pain mild, moderate or severe? Grading pain severity by its interference with function. Pain 1995;61:277-284. Available at: http://www.ncbi.nlm.nih.gov/pubmed/7659438.

955. Soetenga D, Frank J, Pellino TA. Assessment of the validity and reliability of the University of Wisconsin Children's Hospital Pain scale for Preverbal and Nonverbal Children. Pediatr Nurs 1999;25:670-676. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12024390.

956. Ware LJ, Epps CD, Herr K, Packard A. Evaluation of the Revised Faces Pain Scale, Verbal Descriptor Scale, Numeric Rating Scale, and Iowa Pain Thermometer in older minority adults. Pain Manag Nurs 2006;7:117-125. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16931417.

957. Levy MH, Chwistek M, Mehta RS. Management of chronic pain in cancer survivors. Cancer J 2008;14:401-409. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19060605.

958. Moryl N, Coyle N, Essandoh S, Glare P. Chronic pain management in cancer survivors. J Natl Compr Canc Netw 2010;8:1104-1110. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20876547.

959. Caraceni A, Zecca E, Bonezzi C, et al. Gabapentin for neuropathic cancer pain: a randomized controlled trial from the Gabapentin Cancer Pain Study Group. J Clin Oncol 2004;22:2909-2917. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15254060.

960. Jongen JL, Huijsman ML, Jessurun J, et al. The evidence for pharmacologic treatment of neuropathic cancer pain: beneficial and adverse effects. J Pain Symptom Manage 2013;46:581-590 e581. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23415040.

961. Moore RA, Wiffen PJ, Derry S, McQuay HJ. Gabapentin for chronic neuropathic pain and fibromyalgia in adults. Cochrane Database Syst Rev 2011:CD007938. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21412914.

962. Huang R, Jiang L, Cao Y, et al. Comparative efficacy of therapeutics for chronic cancer pain: A Bayesian network meta-analysis. J Clin Oncol 2019;37:1742-1752. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30939089.

963. NUCYNTA® (tapentadol) tablets for oral use C-II. Newark, CA: Depomed, Inc.; 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/022304s022lbl.pdf. Accessed June 5, 2020.

964. Schwartz S, Etropolski M, Shapiro DY, et al. Safety and efficacy of tapentadol ER in patients with painful diabetic peripheral neuropathy: results of a randomized-withdrawal, placebo-controlled trial. Curr Med Res Opin 2011;27:151-162. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21162697.

965. Vinik AI, Shapiro DY, Rauschkolb C, et al. A randomized withdrawal, placebo-controlled study evaluating the efficacy and tolerability of tapentadol extended release in patients with chronic painful diabetic peripheral neuropathy. Diabetes Care 2014;37:2302-2309. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24848284.

966. Imanaka K, Tominaga Y, Etropolski M, et al. Efficacy and safety of oral tapentadol extended release in Japanese and Korean patients with moderate to severe, chronic malignant tumor-related pain. Curr Med Res Opin 2013;29:1399-1409. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23937387.

967. Kress HG, Koch ED, Kosturski H, et al. Tapentadol prolonged release for managing moderate to severe, chronic malignant tumor-related pain.

Pain Physician 2014;17:329-343. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25054392.

968. Koyyalagunta D, Bruera E, Solanki DR, et al. A systematic review of randomized trials on the effectiveness of opioids for cancer pain. Pain Physician 2012;15:ES39-58. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22786461.

969. Chou R, Turner JA, Devine EB, et al. The effectiveness and risks of long-term opioid therapy for chronic pain: a systematic review for a National Institutes of Health Pathways to Prevention Workshop. Ann Intern Med 2015;162:276-286. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25581257.

970. Sutradhar R, Lokku A, Barbera L. Cancer survivorship and opioid prescribing rates: A population-based matched cohort study among individuals with and without a history of cancer. Cancer 2017;123:4286-4293. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28782114.

971. Salz T, Lavery JA, Lipitz-Snyderman AN, et al. Trends in opioid use among older survivors of colorectal, lung, and breast cancers. J Clin Oncol 2019;37:1001-1011. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30817249.

972. Lee JS, Hu HM, Edelman AL, et al. New persistent opioid use among patients with cancer after curative-intent surgery. J Clin Oncol 2017;35:4042-4049. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29048972.

973. Akbik H, Butler SF, Budman SH, et al. Validation and clinical application of the Screener and Opioid Assessment for Patients with Pain (SOAPP). J Pain Symptom Manage 2006;32:287-293. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16939853.

974. Butler SF, Fernandez K, Benoit C, et al. Validation of the revised Screener and Opioid Assessment for Patients with Pain (SOAPP-R). J Pain 2008;9:360-372. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18203666.

975. Chou R, Fanciullo GJ, Fine PG, et al. Opioids for chronic noncancer pain: prediction and identification of aberrant drug-related behaviors: a review of the evidence for an American Pain Society and American Academy of Pain Medicine clinical practice guideline. J Pain 2009;10:131-146. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19187890.

976. Passik SD, Kirsh KL. The interface between pain and drug abuse and the evolution of strategies to optimize pain management while minimizing drug abuse. Exp Clin Psychopharmacol 2008;16:400-404. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18837636.

977. Webster LR, Webster RM. Predicting aberrant behaviors in opioid-treated patients: preliminary validation of the Opioid Risk Tool. Pain Med 2005;6:432-442. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16336480.

978. U.S. Food and Drug Administration. Approved Risk Evaluation and Mitigation Strategies (REMS). Available at: http://www.accessdata.fda.gov/scripts/cder/rems/index.cfm. Accessed June 5, 2020.

979. National Comprehensive Cancer Center. NCCN Resource Tool: Risk Evaluation & Mitigation Strategies (REMS). Plymouth Meeting, PA: Available at: http://www.nccn.org/rems/default.asp. Accessed June 5, 2020.

980. U.S. Food and Drug Administration. Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS). 2019. Available at: https://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm163647.htm. Accessed June 5, 2020.

981. TRANSMUCOSAL IMMEDIATE RELEASE FENTANYL (TIRF) RISK EVALUATION AND MITIGATION STRATEGY (REMS). 2014. Available at: http://www.fda.gov/downloads/drugs/drugsafety/postmarketdrugsafetyinformationforpatientsandproviders/ucm289730.pdf. Accessed June 5, 2020.

982. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain - United States, 2016. MMWR Recomm Rep

2016;65:1-49. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26987082.

983. ASCO Policy Statement on Opioid Therapy: Protecting Access to Treatment for Cancer-Related Pain; 2016. Available at: http://www.asco.org/sites/new-www.asco.org/files/content-files/advocacy-and-policy/documents/2016-ASCO-Opioid-policy-brief.pdf.

984. Fisch MJ, Chang VT. Striving for safe, effective, affordable care for cancer survivors with chronic pain: Another kind of moonshot. JAMA Oncol 2016;2:862-864. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27054656.

985. Hantel A, Levine S, Siegler M. Creating coherent strategies to combat the crises of opioid scarcity and abuse. J Clin Oncol 2018:Jco2018791079. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30001169.

986. Bennett MI. Effectiveness of antiepileptic or antidepressant drugs when added to opioids for cancer pain: systematic review. Palliat Med 2011;25:553-559. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20671006.

987. Finnerup NB, Sindrup SH, Jensen TS. The evidence for pharmacological treatment of neuropathic pain. Pain 2010;150:573-581. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20705215.

988. Saarto T, Wiffen PJ. Antidepressants for neuropathic pain: a Cochrane review. J Neurol Neurosurg Psychiatry 2010;81:1372-1373. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20543189.

989. Smith EM, Pang H, Cirrincione C, et al. Effect of duloxetine on pain, function, and quality of life among patients with chemotherapy-induced painful peripheral neuropathy: a randomized clinical trial. JAMA 2013;309:1359-1367. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23549581.

990. Henry NL, Unger JM, Schott AF, et al. Randomized, multicenter, placebo-controlled clinical trial of duloxetine versus placebo for aromatase inhibitor-associated arthralgias in early-stage breast cancer: SWOG S1202. J Clin Oncol 2018;36:326-332. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29136387.

991. Nguyen VH, Lawrence HJ. Use of gabapentin in the prevention of taxane-induced arthralgias and myalgias. J Clin Oncol 2004;22:1767-1769. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15118009.

992. Baron R, Brunnmuller U, Brasser M, et al. Efficacy and safety of pregabalin in patients with diabetic peripheral neuropathy or postherpetic neuralgia: Open-label, non-comparative, flexible-dose study. Eur J Pain 2008;12:850-858. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18242109.

993. Finnerup NB, Attal N, Haroutounian S, et al. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. Lancet Neurol 2015;14:162-173. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25575710.

994. Johannessen Landmark C. Antiepileptic drugs in non-epilepsy disorders: relations between mechanisms of action and clinical efficacy. CNS Drugs 2008;22:27-47. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18072813.

995. Rao RD, Michalak JC, Sloan JA, et al. Efficacy of gabapentin in the management of chemotherapy-induced peripheral neuropathy: a phase 3 randomized, double-blind, placebo-controlled, crossover trial (N00C3). Cancer 2007;110:2110-2118. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17853395.

996. Jiang J, Li Y, Shen Q, et al. Effect of pregabalin on radiotherapy-related neuropathic pain in patients with head and neck cancer: A randomized controlled trial. J Clin Oncol 2019;37:135-143. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30457920.

997. Paulsen O, Klepstad P, Rosland JH, et al. Efficacy of methylprednisolone on pain, fatigue, and appetite loss in patients with advanced cancer using opioids: a randomized, placebo-controlled, double-

blind trial. J Clin Oncol 2014;32:3221-3228. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25002731.

998. Nabal M, Librada S, Redondo MJ, et al. The role of paracetamol and nonsteroidal anti-inflammatory drugs in addition to WHO Step III opioids in the control of pain in advanced cancer. A systematic review of the literature. Palliat Med 2012;26:305-312. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22126843.

999. Richards BL, Whittle SL, Buchbinder R. Muscle relaxants for pain management in rheumatoid arthritis. Cochrane Database Syst Rev 2012;1:CD008922. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22258993.

1000. Richards BL, Whittle SL, van der Heijde DM, Buchbinder R. The efficacy and safety of muscle relaxants in inflammatory arthritis: a Cochrane systematic review. J Rheumatol Suppl 2012;90:34-39. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22942327.

1001. Cassileth BR, Keefe FJ. Integrative and behavioral approaches to the treatment of cancer-related neuropathic pain. Oncologist 2010;15 Suppl 2:19-23. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20489193.

1002. Huang ST, Good M, Zauszniewski JA. The effectiveness of music in relieving pain in cancer patients: a randomized controlled trial. Int J Nurs Stud 2010;47:1354-1362. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20403600.

1003. Kwekkeboom KL, Cherwin CH, Lee JW, Wanta B. Mind-body treatments for the pain-fatigue-sleep disturbance symptom cluster in persons with cancer. J Pain Symptom Manage 2010;39:126-138. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19900778.

1004. Montgomery GH, Weltz CR, Seltz M, Bovbjerg DH. Brief presurgery hypnosis reduces distress and pain in excisional breast biopsy patients. Int J Clin Exp Hypn 2002;50:17-32. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11778705.

1005. Pfister DG, Cassileth BR, Deng GE, et al. Acupuncture for pain and dysfunction after neck dissection: results of a randomized controlled trial. J Clin Oncol 2010;28:2565-2570. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20406930.

1006. Stoelb BL, Molton IR, Jensen MP, Patterson DR. The efficacy of hypnotic analgesia in adults: a review of the literature. Contemp Hypn 2009;26:24-39. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20161034.

1007. Johannsen M, O'Connor M, O'Toole MS, et al. Efficacy of mindfulness-based cognitive therapy on late post-treatment pain in women treated for primary breast cancer: a randomized controlled trial. J Clin Oncol 2016;34:3390-3399. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27325850.

1008. Keefe FJ, Abernethy AP, L CC. Psychological approaches to understanding and treating disease-related pain. Annu Rev Psychol 2005;56:601-630. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15709948.

1009. Sheinfeld Gorin S, Krebs P, Badr H, et al. Meta-analysis of psychosocial interventions to reduce pain in patients with cancer. J Clin Oncol 2012;30:539-547. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22253460.

1010. Montgomery GH, Schnur JB, Kravits K. Hypnosis for cancer care: over 200 years young. CA Cancer J Clin 2013;63:31-44. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23168491.

1011. Chan BL, Witt R, Charrow AP, et al. Mirror therapy for phantom limb pain. N Engl J Med 2007;357:2206-2207. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18032777.

1012. Clerici CA, Spreafico F, Cavallotti G, et al. Mirror therapy for phantom limb pain in an adolescent cancer survivor. Tumori 2012;98:e27-30. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22495728.

1013. Johannsen M, Farver I, Beck N, Zachariae R. The efficacy of psychosocial intervention for pain in breast cancer patients and survivors: a systematic review and meta-analysis. Breast Cancer Res Treat 2013;138:675-690. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23553565.

1014. Carvalho AP, Vital FM, Soares BG. Exercise interventions for shoulder dysfunction in patients treated for head and neck cancer. Cochrane Database Syst Rev 2012;4:CD008693. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22513964.

1015. Cantarero-Villanueva I, Fernandez-Lao C, Fernandez-de-Las-Penas C, et al. Effectiveness of water physical therapy on pain, pressure pain sensitivity, and myofascial trigger points in breast cancer survivors: a randomized, controlled clinical trial. Pain Med 2012;13:1509-1519. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22958507.

1016. Fernandez-Lao C, Cantarero-Villanueva I, Fernandez-de-Las-Penas C, et al. Effectiveness of a multidimensional physical therapy program on pain, pressure hypersensitivity, and trigger points in breast cancer survivors: a randomized controlled clinical trial. Clin J Pain 2012;28:113-121. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21705873.

1017. McNeely ML, Parliament MB, Seikaly H, et al. Effect of exercise on upper extremity pain and dysfunction in head and neck cancer survivors: a randomized controlled trial. Cancer 2008;113:214-222. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18457329.

1018. Irwin ML, Cartmel B, Gross CP, et al. Randomized exercise trial of aromatase inhibitor-induced arthralgia in breast cancer survivors. J Clin Oncol 2015;33:1104-1111. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25452437.

1019. Sweeney FC, Demark-Wahnefried W, Courneya KS, et al. Aerobic and resistance exercise improves shoulder function in women who are overweight or obese and have breast cancer: A randomized controlled trial. Phys Ther 2019;99:1334-1345. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31309977.

1020. Peppone LJ, Janelsins MC, Kamen C, et al. The effect of YOCAS(c)(R) yoga for musculoskeletal symptoms among breast cancer survivors on hormonal therapy. Breast Cancer Res Treat 2015;150:597-604. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25814054.

1021. Argoff CE. Topical analgesics in the management of acute and chronic pain. Mayo Clin Proc 2013;88:195-205. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23374622.

1022. Barros GA, Miot HA, Braz AM, et al. Topical (S)-ketamine for pain management of postherpetic neuralgia. An Bras Dermatol 2012;87:504-505. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22714779.

1023. Hempenstall K, Nurmikko TJ, Johnson RW, et al. Analgesic therapy in postherpetic neuralgia: a quantitative systematic review. PLoS Med 2005;2:e164. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16013891.

1024. Ho KY, Huh BK, White WD, et al. Topical amitriptyline versus lidocaine in the treatment of neuropathic pain. Clin J Pain 2008;24:51-55. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18180637.

1025. Lin PL, Fan SZ, Huang CH, et al. Analgesic effect of lidocaine patch 5% in the treatment of acute herpes zoster: a double-blind and vehicle-controlled study. Reg Anesth Pain Med 2008;33:320-325. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18675742.

1026. Lynch ME, Clark AJ, Sawynok J, Sullivan MJ. Topical amitriptyline and ketamine in neuropathic pain syndromes: an open-label study. J Pain 2005;6:644-649. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16202956.

1027. Barton DL, Wos EJ, Qin R, et al. A double-blind, placebo-controlled trial of a topical treatment for chemotherapy-induced peripheral neuropathy: NCCTG trial N06CA. Support Care Cancer 2011;19:833-841. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20496177.

1028. Fleming JA, O'Connor BD. Use of lidocaine patches for neuropathic pain in a comprehensive cancer centre. Pain Res Manag 2009;14:381-388. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19862373.

1029. Gammaitoni AR, Alvarez NA, Galer BS. Safety and tolerability of the lidocaine patch 5%, a targeted peripheral analgesic: a review of the literature. J Clin Pharmacol 2003;43:111-117. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12616661.

1030. Lynch ME, Clark AJ, Sawynok J, Sullivan MJ. Topical 2% amitriptyline and 1% ketamine in neuropathic pain syndromes: a randomized, double-blind, placebo-controlled trial. Anesthesiology 2005;103:140-146. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15983466.

1031. Kopsky DJ, Hesselink JM. High doses of topical amitriptyline in neuropathic pain: two cases and literature review. Pain Pract 2012;12:148-153. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21676162.

1032. Gewandter JS, Mohile SG, Heckler CE, et al. A phase III randomized, placebo-controlled study of topical amitriptyline and ketamine for chemotherapy-induced peripheral neuropathy (CIPN): a University of Rochester CCOP study of 462 cancer survivors. Support Care Cancer 2014;22:1807-1814. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24531792.

1033. Brutcher RE, Kurihara C, Bicket MC, et al. Compounded topical pain creams to treat localized chronic pain: A randomized controlled trial. Ann Intern Med 2019;170:309-318. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30716769.

1034. Hurlow A, Bennett MI, Robb KA, et al. Transcutaneous electric nerve stimulation (TENS) for cancer pain in adults. Cochrane Database Syst Rev 2012;3:CD006276. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22419313.

1035. Chiu HY, Hsieh YJ, Tsai PS. Systematic review and meta-analysis of acupuncture to reduce cancer-related pain. Eur J Cancer Care (Engl) 2017;26. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26853524.

1036. Choi TY, Lee MS, Kim TH, et al. Acupuncture for the treatment of cancer pain: a systematic review of randomised clinical trials. Support Care Cancer 2012;20:1147-1158. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22447366.

1037. Garcia MK, McQuade J, Haddad R, et al. Systematic review of acupuncture in cancer care: a synthesis of the evidence. J Clin Oncol 2013;31:952-960. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23341529.

1038. Mao JJ, Xie SX, Farrar JT, et al. A randomised trial of electro-acupuncture for arthralgia related to aromatase inhibitor use. Eur J Cancer 2014;50:267-276. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24210070.

1039. Hershman DL, Unger JM, Greenlee H, et al. Effect of acupuncture vs sham acupuncture or waitlist control on joint pain related to aromatase inhibitors among women with early-stage breast cancer: A randomized clinical trial. JAMA 2018;320:167-176. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29998338.

1040. Lu W, Giobbie-Hurder A, Freedman RA, et al. Acupuncture for chemotherapy-induced peripheral neuropathy in breast cancer survivors: A randomized controlled pilot trial. Oncologist 2020;25:310-318. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32297442.

1041. Bober SL, Varela VS. Sexuality in adult cancer survivors: challenges and intervention. J Clin Oncol 2012;30:3712-3719. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23008322.

1042. Donovan KA, Thompson LM, Hoffe SE. Sexual function in colorectal cancer survivors. Cancer Control 2010;17:44-51. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20010518.

1043. Jackson SE, Wardle J, Steptoe A, Fisher A. Sexuality after a cancer diagnosis: A population-based study. Cancer 2016;122:3883-3891. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27531631.

1044. Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States: prevalence and predictors. JAMA 1999;281:537-544. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10022110.

1045. Morreale MK. The impact of cancer on sexual function. Adv Psychosom Med 2011;31:72-82. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22005205.

1046. Vomvas D, Iconomou G, Soubasi E, et al. Assessment of sexual function in patients with cancer undergoing radiotherapy--a single centre prospective study. Anticancer Res 2012;32:657-664. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22287759.

1047. Bober SL, Carter J, Falk S. Addressing female sexual function after cancer by internists and primary care providers. J Sex Med 2013;10 Suppl 1:112-119. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23387916.

1048. Forbat L, White I, Marshall-Lucette S, Kelly D. Discussing the sexual consequences of treatment in radiotherapy and urology consultations with couples affected by prostate cancer. BJU Int 2012;109:98-103. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21631697.

1049. Reese JB, Sorice K, Beach MC, et al. Patient-provider communication about sexual concerns in cancer: a systematic review. J Cancer Surviv 2017;11:175-188. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27858322.

1050. Sporn NJ, Smith KB, Pirl WF, et al. Sexual health communication between cancer survivors and providers: how frequently does it occur and which providers are preferred? Psychooncology 2015;24:1167-1173. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25534170.

1051. White ID, Allan H, Faithfull S. Assessment of treatment-induced female sexual morbidity in oncology: is this a part of routine medical follow-up after radical pelvic radiotherapy? Br J Cancer 2011;105:903-910. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21897386.

1052. Barbera L, Zwaal C, Elterman D, et al. Interventions to address sexual problems in people with cancer. Curr Oncol 2017;24:192-200. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28680280.

1053. ACOG Practice Bulletin No. 119: Female sexual dysfunction. Obstet Gynecol 2011;117:996-1007. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21422879.

1054. Gilbert E, Ussher JM, Perz J. Sexuality after breast cancer: a review. Maturitas 2010;66:397-407. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20439140.

1055. Krychman M, Millheiser LS. Sexual health issues in women with cancer. J Sex Med 2013;10 Suppl 1:5-15. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23387907.

1056. Barni S, Mondin R. Sexual dysfunction in treated breast cancer patients. Ann Oncol 1997;8:149-153. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9093723.

1057. Frumovitz M, Sun CC, Schover LR, et al. Quality of life and sexual functioning in cervical cancer survivors. J Clin Oncol 2005;23:7428-7436. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16234510.

1058. Ganz PA, Desmond KA, Belin TR, et al. Predictors of sexual health in women after a breast cancer diagnosis. J Clin Oncol 1999;17:2371-2380. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10561299.

1059. Ganz PA, Rowland JH, Desmond K, et al. Life after breast cancer: understanding women's health-related quality of life and sexual functioning. J Clin Oncol 1998;16:501-514. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9469334.

1060. Lindau ST, Gavrilova N, Anderson D. Sexual morbidity in very long term survivors of vaginal and cervical cancer: a comparison to national norms. Gynecol Oncol 2007;106:413-418. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17582473.

1061. Rodrigues AC, Teixeira R, Teixeira T, et al. Impact of pelvic radiotherapy on female sexuality. Arch Gynecol Obstet 2012;285:505-514. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21769555.

1062. Gershenson DM, Miller AM, Champion VL, et al. Reproductive and sexual function after platinum-based chemotherapy in long-term ovarian germ cell tumor survivors: a Gynecologic Oncology Group Study. J Clin Oncol 2007;25:2792-2797. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17602084.

1063. Lammerink EA, de Bock GH, Pras E, et al. Sexual functioning of cervical cancer survivors: a review with a female perspective. Maturitas 2012;72:296-304. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22704291.

1064. Fobair P, Stewart SL, Chang S, et al. Body image and sexual problems in young women with breast cancer. Psychooncology 2006;15:579-594. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16287197.

1065. Syrjala KL, Kurland BF, Abrams JR, et al. Sexual function changes during the 5 years after high-dose treatment and hematopoietic cell transplantation for malignancy, with case-matched controls at 5 years. Blood 2008;111:989-996. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17878404.

1066. Thygesen KH, Schjodt I, Jarden M. The impact of hematopoietic stem cell transplantation on sexuality: a systematic review of the literature. Bone Marrow Transplant 2012;47:716-724. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21874054.

1067. Watson M, Wheatley K, Harrison GA, et al. Severe adverse impact on sexual functioning and fertility of bone marrow transplantation, either allogeneic or autologous, compared with consolidation chemotherapy alone: analysis of the MRC AML 10 trial. Cancer 1999;86:1231-1239. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10506708.

1068. Zantomio D, Grigg AP, MacGregor L, et al. Female genital tract graft-versus-host disease: incidence, risk factors and recommendations for management. Bone Marrow Transplant 2006;38:567-572. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16953208.

1069. NIH consensus conference. Impotence. NIH consensus development panel on impotence. JAMA 1993;270:83-90. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8510302.

1070. Management of Erectile Dysfunction. American Urological Association 2018. Available at: https://www.auanet.org/guidelines/male-sexual-dysfunction-erectile-dysfunction-(2018). Accessed June 5, 2020.

1071. Cappelleri JC, Rosen RC. The Sexual Health Inventory for Men (SHIM): a 5-year review of research and clinical experience. Int J Impot Res 2005;17:307-319. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15875061.

1072. Monga M, Bettencourt R, Barrett-Connor E. Community-based study of erectile dysfunction and sildenafil use: the Rancho Bernardo study. Urology 2002;59:753-757. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11992854.

1073. Ellis R, Smith A, Wilson S, et al. The prevalence of erectile dysfunction in post-treatment colorectal cancer patients and their interests in seeking treatment: a cross-sectional survey in the west-midlands. J Sex Med 2010;7:1488-1496. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19694923.

1074. Hendren SK, O'Connor BI, Liu M, et al. Prevalence of male and female sexual dysfunction is high following surgery for rectal cancer. Ann Surg 2005;242:212-223. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16041212.

1075. Potosky AL, Davis WW, Hoffman RM, et al. Five-year outcomes after prostatectomy or radiotherapy for prostate cancer: the prostate cancer outcomes study. J Natl Cancer Inst 2004;96:1358-1367. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15367568.

1076. Resnick MJ, Koyama T, Fan KH, et al. Long-term functional outcomes after treatment for localized prostate cancer. N Engl J Med 2013;368:436-445. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23363497.

1077. Schover LR, Fouladi RT, Warneke CL, et al. Defining sexual outcomes after treatment for localized prostate carcinoma. Cancer 2002;95:1773-1785. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12365027.

1078. Siegel T, Moul JW, Spevak M, et al. The development of erectile dysfunction in men treated for prostate cancer. J Urol 2001;165:430-435. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11176390.

1079. Stanford JL, Feng Z, Hamilton AS, et al. Urinary and sexual function after radical prostatectomy for clinically localized prostate cancer: the Prostate Cancer Outcomes Study. JAMA 2000;283:354-360. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10647798.

1080. Khera M, Broderick GA, Carson CC, 3rd, et al. Adult-Onset Hypogonadism. Mayo Clin Proc 2016;91:908-926. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27343020.

1081. Loren AW, Mangu PB, Beck LN, et al. Fertility preservation for patients with cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol 2013;31:2500-2510. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23715580.

1082. Armuand GM, Wettergren L, Rodriguez-Wallberg KA, Lampic C. Desire for children, difficulties achieving a pregnancy, and infertility distress 3 to 7 years after cancer diagnosis. Support Care Cancer 2014;22:2805-2812. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24817617.

1083. Kort JD, Eisenberg ML, Millheiser LS, Westphal LM. Fertility issues in cancer survivorship. CA Cancer J Clin 2014;64:118-134. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24604743.

1084. Murphy D, Orgel E, Termuhlen A, et al. Why Healthcare Providers Should Focus on the Fertility of AYA Cancer Survivors: It's Not Too Late! Front Oncol 2013;3:248. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24109589.

1085. Quinn MM, Letourneau JM, Rosen MP. Contraception after cancer treatment: describing methods, counseling, and unintended pregnancy risk. Contraception 2014;89:466-471. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24576795.

1086. Bartula I, Sherman KA. Development and validation of the Female Sexual Function Index adaptation for breast cancer patients (FSFI-BC). Breast Cancer Res Treat 2015;152:477-488. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26198992.

1087. Hatzichristou D, Rosen RC, Derogatis LR, et al. Recommendations for the clinical evaluation of men and women with sexual dysfunction. J Sex Med 2010;7:337-348. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20092443.

1088. McGahuey CA, Gelenberg AJ, Laukes CA, et al. The Arizona Sexual Experience Scale (ASEX): reliability and validity. J Sex Marital Ther 2000;26:25-40. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10693114.

1089. Rosen R, Brown C, Heiman J, et al. The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. J Sex Marital Ther 2000;26:191-208. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10782451.

1090. Abraham L, Symonds T, Morris MF. Psychometric validation of a sexual quality of life questionnaire for use in men with premature ejaculation or erectile dysfunction. J Sex Med 2008;5:595-601. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18208501.

1091. Assessment Center. Available at: http://www.assessmentcenter.net/. Accessed June 5, 2020.

1092. Baser RE, Li Y, Carter J. Psychometric validation of the Female Sexual Function Index (FSFI) in cancer survivors. Cancer 2012;118:4606-4618. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22359250.

1093. Jeffery DD, Tzeng JP, Keefe FJ, et al. Initial report of the cancer Patient-Reported Outcomes Measurement Information System (PROMIS)

sexual function committee: review of sexual function measures and domains used in oncology. Cancer 2009;115:1142-1153. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19195044.

1094. Bartula I, Sherman KA. Screening for sexual dysfunction in women diagnosed with breast cancer: systematic review and recommendations. Breast Cancer Res Treat 2013;141:173-185. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24013707.

1095. Flynn P, Kew F, Kisely SR. Interventions for psychosexual dysfunction in women treated for gynaecological malignancy. Cochrane Database Syst Rev 2009:CD004708. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19370605.

1096. Katz A. Interventions for sexuality after pelvic radiation therapy and gynecological cancer. Cancer J 2009;15:45-47. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19197173.

1097. Brotto LA, Erskine Y, Carey M, et al. A brief mindfulness-based cognitive behavioral intervention improves sexual functioning versus wait-list control in women treated for gynecologic cancer. Gynecol Oncol 2012;125:320-325. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22293042.

1098. Hummel SB, van Lankveld J, Oldenburg HSA, et al. Efficacy of internet-based cognitive behavioral therapy in improving sexual functioning of breast cancer survivors: results of a randomized controlled trial. J Clin Oncol 2017;35:1328-1340. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28240966.

1099. Hickey M, Marino JL, Braat S, Wong S. A randomized, double-blind, crossover trial comparing a silicone- versus water-based lubricant for sexual discomfort after breast cancer. Breast Cancer Res Treat 2016;158:79-90. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27306420.

1100. Goetsch MF, Lim JY, Caughey AB. A practical solution for dyspareunia in breast cancer survivors: a randomized controlled trial. J Clin Oncol 2015;33:3394-3400. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26215946.

1101. Yang EJ, Lim JY, Rah UW, Kim YB. Effect of a pelvic floor muscle training program on gynecologic cancer survivors with pelvic floor dysfunction: a randomized controlled trial. Gynecol Oncol 2012;125:705-711. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22472463.

1102. Miles T, Johnson N. Vaginal dilator therapy for women receiving pelvic radiotherapy. Cochrane Database Syst Rev 2010:CD007291. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20824858.

1103. Melisko ME, Goldman ME, Hwang J, et al. Vaginal testosterone cream vs estradiol vaginal ring for vaginal dryness or decreased libido in women receiving aromatase inhibitors for early-stage breast cancer: a randomized clinical trial. JAMA Oncol 2017;3:313-319. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27832260.

1104. Archer DF, Labrie F, Bouchard C, et al. Treatment of pain at sexual activity (dyspareunia) with intravaginal dehydroepiandrosterone (prasterone). Menopause 2015;22:950-963. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25734980.

1105. Archer DF, Labrie F, Montesino M, Martel C. Comparison of intravaginal 6.5mg (0.50%) prasterone, 0.3mg conjugated estrogens and 10mug estradiol on symptoms of vulvovaginal atrophy. J Steroid Biochem Mol Biol 2017;174:1-8. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28323042.

1106. Labrie F, Archer DF, Bouchard C, et al. Intravaginal dehydroepiandrosterone (prasterone), a highly efficient treatment of dyspareunia. Climacteric 2011;14:282-288. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21244215.

1107. Labrie F, Archer DF, Koltun W, et al. Efficacy of intravaginal dehydroepiandrosterone (DHEA) on moderate to severe dyspareunia and vaginal dryness, symptoms of vulvovaginal atrophy, and of the genitourinary syndrome of menopause. Menopause 2016;23:243-256. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26731686.

1108. Labrie F, Archer DF, Bouchard C, et al. Prasterone has parallel beneficial effects on the main symptoms of vulvovaginal atrophy: 52-week open-label study. Maturitas 2015;81:46-56. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25771041.

1109. Scheffers CS, Armstrong S, Cantineau AE, et al. Dehydroepiandrosterone for women in the peri- or postmenopausal phase. Cochrane Database Syst Rev 2015;1:CD011066. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25879093.

1110. INTRAROSA (prasterone) vaginal inserts. Shionogi Inc.; 2018. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/208470s001lbl.pdf. Accessed June 5, 2020.

1111. OSPHENA (ospemifene). Shionogi Inc.; 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/203505s015lbl.pdf. Accessed June 5, 2020.

1112. Bachmann GA, Komi JO. Ospemifene effectively treats vulvovaginal atrophy in postmenopausal women: results from a pivotal phase 3 study. Menopause 2010;17:480-486. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20032798.

1113. Goldstein SR, Bachmann GA, Koninckx PR, et al. Ospemifene 12-month safety and efficacy in postmenopausal women with vulvar and vaginal atrophy. Climacteric 2014;17:173-182. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23984673.

1114. Portman DJ, Bachmann GA, Simon JA. Ospemifene, a novel selective estrogen receptor modulator for treating dyspareunia associated with postmenopausal vulvar and vaginal atrophy. Menopause 2013;20:623-630. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23361170.

1115. De Rosa N, Lavitola G, Giampaolino P, et al. Impact of ospemifene on quality of life and sexual function in young survivors of cervical cancer: A prospective study. Biomed Res Int 2017;2017:7513610. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28781968.

1116. ADDYI (flibanserin). Sprout Pharmaceuticals, Inc.; 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/022526s008lbl.pdf. Accessed June 5, 2020.

1117. Jaspers L, Feys F, Bramer WM, et al. Efficacy and safety of flibanserin for the treatment of hypoactive sexual desire disorder in women: a systematic review and meta-analysis. JAMA Intern Med 2016;176:453-462. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26927498.

1118. Gao Z, Yang D, Yu L, Cui Y. Efficacy and safety of flibanserin in women with hypoactive sexual desire disorder: a systematic review and meta-analysis. J Sex Med 2015;12:2095-2104. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26745616.

1119. VYLEESI (bremelanotide injection), for subcutaneous use. Waltham, MA: AMAG Pharmaceuticals, Inc.; 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/210557s000lbl.pdf. Accessed April 29, 2020.

1120. Kingsberg SA, Clayton AH, Portman D, et al. Bremelanotide for the treatment of hypoactive sexual desire disorder: Two randomized phase 3 trials. Obstet Gynecol 2019;134:899-908. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31599840.

1121. Goldstein I, Kim NN, Clayton AH, et al. Hypoactive sexual desire disorder: International Society for the Study of Women's Sexual Health (ISSWSH) expert consensus panel review. Mayo Clin Proc 2017;92:114-128. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27916394.

1122. Segraves RT, Croft H, Kavoussi R, et al. Bupropion sustained release (SR) for the treatment of hypoactive sexual desire disorder (HSDD) in nondepressed women. J Sex Marital Ther 2001;27:303-316. Available at: https://www.ncbi.nlm.nih.gov/pubmed/11354935.

1123. Segraves RT, Clayton A, Croft H, et al. Bupropion sustained release for the treatment of hypoactive sexual desire disorder in premenopausal

women. J Clin Psychopharmacol 2004;24:339-342. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15118489.

1124. Landen M, Eriksson E, Agren H, Fahlen T. Effect of buspirone on sexual dysfunction in depressed patients treated with selective serotonin reuptake inhibitors. J Clin Psychopharmacol 1999;19:268-271. Available at: https://www.ncbi.nlm.nih.gov/pubmed/10350034.

1125. Cavalcanti AL, Bagnoli VR, Fonseca AM, et al. Effect of sildenafil on clitoral blood flow and sexual response in postmenopausal women with orgasmic dysfunction. Int J Gynaecol Obstet 2008;102:115-119. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18589423.

1126. Yang CC, Cao YY, Guan QY, et al. Influence of PDE5 inhibitor on MRI measurement of clitoral volume response in women with FSAD: a feasibility study of a potential technique for evaluating drug response. Int J Impot Res 2008;20:105-110. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18059502.

1127. Alexander MS, Rosen RC, Steinberg S, et al. Sildenafil in women with sexual arousal disorder following spinal cord injury. Spinal Cord 2011;49:273-279. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20733587.

1128. Basson R, McInnes R, Smith MD, et al. Efficacy and safety of sildenafil citrate in women with sexual dysfunction associated with female sexual arousal disorder. J Womens Health Gend Based Med 2002;11:367-377. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12150499.

1129. Basson R, Brotto LA. Sexual psychophysiology and effects of sildenafil citrate in oestrogenised women with acquired genital arousal disorder and impaired orgasm: a randomised controlled trial. BJOG 2003;110:1014-1024. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14592587.

1130. Berman JR, Berman LA, Toler SM, et al. Safety and efficacy of sildenafil citrate for the treatment of female sexual arousal disorder: a double-blind, placebo controlled study. J Urol 2003;170:2333-2338. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14634409.

1131. Caruso S, Intelisano G, Lupo L, Agnello C. Premenopausal women affected by sexual arousal disorder treated with sildenafil: a double-blind, cross-over, placebo-controlled study. BJOG 2001;108:623-628. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11426898.

1132. Caruso S, Rugolo S, Agnello C, et al. Sildenafil improves sexual functioning in premenopausal women with type 1 diabetes who are affected by sexual arousal disorder: a double-blind, crossover, placebo-controlled pilot study. Fertil Steril 2006;85:1496-1501. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16579999.

1133. Esposito K, Giugliano F, Di Palo C, et al. Effect of lifestyle changes on erectile dysfunction in obese men: a randomized controlled trial. JAMA 2004;291:2978-2984. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15213209.

1134. Lamina S, Okoye CG, Dagogo TT. Therapeutic effect of an interval exercise training program in the management of erectile dysfunction in hypertensive patients. J Clin Hypertens (Greenwich) 2009;11:125-129. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19302423.

1135. Khoo J, Piantadosi C, Duncan R, et al. Comparing effects of a low-energy diet and a high-protein low-fat diet on sexual and endothelial function, urinary tract symptoms, and inflammation in obese diabetic men. J Sex Med 2011;8:2868-2875. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21819545.

1136. Khoo J, Piantadosi C, Worthley S, Wittert GA. Effects of a low-energy diet on sexual function and lower urinary tract symptoms in obese men. Int J Obes (Lond) 2010;34:1396-1403. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20404829.

1137. Maio G, Saraeb S, Marchiori A. Physical activity and PDE5 inhibitors in the treatment of erectile dysfunction: results of a randomized controlled study. J Sex Med 2010;7:2201-2208. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20367777.

1138. Andersson E, Walen C, Hallberg J, et al. A randomized controlled trial of guided Internet-delivered cognitive behavioral therapy for erectile

dysfunction. J Sex Med 2011;8:2800-2809. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21797983.

1139. Aubin S, Heiman JR, Berger RE, et al. Comparing sildenafil alone vs. sildenafil plus brief couple sex therapy on erectile dysfunction and couples' sexual and marital quality of life: a pilot study. J Sex Marital Ther 2009;35:122-143. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19266381.

1140. Banner LL, Anderson RU. Integrated sildenafil and cognitive-behavior sex therapy for psychogenic erectile dysfunction: a pilot study. J Sex Med 2007;4:1117-1125. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17627724.

1141. Boddi V, Castellini G, Casale H, et al. An integrated approach with vardenafil orodispersible tablet and cognitive behavioral sex therapy for treatment of erectile dysfunction: a randomized controlled pilot study. Andrology 2015;3:909-918. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26311340.

1142. Wylie KR. Treatment outcome of brief couple therapy in psychogenic male erectile disorder. Arch Sex Behav 1997;26:527-545. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9343637.

1143. Canada AL, Neese LE, Sui D, Schover LR. Pilot intervention to enhance sexual rehabilitation for couples after treatment for localized prostate carcinoma. Cancer 2005;104:2689-2700. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16294343.

1144. Schover LR, Canada AL, Yuan Y, et al. A randomized trial of internet-based versus traditional sexual counseling for couples after localized prostate cancer treatment. Cancer 2012;118:500-509. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21953578.

1145. Fink HA, Mac Donald R, Rutks IR, et al. Sildenafil for male erectile dysfunction: a systematic review and meta-analysis. Arch Intern Med 2002;162:1349-1360. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12076233.

1146. Nehra A. Erectile dysfunction and cardiovascular disease: efficacy and safety of phosphodiesterase type 5 inhibitors in men with both conditions. Mayo Clin Proc 2009;84:139-148. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19181648.

1147. Hubanks JM, Umbreit EC, Karnes RJ, Myers RP. Open radical retropubic prostatectomy using high anterior release of the levator fascia and constant haptic feedback in bilateral neurovascular bundle preservation plus early postoperative phosphodiesterase type 5 inhibition: a contemporary series. Eur Urol 2012;61:878-884. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22154730.

1148. Yang L, Qian S, Liu L, et al. Phosphodiesterase-5 inhibitors could be efficacious in the treatment of erectile dysfunction after radiotherapy for prostate cancer: a systematic review and meta-analysis. Urol Int 2012;90:339-347. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23221333.

1149. Kloner RA, Hutter AM, Emmick JT, et al. Time course of the interaction between tadalafil and nitrates. J Am Coll Cardiol 2003;42:1855-1860. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14642699.

1150. Webb DJ, Freestone S, Allen MJ, Muirhead GJ. Sildenafil citrate and blood-pressure-lowering drugs: results of drug interaction studies with an organic nitrate and a calcium antagonist. Am J Cardiol 1999;83:21C-28C. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10078539.

1151. Zhao C, Kim SW, Yang DY, et al. Efficacy and safety of once-daily dosing of udenafil in the treatment of erectile dysfunction: results of a multicenter, randomized, double-blind, placebo-controlled trial. Eur Urol 2011;60:380-387. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21458153.

1152. Rajfer J, Aliotta PJ, Steidle CP, et al. Tadalafil dosed once a day in men with erectile dysfunction: a randomized, double-blind, placebo-controlled study in the US. Int J Impot Res 2007;19:95-103. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16871272.

1153. Porst H, Giuliano F, Glina S, et al. Evaluation of the efficacy and safety of once-a-day dosing of tadalafil 5mg and 10mg in the treatment of erectile dysfunction: results of a multicenter, randomized, double-blind, placebo-controlled trial. Eur Urol 2006;50:351-359. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16766116.

1154. Shim YS, Pae CU, Cho KJ, et al. Effects of daily low-dose treatment with phosphodiesterase type 5 inhibitor on cognition, depression, somatization and erectile function in patients with erectile dysfunction: a double-blind, placebo-controlled study. Int J Impot Res 2014;26:76-80. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24285284.

1155. Bhasin S, Cunningham GR, Hayes FJ, et al. Testosterone therapy in men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2010;95:2536-2559. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20525905.

1156. Snyder PJ, Bhasin S, Cunningham GR, et al. Effects of testosterone treatment in older men. N Engl J Med 2016;374:611-624. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26886521.

1157. Cunningham GR, Stephens-Shields AJ, Rosen RC, et al. Testosterone treatment and sexual function in older men with low testosterone levels. J Clin Endocrinol Metab 2016;101:3096-3104. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27355400.

1158. Buvat J, Montorsi F, Maggi M, et al. Hypogonadal men nonresponders to the PDE5 inhibitor tadalafil benefit from normalization of testosterone levels with a 1% hydroalcoholic testosterone gel in the treatment of erectile dysfunction (TADTEST study). J Sex Med 2011;8:284-293. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20704642.

1159. Corona G, Vignozzi L, Sforza A, Maggi M. Risks and benefits of late onset hypogonadism treatment: an expert opinion. World J Mens Health 2013;31:103-125. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24044106.

1160. Khera M, Bhattacharya RK, Blick G, et al. Improved sexual function with testosterone replacement therapy in hypogonadal men: real-world data from the Testim Registry in the United States (TRiUS). J Sex Med 2011;8:3204-3213. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21834870.

1161. Rosenthal BD, May NR, Metro MJ, et al. Adjunctive use of AndroGel (testosterone gel) with sildenafil to treat erectile dysfunction in men with acquired androgen deficiency syndrome after failure using sildenafil alone. Urology 2006;67:571-574. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16527581.

1162. Hwang TI, Chen HE, Tsai TF, Lin YC. Combined use of androgen and sildenafil for hypogonadal patients unresponsive to sildenafil alone. Int J Impot Res 2006;18:400-404. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16395321.

1163. Zitzmann M, Mattern A, Hanisch J, et al. IPASS: a study on the tolerability and effectiveness of injectable testosterone undecanoate for the treatment of male hypogonadism in a worldwide sample of 1,438 men. J Sex Med 2013;10:579-588. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22812645.

1164. Campbell SE, Glazener CM, Hunter KF, et al. Conservative management for postprostatectomy urinary incontinence. Cochrane Database Syst Rev 2012;1:CD001843. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22258946.

1165. Geraerts I, Van Poppel H, Devoogdt N, et al. Pelvic floor muscle training for erectile dysfunction and climacturia 1 year after nerve sparing radical prostatectomy: a randomized controlled trial. Int J Impot Res 2016;28:9-13. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26538105.

1166. Prota C, Gomes CM, Ribeiro LH, et al. Early postoperative pelvic-floor biofeedback improves erectile function in men undergoing radical prostatectomy: a prospective, randomized, controlled trial. Int J Impot Res 2012;24:174-178. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22573231.

1167. Nelson CJ, Ahmed A, Valenzuela R, et al. Assessment of penile vibratory stimulation as a management strategy in men with secondary retarded orgasm. Urology 2007;69:552-555; discussion 555-556. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17382163.

1168. Cooper K, Martyn-St James M, Kaltenthaler E, et al. Interventions to treat premature ejaculation: a systematic review short report. Health Technol Assess 2015;19:1-180, v-vi. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25768099.

1169. Giuliano F, Clement P. Pharmacology for the treatment of premature ejaculation. Pharmacol Rev 2012;64:621-644. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22679220.

1170. Kim SC, Seo KK. Efficacy and safety of fluoxetine, sertraline and clomipramine in patients with premature ejaculation: a double-blind, placebo controlled study. J Urol 1998;159:425-427. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9649255.

1171. Waldinger MD, Zwinderman AH, Olivier B. On-demand treatment of premature ejaculation with clomipramine and paroxetine: a randomized, double-blind fixed-dose study with stopwatch assessment. Eur Urol 2004;46:510-515; discussion 516. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15363569.

1172. SMSNA Position Statement on Restorative Therapies for ED Sexual Medicine Society of North America, Inc. ; Available at: http://www.smsna.org/V1/news/433-smsna-position-statement-on-restorative-therapies-for-ed. Accessed June 5, 2020.

1173. Berger AM, Mitchell SA. Modifying cancer-related fatigue by optimizing sleep quality. J Natl Compr Canc Netw 2008;6:3-13. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18267055.

1174. Ancoli-Israel S, Moore PJ, Jones V. The relationship between fatigue and sleep in cancer patients: a review. Eur J Cancer Care (Engl) 2001;10:245-255. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11806675.

1175. Ancoli-Israel S. Recognition and treatment of sleep disturbances in cancer. J Clin Oncol 2009;27:5864-5866. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19884528.

1176. Berrett-Abebe J, Cadet T, Pirl W, Lennes I. Exploring the relationship between fear of cancer recurrence and sleep quality in cancer survivors. J Psychosoc Oncol 2015;33:297-309. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25751193.

1177. Carney S, Koetters T, Cho M, et al. Differences in sleep disturbance parameters between oncology outpatients and their family caregivers. J Clin Oncol 2011;29:1001-1006. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21282549.

1178. Fiorentino L, Ancoli-Israel S. Insomnia and its treatment in women with breast cancer. Sleep Med Rev 2006;10:419-429. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16963293.

1179. Fiorentino L, Ancoli-Israel S. Sleep dysfunction in patients with cancer. Curr Treat Options Neurol 2007;9:337-346. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17716597.

1180. Flynn KE, Shelby RA, Mitchell SA, et al. Sleep-wake functioning along the cancer continuum: focus group results from the Patient-Reported Outcomes Measurement Information System (PROMIS((R))). Psychooncology 2010;19:1086-1093. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20013938.

1181. Forsythe LP, Helzlsouer KJ, MacDonald R, Gallicchio L. Daytime sleepiness and sleep duration in long-term cancer survivors and non-cancer controls: results from a registry-based survey study. Support Care Cancer 2012;20:2425-2432. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22218738.

1182. Liu L, Ancoli-Israel S. Sleep disturbances in cancer. Psychiatr Ann 2008;38:627-634. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21243092.

1183. Zee PC, Ancoli-Israel S. Does effective management of sleep disorders reduce cancer-related fatigue? Drugs 2009;69 Suppl 2:29-41. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20047349.

1184. Slade AN, Waters MR, Serrano NA. Long-term sleep disturbance and prescription sleep aid use among cancer survivors in the United States. Support Care Cancer 2020;28:551-560. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31081525.

1185. Palesh O, Aldridge-Gerry A, Ulusakarya A, et al. Sleep disruption in breast cancer patients and survivors. J Natl Compr Canc Netw 2013;11:1523-1530. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24335687.

1186. Buysse DJ, Yu L, Moul DE, et al. Development and validation of patient-reported outcome measures for sleep disturbance and sleep-related impairments. Sleep 2010;33:781-792. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20550019.

1187. Omachi TA. Measures of sleep in rheumatologic diseases: Epworth Sleepiness Scale (ESS), Functional Outcome of Sleep Questionnaire (FOSQ), Insomnia Severity Index (ISI), and Pittsburgh Sleep Quality Index (PSQI). Arthritis Care Res (Hoboken) 2011;63 Suppl 11:S287-296. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22588751.

1188. Savard MH, Savard J, Simard S, Ivers H. Empirical validation of the Insomnia Severity Index in cancer patients. Psychooncology 2005;14:429-441. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15376284.

1189. Yu L, Buysse DJ, Germain A, et al. Development of short forms from the PROMIS sleep disturbance and Sleep-Related Impairment item banks. Behav Sleep Med 2011;10:6-24. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22250775.

1190. Evenson KR, Goto MM, Furberg RD. Systematic review of the validity and reliability of consumer-wearable activity trackers. Int J Behav Nutr Phys Act 2015;12:159. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26684758.

1191. de Zambotti M, Claudatos S, Inkelis S, et al. Evaluation of a consumer fitness-tracking device to assess sleep in adults. Chronobiol Int 2015;32:1024-1028. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26158542.

1192. Gruwez A, Libert W, Ameye L, Bruyneel M. Reliability of commercially available sleep and activity trackers with manual switch-to-sleep mode activation in free-living healthy individuals. Int J Med Inform 2017;102:87-92. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28495352.

1193. Ko PR, Kientz JA, Choe EK, et al. Consumer sleep technologies: a review of the landscape. J Clin Sleep Med 2015;11:1455-1461. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26156958.

1194. Mantua J, Gravel N, Spencer RM. Reliability of sleep measures from four personal health monitoring devices compared to research-based actigraphy and polysomnography. Sensors (Basel) 2016;16. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27164110.

1195. Montgomery-Downs HE, Insana SP, Bond JA. Movement toward a novel activity monitoring device. Sleep Breath 2012;16:913-917. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21971963.

1196. Chung F, Yegneswaran B, Liao P, et al. STOP questionnaire: a tool to screen patients for obstructive sleep apnea. Anesthesiology 2008;108:812-821. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18431116.

1197. Netzer NC, Stoohs RA, Netzer CM, et al. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. Ann Intern Med 1999;131:485-491. Available at: https://www.ncbi.nlm.nih.gov/pubmed/10507956.

1198. Silva GE, Vana KD, Goodwin JL, et al. Identification of patients with sleep disordered breathing: comparing the four-variable screening tool, STOP, STOP-Bang, and Epworth Sleepiness Scales. J Clin Sleep Med 2011;7:467-472. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22003341.

1199. Buchfuhrer MJ. Strategies for the treatment of restless legs syndrome. Neurotherapeutics 2012;9:776-790. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22923001.

1200. Moyer DE, Zayas-Bazan J, Reese G. Restless legs syndrome: diagnostic time-savers, Tx tips. J Fam Pract 2009;58:415-423. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19679021.

1201. Morgenthaler T, Kramer M, Alessi C, et al. Practice parameters for the psychological and behavioral treatment of insomnia: an update. An american academy of sleep medicine report. Sleep 2006;29:1415-1419. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17162987.

1202. Morgenthaler TI, Kapur VK, Brown T, et al. Practice parameters for the treatment of narcolepsy and other hypersomnias of central origin. Sleep 2007;30:1705-1711. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18246980.

1203. Insomnia: assessment and management in primary care. National Heart, Lung, and Blood Institute Working Group on Insomnia. Am Fam Physician 1999;59:3029-3038. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10392587.

1204. Kupfer DJ, Reynolds CF, 3rd. Management of insomnia. N Engl J Med 1997;336:341-346. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9011788.

1205. Lippmann S, Mazour I, Shahab H. Insomnia: therapeutic approach. South Med J 2001;94:866-873. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11592743.

1206. Kline CE, Sui X, Hall MH, et al. Dose-response effects of exercise training on the subjective sleep quality of postmenopausal women: exploratory analyses of a randomised controlled trial. BMJ Open 2012;2. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22798253.

1207. Rubio-Arias JA, Marin-Cascales E, Ramos-Campo DJ, et al. Effect of exercise on sleep quality and insomnia in middle-aged women: a systematic review and meta-analysis of randomized controlled trials. Maturitas 2017;100:49-56. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28539176.

1208. Yang PY, Ho KH, Chen HC, Chien MY. Exercise training improves sleep quality in middle-aged and older adults with sleep problems: a systematic review. J Physiother 2012;58:157-163. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22884182.

1209. Cheville AL, Kollasch J, Vandenberg J, et al. A home-based exercise program to improve function, fatigue, and sleep quality in patients with Stage IV lung and colorectal cancer: a randomized controlled trial. J Pain Symptom Manage 2013;45:811-821. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23017624.

1210. Mishra SI, Scherer RW, Snyder C, et al. Exercise interventions on health-related quality of life for people with cancer during active treatment. Cochrane Database Syst Rev 2012;8:CD008465. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22895974.

1211. Mustian KM, Sprod LK, Janelsins M, et al. Multicenter, randomized controlled trial of yoga for sleep quality among cancer survivors. J Clin Oncol 2013;31:3233-3241. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23940231.

1212. Payne JK, Held J, Thorpe J, Shaw H. Effect of exercise on biomarkers, fatigue, sleep disturbances, and depressive symptoms in older women with breast cancer receiving hormonal therapy. Oncol Nurs Forum 2008;35:635-642. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18591167.

1213. Rogers LQ, Fogleman A, Trammell R, et al. Effects of a physical activity behavior change intervention on inflammation and related health outcomes in breast cancer survivors: pilot randomized trial. Integr Cancer Ther 2013;12:323-335. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22831916.

1214. Van Gerpen RE, Becker BJ. Development of an evidence-based exercise and education cancer recovery program. Clin J Oncol Nurs

2013;17:539-543. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24080053.

1215. Mustian KM. Yoga as treatment for insomnia among cancer patients and survivors: a systematic review. Eur Med J Oncol 2013;1:106-115. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25343044.

1216. Rogers LQ, Courneya KS, Oster RA, et al. Physical activity and sleep quality in breast cancer survivors: A randomized trial. Med Sci Sports Exerc 2017;49:2009-2015. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28538261.

1217. Qaseem A, Kansagara D, Forciea MA, et al. Management of chronic insomnia disorder in adults: a clinical practice guideline from the American College of Physicians. Ann Intern Med 2016;165:125-133. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27136449.

1218. Savard J, Ivers H, Savard MH, Morin CM. Is a video-based cognitive behavioral therapy for insomnia as efficacious as a professionally administered treatment in breast cancer? Results of a randomized controlled trial. Sleep 2014;37:1305-1314. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25083010.

1219. Zachariae R, Amidi A, Damholdt MF, et al. Internet-delivered cognitive-behavioral therapy for insomnia in breast cancer survivors: A randomized controlled trial. J Natl Cancer Inst 2018. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29471478.

1220. Garland SN, Roscoe JA, Heckler CE, et al. Effects of armodafinil and cognitive behavior therapy for insomnia on sleep continuity and daytime sleepiness in cancer survivors. Sleep Med 2016;20:18-24. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27318221.

1221. Matthews EE, Berger AM, Schmiege SJ, et al. Cognitive behavioral therapy for insomnia outcomes in women after primary breast cancer treatment: a randomized, controlled trial. Oncol Nurs Forum 2014;41:241-253. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24650832.

1222. Roscoe JA, Garland SN, Heckler CE, et al. Randomized placebo-controlled trial of cognitive behavioral therapy and armodafinil for insomnia after cancer treatment. J Clin Oncol 2015;33:165-171. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25452447.

1223. Johnson JA, Rash JA, Campbell TS, et al. A systematic review and meta-analysis of randomized controlled trials of cognitive behavior therapy for insomnia (CBT-I) in cancer survivors. Sleep Med Rev 2016;27:20-28. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26434673.

1224. Nakamura Y, Lipschitz DL, Kuhn R, et al. Investigating efficacy of two brief mind-body intervention programs for managing sleep disturbance in cancer survivors: a pilot randomized controlled trial. J Cancer Surviv 2013;7:165-182. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23338490.

1225. Lengacher CA, Reich RR, Paterson CL, et al. The effects of mindfulness-based stress reduction on objective and subjective sleep parameters in women with breast cancer: a randomized controlled trial. Psychooncology 2015;24:424-432. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24943918.

1226. Garland SN, Carlson LE, Stephens AJ, et al. Mindfulness-based stress reduction compared with cognitive behavioral therapy for the treatment of insomnia comorbid with cancer: a randomized, partially blinded, noninferiority trial. J Clin Oncol 2014;32:449-457. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24395850.

1227. Irwin MR, Olmstead R, Carrillo C, et al. Tai Chi Chih compared with cognitive behavioral therapy for the treatment of insomnia in survivors of breast cancer: a randomized, partially blinded, noninferiority trial. J Clin Oncol 2017:JCO2016710285. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28489508.

1228. National Institutes of Health State of the Science Conference statement on Manifestations and Management of Chronic Insomnia in Adults, June 13-15, 2005. Sleep 2005;28:1049-1057. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16268373.

1229. Neubauer DN. The evolution and development of insomnia pharmacotherapies. J Clin Sleep Med 2007;3:S11-15. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17824496.

1230. Kim SW, Shin IS, Kim JM, et al. Effectiveness of mirtazapine for nausea and insomnia in cancer patients with depression. Psychiatry Clin Neurosci 2008;62:75-83. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18289144.

1231. Jonas DE, Amick HR, Feltner C, et al. Screening for obstructive sleep apnea in adults: evidence report and systematic review for the US Preventive Services Task Force. JAMA 2017;317:415-433. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28118460.

1232. Kline CE, Crowley EP, Ewing GB, et al. The effect of exercise training on obstructive sleep apnea and sleep quality: a randomized controlled trial. Sleep 2011;34:1631-1640. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22131599.

1233. Sengul YS, Ozalevli S, Oztura I, et al. The effect of exercise on obstructive sleep apnea: a randomized and controlled trial. Sleep Breath 2011;15:49-56. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19898884.

1234. Gottlieb DJ, Punjabi NM, Mehra R, et al. CPAP versus oxygen in obstructive sleep apnea. N Engl J Med 2014;370:2276-2285. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24918372.

1235. Bassetti CL, Bornatico F, Fuhr P, et al. Pramipexole versus dual release levodopa in restless legs syndrome: a double blind, randomised, cross-over trial. Swiss Med Wkly 2011;141:w13274. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22101745.

1236. Ferini-Strambi L, Aarskog D, Partinen M, et al. Effect of pramipexole on RLS symptoms and sleep: a randomized, double-blind, placebo-controlled trial. Sleep Med 2008;9:874-881. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18952497.

1237. Kaplan PW, Allen RP, Buchholz DW, Walters JK. A double-blind, placebo-controlled study of the treatment of periodic limb movements in sleep using carbidopa/levodopa and propoxyphene. Sleep 1993;16:717-723. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8165385.

1238. Manconi M, Ferri R, Zucconi M, et al. Pramipexole versus ropinirole: polysomnographic acute effects in restless legs syndrome. Mov Disord 2011;26:892-895. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21370262.

1239. Montplaisir J, Nicolas A, Denesle R, Gomez-Mancilla B. Restless legs syndrome improved by pramipexole: a double-blind randomized trial. Neurology 1999;52:938-943. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10102409.

1240. Oertel WH, Stiasny-Kolster K, Bergtholdt B, et al. Efficacy of pramipexole in restless legs syndrome: a six-week, multicenter, randomized, double-blind study (effect-RLS study). Mov Disord 2007;22:213-219. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17133582.

1241. Trenkwalder C, Garcia-Borreguero D, Montagna P, et al. Ropinirole in the treatment of restless legs syndrome: results from the TREAT RLS 1 study, a 12 week, randomised, placebo controlled study in 10 European countries. J Neurol Neurosurg Psychiatry 2004;75:92-97. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14707315.

1242. Walters AS, Ondo WG, Dreykluft T, et al. Ropinirole is effective in the treatment of restless legs syndrome. TREAT RLS 2: a 12-week, double-blind, randomized, parallel-group, placebo-controlled study. Mov Disord 2004;19:1414-1423. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15390050.

1243. Wilt TJ, MacDonald R, Ouellette J, et al. Pharmacologic therapy for primary restless legs syndrome: a systematic review and meta-analysis. JAMA Intern Med 2013;173:496-505. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23460396.

1244. Hornyak M, Scholz H, Kohnen R, et al. What treatment works best for restless legs syndrome? Meta-analyses of dopaminergic and non-dopaminergic medications. Sleep Med Rev 2014;18:153-164. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23746768.

1245. Bega D, Malkani R. Alternative treatment of restless legs syndrome: an overview of the evidence for mind-body interventions, lifestyle interventions, and neutraceuticals. Sleep Med 2016;17:99-105. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26847981.

1246. Winkelman JW, Armstrong MJ, Allen RP, et al. Practice guideline summary: Treatment of restless legs syndrome in adults: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology 2016;87:2585-2593. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27856776.