



National Comprehensive
Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Older Adult Oncology

Version 1.2024 — December 08, 2023

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[NCCN Older Adult Oncology Panel Members](#) [Summary of the Guidelines Updates](#)

- [Definition and Purpose of the NCCN Guidelines for Older Adult Oncology \(OAO-1\)](#)
- [Approach to Shared Decision-Making in the Older Adult Prior to Therapy \(OAO-2\)](#)
- [Pre-Treatment Evaluation \(OAO-3\)](#)
- [Considerations for Older Adults Undergoing Cancer-Specific Treatment \(OAO-4 and OAO-5\)](#)
- [Management of Common Side Effects in Older Adults Undergoing Cancer-Specific Treatment \(OAO-6\)](#)
- [Life Expectancy of General Population \(OAO-A\)](#)
- [Optimizing Communication with Older Adults \(OAO-B\)](#)
- [Geriatric Screening Tools \(OAO-C\)](#)
- [Geriatric Assessment \(OAO-D\)](#)
- [Falls Assessment and Interventions \(OAO-E\)](#)
- [Assessment of Cognitive Function \(OAO-F\)](#)
- [Insomnia \(OAO-G\)](#)
- [Medications Commonly Used for Supportive Care that Are of Concern in Older Patients \(OAO-H\)](#)
- [Approach to Cancer Screening for Older Adult Cancer Survivors \(OAO-I\)](#)
- [Approach to Surveillance Testing for Older Adult Cancer Survivors with No Evidence of Disease \(OAO-J\)](#)
- [Abbreviations \(ABBR-1\)](#)

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.

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

See [NCCN Categories of Evidence and Consensus](#).

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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 Older Adult Oncology from Version 2.2023 include:

Global changes

- References were updated throughout the guidelines.
- Comprehensive Geriatric Assessment (CGA) changed to Geriatric Assessment (GA).

OAO-4

- New subheading added: General considerations.
- Age-Friendly Health Systems section moved here from OAO-6.
- New subheading added: Specific considerations by treatment type.

OAO-5

- Considerations for Older Adults Undergoing Cancer-Specific Treatment
 - ▶ Systemic therapy subheading changed to Chemotherapy
 - ◇ 1st bullet modified: ~~General~~ Chemotherapy toxicity risk calculators (predominantly solid tumors).
 - 2nd sub bullet modified: Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score (<https://moffitt.org/eforms/crashscoreform>).
 - 3rd sub bullet modified: Cancer and Aging Research Group-Breast Cancer (CARG-BC) score for older adults (for adjuvant/neoadjuvant therapy only) (https://www.cancercalc.com/carg_bc.php).
 - ▶ Chimeric Antigen Receptor (CAR) T-cell therapy section moved here from OAO-6.

OAO-6

- Management of Common Side Effects in Older Adults Undergoing Cancer-Specific Treatment
 - ▶ Renal toxicity row modified: Serum creatinine is not a good indicator of renal function in older adults. Calculation of *estimated* creatinine clearance is recommended to assess renal function and adjust dose to reduce systemic toxicity.

OAO-B

- Optimizing Communication with Older Adults
 - ▶ Assess barriers to optimal communication
 - ◇ 1st bullet modified: *Assess for* cognitive impairment

OAO-D 2 OF 10

- Subheading removed: Recommended Assessment Tools and Interventions for CGA of Older Adults with Cancer (Also for OAO-D 3, OAO-D 4 and OAO-D 5)
- Self-reported Function and Mobility
 - ▶ Activities of Daily Living (ADL)
 - ◇ 2nd sub bullet added: OARS (Older Americans Resources and Services)
- 3rd column heading revised: *Additional Assessments/Potential Interventions* (Also for OAO-D 3, OAO-D 4 and OAO-D 5)
 - ▶ 1st bullet modified: Occupational therapy (OT) *and physical therapy (PT)* referral

**Updates in Version 1.2024 of the NCCN Guidelines for Older Adult Oncology from Version 2.2023 include:**[OAO-D 3 OF 10](#)

• Social Functioning and Support

▶ 3rd column

- ◊ 1st bullet, 5th sub bullet modified: *Food/housing* insecurity.
- ◊ 1st bullet, 6th sub bullet added: Caregiver status assessment.
- ◊ 1st bullet, 7th sub bullet added: Elder abuse screening; ask the patient, "Do you feel safe at home?"
- ◊ 4th bullet removed: Ask about caregiver burden
- ◊ 6th bullet removed: Screen for elder abuse; ask the patient, "Do you feel safe at home?"

[OAO-D 4 OF 10](#)

• Cognition

▶ 3rd column

- ◊ 6th bullet added: Provide written summary.
- ◊ 8th bullet added: Consider referral for cognitive rehabilitation.

• Psychological

▶ 3rd column

- ◊ 8th bullet added: Assess for substance and alcohol use disorder

[OAO-D 5 OF 10](#)

• Medication Management

▶ 2nd column

- ◊ 2nd row modified: ~~2019~~ 2023 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication use in Older Adults

[OAO-E](#)

• Falls Assessment and Interventions

▶ Check orthostatic blood pressure

- ◊ 3rd bullet modified: Address salt intake, adequate hydration, and compensatory strategies (eg, elevating head of bed, rising slowly, using pressure stockings *or an abdominal binder*)

[OAO-F 3 OF 4](#)

• Assessment of Cognitive Function

▶ Screening Tool

- ◊ Mild Cognitive Impairment modified: Clinical interview with cognitive (Mini-Cog), *MMSE*, *MoCA*, *SLUMS*, and ...

[OAO-F 4 OF 4](#)

• Risk factors For The Development of Delirium in Older Patients with Cancer

▶ Predisposing factors

- ◊ History of Alcohol Abuse revised to History of Alcohol Use Disorder

[OAO-H 3 OF 7](#)

• Medications Commonly Used For Supportive Care That are of Concern in Older Patients

▶ 2nd row, 3rd column

- ◊ 1st bullet modified: Avoid *metoclopramide*, unless use for patients with gastroparesis.
- ◊ 2nd bullet modified: If benefit outweighs risk, use the lowest *metoclopramide* dose possible, and avoid exceeding 5 mg.



DEFINITION AND PURPOSE

Definition of the Older Adult Oncology Population

- There is no chronologic age threshold to define an older adult. Age 65 years and over is generally considered the chronologic definition of an older adult, as this is the usual age of eligibility for Medicare benefits. The guidelines herein focus on physiologic age and function to define the older adult oncology population.

Purpose of the NCCN Guidelines for Older Adult Oncology

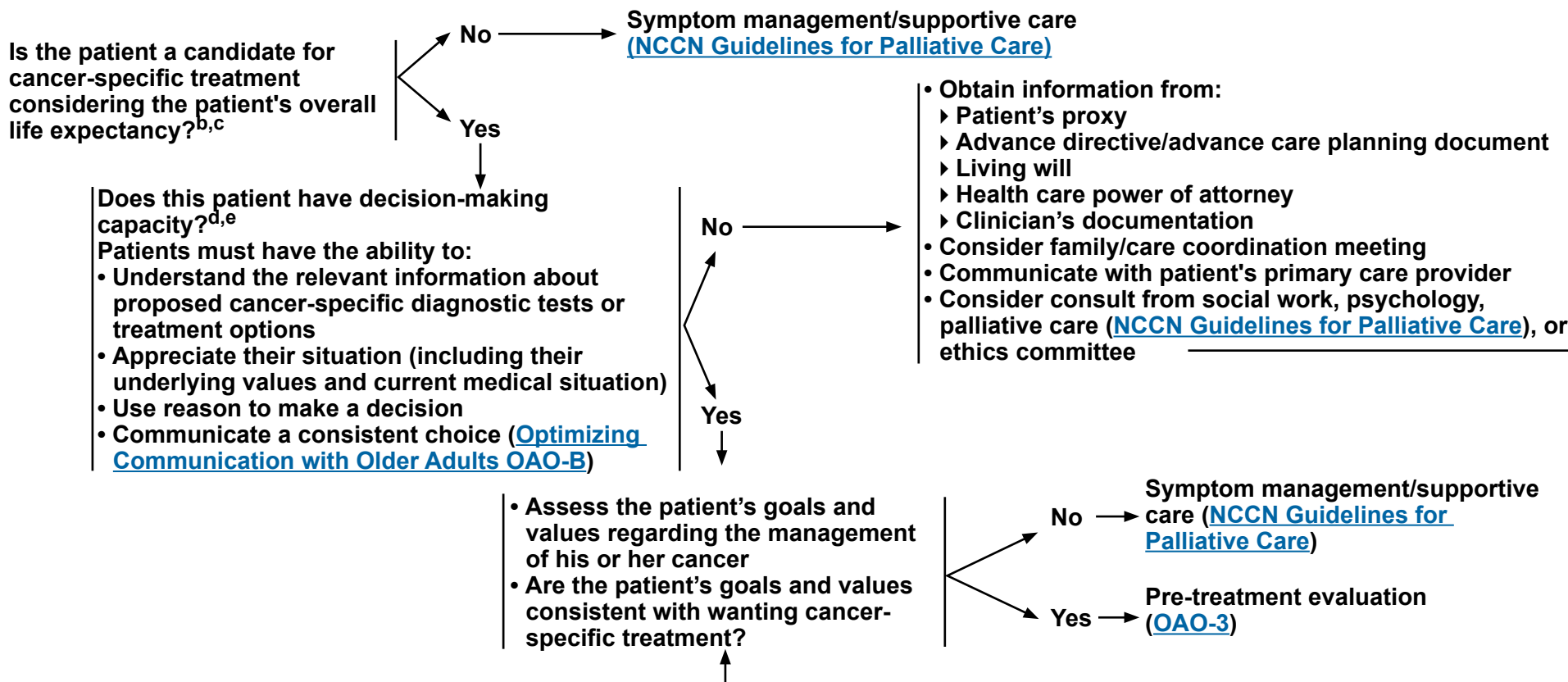
- There are unique issues to consider when caring for an older adult with cancer.
- The biologic characteristics of certain cancers and their responsiveness to therapy may be different in older patients compared to their younger counterparts.
- The psychologic and psychosocial changes associated with aging may impact an older adult's ability to tolerate cancer therapy and should be considered in the treatment decision-making process. See [NCCN Guidelines for Distress Management](#).
- Advanced age alone should not be the only criterion to preclude effective treatment that could improve quality of life (QOL) or lead to a survival benefit in older patients.
- Multidisciplinary team management, patient-specific treatment approach with shared decision-making, and palliative/supportive care for symptom management should be an integral part of cancer care in older adults. See [NCCN Guidelines for Supportive Care](#) and [NCCN Guidelines for Palliative Care](#).
- These age-related issues form the basis for the development of NCCN Guidelines for Older Adult Oncology that address special considerations in older patients with cancer.

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APPROACH TO SHARED DECISION-MAKING IN THE OLDER ADULT PRIOR TO CANCER-SPECIFIC TREATMENT^a



^a Assessment of the patient's goals and objectives with regard to cancer diagnosis should be completed prior to initiation of cancer-specific treatment. Supportive and palliative care assessment is recommended for any older adult with cancer.

^b Life expectancy calculators are available at www.e prognosis.com. Note that these calculators are used to determine anticipated life expectancy (independent of the cancer). They could be utilized in clinical decision-making to weigh whether the cancer is likely to shorten the patient's life expectancy or whether the patient is likely to become symptomatic from cancer during anticipated life expectancy.

^c [Life Expectancy of General Population \(OAO-A\)](#).

^d Sessums LL, et al. JAMA 2011;306:420-427.

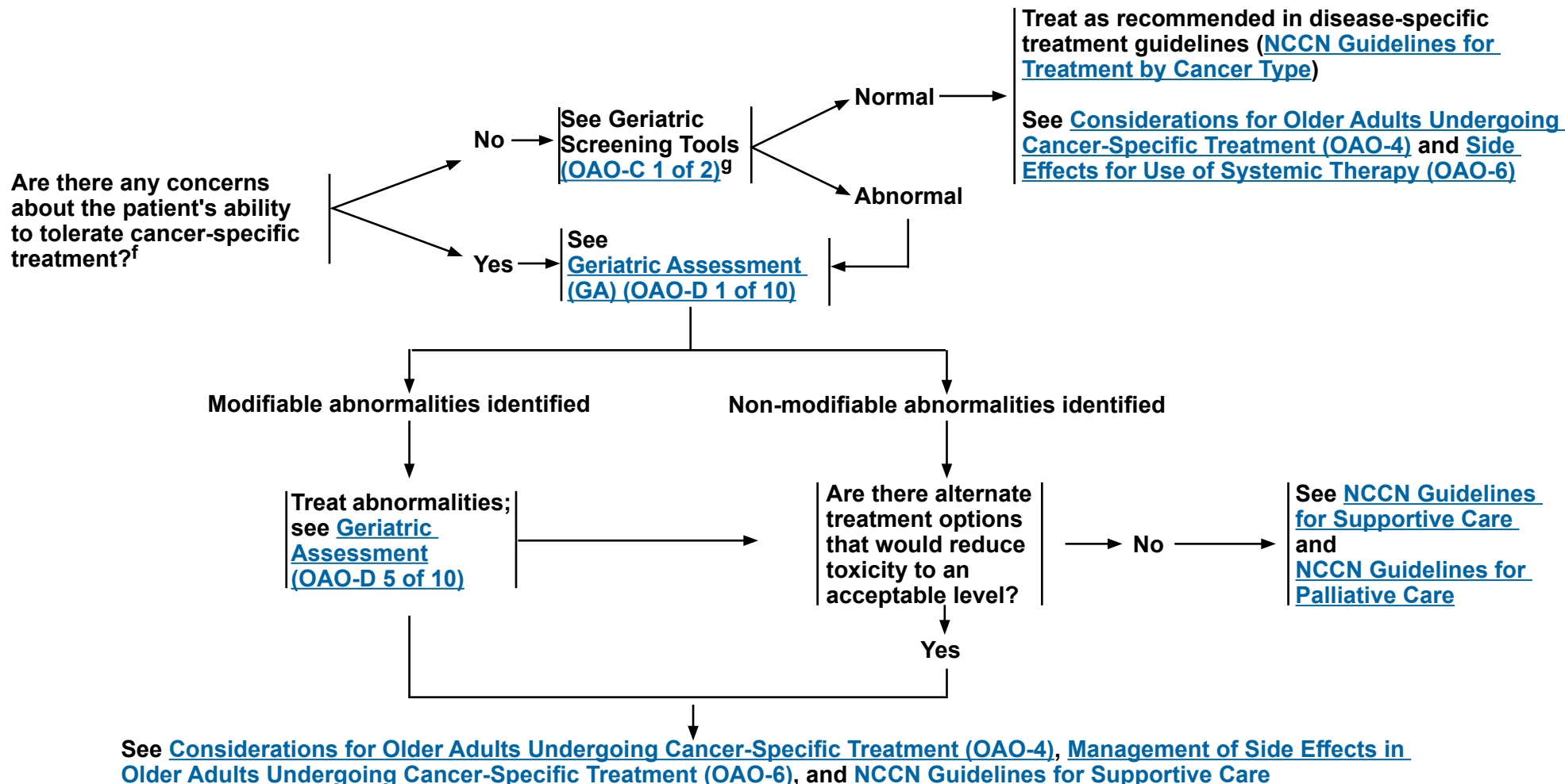
^e McKoy JM, et al. J Natl Compr Canc Netw 2014;12:138-144.

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PRE-TREATMENT EVALUATION^a



^a Assessment of the patient's goals and objectives with regard to cancer diagnosis should be completed prior to initiation of cancer-specific treatment. Supportive and palliative care assessment is recommended for any older adult with cancer ([OAO-2](#)).

^f Concerns can come from the patient, family, or clinician and can be related to the patient's performance status and/or comorbidities.

^g Multiple screening tools have been tested and validated in this setting. Selected geriatric screening tools that have been used to determine if a GA would be beneficial for older patients with cancer are listed on [OAO-C 1 of 2](#).

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**CONSIDERATIONS FOR OLDER ADULTS UNDERGOING CANCER-SPECIFIC TREATMENT^a****General Considerations**

- Patient's goals and objectives should be assessed in context with life expectancy; comorbidities; cognitive, functional, psychological/psychosocial, and nutritional status; aggressiveness of the disease; and treatment approach ([OAO-3](#)).
- There are data to suggest correlation between low social support and a higher risk for mortality. In patients with low levels of social support, consider referral to social work and/or case management to explore home supports and community resources.
- Multidisciplinary team management, patient-specific treatment approach with shared decision-making, and palliative/supportive care for symptom management should be an integral part of cancer care in older adults. See [NCCN Guidelines for Supportive Care](#) and [NCCN Guidelines for Palliative Care](#).
- Age-Friendly Health Systems provide a set of four evidence-based elements of high-quality care to all older adults known as the 4Ms.¹
 - ▶ **What Matters most:** Care is aligned with individual goals and preferences
 - ▶ **Mobility:** Move safely and maintain function
 - ▶ **Medication:** Treatment is necessary and non-redundant
 - ▶ **Mentation:** Prevent, identify, treat, and manage dementia, depression, and delirium.

Specific Considerations by Treatment Type

Surgery →

- Chronologic age is not the primary consideration for surgical risk²; all older adults undergoing surgery should undergo an assessment for components of frailty including comorbidities, cognition, mobility, functional status, and nutrition.
- The [American College of Surgeons \(ACS\) Geriatric Surgery Verification \(GSV\) Program](#) provides a framework for hospitals to take an interdisciplinary approach to continuously optimize surgical care for older adults. The GSV Program includes 32 standards to improve surgical care for older adults with an emphasis on goals of care and shared decision-making, assessment of geriatric-specific vulnerabilities (eg, cognition, mobility), and interdisciplinary postoperative care.³
- The [ACS National Surgical Quality Improvement Program Surgical Risk Calculator](#) includes both geriatric-specific predictors and geriatric-specific outcomes; the ACS Surgical Risk Calculator can be a useful tool for sharing patient-specific predicted outcomes after surgery and facilitating a more informed discussion regarding risks of surgery.⁴
- Delirium is preventable and the most common postoperative complication in older adults; the American Geriatrics Society (AGS) practice guideline on postoperative delirium in older adults covers the topic areas of delirium risk factors, diagnosis and screening, prevention, medical evaluation, and pharmacologic treatment.^{5,6} See [OAO-F 2 of 4](#).

^a Assessment of the patient's goals and objectives with regard to cancer diagnosis should be completed prior to initiation of cancer-specific treatment. Supportive and palliative care assessment is recommended for any older adult with cancer ([OAO-2](#)).

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[References](#)

**CONSIDERATIONS FOR OLDER ADULTS UNDERGOING CANCER-SPECIFIC TREATMENT^a****Radiation
therapy⁷⁻¹⁵**

- Improvements in radiation therapy techniques including intensity-modulated radiation therapy (IMRT), image-guided radiation therapy (IGRT), and stereotactic ablative radiotherapy (SABR) have improved the tolerability and therapeutic ratio of radiation therapy in older adults.
- Considerations of older patients undergoing radiation therapy should be informed by the benefits versus risks based on the anatomic site being radiated and the dose/fractionation chosen. Chronologic age by itself should not exclude patients from evaluation for curative radiation therapy.
- Use caution with concurrent chemoradiation therapy. Dose modification of chemotherapy or chemoradiation, additional supportive services, and more frequent monitoring may be necessary. See disease-specific [NCCN Guidelines for Treatment by Cancer Type](#).
- Hypofractionation and SABR may be considered to decrease the number of treatments, especially in patients who are frail and/or less mobile.
- Local ablative radiation therapy should be considered as an adjunct or alternative to systemic therapy in older adults with oligometastatic disease.

Chemotherapy

- Chemotherapy toxicity risk calculators (predominantly solid tumors)¹⁶
 - ▶ Cancer and Aging Research Group (CARG) Chemo Toxicity Calculator (http://www.mycarg.org/Chemo_Toxicity_Calculator).
 - ▶ Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score¹⁷.
 - ▶ Cancer and Aging Research Group-Breast Cancer (CARG-BC) score for older adults (for adjuvant/neoadjuvant therapy only) (https://www.cancercalc.com/carg_bc.php).¹⁸

Immunotherapy¹⁹⁻²¹

- Older adults are underrepresented in clinical trials studying immunotherapy across multiple cancers. Most subgroup analyses and retrospective studies report a similar clinical benefit in older and younger patients, with some concerns for increase in toxicity rates.

Targeted therapy

See [NCCN Guidelines for Treatment by Cancer Type](#)

**Chimeric antigen
receptor (CAR)
T-cell therapy**

- CAR T-cell therapy has been shown to be an effective therapeutic option for older adults with similar response rates, and age should not be an absolute contraindication for the use of these therapies for these patients. However, older adults, especially those who are frail or unfit, may have a higher incidence of neurologic toxicities and require close monitoring ([NCCN Guidelines for the Management of Immunotherapy-Related Toxicities](#)).²²⁻²⁵

^a Assessment of the patient's goals and objectives with regard to cancer diagnosis should be completed prior to initiation of cancer-specific treatment. Supportive and palliative care assessment is recommended for any older adult with cancer ([OAO-2](#)).

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[References](#)

OAO-5

**MANAGEMENT OF COMMON SIDE EFFECTS IN OLDER ADULTS UNDERGOING CANCER-SPECIFIC TREATMENT^a**

Diarrhea	NCCN Guidelines for Palliative Care
Constipation	NCCN Guidelines for Palliative Care
Nausea/Vomiting	NCCN Guidelines for Antiemesis and NCCN Guidelines for Palliative Care
Mucositis	<ul style="list-style-type: none"> • Early hospitalization is needed for patients with mucositis who also develop dysphagia/diarrhea. • Provide nutritional support. See NCCN Task Force: Prevention and Management of Mucositis in Cancer Care.
Bone marrow suppression	NCCN Guidelines for Hematopoietic Growth Factors
Neurotoxicity	<ul style="list-style-type: none"> • Monitor hearing loss and avoid neurotoxic agents if significant hearing loss is present. • Monitor cerebellar function if treated with high-dose cytarabine. • Monitor for peripheral neuropathy. • Monitor for cognitive dysfunction (OAO-F).
Falls	<ul style="list-style-type: none"> • Periodic assessment of history of falls, balance, and gait difficulties is recommended for all patients as fall risk may change over time²⁶ (OAO-E). • The use of early and preventive use of durable medical equipment and in-home safety evaluations is recommended for patients at high risk for falls.
Cardiac toxicity	<ul style="list-style-type: none"> • Monitor for symptomatic or asymptomatic congestive heart failure (CHF). <ul style="list-style-type: none"> ▶ Caution with use of anthracyclines; consider alternative treatment dosing schedule or treatment as appropriate per disease site (NCCN Guidelines for Treatment of Cancer by Site). ▶ Caution with use of trastuzumab (among patients with normal left ventricular ejection fraction [LVEF], risk factors for CHF include older age, receipt of an anthracycline-based regimen, baseline LVEF of 50%–54%, coronary artery disease, hypertension, and weekly trastuzumab administration) (see SCARDIO-1, SCARDIO-2, and SCARDIO-3 in NCCN Guidelines for Survivorship).²⁷
Renal toxicity	<ul style="list-style-type: none"> • Serum creatinine is not a good indicator of renal function in older adults. Calculation of estimated creatinine clearance is recommended to assess renal function and adjust dose to reduce systemic toxicity.
Insomnia (OAO-G)	<ul style="list-style-type: none"> • Benzodiazepines or other sedative-hypnotics should not be used as first-line treatment for insomnia in older adults²⁸; non-pharmacologic methods such as cognitive behavioral therapy (CBT) and lifestyle modifications are preferred (Sleep Disorders in NCCN Guidelines for Survivorship).
Immune-related adverse events (irAEs)	<ul style="list-style-type: none"> • High-dose steroids for the management of treatment-related toxicities must be used with caution in older patients as it may worsen other comorbidities or cognitive function. • NCCN Guidelines for the Management of Immunotherapy-Related Toxicities

^a Assessment of the patient's goals and objectives with regard to cancer diagnosis should be completed prior to initiation of cancer-specific treatment. Supportive and palliative care assessment is recommended for any older adult with cancer ([OAO-2](#)).

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[References](#)

OAO-6

**REFERENCES**

- 1 <https://www.ihl.org/Engage/Initiatives/Age-Friendly-Health-Systems/Pages/default.aspx>.
- 2 Montroni I, Ugolini G, Saur NM, et al. Quality of life in older adults after major cancer surgery: The GOSAFE International Study. *J Natl Cancer Inst* 2022;114:969-978.
- 3 The American College of Surgeons Geriatric Surgery Verification Program. Available at: <https://www.facs.org/Quality-Programs/geriatric-surgery>. Accessed December 16, 2020.
- 4 Hornor MA, Ma M, Zhou L, et al. Enhancing the American College of Surgeons NSQIP Surgical Risk Calculator to predict geriatric outcomes. *J Am Coll Surg* 2020;230:88-100.
- 5 American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults. American Geriatrics Society abstracted clinical practice guideline for postoperative delirium in older adults. *J Am Geriatr Soc* 2015;63:142-150.
- 6 American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults. Postoperative delirium in older adults: best practice statement from the American Geriatrics Society. *J Am Coll Surg* 2015;220:136-148.
- 7 Popescu T, Karlsson U, Vinh-Hung V, et al. Challenges facing radiation oncologists in the management of older cancer patients: Consensus of The International Geriatric Radiotherapy Group. *Cancers (Basel)* 2019;11:371.
- 8 Amini A, Morris L, Ludmir EB, et al. Radiation therapy in older adults with cancer: A critical modality in geriatric oncology. *J Clin Oncol* 2022;40:1806-1811.
- 9 Lancellotta V, Kovács G, Tagliaferri L, et al. Age is not a limiting factor in interventional radiotherapy (brachytherapy) for patients with localized cancer. *Biomed Res Int* 2018;2018:2178469.
- 10 Lee CH. Assessment of tumor volume change and movement during stereotactic body radiation therapy (SBRT) lung cancer: is adaptive radiation therapy (ART) necessary? *Medical Physics* 2015;42:3306.
- 11 Batenburg MCT, Bartels M, Maarse W, et al. Factors associated with late local radiation toxicity after post-operative breast irradiation. *Breast J* 2022;2022:6745954.
- 12 Wu YH, Yang WC, Hu YW, et al. Definitive radiotherapy for older patients with prostate cancer: experience of a medical center in Taiwan. *Sci Rep* 2017;7:13880.
- 13 O'Donovan A, Morris L. Palliative radiation therapy in older adults with cancer: age-related considerations. *Clin Oncol (R Coll Radiol)* 2020;32:766-774.
- 14 Extermann M, Chetty IJ, Brown SL, et al. Predictors of toxicity among older adults with cancer. *Semin Radiat Oncol* 2022;32:179-185.
- 15 Morse RT, Ganju RG, Gan GN, et al. Sarcopenia and treatment toxicity in older adults undergoing chemoradiation for head and neck cancer: identifying factors to predict frailty. *Cancers (Basel)* 2022;14:2094.
- 16 Ortland I, Mendel Ott M, Kowar M, et al. Comparing the performance of the CARG and the CRASH score for predicting toxicity in older patients with cancer. *J Geriatr Oncol* 2020;11:997-1005.
- 17 Extermann M, Boler I, Reich RR, et al. Predicting the risk of chemotherapy toxicity in older patients: the Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score. *Cancer* 2012;118:3377-3386.
- 18 Magnuson A, Sedrak MS, Gross CP, et al. Development and validation of a risk tool for predicting severe toxicity in older adults receiving chemotherapy for early-stage breast cancer. *J Clin Oncol* 2021;39:608-618.
- 19 Yang F, Markovic SN, Molina JR, et al. Association of sex, age, and Eastern Cooperative Oncology Group Performance Status with survival benefit of cancer immunotherapy in randomized clinical trials: A systematic review and meta-analysis. *JAMA Netw Open* 2020;3:e2012534.
- 20 Luciani A, Ghidini A, Dottorini L, Petrelli. Safety and effectiveness of immune checkpoint inhibitors in older patients with cancer: a systematic review of 48 real-world studies. *Drugs Aging* 2021;38:1055-1065.

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REFERENCES

- ²¹ Nebhan CA, Cortellini A, Ma W, et al. Clinical outcomes and toxic effects of single-agent immune checkpoint inhibitors among patients aged 80 years or older with cancer: a multicenter international cohort study. *JAMA Oncol* 2021;7:1856-1861.
- ²² Neelapu SS, Jacobson CA, Oluwole OO, et al. Outcomes of older patients in ZUMA-1, a pivotal study of axicabtagene ciloleucel in refractory large B-cell lymphoma. *Blood* 2020;135:2106-2109.
- ²³ Bishop MR. The benefit of CAR T cells in older patients. *Blood* 2020;135:2020-2021.
- ²⁴ Zhang H, Liu M, Li Q, et al. Evaluation of the safety and efficacy of humanized anti-CD19 chimeric antigen receptor T-cell therapy in older patients with relapsed/refractory diffuse large B-cell lymphoma based on the comprehensive geriatric assessment system. *Leuk Lymphoma* 2022;63:353-361.
- ²⁵ Sehgal A, Hoda D, Riedell PA, et al. Lisocabtagene maraleucel as second-line therapy in adults with relapsed or refractory large B-cell lymphoma who were not intended for haematopoietic stem cell transplantation (PILOT): an open-label, phase 2 study. *Lancet Oncol* 2022;23:1066-1077.
- ²⁶ Tinetti ME. Clinical practice. Preventing falls in elderly persons. *N Engl J Med* 2003;348:42-49.
- ²⁷ Chavez-MacGregor M, Zhang N, Buchholz TA, et al. Trastuzumab-related cardiotoxicity among older patients with breast cancer. *J Clin Oncol* 2013;31:4222-4228.
- ²⁸ American Geriatrics Society 2023 updated AGS Beers Criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc* 2023;71:2052-2081.

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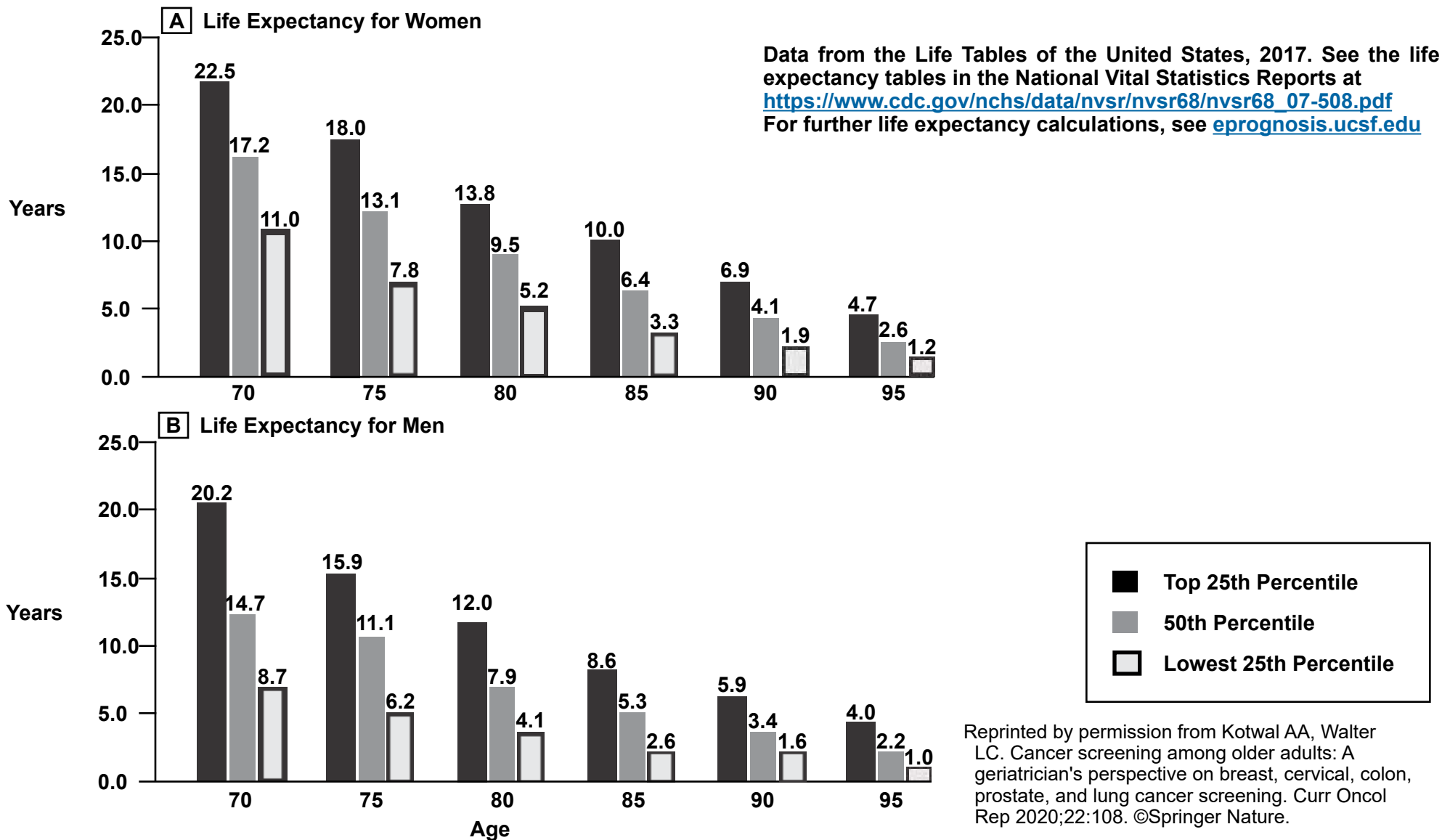


NCCN Guidelines Version 1.2024

Older Adult Oncology

LIFE EXPECTANCY OF GENERAL POPULATION

UPPER, MIDDLE, AND LOWER QUARTILES OF OVERALL AGE-SPECIFIC LIFE EXPECTANCY FOR WOMEN AND MEN



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**OPTIMIZING COMMUNICATION WITH OLDER ADULTS^a****Assess barriers to optimal communication:**

- Assess for cognitive impairment ([OAO-F](#))
- Optimize vision – glasses if needed
- Optimize hearing – hearing aid, amplifying device (eg, pocket talker, provision of American Sign Language translators)
 - Ask the patient how best to communicate, and if hearing is better in one ear or the other
 - Speak toward the better ear and use a lower-pitched voice; minimize background noise
- Avoid jargon (eg, instead of “benign” use “not cancer” or instead of “metastasized” use “the cancer has spread”)
- Offer to include family and/or caregiver(s)

Written materials:

- Write materials at the 5th grade level
- Use a large font (14 pt or larger)
- Use pictures that enhance the text
- Use black ink on white paper to optimize contrast

Oral communication:

- Have the patient sit with his/her back to a wall (to help reflect sound)
- Face the patient when speaking, speak slowly and distinctly; don't shout
- Rephrase rather than repeat
- Pause at the end of phrases or ideas
- For major concepts (prognosis, expected side effects, outcomes of treatment, and informed consent) always use the “teach back” (see [Teach-Back](#)) or “teach goal” method, by querying the patient for understanding. Use questions such as: “I just gave you a lot of information and that can be confusing or a lot to absorb at once. Can you tell me in your own words what this chemotherapy will do for you/ how you will take your medicine, etc?”
- After each key concept, topic, or instruction, stop and ask, “What questions do you have?”
- Use a black board/white board or written materials to reinforce key concepts.
- Recognize the presence of, and avoid the use of, “elderspeak,” a form of communication used with older adults that is similar to “baby-talk” and may impact clinician-patient interactions and result in poor patient outcomes.^b

^a With permission from Reuben DB, Herr KA, Pacala JT, et al. Geriatrics At Your Fingertips: 2016, 18th Edition. New York: The American Geriatrics Society; 2016.

^b Corwin AI. Overcoming elderspeak: A qualitative study of three alternatives. Gerontologist 2018;58:724-729.

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GERIATRIC SCREENING TOOLS

Geriatric screening tools are used to identify older adults with cancer who would benefit from a Geriatric Assessment (GA) ([OAO-D 1 of 10](#)).

- Abbreviated Comprehensive Geriatric Assessment (aCGA)^{1,2}
- Barber Questionnaire³
- Fried Frailty Criteria^{4,5}
- Geriatric 8 (G-8) Questionnaire^{6,7}
- Groningen Frailty Index²
- Senior Adult Oncology Program (SAOP) 2^{8,9}
- Triage Risk Screening Tool (TRST)¹⁰
- Vulnerable Elders Survey-13 (VES-13)^{11,12,13}
- Self-Rated Health (SRH)¹⁴

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REFERENCES

- 1 Overcash JA, Beckstead J, Moody L, et al. The abbreviated comprehensive geriatric assessment (aCGA) for use in the older cancer patient as a prescreen: scoring and interpretation. *Crit Rev Oncol Hematol* 2006;59:205-210.
- 2 Kellen E, Bulens P, Deckx L, et al. Identifying an accurate pre-screening tool in geriatric oncology. *Crit Rev Oncol Hematol* 2010;75:243-248.
- 3 Molina-Garrido MJ, Guillen-Ponce C. Comparison of two frailty screening tools in older women with early breast cancer. *Crit Rev Oncol Hematol* 2011;79:51-64.
- 4 Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56:M146-M156.
- 5 Walston J, Buta B, Xue QL. Frailty screening and interventions: considerations for clinical practice. *Clin Geriatr Med* 2018;34:25-38.
- 6 van Walree IC, Scheepers E, van Huis-Tanja L, et al. A systematic review on the association of the G8 with geriatric assessment, prognosis and course of treatment in older patients with cancer. *J Geriatr Oncol* 2019;10:847-858.
- 7 Kenis C, Bron D, Libert Y, et al. Relevance of a systematic geriatric screening and assessment in older patients with cancer: results of a prospective multicentric study. *Ann Oncol* 2013;24:1306-1312.
- 8 Russo C, Giannotti C, Signori A, et al. Predictive values of two frailty screening tools in older patients with solid cancer: a comparison of SAOP2 and G8. *Oncotarget* 2018;9:35056-35068.
- 9 Extermann M. Evaluation of the senior cancer patient: Comprehensive geriatric assessment and screening tools for the elderly. *Handbook of cancer in the senior patient*. Informa Healthcare 2010; 2010:13-21.
- 10 Erden A, Merih Y, Ozlem K, et al. Evaluation of elderly patients with hematological malignancies by two different geriatric risk scoring systems: G8 and Flemish version of the Triage Risk Screening Tool (FTRST). *Blood* 2018;132:5902.
- 11 Mohile SG, Bylow K, Dale W, et al. A pilot study of the vulnerable elders survey-13 compared with the comprehensive geriatric assessment for identifying disability in older patients with prostate cancer who receive androgen ablation. *Cancer* 2007;109:802-810.
- 12 Luciani A, Ascione G, Bertuzzi C, et al. Detecting disabilities in older patients with cancer: comparison between comprehensive geriatric assessment and vulnerable elders survey-13. *J Clin Oncol* 2010;28:2046-2050.
- 13 Owusu C, Koroukian SM, Schluchter M, et al. Screening older cancer patients for a Comprehensive Geriatric Assessment: A comparison of three instruments. *J Geriatr Oncol* 2011;2:121-129.
- 14 Giri S, Mir N, Al-Obaidi M, et al. Use of single-item self-rated health measure to identify frailty and geriatric assessment-identified impairments among older adults with cancer. *Oncol* 2022;27:e45-e52.

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GERIATRIC ASSESSMENT (GA)

GA is a multidisciplinary, in-depth evaluation that assesses the objective health of the older adult while evaluating multiple domains, which may affect cancer prognosis and treatment choices and tolerance. Appropriate use of geriatric screening tools and/or GA enables physicians to develop a coordinated plan for cancer treatment and to guide interventions tailored to the individual patient.

Reasons to Perform GA^{1,2}

- GA can be helpful in re-assessing the patient's status throughout therapy.
- GA can reveal/detect reversible geriatric problems not found by routine oncology care.
- GA can predict risk of toxicity/adverse effects from cancer treatment.
- GA has important prognostic information that can be helpful in estimating life expectancy, which is of paramount importance when making treatment decisions.
- GA-guided care can reduce toxicity, and allows for targeted intervention, which can improve QOL and adherence to therapy.^{3,4}
- GA can be helpful in improving communication.⁵

Collaboration Between Geriatric Trained Clinician and Oncologist in the Care of an Older Patient with Cancer

Older adults may benefit from a referral to a geriatric trained clinician for assessment of vulnerability prior to cancer treatment, to develop a coordinated care plan with the oncologist and/or to manage geriatric syndromes that could jeopardize outcomes of cancer treatment. The geriatric trained clinician thus may be able to assist the oncologist in optimizing the management of the non-cancer aspects of the patient's care, which in turn may enable more effective delivery of direct cancer care. Consider consultation with a geriatric trained clinician for the following:

- Cognitive impairment
 - Dementia/delirium
 - Decision-making capacity evaluation
 - Life expectancy, advance directive/advance care planning, or guardianship ([NCCN Guidelines for Palliative Care](#))
- Functional or physical impairment, mobility issues, or disability
 - Falls evaluation and/or advice on falls prevention
 - Promote independent living or supportive living
- Multimorbidity including vision and hearing impairments

Medication Management

- Polypharmacy evaluation
- When considering a high-risk procedure, such as:
 - Chemotherapy and radiotherapy
 - Hematopoietic cell transplantation
 - Complex surgeries (eg, cystectomy)
- Presence of geriatric syndromes such as frailty, osteoporosis, depression, pressure ulcers, urinary incontinence, neglect or abuse, failure to thrive, or sarcopenia
- Weight loss (≥5% unintentional weight loss in last 3 months) and anorexia
- Caregiver support
- Assistance with social support resources

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GERIATRIC ASSESSMENT (GA)^a

- GA can be performed in a number of ways, the most extensive being with a geriatric trained clinician conducting a full assessment. Alternatively, there are tools that allow the clinician and/or patient to perform these assessments as listed below.
- Patient's wishes/goals and objectives with regard to his/her cancer diagnosis should be assessed prior to any treatment decision. Supportive and palliative care assessment is recommended for all older adults with cancer. See [NCCN Guidelines for Supportive Care](#) and [NCCN Guidelines for Palliative Care](#).

Domain	Assessment Tools ^b /Description	Additional Assessments/Potential Interventions
Self-reported Function and Mobility (OAO-D, 6 of 10)	Activities of Daily Living (ADL) • Measures limitations in physical function activities, including bathing and dressing ▶ Katz Index of Independence in Activities of Daily Living (ADL) ▶ OARS (Older Americans Resources and Services)	<ul style="list-style-type: none"> • Occupational therapy (OT) and physical therapy (PT) referral • Physical medicine & rehabilitation referral • Home safety evaluation health care • Promote physical activity and exercise • Referral to geriatric trained clinician or primary care physician
	Instrumental Activities of Daily Living (IADL) • Measures ability to complete activities required to maintain independence ranging from making telephone calls to money management ▶ OARS (Older Americans Resources and Services) ▶ Lawton-Brody Instrumental Activities of Daily Living (IADL) Scale	
	Falls (OAO-E) • Number of falls within the last 6 months	
Objective Function and Mobility (OAO-E)	Time it takes for individuals to stand up, walk 10 feet, return to chair, and sit back down Timed "Up and Go" (TUG)	
	Assesses functional mobility Timed 10-Meter Walk Test	
	Short Physical Performance Battery (SPPB) Evaluation of lower extremity functioning	
	Physical Performance Status (Refer to Karnofsky or Eastern Cooperative Oncology Group [ECOG])	

Adapted with permission from Mohile SG, Velarde C, Hurria A, et al. J Natl Compr Canc Netw 2015;13:1120-1130.

^a Completion of the proposed GA will take an average of 20 minutes. Alternative tools that could be utilized are listed in the domain-specific section.

^b All of these assessments can be performed in less than 5 minutes.

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[Continued](#)

GERIATRIC ASSESSMENT (GA)^a

Domain	Assessment Tools ^b /Description	Additional Assessments/Potential Interventions
Comorbidity ^c	<ul style="list-style-type: none"> Assess the presence or absence of comorbidities <ul style="list-style-type: none"> Charlson Comorbidity Index (CCI) Cumulative Illness Rating Scale-Geriatric (CIRS-G) OARS Questionnaire^{6,7} 	<ul style="list-style-type: none"> Optimize each medical condition prior to therapy Coordinate with primary care physician and other specialists Evaluation of life expectancy (Life Expectancy Table)
	<ul style="list-style-type: none"> Assess different categories of organ dysfunction and non-relapsed mortality risk <ul style="list-style-type: none"> Hematopoietic Cell Transplantation-Specific Comorbidity Index (HCT-CI) 	
Social Functioning and Support (OAO-D 6 of 10)	<ul style="list-style-type: none"> Measure the availability of social support and engagement in physical or social activities <ul style="list-style-type: none"> MOS Social Support Survey 	<ul style="list-style-type: none"> Refer to social work for: <ul style="list-style-type: none"> Transportation assistance Financial toxicity⁸ Home health care Support groups Food/housing insecurity Caregiver status assessment Elder abuse screening; ask the patient, "Do you feel safe at home?" Language barrier and need for interpreter support Medication assistance programs, change in level of care, facilitations to assisted living, respite care, skilled nursing facilities, arrangement to local agencies on aging and community resources Home safety evaluation/referral for medical alert devices Refer to psychiatry/psychology Spiritual care
	<ul style="list-style-type: none"> Evaluate the self-reported availability of emotional/informational social support <ul style="list-style-type: none"> RAND Health Care Social Support Survey Instrument: Emotional/Informational Subscale 	
	<ul style="list-style-type: none"> Evaluate the self-reported availability of tangible physical social support <ul style="list-style-type: none"> RAND Health Care Social Support Survey: Tangible Subscale 	

Adapted with permission from Mohile SG, Velarde C, Hurria A, et al. J Natl Compr Canc Netw 2015;13:1120-1130. Abbreviation: MOS, Medical Outcomes Study.

^a Completion of the proposed GA will take an average of 20 minutes. Alternative tools that could be utilized are listed in the domain-specific section.

^b All of these assessments can be performed in less than 5 minutes.

^c Comorbidity is being used instead of multi-morbidity, since cancer is the predominant disease.

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GERIATRIC ASSESSMENT (GA)^a

Domain	Assessment Tools ^b /Description	Additional Assessments/Potential Interventions
Cognition (OAO-F)	<ul style="list-style-type: none"> Evaluate the level of cognitive impairment, if any <ul style="list-style-type: none"> Mini-Cog Mini-Mental State Examination (MMSE)^{d,e} Blessed Orientation Memory Concentration Test (BOMC) Montreal Cognitive Assessment (MoCA)^e Saint Louis University Mental Status Exam (SLUMS) 	<ul style="list-style-type: none"> Involve family/caregiver Assess/minimize potentially inappropriate medications (OAO-H) Prevent delirium (OAO-F 4 of 4) Assess capacity and ability to consent to treatment (OAO-2) Identify health care proxy/collaborative decision maker Provide written summary Provide cognitive testing/referral to neuropsychologist/geriatric trained clinician Consider referral for cognitive rehabilitation
Psychological	<ul style="list-style-type: none"> Evaluate for the risk for depression <ul style="list-style-type: none"> Geriatric Depression Scale-4 (GDS-4) Patient Health Questionnaire (PHQ-2 and PHQ-9)⁹ Evaluates the level of depression and anxiety experienced in the last month <ul style="list-style-type: none"> Mental Health Inventory (MHI-17) Evaluates the level of distress <ul style="list-style-type: none"> Distress thermometer (NCCN Guidelines for Distress Management) 	<ul style="list-style-type: none"> Provide complementary (non-pharmacologic) modalities such as guided imagery, meditation, relaxation, acupuncture, etc. Refer to integrative medicine Provide counseling by a qualified professional Refer to psychiatry/psychology Start medication to treat anxiety/depression Provide support programs Provide spiritual care Assess for substance and alcohol use disorder

Adapted with permission from Mohile SG, Velarde C, Hurria A, et al. J Natl Compr Canc Netw 2015;13:1120-1130.

^a Completion of the proposed GA will take an average of 20 minutes. Alternative tools that could be utilized are listed in the domain specific section.

^b All of these assessments can be performed in less than 5 minutes.

^d 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.

^e Licensing is required for using these tools.

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GERIATRIC ASSESSMENT (GA)^a

Domain	Assessment Tools ^b /Description	Additional Assessments/Potential Interventions
Nutrition^{2,10,11} (OAO-D, 7 of 10)	Body Mass Index (BMI) Weight (kg)/Height (m ²)	<ul style="list-style-type: none"> • Nutrition consult • Make specific dietary recommendations • Oral care • Supplemental nutrition • OT for assistive devices • Speech therapy and swallowing assessment • Oral and dental evaluation for dentures • Evaluation for appetite stimulants/nausea control/calorie/protein fluid recommendations/food insecurity (eg, local food banks, Meals on Wheels), treatment with dietary supplements
	Percent unintentional weight loss in last 6 months	
	Mini-Nutritional Assessment (MNA)[®] Validated self-reported tool that can identify older adults who are malnourished or at risk for malnutrition	
	Guide to Nutritional Intervention from NCI Nutrition in Cancer Care (PDQ)	
Medication Management¹²⁻¹⁵ (OAO-D, 8 of 10)	Medications Prescription and over-the-counter medication list	<ul style="list-style-type: none"> • Medication reconciliation with patient and other care providers • Discontinue inappropriate or unnecessary medications • Evaluate for drug-drug and drug-disease interactions • Evaluate for the use of supplements and herbal therapies
	2023 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults	
	Screening Tool of Older Persons' Prescriptions (STOPP)	
	Screening Tool to Alert to Right Treatment (START) criteria	
	Medication Appropriateness Index (MAI)	

Adapted with permission from Mohile SG, Velarde C, Hurria A, et al. J Natl Compr Canc Netw 2015;13:1120-1130.

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^b All of these assessments can be performed in less than 5 minutes.

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**GERIATRIC ASSESSMENT (GA)****Functional Status**

- **ADL - Self-feeding, dressing, continence, grooming, transferring, using the bathroom**
- **IADL - Using transportation, managing money, taking medications, shopping, preparing meals, doing laundry, doing housework, using the telephone**
- **Physical Performance Status (refer to Karnofsky or ECOG)**
- **Visual function and/or hearing impairment**
- **Falls and/or unstable gait**
 - ▶ **Falls are more common in older adults with cancer than those without cancer**
 - ▶ **Factors that have been prospectively associated with increased risk of subsequent falls in older adults with cancer include: prior falls, benzodiazepine use, cancer pain, and neurotoxic chemotherapy**
 - ▶ **In patients who are at risk, such as those who have experienced a fall in the last 6 months or if the patient is “afraid of falling,” consider the following evaluations:**
 - ◊ **Assessment of gait by evaluating gait speed¹⁶ or using the TUG test ([OAO-E](#))**
 - ◊ **Exercise promotion including PT or OT evaluation, as needed**
 - ◊ **Checking vitamin D levels and supplementing vitamin D if low**
 - ◊ **Referral to geriatrics or primary care physician**
 - ◊ **Home safety evaluation and home modifications as indicated**
 - ◊ **Medications that put patients at risk for adverse outcomes ([Medications Commonly Used for Supportive Care that Are of Concern in Older Patients \(OAO-H\)](#))**

Socioeconomic Considerations

Evaluate/assess for the following (refer to social work as appropriate):

- **Language barriers and need for interpreter support**
- **Cultural considerations**
- **Living conditions**
 - ▶ **Family/caregiver or social support**
 - ▶ **Income**
 - ▶ **Elder abuse**
 - ▶ **Safety at home**
- **Transportation barriers/access problems**
- **Food insecurity**
- **Financial toxicity (eg, underinsurance and/or high out-of-pocket costs)⁸**

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GERIATRIC ASSESSMENT (GA)

Nutritional Status

Patients with cancer are at risk for severe malnutrition that is underdiagnosed.¹⁷

- Poor nutritional status is associated with increased mortality and poor chemotherapy tolerance.
- Malnutrition among hospitalized patients with cancer is associated with increased length of stay.¹⁷
- ▶ Practical consideration to guide further nutritional assessment of patients at risk for malnutrition includes:
 - ◇ Unintentional weight loss of greater than 5% over 6 months.¹⁸ As per ASPEN guidelines, unintentional weight loss is considered: greater than or equal to 5% in 1 month, greater than or equal to 10% in 6 months.¹⁹
 - ◇ BMI of 22 or below
 - ◇ Weighing less than 80% of ideal body weight²⁰
 - ◇ Practical suggestions for evaluation of and treatment for optimizing nutrition among patients with cancer:
 - [Guide to Nutritional Intervention from NCI Nutrition in Cancer Care \(PDQ\)](#)
 - [MNA](#)[®]
 - ◇ Referral to speech and language pathologist to assess for swallowing issues

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**GERIATRIC ASSESSMENT (GA)**
MEDICATION MANAGEMENT

Medication Reconciliation^f: Reconcile medications at every visit, including prescription and over-the-counter medications, vitamins, and supplements.

Medication Review^{g,h,12-15,21-23}: Medication review is indicated with transitions of care, any initiation or change in oncologic treatment, change in comorbid disease management, or change in clinical condition.

- Does every medication match a known medical problem or chronic condition? Any deficiencies or duplications?
- Are the dosages appropriate for each medication for the patient's age, renal function, or liver function?
- Are there potential drug-drug or drug-disease interactionsⁱ or other adverse effects of the medication?
- Could a medication-related problem be responsible for current complaints or presenting problems?
- Can the medication regimen be simplified? Consider deprescribing as appropriate.
- Are there any less expensive alternative medications that are of equal utility?

Potential Inappropriate Prescribing

- Carefully review indications, duration of therapy, and dosage when using these medications or classes of medications that are not recommended for older adults. See [Medications Commonly Used for Supportive Care that Are of Concern in Older Patients \(OAO-H\)](#).
- Are there any high-risk/low-benefit or inappropriate medications?
- Use an evidenced-base instrument for the determination of a medication appropriateness: Beers Criteria,²⁴ STOPP,²⁵ START criteria,²⁶ MAI²⁷

Medication Adherence

- Always assess risk of non-adherence, especially when considering a treatment regimen that will include an oral agent.²⁸

- Risk factors for non-adherence in the older adult include:
 - ▶ Decreased propensity of older adults to ask questions about benefits and risks of treatments
 - ▶ Increased numbers of comorbidities and associated medications leading to regimen complexity, multiple providers, and/or multiple pharmacies
 - ▶ Side effects adversely affecting comorbidities
 - ▶ Prior experience with medication side effects
 - ▶ Acquisition barriers such as out-of-pocket costs, mobility/transportation difficulties, and lack of synchronized refill dates
 - ▶ Cognitive impairment
- Strategies to minimize non-adherence include:
 - ▶ Ask patient to bring in all bottles of prescribed, over-the-counter medications and supplements to review
 - ▶ Reduce regimen complexity, if possible
 - ▶ Consider financial burden: insurance coverage and out-of-pocket cost
 - ▶ Prioritize clinical pharmacist involvement in adherence management²⁹
 - ▶ Synchronize medication refills whenever possible³⁰
 - ▶ Prepare the patient regarding anticipated side effects to avoid inappropriate medication discontinuation and ensure that the patient and caregivers understand the benefits/rationale for the medication and the risks of not taking it³¹
 - ▶ Provide written instructions at the fifth-grade level^j and have them repeat back their understanding of how to take the medication, common side effects, and “when to worry” and “what to do if worried”
 - ▶ At each follow-up visit provide additional cues or reminders
 - ▶ Reinforce benefits and ask about side effects: if tolerable, stay the course; if intolerable, select an alternative

^f Medication reconciliation refers to the process of developing an accurate list of medications a patient is taking.

^g Medication review refers to the process of providing a structural, critical evaluation of a patient's medication list in order to optimize care and avoid harm.

^h Memorial Sloan Kettering Cancer Center Search About Herbs. Available at: <https://www.mskcc.org/cancer-care/diagnosis-treatment/symptom-management/integrative-medicine/herbs/search>.

ⁱ <http://medicine.iupui.edu/clinpharm/ddis/>

^j Confirm ability to read and comprehend written instructions (eg, vision, literacy).

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References

**GERIATRIC ASSESSMENT (GA)**
REFERENCES

- 1 Wildiers H, Heeren P, Puts M, et al. International Society of Geriatric Oncology consensus on geriatric assessment in older patients with cancer. *J Clin Oncol* 2014;32:2595-2603.
- 2 Hamaker M, Lund C, Te Molder M, et al. Geriatric assessment in the management of older patients with cancer - A systematic review (update). *J Geriatr Oncol* 2022;13:761-777.
- 3 Li D, Sun CL, Kim H, et al. Geriatric Assessment–Driven Intervention (GAIN) on chemotherapy-related toxic effects in older adults with cancer: a randomized clinical trial. *JAMA Oncol* 2021;7:e214158.
- 4 Mohile SG, Mohamed MR, Xu H, et al. Evaluation of geriatric assessment and management on the toxic effects of cancer treatment (GAP70+): a cluster-randomised study. *Lancet* 2021;398:1894-1904.
- 5 Mohile SG, Epstein RM, Hurria A, et al. Communication with older patients with cancer using geriatric assessment: A cluster-randomized clinical trial from the National Cancer Institute Community Oncology Research Program. *JAMA Oncol* 2020;6:196-204.
- 6 Williams GR, Deal AM, Lund JL, et al. Patient-reported comorbidity and survival in older adults with cancer. *Oncologist* 2018;23:433-439.
- 7 Klepin HD, Pitcher BN, Ballman KV, et al. Comorbidity, chemotherapy toxicity, and outcomes among older women receiving adjuvant chemotherapy for breast cancer on a clinical trial: CALGB 49907 and CALGB 361004 (alliance). *J Oncol Pract* 2014;10:e285-292.
- 8 de Souza JA, Yap BJ, Wroblewski K, et al. Measuring financial toxicity as a clinically relevant patient-reported outcome: The validation of the COmprehensive Score for financial Toxicity (COST). *Cancer* 2017;123:476-484.
- 9 Levis B, Sun Y, He C, et al. Accuracy of the PHQ-2 alone and in combination with the PHQ-9 for screening to detect major depression: Systematic review and meta-analysis. *JAMA* 2020;323:2290-2300.
- 10 Zhang X, Edwards BJ. Malnutrition in older adults with cancer. *Curr Oncol Rep* 2019;21:80.
- 11 Vellas B, Guigoz Y, Garry PJ, et al. The Mini Nutritional Assessment (MNA) and its use in grading the nutritional state of elderly patients. *Nutrition* 1999;15:116-122.
- 12 Nightingale G, Skonecki E, Boparai MK. The impact of polypharmacy on patient outcomes in older adults with cancer. *Cancer J* 2017;23:211-218.
- 13 Nightingale G, Pizzi LT, Barlow A, et al. The prevalence of major drug-drug interactions in older adults with cancer and the role of clinical decision support software. *J Geriatr Oncol* 2018;9:526-533
- 14 Kantilal K, Kantilal K, Nightingale et al. How-to guide for medication reviews in older adults with cancer: A young international Society of Geriatric Oncology and Nursing & Allied Health Interest Group initiative. *J Geriatr Oncol* 2022;13:1283-1286.
- 15 Mohamed MR, Ramsdale E, Loh KP, et al. Associations of polypharmacy and inappropriate medications with adverse outcomes in older adults with cancer: a systematic review and meta-Analysis. *Oncologist* 2020;25:94-108.
- 16 Studenski S, Perera S, Patel K, et al. Gait speed and survival in older adults. *JAMA* 2011;305:50-58.
- 17 Pressoir M, Desne S, Berchery D, et al. Prevalence, risk factors and clinical implications of malnutrition in French Comprehensive Cancer Centres. *Br J Cancer* 2010;102:966-971.
- 18 Fearon K, Strasser F, Anker SD, et al. Definition and classification of cancer cachexia: an international consensus. *Lancet Oncol* 2011;12:489-495.
- 19 White JV, Guenter P, Jensen G, et al. Consensus Statement: Academy of Nutrition and Dietetics and American Society for Parenteral and Enteral Nutrition. *JPEN J Parenter Enteral Nutr* 2012;36:275-283.
- 20 Dotan E, Tew WP, Mohile SG, et al. Associations between nutritional factors and chemotherapy toxicity in older adults with solid tumors. *Cancer* 2020;126:1708-1716.
- 21 Barlow A, Skonecki E, Barlow B et al. Interventions to reduce polypharmacy and optimize medication use in older adults with cancer. *J Geriatr Oncol* 2021;12:863-871.
- 22 Nightingale G, Hajjar E, Swartz K, et al. Evaluation of a pharmacist-led medication assessment used to identify prevalence of and associations with polypharmacy and potentially inappropriate medication use among ambulatory senior adults with cancer. *J Clin Oncol* 2015;33:1453-1459.
- 23 Mohamed MR, Ramsdale E, Loh KP, et al. Association of polypharmacy and potentially inappropriate medications with physical functional impairments in older adults with cancer. *J Natl Compr Canc Netw* 2021;19:267-274.
- 24 American Geriatrics Society 2023 Beers Criteria Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc* 2023;71:2052-2081.

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GERIATRIC ASSESSMENT (GA) REFERENCES

- ²⁵ Gallagher P, O'Mahony D. STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions): application to acutely ill elderly patients and comparison with Beers' criteria. *Age Ageing* 2008;37:673-679.
- ²⁶ Barry PJ, Gallagher P, Ryan C, O'Mahony D. START (screening tool to alert doctors to the right treatment)--an evidence-based screening tool to detect prescribing omissions in elderly patients. *Age Ageing* 2007;36:632-638.
- ²⁷ Samsa GP, Hanlon JT, Schmader KE, et al. A summated score for the medication appropriateness index: development and assessment of clinimetric properties including content validity. *J Clin Epidemiol* 1994;47:891-896.
- ²⁸ Mislav AR, Wildes TM, Kanesvaran R, et al. Adherence to oral cancer therapy in older adults: The International Society of Geriatric Oncology (SIOG) taskforce recommendations. *Cancer Treat Rev* 2017;57:58-66.
- ²⁹ Muluneh B, Schneider M, Faso A, et al. Improved adherence rates and clinical outcomes of an integrated, closed-loop, pharmacist-led oral chemotherapy management program. *J Oncol Pract* 2018;14:e324-e334.
- ³⁰ Lasala R, Santoleri F. Association between adherence to oral therapies in cancer patients and clinical outcome: A systematic review of the literature. *Br J Clin Pharmacol* 2022;88:1999-2018.
- ³¹ Puts MTE, Tu HA, Tourangeau A, et al. Factors influencing adherence to cancer treatment in older adults with cancer: a systematic review. *Ann Oncol* 2014;25:564-577.

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**FALLS ASSESSMENT AND INTERVENTIONS****Assessment of gait by evaluating gait speed or using the TUG test^{1,2,3} ([OAO-D, 2 of 10](#))**

- ▶ The TUG test is calculated as the time in seconds it takes a patient to stand up from a chair (without using his or her arms), walk 10 feet straight ahead, turn back, and return to the chair and sit down. The patient may use an assistive device, such as a cane or walker, but may not have assistance from another person.
- ▶ A normal TUG test score is less than 13 seconds. For patients with above-normal TUG test scores, consider comprehensive evaluation as indicated below.

ASSESSMENT	INTERVENTIONS
Assess proximal muscle strength	<ul style="list-style-type: none"> • Diagnose and treat underlying causes • Consider PT evaluation
Mobility aids assessment	<ul style="list-style-type: none"> • Assess for type, condition, usage technique, and fit of mobility aid • Consider referral for OT/PT evaluation • Physical medicine and rehabilitation referral
Check orthostatic blood pressure	<ul style="list-style-type: none"> • Diagnose and treat underlying causes • Review medications • Address salt intake, adequate hydration, and compensatory strategies (eg, elevating head of bed, rising slowly, using pressure stockings or an abdominal binder⁴)
Ask about vision changes	<ul style="list-style-type: none"> • Diagnose and treat underlying cause of vision changes • Consider referral to ophthalmologist • Consider neurologic evaluation • OT referral
Assess for neurologic changes	<ul style="list-style-type: none"> • Evaluate if cancer or cancer treatment-related and modify treatment if possible • Consider neurologic evaluation
Review medications	<ul style="list-style-type: none"> • See "Medication Management" (OAO-D, 8 of 10)
Environmental hazards	<ul style="list-style-type: none"> • Consider home safety evaluation • Educate patients to reduce risk (http://www.cdc.gov/HomeandRecreationalSafety/Falls/CheckListForSafety.html)
Footwear assessment	<ul style="list-style-type: none"> • Assess type, condition, and fit of shoes • Perform foot examination • Consider referral to podiatrist

¹ Pondal M, et al. J Geriatr Phys Ther 2008;31:57-63.² Lui MA, et al. Blood 2019;134:374-382.³ Vande Walle N, et al. BMC Geriatr 2014;14:135.⁴ Figueroa JJ, et al. Arch Phys Med Rehabil 2015;96:505-510; Fanciulli A, et al. Mov Disord Clin Pract 2015;3:156-160; Okamoto LE, et al. Hypertension 2016;68:418-426.**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.**



ASSESSMENT OF COGNITIVE FUNCTION^{1,2}

When to Assess for Cognitive Function	Recommendations
<p>Would impaired cognitive function affect the planning or delivery of care? (eg, impact life expectancy or risk/benefit, impact adherence to treatment plan)</p>	
<p>Is the medical team concerned about decision-making capacity? See OAO-2</p>	
<p>Does the patient have a history of recent delirium or late onset of depression?</p>	
<p>Does the medical team suspect impaired cognitive function?</p>	
<p>Has the patient or patient's family/caregiver suggested that the patient has impaired cognitive function?</p>	

¹ Cordell CB, Borson S, Boustani M, et al; Medicare Detection of Cognitive Impairment Workgroup. Alzheimer's Association recommendations for operationalizing the detection of cognitive impairment during the Medicare Annual Wellness Visit in a primary care setting. *Alzheimers Dement* 2013;9:141-150.

² Simpson JR. DSM-5 and neurocognitive disorders. *J Am Acad Psychiatry Law* 2014;42:159-164.

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[Continued](#)



ASSESSMENT OF COGNITIVE FUNCTION^{1,2,3}

	Mild Cognitive Impairment	Dementia	Delirium
Definition	An intermediate state between normal cognition and dementia characterized by: Subjective memory impairment Preserved general cognitive function Intact ability to perform daily functions	A progressive condition characterized by: Evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains Interference with ability to perform daily functions (ADL/IADL , OAO-D, 2 of 10)	Disturbance in attention and awareness: Onset over a short period of time (usually hours to days) Fluctuation during the course of the day See OAO-F 4 of 4 for risk factors and strategies for the prevention of delirium
Distinguishing Features	Subjective memory complaints and awareness of memory changes Preserved function	Progressive (not sudden) loss of multiple cognitive abilities Affects the ability to function independently	Acute onset Waxing and waning attention Associated with physiologic disturbances Increased in postoperative setting ⁴
Differential Diagnosis (confounding factors)	Central nervous system (CNS) metastases Psychiatric disease (depression, anxiety, apathy) Endocrine dysfunction (thyroid) Metabolic causes (B12 deficiency) Drug dependency (including alcohol) Medication related Sleep disturbance Common geriatric conditions (pain, infection, constipation)		

¹ Cordell CB, Borson S, Boustani M, et al; Medicare Detection of Cognitive Impairment Workgroup. Alzheimer's Association recommendations for operationalizing the detection of cognitive impairment during the Medicare Annual Wellness visit in a primary care setting. *Alzheimers Dement* 2013;9:141-150.

² Simpson JR. DSM-5 and neurocognitive disorders. *J Am Acad Psychiatry Law* 2014;42:159-164.

³ If you have concerns about decision-making capacity, see [\(OAO-2\)](#).

⁴ American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults. American Geriatrics Society abstracted clinical practice guideline for postoperative delirium in older adults. *J Am Geriatr Soc* 2015;63:142-150.

[Continued](#)

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ASSESSMENT OF COGNITIVE FUNCTION^{1,2,3}

	Mild Cognitive Impairment	Dementia	Delirium
Screening Tool	Clinical interview with cognitive (Mini-Cog), MMSE, ^{5,6} MoCA, ⁶ SLUMS , and functional (ADL/IADL , OAO-D, 2 of 10) assessment	Clinical interview with cognitive (Mini-Cog) and functional (ADL/IADL , OAO-D, 2 of 10) assessment	Confusion Assessment Method (CAM) ⁷
Further Evaluation	Reassess periodically and with major changes in condition or when considering changes to treatment plan If screening is abnormal, consult with a clinician experienced in cognitive evaluation	Consult with a clinician experienced in cognitive evaluation and treatment Neuropsychological testing may be indicated Evaluation: B12, thyroid-stimulating hormone (TSH), brain imaging See DIS-7 and DIS-8 in NCCN Guidelines for Distress Management	Evaluate and treat all potential causes of delirium If screening is abnormal consult with a clinician experienced in cognitive evaluation See DIS-7 and DIS-8 in NCCN Guidelines for Distress Management
Communication		Refer to guidance from the Alzheimer's Association: https://www.alz.org/help-support/caregiving/daily-care/communications .	

¹ Cordell CB, Borson S, Boustani M, et al; Medicare Detection of Cognitive Impairment Workgroup. Alzheimer's Association recommendations for operationalizing the detection of cognitive impairment during the Medicare Annual Wellness visit in a primary care setting. *Alzheimers Dement* 2013;9:141-150.

² Simpson JR. DSM-5 and neurocognitive disorders. *J Am Acad Psychiatry Law* 2014;42:159-164.

³ If you have concerns about decision-making capacity, see [\(OAO-2\)](#).

⁵ 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.

⁶ Licensing is required for using these tools.

⁷ Confusion Assessment Method. © 1988, 2003, Hospital Elder Life Program. All rights reserved. Adapted from: Inouye SK, et al. *Ann Intern Med* 1990;113:941-948.

[Continued](#)

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ASSESSMENT OF COGNITIVE FUNCTION^{1,2,3} Risk Factors For The Development of Delirium In Older Patients With Cancer^{8,9}

PREDISPOSING FACTORS	PRECIPITATING FACTORS	CANCER-RELATED FACTORS
Advanced Age	New psychoactive drugs	Primary CNS tumors
Preexisting Cognitive Impairment	Dehydration and/or electrolyte disturbance	Secondary CNS tumors: Brain or meningeal metastasis
Previous History of Delirium	Immobility	Para-neoplastic neurological syndromes
Polypharmacy	Constipation/fecal impaction	Toxicities from anticancer treatment: radiation to the brain, chemotherapy, immunotherapy
Sensory Impairment (vision, hearing)	Urinary retention/bladder catheters	Toxicities from chemotherapy support (eg, antihistamines, steroids, antiemetics, anxiolytics, opioids)
Functional Dependency	Malnutrition	
History of Alcohol Use Disorder	Pain	
Multiple Comorbid Conditions	Use of physical restrains	
Malnutrition	Severe illness (eg, sepsis, stroke)	

Strategies for Prevention of Delirium

- The strongest evidence supports the reduction of the common risk factors such as polypharmacy, sleep deprivation, immobility, visual and hearing impairment, malnutrition, and dehydration.
- Reduce psychoactive medications as a first step wherever possible.
- Reserve pharmacologic interventions for patients with severe agitation, which will result in interruption of essential medical therapies or poses a danger for self-injury; or for those with distressing psychotic symptoms (eg, hallucinations, delusions).
- Patients with one or more of these risk factors should receive non-pharmacologic interventions to address them.

Non-pharmacologic Interventions for the Treatment of Delirium

- Non-pharmacologic interventions are the cornerstone of delirium treatment.
- These interventions include:
 - Identification and elimination of factors contributing to delirium
 - Frequent reorientation
 - Involvement of family members
 - Symptom management; treat dehydration and constipation
 - Thorough medication review, promotion of mobility and sleep hygiene

¹ Cordell CB, Borson S, Boustani M, et al; Medicare Detection of Cognitive Impairment Workgroup. Alzheimer's Association recommendations for operationalizing the detection of cognitive impairment during the Medicare Annual Wellness visit in a primary care setting. *Alzheimers Dement* 2013;9:141-150.

² Simpson JR. DSM-5 and neurocognitive disorders. *J Am Acad Psychiatry Law* 2014;42:159-164.

³ If you have concerns about decision-making capacity, see [\(OAO-2\)](#).

⁸ Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. *Lancet* 2014;383:911-922.

⁹ Bush SH, Lawlor PG, Ryan K, et al. Delirium in adult cancer patients: ESMO Clinical Practice Guidelines. *Ann Oncol* 2018;29:iv143-iv165.

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INSOMNIA

- The AGS provides recommendations for the diagnosis, evaluation, and management of insomnia.
- Benzodiazepines or other sedative-hypnotics should not be used as first-line treatment for insomnia in older adults.^a
- Non-pharmacologic methods such as sleep hygiene, CBT, and lifestyle modifications are preferred.
- Patient should be cautioned that most over-the-counter sleep medications contain antihistamines and should not be used in older adults.
- If pharmacologic therapy is to be utilized, it is recommended for short-term use only with the lowest dose that is effective. The risks and benefits of the therapy should be discussed.^b
- Please note that if zolpidem is considered, the U.S. Food and Drug Administration (FDA) has advised that the recommended dose of zolpidem for females should be lowered from 10 mg to 5 mg for immediate-release products and from 12.5 mg to 6.25 mg for extended-release products.^c
- Patient information regarding optimizing sleep is available through the National Institute on Aging.^d
- See sleep medication recommendations ([OAO-H, 2 of 7](#)).

^a See American Geriatrics Society: Ten Things Clinicians and Patients Should Question (<http://www.choosingwisely.org/doctor-patient-lists/american-geriatrics-society/>).

^b See AGS Geriatrics Evaluation & Management Tools (GEMS): <http://www.americangeriatrics.org>.

^c See <https://www.fda.gov/drugs/drugsafety/ucm334041.htm>.

^d See <http://www.nia.nih.gov/health/publication/good-nights-sleep>.

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MEDICATIONS COMMONLY USED FOR SUPPORTIVE CARE THAT ARE OF CONCERN IN OLDER PATIENTS

Consider initiating all medications at the lowest possible dose and increase dose gradually (as tolerated).

Therapeutic Class/Medication(s)	Negative Effects/ Condition the Drug May Adversely Affect	Recommendation	Alternative(s)
<p>Corticosteroids (oral)^{1,2,3,4,5,6:}</p> <ul style="list-style-type: none"> • hydrocortisone • methylprednisolone • prednisone • prednisolone • dexamethasone 	<ul style="list-style-type: none"> • Weight gain • Muscle weakness • Agitation • Hyperglycemia/Diabetes • Cushing syndrome • Osteoporosis • Delirium • Insomnia • Increased risk of gastrointestinal (GI) bleed, infection, fracture, thromboembolism 	<ul style="list-style-type: none"> • When used for supportive care, carefully consider the dose and duration of therapy. • Use the lowest possible dose ideally for short-term therapy (1–3 weeks). • Short-term use as an adjuvant for pain or antiemetic, for spinal cord compression, increased intracranial pressure, and bowel obstruction is appropriate (when benefit outweighs risk). • For management of irAE, use the lowest possible effective dose. 	<p>When risk outweighs benefit:</p> <ul style="list-style-type: none"> • For pain, consider other adjuvant pain medications (eg, gabapentin,^a serotonin-norepinephrine reuptake inhibitor [SNRI] antidepressants,^b lamotrigine,^a topical lidocaine, as indicated by type of pain and response). • For nausea, consider alternative antiemetics (eg, serotonin antagonists, aprepitant).

^a Unlabeled use.

^b Not all medications in this class are labeled for this use.

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MEDICATIONS COMMONLY USED FOR SUPPORTIVE CARE THAT ARE OF CONCERN IN OLDER PATIENTS

Consider initiating all medications at the lowest possible dose and increase dose gradually (as tolerated).

Therapeutic Class/Medication(s)	Negative Effects/ Condition the Drug May Adversely Affect	Recommendation	Alternative(s)
Benzodiazepines^{4,5,7,8:} <ul style="list-style-type: none"> alprazolam estazolam lorazepam oxazepam temazepam triazolam clorazepate chlordiazepoxide clonazepam diazepam flurazepam quazepam 	<ul style="list-style-type: none"> Older adults have increased sensitivity and slower metabolism of benzodiazepines Increased risk for falls, cognitive impairment, delirium 	<ul style="list-style-type: none"> Avoid for treatment of insomnia,⁹ agitation, or delirium. Potentially appropriate for seizures, rapid eye movement sleep disorders, benzodiazepine withdrawal, alcohol withdrawal, severe generalized anxiety disorders, and end-of-life care. Reduce dose and/or lengthen the dosing interval when using for supportive care during chemotherapy administration. Avoid abrupt discontinuation or quick taper after chronic use in order to prevent significant withdrawal symptoms. 	<ul style="list-style-type: none"> For anxiety, consider buspirone, selective serotonin reuptake inhibitors (SSRIs),^a or SNRIs.^a For sleep, use sleep hygiene education, sleep restriction or sleep compression,^c or CBT. See Insomnia (OAO-G). See NCCN Guidelines for Survivorship. For nausea, consider an alternative agent. See NCCN Guidelines for Antiemesis.
Non-benzodiazepine sedative hypnotics^{7,8:} <ul style="list-style-type: none"> zolpidem eszopiclone zaleplon 	<ul style="list-style-type: none"> Similar adverse effects to benzodiazepines with minimal improvement in sleep latency and duration Delirium Falls/fractures 	<ul style="list-style-type: none"> Use no more than 2 to 3 days per week for up to 90 days. Avoid chronic use. If zolpidem is used, the dose in females should not exceed 5 mg. 	<ul style="list-style-type: none"> Use sleep hygiene education, sleep restriction or compression, or CBT. In the right setting, if pharmacologic therapy is deemed necessary, agents such as trazodone,^a mirtazapine,^a melatonin,^a ramelteon, or other medications could be considered, keeping in mind the risks and benefits of each individual therapy. See Insomnia (OAO-G). See Sleep Disorders in NCCN Guidelines for Survivorship.

^a Unlabeled use.

^c Sleep compression is an incremental decrease of time spent in bed.

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MEDICATIONS COMMONLY USED FOR SUPPORTIVE CARE THAT ARE OF CONCERN IN OLDER PATIENTS

Consider initiating all medications at the lowest possible dose and increase dose gradually (as tolerated).

Therapeutic Class/Medication(s)	Negative Effects/ Condition the Drug May Adversely Affect	Recommendation	Alternative(s)
First-generation antihistamines^{4,5,7,8}: <ul style="list-style-type: none"> diphenhydramine hydroxyzine promethazine brompheniramine carbinoxamine clemastine cyproheptadine dexbrompheniramine dexchlorpheniramine doxylamine triprolidine 	<ul style="list-style-type: none"> Anticholinergic toxicities Confusion Cognitive impairment Delirium Dry mouth Constipation Urinary retention Clearance is reduced 	<ul style="list-style-type: none"> Use only for supportive care when convincing benefit exists. Appropriate for acute treatment of severe allergic reactions. 	<ul style="list-style-type: none"> Consider second-generation antihistamines (ie, cetirizine, desloratadine, fexofenadine, levocetirizine), intranasal antihistamines, intranasal anticholinergics, or leukotriene inhibitors. For sleep, use sleep hygiene education, sleep restriction or sleep compression, or CBT. See Insomnia (OAO-G). See NCCN Guidelines for Survivorship.
Antiemetic, prokinetic^{6,7,8}: <ul style="list-style-type: none"> metoclopramide NK-1 antagonists <ul style="list-style-type: none"> Aprepitant Fosaprepitant Rolapitant Phenothiazine antiemetics⁷: <ul style="list-style-type: none"> prochlorperazine 	<ul style="list-style-type: none"> May cause extrapyramidal effects Greater risk of falls in older patients Can worsen parkinsonian symptoms 	<ul style="list-style-type: none"> Avoid metoclopramide, unless use is for patients with gastroparesis. If benefit outweighs risk, use the lowest metoclopramide dose possible, and avoid exceeding 5 mg. Renally dose adjust metoclopramide. 	<ul style="list-style-type: none"> Consider serotonin antagonists (ie, dolasetron, granisetron, ondansetron, palonosetron, tropisetron), short-term corticosteroids (ie, dexamethasone, prednisone), or other antiemetics. See NCCN Guidelines for Antiemesis.
Histamine-2 receptor blockers⁷: <ul style="list-style-type: none"> famotidine ranitidine cimetidine 	<ul style="list-style-type: none"> Delirium Cognitive impairment Can worsen dementia 	<ul style="list-style-type: none"> Avoid in patients at risk for delirium. 	<ul style="list-style-type: none"> Proton pump inhibitors (eg, omeprazole, esomeprazole, pantoprazole, lansoprazole) An alternative to H2 blockers may be antacids such as calcium carbonate, in addition to proton pump inhibitors, if hypercalcemia of malignancy is not a concern.

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Consider initiating all medications at the lowest possible dose and increase dose gradually (as tolerated).

Therapeutic Class/Medication(s)	Negative Effects/ Condition the Drug May Adversely Affect	Recommendation	Alternative(s)
<p>Selective serotonin reuptake inhibitor antidepressants (SSRIs)^{4,5,7,8,10}:</p> <ul style="list-style-type: none"> • fluoxetine • paroxetine • sertraline • fluvoxamine • citalopram • escitalopram 	<ul style="list-style-type: none"> • Can induce ataxia, impair psychomotor function • Increases risk for syncope • Increases risk for falls • Exacerbates hyponatremia, particularly in older adults by syndrome of inappropriate secretion of antidiuretic hormone (SIADH) • Increases risk for GI bleeding, particularly when using with nonsteroidal anti-inflammatory drugs (NSAIDs), aspirin, or anticoagulation • Can increase QT interval 	<ul style="list-style-type: none"> • Consider side-effect profile and drug interactions prior to the selection of antidepressants. • Review the need for continued treatment for depression at least 6 months after remission of the episode, based on number of prior episodes, residual symptoms, current medical problems, and psychosocial difficulties. • Consider stopping by gradually reducing the dose over a 4-week period in patients who no longer need antidepressants. • Avoid in patients with falls, unless alternatives are not available. • Avoid in patients with SIADH. • Avoid paroxetine (and possibly fluoxetine) in patients taking tamoxifen. • Consider baseline electrocardiogram (ECG) before initiation of therapy. 	<ul style="list-style-type: none"> • For patients with falls, consider SNRIs (eg, venlafaxine, desvenlafaxine, duloxetine) or bupropion. • Consider the use of a gastroprotective medication (proton pump inhibitors such as omeprazole, esomeprazole, or misoprostol) if SSRIs must be combined with nonsteroidal anti-inflammatory drugs (NSAIDs), aspirin, or antiplatelet agents. • For patients taking warfarin, heparin, or anticoagulants, consider mirtazapine. • Consider complementary or alternative therapy (eg, CBT).

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Therapeutic Class/Medication(s)	Negative Effects/ Condition the Drug May Adversely Affect	Recommendation	Alternative(s)
<p>Antipsychotics^{4,5,7,8,11-14:}</p> <ul style="list-style-type: none"> • chlorpromazine • fluphenazine • haloperidol • loxapine • molindone • perphenazine • pimozide • promazine • thioridazine • thiothixene • trifluoperazine • triflupromazine • aripiprazole • asenapine • clozapine • iloperidone • lurasidone • olanzapine • paliperidone • quetiapine • risperidone • ziprasidone 	<ul style="list-style-type: none"> • Some agents have anti-anticholinergic effects (especially chlorpromazine, clozapine, loxapine, olanzapine, thioridazine, and trifluoperazine) • Increased risk of cerebrovascular accident (CVA) • Increased risk of mortality in patients with dementia • Hyperglycemia • Increased risk of falls and fractures, especially in patients at risk • Concern for QT prolongation, especially in combination with serotonin antagonists, antidepressants, and in patients with underlying cardiac diseases 	<ul style="list-style-type: none"> • In the presence of psychosis and danger to self/others, use low-dose non-anticholinergic agent for the shortest duration possible. • May be appropriate for short-duration treatment of refractory chemotherapy-induced nausea and vomiting. • May be appropriate for short-term management of delirium. • With concern for QT prolongation, start at the lowest dose with slow up-titration. Consider baseline ECG before initiation of therapy. 	<ul style="list-style-type: none"> • For delirium, short-term use (no more than 5 days) of one of the following at low dose: <ul style="list-style-type: none"> ▶ Haloperidol^a (0.25–1 mg PO up to q8h) ▶ Olanzapine^a (2.5–5 mg PO daily) ▶ Risperidone^a (0.25–0.5 mg PO daily) ▶ For patients with parkinsonism, quetiapine^a (12.5–25 PO daily or q12h) • If using an antipsychotic, attempt to reduce, taper, or stop other antipsychotics and/or drugs acting on the CNS that can worsen the risk of falls or cognitive decline. • For nausea, consider other antiemetics (serotonin antagonists such as ondansetron, dexamethasone, or aprepitant) if risk outweighs the benefit of using an antipsychotic. • Monitor for extrapyramidal symptoms; tools such as the Abnormal Involuntary Movement Scale are useful. • See NCCN Guidelines for Antiemesis

^a Unlabeled use.

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Therapeutic Class/ Medication(s)	Negative Effects/ Condition the Drug May Adversely Affect	Recommendation	Alternative(s)
Antiepileptic drugs (AEDs)¹⁵: <ul style="list-style-type: none"> phenobarbital primidone phenytoin carbamazepine 	<ul style="list-style-type: none"> Induce multiple cytochrome P450 enzymes, resulting in clinically significant drug interactions Falls 	<ul style="list-style-type: none"> Avoid for newly diagnosed epilepsy in persons aged ≥60 years not currently on antiepileptic therapy, unless at least two other AEDs have been unsuccessful in stopping seizures or have intolerable adverse effects. Carefully check drug interactions when using these agents. 	<ul style="list-style-type: none"> Examples of multiple AEDs that do not induce cytochrome P450 enzymes: lamotrigine, levetiracetam, tiagabine, and topiramate.
Opioids <ul style="list-style-type: none"> morphine codeine tramadol hydrocodone oxycodone hydromorphone fentanyl methadone 	<ul style="list-style-type: none"> Sedation Impaired balance and falls Nausea/vomiting Constipation Respiratory depression, especially in patients with sleep apnea Urinary retention Dependence Long-term use is associated with bone loss Confusion Delirium 	<ul style="list-style-type: none"> Start low and escalate slowly, use longer intervals. Start with short-acting agents. Make sure patients are on a bowel regimen to avoid severe constipation. Caution when prescribing with underlying dementia. Half-life may be longer in older adults who have renal or hepatic dysfunction. 	<ul style="list-style-type: none"> Consider using nonopioids if possible; NSAIDs, acetaminophen Consider radiation or nerve block in localized pain For neuropathic pain, consider non-opioids See NCCN Guidelines for Adult Cancer Pain

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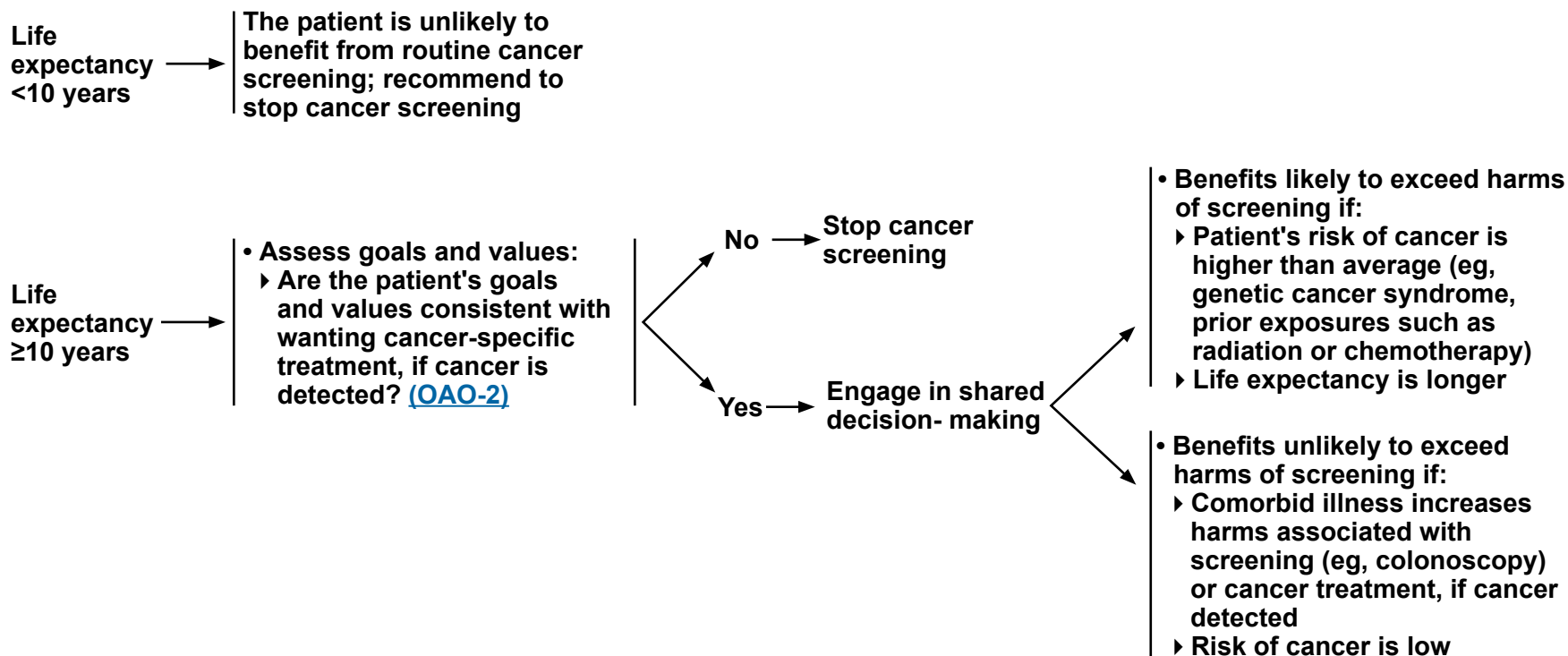
REFERENCES

- ¹ Vyvey M. Steroids as pain relief adjuvants. *Can Fam Physician* 2010;56:1295-1297.
- ² Sturdza A, Millar BA, Bana N, et al. The use and toxicity of steroids in the management of patients with brain metastases. *Support Care Cancer* 2008;16:1041-1048.
- ³ American Geriatrics Society Panel on Pharmacological Management of Persistent Pain in Older Persons. Pharmacological management of persistent pain in older persons. *J Amer Geriatr Soc* 2009;57:1331-1346.
- ⁴ Hilmer SN, Mager DE, Simonsick EM, et al. A drug burden index to define the functional burden of medications in older people. *Arch Intern Med* 2007;167:781-787.
- ⁵ Chew ML, Mulsant BH, Pollock BG, et al. Anticholinergic activity of the 107 medications commonly used by older adults. *J Am Geriatr Soc* 2008;56:1333-1341.
- ⁶ Malik I, Moid I, Khan Z, Hussain M. Prospective randomized comparison of tropisetron with and without dexamethasone against high-dose metoclopramide in prophylaxis of acute and delayed cisplatin-induced nausea and vomiting. *Am J Clin Oncol* 1999;22:126-130.
- ⁷ American Geriatrics Society 2019 Updated AGS Beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc* 2019;67:674-694.
- ⁸ HEDIS: Health Care Effectiveness Data and Information Set, at <https://www.ncqa.org/hedis/>.
- ⁹ Loh KP, Burhenn P, Hurria A, et al. How do I best manage insomnia and other sleep disorders in older adults with cancer? *J Geriatr Oncol* 2016;7:413-421.
- ¹⁰ 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.
- ¹¹ Pugh MJ, Berlowitz DR, Rao JK, et al. The quality of care for adults with epilepsy: an initial glimpse using the QUIET measure. *BMC Health Serv Res* 2011;11:1.
- ¹² O'Neil ME, Freeman M, Christensen V, et al. VA-Evidence-based Synthesis Program Reports Project #05-225, Washington (DC): Department of Veterans Affairs; March 2011.
- ¹³ Porsteinsson AP, Drye LT, Pollock BG, et al. Effect of citalopram on agitation in Alzheimer disease: the CitAD randomized clinical trial. *JAMA* 2014;311:682-691.
- ¹⁴ Hocking CM, Kichenadasse G. Olanzapine for chemotherapy-induced nausea and vomiting: a systematic review. *Support Care Cancer* 2014;22:1143-1151.
- ¹⁵ Fossey J, Ballard C, Juszczak E, et al. Effect of enhanced psychosocial care on antipsychotic use in nursing home residents with severe dementia: cluster randomised trial. *BMJ* 2006;332:756-761.

APPROACH TO CANCER SCREENING FOR OLDER ADULT CANCER SURVIVORS

Note: “Cancer screening” refers to screening for new primary cancers different than the cancer survivor’s prior cancer(s). There is evidence to support routine screening for the following cancers (although evidence in older individuals is limited): breast, colorectal, and lung cancer. There is limited or no evidence to support screening for cervical cancer or prostate cancer in older adults. For specific cancer screening recommendations, including NCCN recommendations regarding the early detection of prostate cancer, please refer to the respective [NCCN Guidelines for Detection, Prevention, and Risk Reduction](#).

Is the cancer survivor a candidate for routine cancer screening considering overall life expectancy?^a



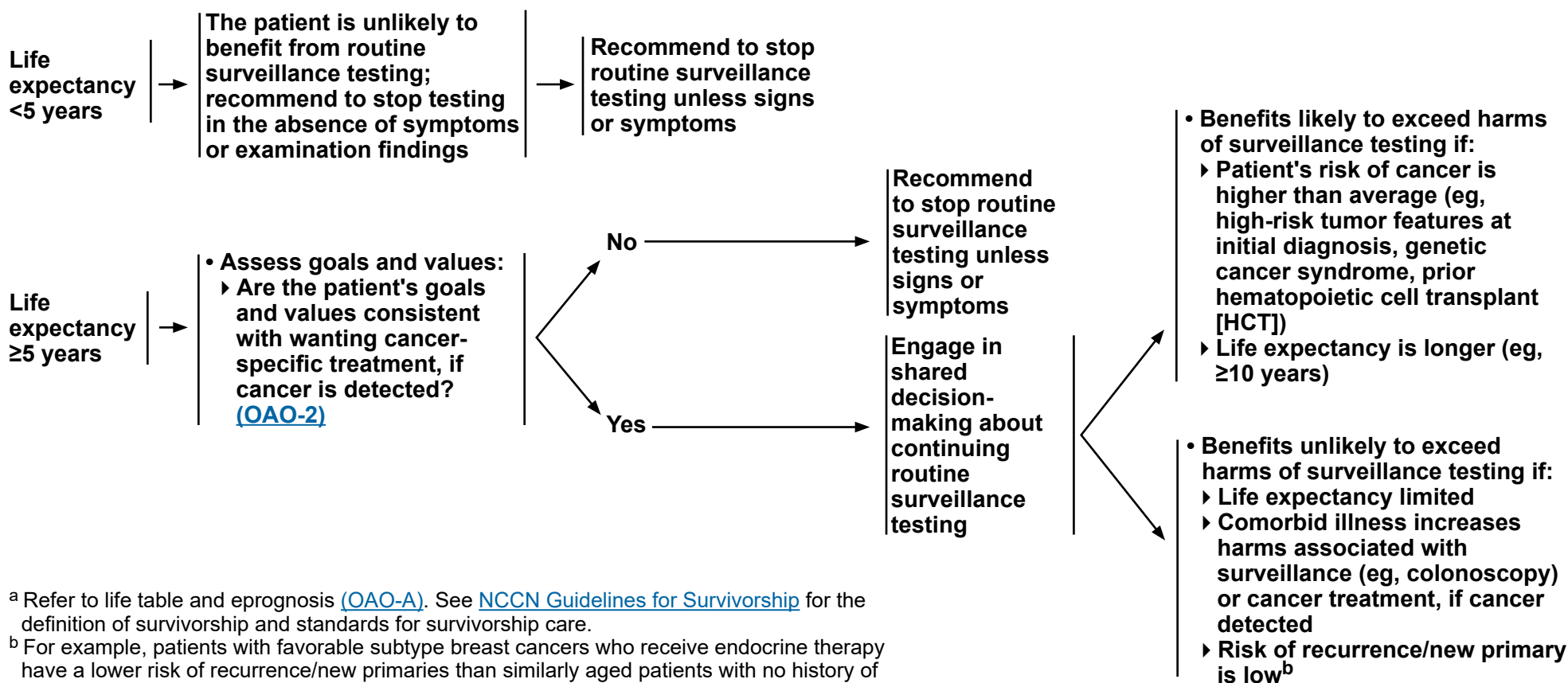
^a Refer to life table and eprognosis [\(OAO-A\)](#). See [NCCN Guidelines for Survivorship](#) for the definition of survivorship and standards for survivorship care.

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.

APPROACH TO SURVEILLANCE TESTING FOR OLDER ADULT CANCER SURVIVORS WITH NO EVIDENCE OF DISEASE

“Surveillance testing” refers to routine assessment (in the absence of symptoms or examination findings) for recurrence or new primary cancers of the same type as the cancer survivor’s prior cancer(s) beyond routine history and physical examination. (Note that patients with symptoms or signs suspicious for cancer on history or physical examination should undergo diagnostic evaluation.)

Is the cancer survivor a candidate for routine surveillance testing considering overall life expectancy?^a



^a Refer to life table and eprognosis (OAO-A). See [NCCN Guidelines for Survivorship](#) for the definition of survivorship and standards for survivorship care.

^b For example, patients with favorable subtype breast cancers who receive endocrine therapy have a lower risk of recurrence/new primaries than similarly aged patients with no history of breast cancer (Freedman RA, et al. JAMA Oncol 2021;7:609-615).

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.

**ABBREVIATIONS**

aCGA	Abbreviated Comprehensive Geriatric Assessment	G-8	Geriatric 8	OT	occupational therapy
ADL	activities of daily living	GA	geriatric assessment	PT	physical therapy
AEDs	antiepileptic drugs	GI	gastrointestinal	QOL	quality of life
AGS	American Geriatrics Society	GSV	Geriatric Surgery Verification	SABR	stereotactic ablative radiotherapy
BMI	body mass index	HCT-CI	Hematopoietic Cell Transplantation-Specific Comorbidity Index	SAOP	Senior Adult Oncology Program
BOMC	Blessed Orientation Memory Concentration Test	IADL	instrumental activities of daily living	SIADH	syndrome of inappropriate secretion of antidiuretic hormone
CAR	chimeric antigen receptor	IGRT	image-guided radiation therapy	SLUMS	Saint Louis University Mental Status Exam
CARG	Cancer and Aging Research Group	IMRT	intensity-modulated radiation therapy	SNRI	serotonin-norepinephrine reuptake inhibitor
CARG-BC	Cancer and Aging Research Group-Breast Cancer	irAE	immune-related adverse event	SPPB	Short Physical Performance Battery
CBT	cognitive behavioral therapy	LVEF	left ventricular ejection fraction	SRH	Self-Rated Health
CCI	Charlson Comorbidity Index	MAI	Medication Appropriateness Index	SSRI	selective serotonin reuptake inhibitor
CHF	congestive heart failure	MMSE	Mini-Mental State Examination	START	Screening Tool to Alert to Right Treatment
CIRS-G	Cumulative Illness Rating Scale-Geriatric	MNA	Mini-Nutritional Assessment	STOPP	The Screening Tool of Older Persons' Prescriptions
CNS	central nervous system	MoCA	Montreal Cognitive Assessment	TRST	Triage Risk Screening Tool
CRASH	Chemotherapy Risk Assessment Scale for High-Age Patients	MOS	Medical Outcomes Study	TSH	thyroid-stimulating hormone
CVA	cerebrovascular accident	NSAID	nonsteroidal anti-inflammatory drug	TUG	Timed Up and Go
ECG	electrocardiogram	OARS	Older Americans Resources and Services	VES-13	Vulnerable Elders Survey
ECOG	Eastern Cooperative Oncology Group				



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.



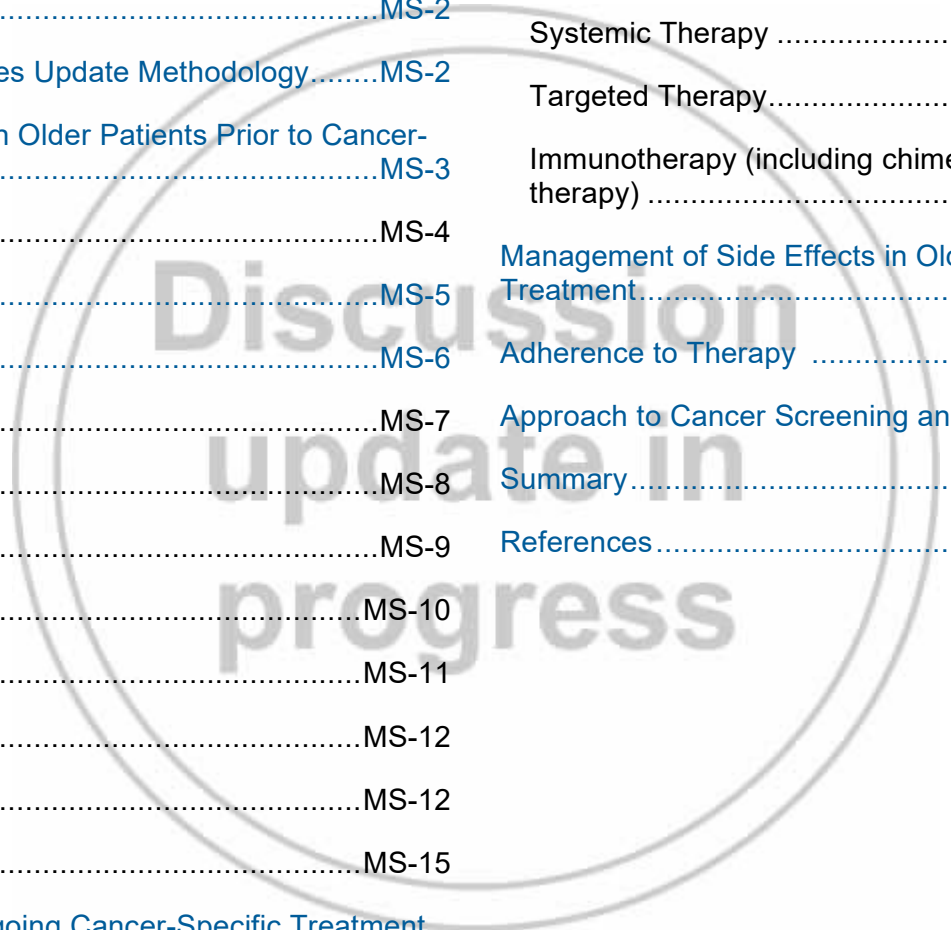
NCCN Guidelines Version 1.2024 Older Adult Oncology

Discussion

This discussion corresponds to the NCCN Guidelines for Older Adult Oncology. Last updated on July 12th, 2022.

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Overview

Cancer is the leading cause of death in patients aged 60 to 79 years.¹ More than 50% of all cancers and more than 70% of cancer-related deaths in the United States occur in patients who are 65 years and older.² It is estimated that by 2030 approximately 70% of all cancers will be diagnosed in adults aged 65 years and older.³ Aging in the U.S. population and greater life expectancy mean that cancer in older adults is becoming an increasingly common problem. Furthermore, older patients with cancer are under-represented in clinical trials for new cancer therapies.⁴ Therefore, less evidence-based information exists to guide the treatment of these patients.

The challenge of managing older patients with cancer is to assess whether the expected benefits of treatment are superior to the risks in a population with decreased life expectancy and decreased tolerance to stress. There are unique issues to consider when caring for an older adult with cancer. The biological characteristics of certain cancers and their responsiveness to therapy are different in older patients compared to their younger counterparts.⁵ In addition, older patients have decreased tolerance to anticancer therapy. Nevertheless, advanced age alone should not be the only criterion to preclude effective treatment that could improve quality of life (QOL) or lead to a survival benefit in older patients.^{6,7} The available data suggest that older patients with good performance status can tolerate commonly used chemotherapy regimens as well as younger patients, particularly when adequate supportive care is provided.⁸⁻¹⁰ However, there have been few studies that have addressed patients at the extremes of age or those with poor performance status. Multidisciplinary team management, a patient-specific treatment approach with shared decision-making, and palliative/supportive care for symptom management should be an integral part of cancer care in older adults.

Together, these age-related issues form the basis for the development of Guidelines that address special considerations in older adults with cancer. Proper selection of patients is the key to administering effective and safe cancer treatment. Treatment that diminishes QOL with no significant survival benefit should be avoided. The physiologic changes associated with aging may impact an older adult's ability to tolerate cancer therapy and should be considered in the treatment decision-making process. The NCCN Guidelines® for Older Adult Oncology address specific issues related to the management of cancer in older adults, including screening and comprehensive geriatric assessment (CGA), assessing the risks and benefits of treatment, preventing or decreasing complications from therapy, and managing patients deemed to be at high risk for toxicity from standard treatment.

Literature Search Criteria and Guidelines Update Methodology

Prior to the update of this version of the NCCN Guidelines for Older Adult Oncology, a literature search was performed to obtain key literature in Older Adult Oncology using the following search terms: older patients and cancer, treatment, allogeneic stem cell transplantation, adherence, comprehensive geriatric assessment, toxicity and chemotherapy, polypharmacy, comorbidities, functional status, cognitive status, nutritional status, falls, frailty, geriatric syndromes, delirium, dementia, depression, and distress.

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; Clinical Trial, Phase IV; Guideline; Randomized Controlled Trial; Meta-Analysis; Systematic Reviews; and Validation Studies.



The data from key PubMed articles selected by the panel for review during the Guidelines update meeting as well as 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. Recommendations for which high-level evidence is lacking are based on the panel's review of lower-level evidence and expert opinion.

NCCN recommendations have been developed to be inclusive of individuals of all sexual and gender identities to the greatest extent possible. When citing data and recommendations from other organizations, the terms men, male, women, and female will be used to be consistent with the cited sources.

The complete details of the Development and Update of the NCCN Guidelines are available at www.NCCN.org.

Approach to Shared Decision-Making in Older Patients Prior to Cancer-Specific Treatment

Older patients can be classified into three categories: 1) young old patients are 65 to 75 years of age; 2) old patients are 76 to 85 years of age, and 3) oldest old patients are older than 85 years of age.⁵ Chronologic age by itself is not reliable in estimating life expectancy, functional reserve, or the risk of treatment complications.¹¹ While it is not possible for a physician to predict the exact life expectancy of an individual patient, it is possible to provide an estimate of whether a patient is likely to live longer or shorter than an average person of similar age.¹²⁻¹⁸

Life expectancy at a given age can be estimated using life table data as suggested by Walter and Schonberg.¹⁹ For example, about 25% of the healthiest 75-year-old patient will live more than 22 years, 50% will live at least 17 years, and 25% will live less than 10 years. Lee and colleagues developed and validated a potentially useful tool for clinicians to estimate

the 4-year mortality risk.¹⁴ Patients can be stratified into three groups of varying risk of mortality (high, intermediate, or low) based on the prognostic index, which incorporates demographic variables (age and sex), self-reported comorbid conditions and functional measures.¹⁴ Carey and colleagues also developed a similar functional morbidity index based on self-reported functional status, age, and gender to stratify elders into varying risk groups for 2-year mortality.¹³

The risk of morbidity from cancer is generally established by the stage at diagnosis, the aggressiveness of the tumor, and the risk of recurrence and progression. More generally, a useful collection of tools to estimate the general mortality risk in older adult can be found online at <https://eprognosis.ucsf.edu>. Life expectancy calculators available on this website can be utilized to determine anticipated life expectancy (independent of cancer) and in clinical decision-making to assess whether 1) the cancer is likely to shorten the patient's life expectancy; or 2) whether the patient is likely to become symptomatic from cancer during the anticipated life expectancy. These calculators should be used in conjunction with clinical judgment.

Patients with a low risk of dying or suffering from their cancer and who have other competing causes of mortality can receive symptom management and supportive care as detailed in the appropriate NCCN Guidelines for Supportive Care. Patients who are at moderate or high risk of suffering from their cancer can be further evaluated to assess their functional dependency, decision-making capacity, overall goals, and desire for the proposed treatment.^{20,21}

A patient's decision-making capacity is generally evaluated based on the patient's ability to understand the relevant information about the diagnosis and proposed cancer-specific diagnostic tests or treatment options; appreciate their underlying values and current medical situation; use



reason to make decisions; and communicate a consistent choice. It is essential that key concepts and information regarding the diagnosis of cancer and cancer-specific treatment be communicated to older patients in a way that they can understand. See *Optimizing Communication with Older Adults* in the algorithm. Sessums et al evaluated a variety of instruments used to assess medical decision-making capacity in adult patients without mental illness and concluded that Aid to Capacity Evaluation (ACE) is the best available instrument to assist physicians in making assessments about a patient's medical decision-making capacity.²¹

Irrespective of age, a person who is functionally independent without serious comorbidities and has good decision-making capacity should be a candidate for most forms of cancer-specific treatment. Patient's goals and objectives should be assessed in context of life expectancy; comorbidities; cognitive, functional, psychological/psychosocial, and nutritional status; aggressiveness of the disease; and treatment approach. There are data to suggest a correlation between low social support and a higher risk for mortality. In patients with low levels of social support, referral to social work should be considered and/or case management to explore home supports and community resources. Multidisciplinary team management, patient-specific treatment approach with shared decision-making, and palliative/supportive care for symptom management should be an integral part of cancer care in older adults. In patients without decision-making capacity, the Guidelines recommend considering consultation with a social worker, psychologist, palliative care specialist, or an ethics committee. Additional information can be obtained from the patient's proxy, advance directive/advance care planning document, health care power of attorney, living will, or clinician's documentation.

Functionally independent patients with contraindications to treatment and patients with major functional impairment with or without complex comorbidity should be managed according to the appropriate NCCN Guidelines for Supportive Care. Patients who are dependent in some instrumental activities of daily living (IADLs), with or without severe comorbidities, are at increased risk of cancer-specific treatment complications. For these patients with intermediate functional impairment who have milder problems (such as dependence in one or more IADLs, milder comorbidity, depression, minor memory disorder, mild dementia, and inadequate caregiver), treatment may still be administered with special individualized precautions.⁵

The potential benefits of cancer-specific treatments include prolonged survival, and improvement of QOL and function, as well as palliation of symptoms. For patients who are able to tolerate treatment, options include surgery, radiation therapy (RT), chemotherapy, targeted therapies, and immunotherapy.

Pre-Treatment Evaluation

The NCCN Older Adult Oncology Panel recommends pre-treatment evaluation using a CGA for all older adults with cancer, especially if there are apprehensions regarding the patient's ability to tolerate treatment. The CGA is a multidisciplinary, in-depth evaluation that assesses the objective health of the older adult through evaluation of multiple domains, which predict overall prognosis as well as fitness and ability to tolerate cancer therapy. The feasibility of conducting a CGA in oncology practice has been demonstrated among older patients with cancer in clinical practice and research settings.²²⁻²⁴ The components of CGA, including comorbid conditions, functional status, cognitive function, geriatric syndromes, polypharmacy, and nutritional status, have been associated with survival and chemotherapy tolerance.²⁵⁻³⁴



For example, in patients 65 years or older diagnosed with stage I–III primary breast cancer, the all-cause and breast-cancer-specific death rates at 5 and 10 years were consistently approximately two times higher in patients with three or more cancer-specific CGA deficits, regardless of age and stage of disease.²⁸ In another prospective study of 375 consecutive older patients with cancer (ELCAPA study), in a multivariate analysis, a lower activities of daily living (ADLs) score and malnutrition were independently associated with changes in the cancer treatment intensity.²⁹ In a prospective multicenter study of 348 previously untreated cancer patients older than 70 years, poor nutritional status, impaired mobility, and advanced tumors were identified as risk factors predictive of early death (<6 months) after initiation of chemotherapy.³⁰ In a phase III study (FFCD 2001-02), impairment in functional status and cognitive function (as assessed by IADLs and Mini-Mental State Exam [MMSE], respectively) were predictive of severe chemotherapy-related toxicity and hospitalization in older patients with metastatic colorectal cancer (CRC).³¹ Similarly, among older patients receiving induction chemotherapy for acute myeloid leukemia (AML), overall survival (OS) was significantly shorter for patients with impaired cognitive and physical function.³² CGA has also been reported to be an efficient method to identify older patients with diffuse large B-cell lymphoma (DLBCL) who can benefit from anthracycline-based chemoimmunotherapy.^{27,35}

Although CGA is helpful for physicians to develop a coordinated plan for cancer treatment as well as to guide appropriate interventions to address problems that were identified during assessment, it can be time-consuming and may not be practical for all patients. Geriatric screening assessment tools can be used to identify older adults with cancer who would benefit from a full CGA. At a minimum, assessment using a geriatric screening tool is recommended for older adults with cancer prior to treatment initiation.

Geriatric Screening Tools

Multiple geriatric screening tools have been tested and validated to identify patients at risk who would benefit from a CGA. The Geriatric 8 (G8),^{36,37} modified G8,³⁸ and Vulnerable Elders Survey (VES-13)³⁹⁻⁴² are the most commonly used screening tools to identify older adults with cancer who would benefit from a CGA.^{43,44}

The abbreviated CGA (aCGA),^{45,46} Barber questionnaire,⁴⁷ Fried Frailty Criteria,^{48,49} Groningen Frailty Index,⁴⁶ Triage Risk Screening Tool (TRST),³⁷ Lachs' screening test,⁵⁰ and Senior Adult Oncology Program 2 (SAOP2)^{51,52} have also been used to identify patients who would benefit from a CGA.

The SAOP2 screening tool developed by Extermann and colleagues is aimed at identifying older patients who would benefit from a multidisciplinary evaluation by a geriatric oncology team. The SAOP2 screening tool includes the assessment of older cancer patients across the following domains using validated measures: self-rated health, cognitive function, nutritional status, comorbidity, ECOG performance status, and functional status.

G8 and aCGA were developed specifically for older patients with cancer. In a systematic review, Hamaker et al assessed the sensitivity and specificity of frailty screening methods that could potentially be useful in the selection of patients for CGA.⁵³ G8 and TRST had the highest sensitivity (87% and 92%, respectively) and aCGA had the highest specificity (97%) for predicting frailty on CGA. A modified six-item version of the G8 screening tool, which was evaluated in a prospective cohort of older patients with cancer from the ELCAPA study, exhibited better diagnostic performance with 89% sensitivity and 79% specificity.³⁸ In the ONCODAGE prospective multicenter cohort study, which evaluated the diagnostic accuracy of G8 and VES-13 as predictive screening tools to identify older patients who would require CGA, G8 was more sensitive and VES-13 was more specific. Abnormal G8 score, advanced stage,



male sex, and poor performance status were independent prognostic factors of 1-year survival.⁴⁴

While all of the screening tools included the assessment of functional status, the assessment of other domains such as psychosocial status, nutritional status, comorbidities, and polypharmacy varied widely. For example, aCGA, Fried Frailty Criteria, and VES-13 had a stronger predictive value for impairment of functional status (ADLs and IADLs) and G8 had a strong predictive value for nutritional status, but not for other geriatric conditions. As a result, none of the screening tools was successful in identifying impairments across all of the domains included in CGA. Given the lack of data supporting the use of any one screening tool for predicting outcome of a CGA, screening tools should not replace CGA in the management of older patients with cancer. However, screening tools could be used to identify those patients who would benefit from a CGA prior to initiation of therapy.^{43,54} In a systematic review of skin cancer patients screened using different frailty screening tools, G8 appeared to be the best tool for assessing frailty although more data are needed to assess its feasibility in the clinic for this patient population.⁵⁵ The appropriate use of geriatric screening tools and/or CGA (as described below) enables physicians to develop a coordinated plan for cancer treatment and to guide interventions tailored to the individual patient.

Comprehensive Geriatric Assessment

The CGA is a multidisciplinary, in-depth evaluation that assesses the objective health of the older adult while evaluating multiple domains, which informs cancer prognosis and predicts treatment tolerance. The appropriate use of geriatric screening tools and/or CGA enables physicians to develop a coordinated plan for cancer treatment and to guide interventions tailored to the individual patient. The CGA includes assessment tools that evaluate the functional age of older patients with cancer based on function and mobility, comorbidities that may interfere

with cancer treatment, polypharmacy, nutritional status, cognitive function, psychological status, socioeconomic issues, and various geriatric syndromes.

CGA can reveal reversible geriatric problems that are not detected by routine oncology care and predict toxicity from cancer treatment. Identifying these issues can enable targeted use of supportive care measures to improve QOL and ensure compliance with adherence to therapy.⁵⁶⁻⁵⁸ Some components of CGA have also been incorporated in tools that have been developed to predict the risk of severe toxicity from chemotherapy in older patients with cancer (eg, Cancer and Aging Research Group [CARG] Chemo Toxicity Calculator and Chemotherapy Risk Assessment Scale for High-Age Patients [CRASH] score; See *Considerations for Older Adults Undergoing Cancer-Specific Treatment - Systemic Therapy* in the algorithm).⁵⁹⁻⁶¹ The CGA may also be useful in estimating life expectancy, which is of paramount importance when making treatment decisions, and allowing for shared decision-making with the patient and/or the caregiver. Furthermore, CGA can also promote improved communication with patients and caregivers.⁶²

Older adults may benefit from a referral to a geriatric-trained clinician for risk stratification prior to cancer treatment, to develop a coordinated plan of care with the oncologist and/or to manage geriatric syndromes that could jeopardize outcomes of cancer treatment. The geriatric-trained clinician thus may be able to assist the oncologist in optimizing the management of non-cancer aspects of the patient's care, which in turn may enable more effective delivery of direct cancer care. Consultation with a geriatric-trained clinician should be considered for the following: cognitive impairment (dementia/delirium, decision-making capacity evaluation, life expectancy, advance directive/advance care planning, and guardianship), functional/physical impairment, vision/hearing impairments, polypharmacy, when considering high-risk procedures, geriatric



syndromes (ie, repeated falls, incontinence), weight loss, and social and caregiver support.

Although typically a thorough CGA is performed by a geriatric-trained clinician, many of the tools can be incorporated into routine practice and administered by providers without any advanced training in this area. The various domains of CGA and the recommended tools for their assessment are discussed below.

Function Status and Mobility

Functional status and mobility in older adults with cancer may be evaluated using either self-reported assessments tools or objective measures. Self-reported assessment tools include ADLs, IADLs, and the number of falls within the past 6 months.^{63,64} ADLs encompass basic self-care skills required to maintain independence at home (eg, bathing, using the bathroom) and IADLs encompass complex skills that are necessary for maintaining independence in the community (eg, shopping). The need for assistance with IADLs has been associated with decreased treatment tolerance and poorer survival in older patients with cancer.^{25-27,65} Objective measures such as the Timed Up and Go (TUG) test, the Timed 10-Meter Walk Test (or gait speed), and the Short Physical Performance Battery (SPPB) test can also be used to assess function and mobility in older patients.

The TUG test is a quick screening test to assess mobility and overall motor function in older adults.^{66,67} The TUG test score is calculated as the time in seconds it takes for a patient to stand up from an armchair without using his or their arms, walk 10 feet forward at his or her usual pace, turn around, walk back to the chair, and then sit down again. The patient may use an assistive device, such as a cane or walker, but may not have assistance from another person. The TUG test score has been shown to predict the risk of falls in older adults.^{68,69} In a preliminary prospective

study, the TUG test was also associated with good sensitivity and specificity in the assessment of falls in older patients with cancer.⁷⁰ A TUG test score of 13 seconds or greater is associated with an increased risk of falls. For these patients, a comprehensive evaluation should be considered. The NCCN Older Adult Oncology Panel recommends including evaluation of ADLs, IADLs, and at least one other objective measure of function and mobility when assessing an older adult with cancer before treatment. See *Falls Assessment and Interventions* in the algorithm. Gait speed has also been used to assess functional status and health outcomes in older adults.^{17,71} It has been reported that decline in gait speed (slow, moderate, and fast) could predict mortality in well-functioning older adults.¹⁶ In a pooled analysis of individual data from 9 large cohort studies that included more than 30,000 participants (≥65 years) living in the community, Studenski and colleagues reported that gait speed was associated with survival in older adults.¹⁵ In this analysis, with 0.8 meter/second as the cutoff, gait speed faster than 1.0 meter/second suggested a better-than-average life expectancy and gait speed faster than 1.2 meters/second suggested exceptional life expectancy. White and colleagues reported that decline in gait speed (slow, moderate, and fast) could predict mortality in well-functioning older adults. A fast decline in gait speed was associated with a 90% greater risk of mortality than a slow decline.¹⁶ The predictive value of gait speed has also been evaluated in older patients with cancer.^{72,73} In the Health, Ageing and Body Composition study that included 429 older patients with cancer, faster gait speed (time taken to cover a 20-meter course) was associated with lower risk of death (hazard ratio [HR] = .89) in patients with metastatic cancer and lower 2-year progression to death or disability in patients with non-metastatic cancer.⁷² In the Physical Frailty in Elder Cancer patients study that included 190 patients (mean age, 80.6 years) with cancer during the first 6 months following a CGA, a gait speed slower than 0.8 meter/second (HR, 5.6; 95% CI, 1.6–19.7; *P* = .007) was significantly associated with early death.⁷³ Gait speed may be helpful in identifying



older patients with a longer life expectancy and who may be candidates for preventive interventions that are associated with long-term benefit.

The SPPB is a tool used to assess lower extremity function and mobility in older adults by measuring gait speed, balance, and strength.⁷⁴ Several studies have validated its ability to predict mobility disability, frailty, ADL disability, nursing home admission, hospitalization, and mortality.⁷⁵⁻⁷⁸ In a prospective cohort study, 1122 individuals aged 71 years or older (with no ADL limitations, the ability to walk one-half mile, and the ability to climb stairs without assistance) were instructed to perform tasks relating to the SPPB and follow-up after a period of 4 years. It was found that lower scores on the SPPB were associated with statistically significant disabilities at follow-up. In fact, those with lower scores at onset were 4.2 to 4.9 times more likely to have a disability at follow-up.⁷⁵ In another study, the association between the SPPB and the loss of the ability to walk 400 meters was evaluated. A total of 542 individuals aged 65 years and older completed the SPPB and 400-meter walk at baseline and following a period of 3 years. It was found that a lower SPPB score (≤ 10 at baseline) was strongly predictive of mobility disability at follow-up (OR, 3.38, 95% CI, 1.32–8.65).⁷⁶

Interventions in the case of limitations in function and mobility are listed within the algorithm under Comprehensive Geriatric Assessment. Potential interventions recommended by the panel include referral to physical medicine and rehabilitation (PM&R) and/or occupational therapy (OT) and/or a geriatric-trained clinician or a primary care physician, a home safety evaluation, and the promotion of physical activity and exercise.

Comorbidities

Older adults have an increased prevalence of comorbidities that may impact cancer prognosis and treatment tolerance.^{79,80} Cardiovascular problems including congestive heart failure (CHF), coronary artery disease

(CAD), diabetes mellitus, renal insufficiency, dementia, depression, anemia, chronic infections, neuropathy, anemia, liver and lung disease, hearing or vision loss, osteoporosis, decubitus or pressure ulcers, and prior cancer diagnosis and treatment are some of the frequently encountered comorbid conditions in older patients with cancer.

Specific comorbidities have been shown to have an impact on prognosis and treatment outcomes in patients with cancer.⁸¹⁻⁸³ In a randomized adjuvant chemotherapy trial of 3759 patients with high-risk stage II and stage III colon cancer, patients with diabetes mellitus experienced a significantly higher rate of overall mortality and cancer recurrence. At 5 years, the disease-free survival (DFS; 48% vs. 59%), OS (57% vs. 66%), and relapse-free survival (RFS; 56% vs. 64%) were significantly worse for patients with diabetes compared with patients without diabetes.⁸¹ In another series of 5077 patients (median age, 69.5 years) with localized or locally advanced prostate cancer, neoadjuvant hormonal therapy was significantly associated with an increased risk of all-cause mortality (26.3% vs. 11.2%) among patients with a history of CAD, CHF, or myocardial infarction after a median follow-up of 5.1 years.⁸² In the SEER-Medicare database analysis of older patients (≥ 66 years) diagnosed with stages I–III breast cancer, those with diabetes had an increased rate of hospitalizations for any chemotherapy toxicity and higher all-cause mortality.⁸³

The interaction of cancer treatment with comorbidities may impact functional status or worsen the comorbidity. Cancer-specific treatment may be overly risky due to the type and severity of the comorbidity. For example, chronic lung disease may affect the ability to perform thoracic surgery, or administer RT to the lungs, and extensive cardiac disease will limit the use of potential cardiotoxic drugs. Renal function carries significant weight when determining treatment approach as many of the chemotherapy agents are excreted by the kidneys, and dose



adjustments to the measured glomerular filtration rate (GFR) should be considered since the GFR decreases with age. Furthermore, comorbidity may influence life expectancy (independent of cancer), thus affecting treatment recommendations. The effect of comorbidity on life expectancy should be evaluated prior to the initiation of treatment.

The Charlson Comorbidity Index (CCI),⁸⁴ Cumulative Illness Rating Scale for Geriatrics (CIRS-G),⁸⁵ Older Americans Resources and Services (OARS) Questionnaire,^{86,87} and Hematopoietic Cell Transplantation-Specific Comorbidity Index (HCT-CI)⁸⁸ are commonly used to determine the risk of mortality associated with comorbidity in older patients. CCI⁸⁹ and CIRS-G^{90,91} have also been used to determine treatment tolerance in older patients with cancer. In a study of 310 older patients (≥70 years) with head and neck cancer, comorbidity as measured by the ACE-27 index was an indicator of OS.⁹² In a randomized trial that compared vinorelbine alone or in combination with gemcitabine in older patients with locally advanced non-small cell lung cancer (NSCLC), a CCI of greater than 2 was associated with a higher risk of early treatment cessation (82% vs. 30%, respectively).⁸⁹ In a phase III trial comparing platinum-doublet therapy as first-line treatment in patients with advanced-stage NSCLC, patients with severe comorbidities (as measured by CIRS-G) benefited from and tolerated platinum-doublet chemotherapy as well as patients with no comorbidities.⁹⁰ However, the former group had a higher risk of neutropenic fever and death from neutropenic infections. The OARS questionnaire assesses the presence of 13 common comorbidities and additionally inquires about the degree to which the individual comorbid conditions interfere with daily activities.⁸⁷ In a study including 539 older patients, 92% reported 1 or more comorbid conditions using the patient-reported OARS questionnaire, with arthritis and hypertension being the most prevalent, and 62% reported functional limitation due to comorbidity. Another study evaluated the association between comorbidity, toxicity, time to relapse, and OS in older patients with good performance status

receiving adjuvant chemotherapy for early-stage breast cancer using OARS. In these patients, comorbidity was associated with shorter OS, but was not associated with increased treatment-related toxicity or relapse.⁸⁶

Finally, in a retrospective cohort study of patients aged 50 years and older who had undergone allogeneic HCT, high HCT-CI score (≥3) was found to be more predictive than age, conditioning intensity, or performance status for a lower OS (HR, 2.2; $P = .02$). Adverse events (grade 3–4) following HCT were also more common in patients with high HCT-CI ($P = .02$).⁹³ It is recommended that for older adults with comorbidities, clinicians optimize each medical condition prior to therapy, evaluate the patient's life expectancy, and coordinate with the patient's primary care physician and team of specialists.

Social Functioning and Support

The availability of social support has been associated with physical health and emotional well-being of patients with cancer.⁹⁴ Older adults with cancer require dependable social support systems to optimize treatment outcomes. Additionally, the lack of social ties has been identified as a significant predictor of mortality in older adults.^{94,95} Therefore, providers should conduct a comprehensive evaluation of the older adult's social support system prior to starting anti-cancer therapy. The patient's living conditions, presence, and adequacy of caregiver and financial status should be considered. Information should be sought as to whether the patient is a caregiver for someone else and whether cancer treatment may impact their ability to provide this care. Finally, the patient's treatment goals should be discussed, clarifying advance directives and the presence of a health care proxy.

The self-administered, 19-item Medical Outcomes Study (MOS) social support survey measures the availability of support in several domains using four subscales (ie, emotional/informational, tangible/instrumental,



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positive social interaction, affection) and one overarching index.^{96,97} To facilitate its administration, the survey has been abridged to a modified, eight-item survey with two subscales, encompassing two domains of social support (emotional and tangible).⁹⁶ In an analysis of 3241 patients who completed either the MOS social support survey or the modified MOS social support survey, the results of the modified survey were found to be comparable to that of the MOS social support survey.⁹⁶ Other assessment tools include the RAND Health Care Social Support Survey Instrument: Emotional/Informational Subscale and the RAND Health Care Social Support Survey: Tangible Subscale.

In the case of deficient social support, the NCCN Older Adult Oncology Panel recommends several potential interventions, including referral to social work for a thorough evaluation, home safety review and issue of medical alert devices, psychiatry/psychology consultation, spiritual care, and screening for elder abuse and caregiver burden.

Cognition

Older patients with cancer who are cognitively impaired have an increased risk of functional dependence, a higher incidence of depression, and a greater risk of death. Cognitive function is also predictive of medication nonadherence across diagnoses, regardless of the complexity of regimen.⁹⁸ Cognitively impaired patients should be cared for by an experienced multidisciplinary geriatric oncology team along with good supportive care throughout treatment.⁹⁹ In addition, the association between cognitive impairment and the ability to weigh the risks and benefits of cancer treatment decisions needs to be considered.

Often present in older patients as a comorbid condition, dementia is a progressive condition characterized by impairment of memory and at least one other cognitive function (such as aphasia, apraxia, agnosia, or executive function) that would interfere with the ability to perform daily

functions independently. Mild cognitive impairment is an intermediate state between normal cognition and dementia. It is characterized by subjective memory impairment, preserved general cognitive function, and intact ability to perform daily functions.¹⁰⁰ Clinical interview with cognitive and functional assessment to screen for mild cognitive impairment or dementia is recommended for all patients, since there is a strong correlation between decline in cognitive status and the loss of functional independence in older adults.¹⁰¹

The MMSE is recommended for the assessment of cognitive function in older adults.¹⁰²⁻¹⁰⁵ MMSE is an 11-item screening test that quantitatively assesses the severity of cognitive impairment and documents cognitive changes occurring over a period of time.^{103,104} However, MMSE is not adequate for mild cognitive impairment and does not predict future decline.

The Guidelines also include the Mini-Cog as a screening tool for the assessment of mild cognitive impairment and dementia in older patients with cancer. Mini-Cog is a 5-point test (consisting of a three-word recall and clock drawing test) used for screening cognitive impairment in the older population.^{106,107} Finally, the Blessed Orientation Memory Concentration Test (BOMC) is also included in the Guidelines. The BOMC is a weighted, six-item survey that evaluates patients' orientation, registration, and attention in order to diagnose dementia.¹⁰⁸

Assessment of cognitive function can also be confounded by fatigue, depression, anxiety, underlying cerebral disease, endocrine dysfunction, nutritional deficiency, alcohol use, and sleep disturbances.¹⁰⁹ Therefore, if dementia is suspected, further evaluation including brain imaging, neuropsychological testing, and evaluation for vitamin B12 deficiency and thyroid dysfunction may be indicated. The use of certain classes of medications (anticholinergics, antipsychotics, benzodiazepines, corticosteroids, and opioids) has been associated with cognitive



impairment and delirium in older adults.¹¹⁰⁻¹¹² Antipsychotic drugs are also associated with higher mortality rates in patients with dementia.¹¹³⁻¹¹⁵ Research suggests that chemotherapy is also responsible for cancer-related cognitive decline. Chemotherapy-related cognitive impairment may persist for months to years following treatment and the reasons are varied. Hilmer and colleagues developed a drug burden index, which is a useful evidence-based tool for assessing the effect of medications on physical and cognitive performance in older adults.¹¹⁶ Special considerations for over- or under-use, duration of therapy, and dosage should be in place with the use of these classes of medications.

For patients with suspected impaired cognitive function that may potentially interfere with their decision-making capacity, the Guidelines recommend consultation with a clinician experienced in cognitive evaluation (geriatric-trained clinician, neurologist, geriatric psychiatrist, or neuropsychologist) for initiation of further evaluation to determine the appropriate diagnosis (eg, mild cognitive impairment, dementia, delirium).¹¹⁷ In addition to the clinical observation by the medical team, any concerns reported by the patient or the patient's family suggestive of impaired cognitive function should also trigger further evaluation. The NCCN Guidelines recommend periodic reassessment of cognitive function, especially when considering changes to treatment plan for all patients, including those with no cognitive impairment.

Psychological

Depression and distress have been identified in about 28% and 41% of older adults with cancer, respectively, and their prevalence can have a significant impact on a patient's ability to receive treatment for his/her cancer.^{118,119} Impaired mobility and functional status, impaired ADL, inadequate social support, cognitive impairment, polypharmacy, multimorbidity, and cancer-related pain were independently associated with clinical depression, whereas poorer physical function and loss of

independence were the key risk factors contributing to distress.^{118,119} Beuplet and colleagues highlight the lack of evidence-based knowledge in evaluating depression in older adult patients with cancer leading to difficulty in guiding the treatment approach in this setting, and stress that psycho-oncologic evaluation through screening tests is a must along with intervention from a trained geriatric clinician.¹²⁰

To screen for depression, the Geriatric Depression Scale (GDS) is a reliable and valid tool for older patients with no or moderate cognitive impairment.¹²¹ GDS was originally developed as a 30-item scale.¹²¹ Shortened versions of GDS have been found to be equally accurate and less time consuming in screening for depression in older adults.^{122,123} Cancer-related fatigue and depression frequently occur together; therefore, patients reporting fatigue could benefit from an assessment for depression.¹²⁴⁻¹²⁶

In the prospective ELCAPA cohort study, the overall prevalence of clinical depression was 28% among older patients with cancer that had not yet been treated.¹¹⁸ In a multivariate analysis, geriatric assessment findings including impaired mobility and functional status, ADLs, inadequate social support, cognitive impairment, polypharmacy, multimorbidity, and cancer-related pain were independently associated with clinical depression.

The Patient Health Questionnaire (PHQ-2 and PHQ-9) is also used as a tool to evaluate for depression in older patients with cancer. PHQ-2 consists of the first two items of PHQ-9, and is a brief screening tool administered prior to the longer questionnaire PHQ-9. In an individual participant data meta-analysis of 10,627 patients, the PHQ-2/PHQ-9 combination had a sensitivity of 82%, specificity of 87%, and area under the receiver operating characteristic (ROC) curve of 0.90.¹²⁷

Similarly, psychological distress is common among patients with cancer. Hurria and colleagues reported that significant distress was identified in



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41% of patients 65 years and older with cancer, and poorer physical function was the best predictor of distress.¹¹⁹ Screening tools have been found to be effective and feasible in reliably identifying distress and the psychosocial needs of patients.¹²⁸⁻¹³⁰ The NCCN Distress Thermometer (DT) and the accompanying 36-item Problem List is a well-known screening tool, specifically developed for patients with cancer by the NCCN Distress Management Panel.^{131,132} The NCCN DT has been validated by several studies in patients with different types of cancer and has revealed good correlation with the more comprehensive Hospital Anxiety and Depression Scale.¹³⁰ Patients can quickly fill out this distress assessment tool in the waiting room and the tool can alert the physician to potential problems. This tool identifies whether patients with cancer have problems in five different categories: practical, family, emotional, spiritual/religious, and physical. See the NCCN Guidelines for Distress Management for more information on the use of DT as a screening tool in patients with cancer.

Finally, the Mental Health Inventory (MHI-17) is a method to evaluate overall emotional functioning by measuring the level of depression and anxiety experienced within the past month. For those detected to have psychological impairment, potential interventions are listed within the algorithm under *Comprehensive Geriatric Assessment*.

Nutrition

Nutritional deficiency or malnutrition is a common and serious condition that is underdiagnosed in older patients with cancer. Poor nutritional status is associated with an increased risk of severe hematologic toxicity, an increased mortality risk, poor chemotherapy tolerance, and an increased length of stay among hospitalized patients with cancer.¹³³⁻¹³⁶ While some of the malnutrition is attributed to the underlying illness, in most of the patients it is due to inadequate intake of calories. Nutritional parameters would help to identify patients for individualized or advanced

intervention. There are many scales for nutritional assessment and no clear data to identify the most sensitive scale. A meta-analysis evaluated the ability of 15 markers of nutritional status to predict patient outcomes and concluded that no single screening tool can distinctly identify malnutrition due to lack of uptake/intake of food from inflammatory causes of weight loss.¹³⁷ The malnutrition universal screening tool uses cutoffs such as a body mass index (BMI) of less than or equal to 22 kg/m² and percent of unintentional weight loss of greater than 5% over 6 months.¹³⁸

The Mini Nutritional Assessment (MNA) is a validated, self-reported tool that can identify older adults who are malnourished or at risk for malnutrition. The summated scores differentiate between those with sufficient nutrition, with protein-calorie malnutrition, or who are at risk of malnutrition. Finally when evaluating patients for potential nutritional deficits, special attention should also be devoted to vitamin D deficiency since that may be related to osteoporosis and fractures.¹³⁹

For those detected to have nutritional deficits, the NCCN Older Adult Oncology Panel recommends a nutrition consult, specific dietary interventions, oral care, supplemental nutrition, OT for assistive devices, speech therapy and swallowing assessment, oral/dental evaluation for dentures, screening for food insecurity, social/caregiver support, and evaluation for appetite stimulants, nausea control, and calorie, protein, and fluid recommendations.

Polypharmacy

Polypharmacy can be defined in various ways, including the use of increased number of medications (≥ 5 , more than is clinically indicated); the use of potentially inappropriate medications; medication underuse; and medication duplication.¹⁴⁰ Although polypharmacy can be an issue across all age groups, it can be more prevalent and pose a serious problem for older patients due to the presence of increased comorbid conditions treated with multiple drugs. The use of cancer therapy as well as



medications for management of treatment-related symptoms or side effects can result in polypharmacy.¹⁴¹⁻¹⁴³

The use of multiple medications can lead to increased incidences of adverse drug reactions, which can lead to functional decline, other geriatric syndromes, and non-adherence.^{144,145} Among patients with cancer receiving systemic anticancer therapy for solid tumors, one or more drug-drug interactions were observed in 27% of patients, which increased to 31% among patients with cancer receiving palliative care only.¹⁴⁶ Older patients and those with comorbid conditions are at greater risk of drug interactions.¹⁴⁶

Alterations in pharmacokinetics and pharmacodynamics of drug metabolism in the older population can also contribute to adverse drug interactions.¹⁴⁷ Most of the commonly prescribed medications such as opioids, antidepressants, antibiotics, and antipsychotics as well as anticancer drugs induce or inhibit cytochrome P-450 enzymes. In a retrospective analysis of 244 older patients (≥70 years), Popa and colleagues assessed the impact of potential drug interactions (PDIs) and their association with chemotherapy tolerance.¹⁴⁸ The results of this study demonstrated that PDIs may contribute to severe non-hematologic toxicities, whereas there was no association between PDIs and hematologic toxicities. Further research regarding PDIs and anti-cancer therapy toxicity is warranted in order to develop interventions and optimize clinical outcomes in older patients receiving these treatments.

The use of one or more potentially inappropriate medications among older patients has also been documented in several studies.¹⁴⁹⁻¹⁵¹ In one study, the use of inappropriate medications increased from 29% to 48% among patients with cancer in the palliative care setting.¹⁵⁰ In a study of 500 older patients with cancer (≥65 years) starting a new chemotherapy regimen, polypharmacy (≥4 drugs) was observed in over 60% of patients and the use of potentially inappropriate medications was commonly seen in less

than or equal to 29% of patients. Polypharmacy did not increase the risk of chemotherapy-related toxicity in this cohort, frequency of hospitalization, or early discontinuation of chemotherapy.¹⁵¹ The use of potentially inappropriate medications (especially hypnotics, sedatives, antidepressants, long-acting benzodiazepines, other psychotropics, and medications with anticholinergic properties) is also associated with an increased risk of falls in older adults (≥65 years).^{152,153}

Evaluation of Polypharmacy

The Guidelines recommend evaluation of adherence to therapy and periodic medication review to check for medication duplication, appropriate use, availability of less expensive alternative medications, and PDIs. The panel also recommends the careful evaluation of the use of supplements and herbal therapies. Although the optimal polypharmacy cut-point for predicting clinically important adverse events in older people with cancer is unclear, the common definition of 5 or more medications is reasonable for identifying patients for medication review.¹⁵⁴ Medication review of existing prescription and over-the-counter medications may be indicated prior to initiation or change in treatment, change in comorbid disease management or in clinical condition, and at other times as determined by the clinical team and during transition of care. A careful review of the indication for treatment, duration of therapy, and dosage should be performed when using specific medications or classes of medications that are not recommended for older adults. See the section on *Medications Commonly Used for Supportive Care that are of Concern in Older Patients* in the algorithm for specific recommendations.

Beers Criteria and the Medication Appropriateness Index (MAI) are two of the most common approaches used to evaluate potentially inappropriate medication use in older patients. The Screening Tool of Older Persons' Prescriptions (STOPP) and the Screening Tool to Alert doctors to Right



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Treatment (START) criteria have been developed to evaluate drug interactions, medication duplication, and medication underuse.

Beers Criteria

The Beers Criteria identify inappropriate medications that have potential risks that outweigh potential benefits based on the risk of toxicity and the presence of potential drug-disease interaction in older patients with cancer.^{155,156} The criteria are appropriate for persons older than 65 years of age and provide a rating of severity for adverse outcomes as well as a descriptive summary of the prescribing information associated with the medication. The updated Beers Criteria have been used to evaluate polypharmacy in older patients with cancer both in an oncology-specific acute care unit (Oncology-Acute Care for Elders [OACE]; n = 47 with a median age of 73.5 years) and in the outpatient setting (n = 154 with a median age of 74 years).^{157,158} The Beers Criteria-based polypharmacy was observed in 21% and 11% of patients, respectively. Both of these studies had implemented medication review and pharmacist-based interventions to improve the appropriateness of prescribing. In the OACE study, 53% had a subsequent alteration in their medication regimen and 28% had a potentially inappropriate medication discontinued, after implementation of recommendation by the OACE team.¹⁵⁷ In the outpatient study, 50% of patients required specific interventions and the use of potentially inappropriate medication was identified in 11% of patients, following geriatric management evaluation.¹⁵⁸

The Beers Criteria were updated by the American Geriatrics Society (AGS) to improve monitoring of drug use, e-prescribing, interventions to decrease adverse events in older adults, and patient outcomes.¹⁵⁹ In the updated criteria, medications that are used in older adults are divided into: medications that should be avoided in most older patients, medications that should be avoided in older patients with select conditions, medications that should be administered with caution as the benefits outweigh the

risks, medication interactions, and dose adjustment of medication based on renal function.¹⁶⁰

Medication Appropriateness Index

MAI was developed to measure appropriate prescribing based on a 10-item list and a 3-point rating scale.¹⁶¹ Samsa and colleagues subsequently modified the MAI to include a single summated MAI score per medication that demonstrated acceptable reliability in assessing medication appropriateness among 1644 medications prescribed to 208 older veterans from the same clinic.¹⁶² This modified MAI appears to be a valid and relatively reliable measure to detect medication appropriateness and inappropriateness in the community pharmacy setting as well as in ambulatory older patients on multiple medications.^{163,164} MAI scores were significantly lower for medications with a high potential for adverse effects compared with those with a low potential (1.8 vs. 2.9; $P < .001$).¹⁶³ Higher MAI scores were also associated with lower self-related health scores in older adults.¹⁶⁵ MAI has not been evaluated extensively in older patients with cancer.

STOPP/START Criteria

STOPP/START criteria were established using the Delphi consensus and an 18-member expert panel from the academic centers of Ireland and the United Kingdom.¹⁶⁶ The STOPP criteria are comprised of 65 indicators for potentially inappropriate prescribing, including drug-drug and drug-disease interactions, therapeutic duplication, and drugs that increase the risks of geriatric syndromes, whereas the START criteria incorporate 22 evidence-based indicators to identify prescribing omissions in older people.^{167,168} In a randomized trial of 400 hospitalized patients (≥65 years), unnecessary polypharmacy, the use of drugs at incorrect doses, and potential drug-drug and drug-disease interactions were significantly lower in the group assigned to screening with STOPP/START criteria with recommendations provided to their attending physicians compared to the



control group assigned to routine pharmaceutical care.¹⁶⁹ Significant improvements in prescribing appropriateness were sustained for 6 months after discharge.

Geriatric Syndromes

Falls, dementia, delirium, depression, distress, osteoporosis, fatigue, and frailty are some of the most common syndromes in older patients with cancer.¹⁷⁰ Older patients with cancer experience a higher prevalence of geriatric syndromes than those without cancer. In an analysis of a national sample of 12,480 community-based elders, 60.3% of patients with cancer reported one or more geriatric syndromes compared with 53.2% of those without cancer.¹⁷¹ In this cohort, the prevalence of hearing trouble, urinary incontinence, depression, and osteoporosis were significantly higher among those with cancer.

Fatigue

Cancer-related fatigue is a persistent, subjective sense of tiredness related to cancer or cancer treatment that interferes with usual functioning.¹⁷² In advanced cancer, the prevalence of fatigue is greater than 50% to 70%.¹⁷³ In a study that evaluated the prevalence of common symptoms in patients with advanced cancer, fatigue was independently associated with chemotherapy, hemoglobin level, and other symptoms such as pain and depression.¹⁷⁴ Patients perceive fatigue to be one of the most distressing symptoms associated with cancer and its treatment, more than pain or nausea and vomiting.^{175,176} In contrast to normal fatigue, cancer-related fatigue is refractory to sleep and rest, perhaps because patients with cancer have aberrant sleep patterns. It is reasonable to expect that fatigue may precipitate functional dependence, especially in patients who are already dependent in IADLs.^{70,177,178}

Multiple factors can contribute to fatigue, including pain, emotional distress, anemia, comorbidities, medications, and/or sleep disturbance;

many of them are treatable. Certainly, the best strategy is avoidance of any fatigue that may precipitate functional dependence in older adults. Energy conservation, exercise programs, stress management, sleep therapy, and psychostimulants are some of the interventions that have proved valuable. Screening for fatigue can be done using a brief screening questionnaire that would enable patients to rate the severity of their fatigue on a scale of 0 (no fatigue) to 10 (worst fatigue). See the NCCN Guidelines for Cancer-Related Fatigue available at www.NCCN.org.

Frailty

Frailty is a biologic syndrome of decreased reserve and resistance to stressors, causing vulnerability to adverse outcomes.¹⁷⁹ Frail patients are at risk for falling, disability, hospitalization, and death. Fried Frailty Criteria and the Balducci Frailty Criteria are the two most common measures used to identify frail patients.^{22,48} A study showed that very few patients were classified as frail based on the oncologist's clinical judgment, and the use of a geriatric assessment can aid the oncologists to better identify frail patients.¹⁸⁰

According to Fried Frailty Criteria, frailty is defined as a clinical syndrome with three or more of the following conditions: unintentional weight loss (≥ 10 lb in the past year), self-reported exhaustion, weakness (grip strength), slow walking speed, and/or low physical activity.⁴⁸ In a prospective, observational study of 5317 patients (≥ 65 years), frailty status based on these criteria was found to be predictive of incident falls, worsening mobility or ADL function, incidence of hospitalization, and death.⁴⁸

The Balducci Frailty Criteria are based on the components of CGA (dependence in one or more ADLs, three or more comorbid conditions, and one or more geriatric syndromes).²² These CGA-frailty criteria have been found to be more useful in identifying frail patients with cancer. In a prospective study that compared the Balducci Frailty Criteria and the



modified version of Fried Frailty Criteria in 176 patients (aged 70–94 years) who underwent elective surgery for CRC, although both frailty measures were predictive of OS, the Balducci Frailty Criteria were more useful than the modified version of the Fried Frailty Criteria in predicting postoperative complications.¹⁸¹

Osteoporosis

Osteoporosis and its associated increased risk of fracture is a major risk factor in patients with cancer, especially in patients receiving chemotherapy or hormonal therapy for breast cancer and in patients receiving hormonal therapy for prostate cancer. Osteoporosis can be prevented with appropriate screening, lifestyle interventions, and therapy. The diagnosis of osteoporosis is based on assessment of bone density by a dual-energy x-ray absorptiometry (DEXA) scan. Management of bone health has become an integral part of comprehensive cancer care. Older patients should be made aware of the impact of cancer therapies on bone health and should adhere to treatment recommendations for maintaining bone health.¹⁸² The NCCN Task Force Report on Bone Health in Cancer Care discusses effective screening and therapeutic options for optimizing bone health in patients with cancer.¹⁸³

Falls

Falls are more common in older adults with a cancer diagnosis than those without cancer. Cancer diagnosis (especially in the first 6 months after diagnosis) and chemotherapy are also associated with a high risk of falls.¹⁸⁴⁻¹⁸⁶ In a prospective study of 185 patients with advanced cancer, 93 (50.3%) patients experienced falls associated with a high risk of physical injury, regardless of age: 35 patients were older than 65 years of age and 58 patients were 65 years of age or older.¹⁸⁴ The median time to a fall was 96 days. In a multivariate analysis, the diagnosis of a primary brain tumor or brain metastasis, number of falls in the preceding 3 months, severity of depression, benzodiazepine dose, and cancer-related pain were identified

as independent risk factors.¹⁸⁴ Another study also reported that the risk of falls increases with each cycle of chemotherapy, and patients treated with taxane-based chemotherapy may be at a greater risk of falls than those treated with platinum-based chemotherapy.¹⁸⁵ In a study that evaluated the occurrence of falls in 937 older adults with cancer, during the follow-up of 2 to 3 months after cancer treatment decision, a fall was reported by 142 patients (17.6%), of whom 51.4% fell more than once. Fall history in the past 12 months, fatigue, ADL dependency, geriatric risk profile by G8, and living alone were identified as independent predictors of 1 or fewer falls within 2 to 3 months after cancer treatment decision.¹⁸⁷ In addition, there are some data indicating the impact of falls in the interruption or cessation of subsequent cancer treatment.¹⁸⁸ These findings suggest that falls are important problems in older patients with cancer and that geriatric assessment can identify patients at risk for falls.

Multifactorial risk assessment and management, exercise, vitamin D supplementation, withdrawal of psychotropic medications, and environmental modifications have been shown to be effective in reducing the risk and/or rate of falls in older patients.¹⁸⁹⁻¹⁹⁴ The Guidelines recommend periodic assessment of history of falls, balance, and gait difficulties for all patients, as fall risk may change over time. The use of early and preventative use of durable medical equipment and in-home safety evaluations are recommended for patients with neurotoxicities at high risk for falls. Assessment of gait by evaluating gait speed¹⁵ or using the TUG test, evaluation for physical therapy or OT, vitamin D supplementation (in patients with low levels of vitamin D), or referral to geriatrics or a primary care physician can be considered for patients who have experienced a fall in the last 6 months or if they are afraid of falling. Finally, risk of falls should be considered carefully when making treatment decisions, as prescribing medications that can induce peripheral neuropathy may significantly increase this risk.



Delirium

Delirium is an acute decline in attention and cognition developed over a short period of time (usually hours to days) and is characterized by disturbance of consciousness with reduced ability to focus, sustain, or shift attention.¹⁹⁵ It is a common, serious, costly, under-recognized and easily overlooked problem in older adults that can contribute to complications such as poorer clinical outcomes, functional decline, impaired communication between the patient and physicians, longer length of hospital stay, and death.¹⁹⁶ Dementia is the leading risk factor for delirium and about two thirds of cases of delirium occur in older patients with dementia.¹⁹⁵

Many other predisposing factors such as vision or hearing impairment, history of alcohol abuse, functional dependency, and multiple comorbidities were consistently identified across patient populations.¹⁹⁵ Precipitating factors such as polypharmacy, dehydration, use of psychoactive drugs, and physical restraints can lead to delirium. Predictive models for delirium can be useful in identification as well as stratification of risks of delirium to assist health care providers in implementing preventive measures and improve outcomes.¹⁹⁵

With respect to older patients with cancer, cognitive dysfunction is one of the most common direct effects of primary and secondary CNS tumors (brain or meningeal metastasis). Para-neoplastic neurologic syndromes are potential causes of delirium. Toxicities from cancer-specific treatment with radiation, chemotherapy, and immunotherapy as well as supportive medications such as antihistamines, antiemetics, and anxiolytics also can lead to delirium and cognitive impairment.^{197,198}

The Confusion Assessment Method (CAM) is the most utilized screening and diagnostic tool based on four important features of delirium: acute onset and fluctuating course, inattention, disorganized thinking, and altered level of consciousness.^{199,200} The Memorial Delirium Assessment

Scale is a 10-item validated instrument developed for repeated use to quantify the severity of delirium symptoms in patients with advanced cancer.²⁰¹ The Nursing Delirium Screening Scale is an observational 5-item scale and has been validated in the oncology inpatient setting and is associated with high sensitivity and specificity.²⁰²

The NCCN Guidelines have included CAM as a screening tool for delirium. Delirium is usually multifactorial. A complete evaluation and treatment of all potential causes of delirium is recommended for all patients with delirium, including a conducting a thorough medication review and deprescribing agents that can contribute to delirium such as psychoactive medications and narcotics.²⁰³⁻²⁰⁵ Other potential contributing factors such as sleep deprivation, immobility, visual and hearing impairment, malnutrition, and dehydration should be addressed and non-pharmacologic approaches should be used. Pharmacologic interventions should be reserved for patients with severe agitation, which could result in interruption of essential medical therapies or could pose a danger for self-injury, or for those with distressing psychotic symptoms (eg, hallucinations, delusions).¹⁹⁵

Considerations for Older Adults Undergoing Cancer-Specific Treatment

Surgery

In general, age is not the primary consideration for surgical risk, although the physiologic status of the patient needs to be assessed.²⁰⁶ All older adults undergoing surgery should undergo an assessment for components of frailty, including comorbidities, mobility, functional status, and nutrition.²⁰⁷ The American College of Surgeons (ACS) Geriatric Surgery Verification (GSV) program provides a framework for hospitals to take an interdisciplinary approach to continuously optimize surgical care of older adults. The GSV program includes 30 standards to improve surgical care for older adults with an emphasis on goals of care and shared decision-



making, assessment of geriatric-specific vulnerabilities (eg, cognition, mobility), and interdisciplinary postoperative care.²⁰⁵ The ACS National Surgical Quality Improvement Program Surgical Risk Calculator includes both geriatric-specific predictors and geriatric-specific outcomes; the ACS Surgical Risk Calculator can be a useful tool for sharing patient-specific predicted outcomes after surgery and facilitating a more informed discussion regarding risks of surgery.²⁰⁸ The tool's functionality was enhanced by collecting data from more than 38,000 older patients and comparing performance in outcomes prediction using the traditional ACS Surgical Risk Calculator with models that also included geriatric risk factors.

Older age is also a risk factor for postoperative delirium, which is the most common postoperative complication in older adults. About 40% of the delirium in older patients is preventable, which makes it a prime candidate for prevention interventions targeted to improve the outcome of older adults after surgery.^{209,210} The AGS practice guidelines have presented both nonpharmacologic and pharmacologic interventions for prevention and treatment of postoperative delirium in older adults. The guidelines cover the topic areas of delirium risk factors, diagnosis and screening, prevention, medical evaluation, and pharmacologic treatment.²⁰⁹

Radiation Therapy

RT (external beam RT [EBRT] or brachytherapy) can be offered either in the curative or palliative setting.^{211,212} Available data from the literature indicate that RT can be highly effective and well tolerated, so that age alone need not be a limiting factor in older patients with cancer.^{213,214} Radiation oncologists, like all other clinicians caring for older patients with cancer, must be careful of the potential to overtreat older adults with substantial competing risks of non-cancer death, as well as the potential to undertreat older adults because of an underestimation of life expectancy in patients with advanced age but few significant comorbid conditions.

It is important to consider several general principles when developing an individualized treatment plan with RT in older patients.²¹² The decision to offer RT to older patients with cancer should be based on the following factors: 1) evaluation of the benefits and risks associated with RT; 2) careful consideration of the patient's underlying functional reserve; and 3) an understanding of the differences in the biology of cancers and their responsiveness to therapy in this patient population. Since the biologic characteristics of certain cancers are different in older patients compared to their younger counterparts, and partly because of the decreased tolerance of treatment by older patients, treatment should be individualized based on the nature of the disease and the performance status of the patient. Nutritional support and pain control for treatment-induced mucositis are recommended for patients receiving RT. Considerations for older patients undergoing RT will heavily depend on the anatomic site being radiated and the dose/fractionation chosen. See disease-specific NCCN Guidelines for Treatment by Cancer Type available at www.NCCN.org. Concurrent chemoradiation, however, should be used with caution; dose modification of chemotherapy may be necessary to reduce toxic side effects.

Incomplete and interrupted courses of RT can compromise the efficacy of treatment as well as the ability to deliver higher doses of RT in the future. Therefore, it is important to consider alternative approaches in patients with extreme functional limitations and ensure maximal supportive care. Advanced RT techniques (eg, intensity-modulated RT [IMRT], image-guided RT [IGRT], and stereotactic body RT [SBRT] or stereotactic ablative radiotherapy [SABR]) facilitate the delivery of large doses of radiation to small target volumes while limiting the risk of radiation-induced damage to normal surrounding tissues and organs at risk (OARs).²¹⁴ Judicious application of these techniques may also help to assuage concerns about the risks of RT in older adults. Hypofractionated RT may



also help to improve treatment tolerability by limiting overall treatment time without compromising clinical outcomes in some patients.²¹⁵

RT, though administered locally, can produce systemic side effects such as fatigue, depression, anorexia, nausea, vomiting, alteration in taste, sleep disturbance, headache, anemia, dry skin, dermatitis, and constipation. Late complications of these therapies also include pharyngitis, esophagitis, laryngitis, persistent dysphagia, fatigue, cardiovascular disease, mucositis, hepatotoxicity, and cognitive deficits.^{216,217}

Systemic Therapy

Several retrospective studies have reported that the toxicity of chemotherapy is not more severe or prolonged in persons older than 70 years of age.²¹⁸⁻²²¹ However, the results of these studies cannot be generalized for the following reasons:

- Only a few patients were 80 years of age or older; therefore, minimal information is available on the oldest patients.
- The older patients involved in these studies were highly selected by the eligibility criteria of the cooperative group protocols and were not representative of the general older population, because they were probably healthier than most older patients.
- Many of the treatment regimens used in these trials had lower dose intensity than those in current use.

Nevertheless, these studies are important, because they demonstrate that age, by itself, is not a contraindication to cancer therapy. Therefore, patient selection is extremely important to maximize the benefits of systemic therapy in older patients with cancer.

More studies have emerged studying impact of chemotherapy on older cancer patients. For example, cognitive functioning (assessed through MMSE) was not worst among breast cancer patients aged 70 to 80 years treated with immunotherapy with chemotherapy combination as compared to those treated with immunotherapy alone.²²² In another retrospective evaluation of NSCLC patients aged 85 years or more, epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI) as first-line therapy showed greater benefit than cytotoxic chemotherapy or best supportive care alone with OS of 16.9, 7.2, and 9.8 months, respectively.²²³

Increased age has been associated with changes in the pharmacokinetics and pharmacodynamics of cancer therapy and increased susceptibility of normal tissues to toxic complications.²²⁴ Pharmacodynamic changes of interest include reduced repair of DNA damage and increased risk of toxicity. Pharmacokinetic changes of major concern include decrease in the GFR and volume of distribution of hydrosoluble drugs. Although the hepatic uptake of drugs and the activity of cytochrome P450 enzymes also decrease with age, the influence of these changes on cancer chemotherapy is not clear. Intestinal absorption may decrease with age, but it does not appear to affect the bioavailability of anticancer agents. The pharmacokinetics of antineoplastic drugs is unpredictable to some extent; thus, drug doses should be adjusted according to the degree of toxicity that develops. However, adequate dosing is necessary to ensure the effectiveness of therapy.

Extermann and colleagues have devised the MAX2 index for estimating the average per-patient risk for toxicity from chemotherapy.²²⁵ In a retrospective analysis, Shayne et al identified advanced age (≥ 65 years), greater body surface area, comorbidities, anthracycline-based regimens, a 28-day schedule, and febrile neutropenia as independent predictors of reduced dose intensity among patients with early-stage breast cancer receiving adjuvant chemotherapy.²²⁶ In another retrospective analysis of



older patients (≥ 65 years) with invasive breast cancer, the type of adjuvant chemotherapy regimen was a better predictor of toxicity than increased age or comorbidity score.²²⁷ Anthracycline-based regimen resulted in greater grade 3 or 4 toxicity, hospitalization, and/or febrile neutropenia, whereas treatment delays due to myelosuppression were more frequent with the cyclophosphamide-containing regimen. Among older patients with ovarian cancer, those receiving standard-dose chemotherapy were more likely to experience cumulative toxicity and delays in therapy versus those receiving reduced-dose intravenous carboplatin/paclitaxel.²²⁸

Other investigators have developed tools incorporating components of CGA to assess the individual risk of severe toxicity from chemotherapy in older patients.⁵⁹⁻⁶¹ Hurria and colleagues have developed a cancer-specific geriatric assessment (CSGA) for predicting treatment-related toxicity in older patients with cancer, which has also been validated in an independent cohort study of 250 older adults (≥ 65 years) with a solid tumor.^{59,60} The following factors were predictive of grade 3 to 5 toxicity: age greater than or equal to 72 years; type of cancer (gastrointestinal [GI] or genitourinary); standard-dose chemotherapy; polychemotherapy; hemoglobin level (male: < 11 g/dL; female: < 10 g/dL); creatinine clearance less than 34 mL/min; hearing impairment described as fair or worse; one or more falls in the last 6 months; limited in walking one block; the need for assistance with taking medications; and decreased social activities due to physical or emotional health. Extermann et al have developed the chemotherapy risk assessment scale for high-age patients (CRASH) score, which could be useful in predicting significant differences in the risk of severe toxicity in older patients with cancer starting a new chemotherapy.⁶¹ In this model, diastolic blood pressure, IADLs, lactate dehydrogenase, and the type of treatment were the best predictors of hematologic toxicity. Performance status, cognitive function, nutritional status, and the type of therapy were the best predictors of non-hematologic toxicity. These tools can aid the oncologist in selecting

and discussing the recommended therapy with an older adult. Such information will allow for shared decision-making weighing the risks and benefits of the proposed treatment approach. A study showed the benefits of performing CGA prior to chemotherapy and delivering CGA guided care along side anti-cancer therapy in reducing toxic effects in older adults with cancer. In this randomized controlled trial (RCT), 613 patients 65 years of age or older were randomized to either the specific geriatric assessment-driven intervention (GAIN) arm or to the standard of care (SOC) arm. Incidence of grade 3 or higher chemotherapy-related toxic effects in the GAIN arm (50.5%; 95% CI, 45.6%–55.4%) were 10.1% lower than the SOC arm (60.6%; 95% CI, 53.9%–67.3%).²²⁹ Another study, the Geriatric Assessment for Patients 70 years and older (GAP70+) trial, also reported a significant reduction in the proportion of patients with grade 3 to 5 toxic effects who were assigned to geriatric assessment intervention before receiving chemotherapy (51% vs. 71% with usual care; relative risk [RR], 0.74; 95% CI, 0.64–0.86; $P = .0001$).²³⁰

Targeted Therapy

The emergence of targeted therapies (monoclonal antibodies and small molecules targeted against specific molecular pathways required for the development of a particular malignancy) has significantly improved outcomes in a variety of malignancies. The use of targeted therapies in older patients appears to be promising in view of their better efficacy and toxicity than conventional chemotherapeutic agents.^{231,232} However, these drugs are also associated with some unique and severe side effects.²³³ For example, cardiovascular complications such as left ventricular dysfunction (LVD) are associated with HER2 inhibitors (trastuzumab) and hypertension and arterial thromboembolic events (ATEs) are associated with vascular endothelial growth factor receptor (VEGFR) inhibitors (ie, bevacizumab),²³⁴⁻²³⁶ whereas dermatologic toxicities (acneiform rash and hand-foot skin reaction) are the major adverse effects of EGFR inhibitors (ie, erlotinib, sunitinib, sorafenib, cetuximab).²³⁷



There are limited but growing data available on the safety and efficacy of targeted therapies in older patients with cancer. Prospective clinical trials that include a sufficiently large number of older patients are needed to accurately determine the efficacy and tolerability of targeted therapies in this cohort of patients. In patients who are not able to tolerate cytotoxic chemotherapy, the risk-benefit ratio should be considered prior to initiation of targeted therapy and the use of targeted therapies should be individualized.

Immunotherapy (including chimeric antigen receptor [CAR] T-cell therapy)

Older adults are underrepresented in clinical trials studying immunotherapy including CAR T-cell therapy across multiple cancers. Participation of this population is limited due to exclusion criteria in studies related to age, comorbidities, and impaired functional status.²³⁸ In general, information derived from subgroup analyses and retrospective studies report a similar clinical benefit in older and younger patients in case of immune checkpoint inhibitor (ICI) therapy (ie, PD-1/PD-L1),^{239,240} with some concerns for increase in toxicity rates. In the Keynote-024 study of pembrolizumab for NSCLC patients with more than half of the population being older than 65 years, a more favorable HR of 0.45 (0.29–0.70; 95% CI) for disease progression or death was observed for older patients compared to younger ones.^{241,242} Subgroup analysis of the Keynote-045 phase 3 study evaluating benefits of pembrolizumab over chemotherapy in older patients aged 65 years and older with advanced urothelial carcinoma, who had progressed after chemotherapy, showed improved OS and fewer adverse events in the pembrolizumab group.²⁴³ Similarly, in a meta-analysis of 34 RCTs with 21,213 patients with advanced cancers (eg, NSCLC, melanoma), which included 69.4% of patients younger than 65 years and 40.6% of patients aged 65 years and older, similar statistically significant advantage in OS of immunotherapy over control

therapy (non-ICI therapy) was observed in both age groups.²⁴⁰ A meta-analysis evaluated 15 phase 3 studies that included patients aged 75 years or more with NSCLC, renal cell carcinoma (RCC), melanoma, head and neck squamous cell carcinoma (SCC), or gastric cancer comparing ICI therapies (mono- or combination therapy) versus standard therapy as first-line and second-line treatment. The HR for the first-line setting was 0.78 (95% CI, 0.61–0.99) versus 1.02 (95% CI, 0.77–1.36) for second-line treatment, which indicated survival benefits of ICI therapy in the first-line setting but not in second-line treatment.²⁴⁴

Safety data of CAR T-cell therapies in the older patient population are sparse that limit the generalization of the effects of CAR T-cell therapy in the older population. The pivotal ZUMA-1 phase 1/2 study evaluating safety of a CAR T-cell therapy for B-cell lymphoma showed no significant differences in the extent of benefits between younger and older patients, although the older patients only represented a small number.²⁴⁵ In a large-scale post-marketing analysis of 804 cases receiving CAR T-cell therapy,²⁴⁶ some of the adverse events noted in older patients receiving CAR T-cell therapy versus the younger population were encephalopathy syndrome (8% vs. 4%, $P = .03$), decreased hemoglobin and hematocrit (13% vs. 7% and 12% vs. 6%, respectively; $P < .01$ for both), decreased blood fibrinogen (2% vs. 0.2%, $P = .04$), increased blood creatinine (2% vs. 0.2%, $P = .04$), rash (2% vs. 0%, $P < .01$), and sepsis (3% vs. 1%, $P = .02$). Younger patients reported more hospitalizations and adverse events such as pyrexia, tachycardia, and thrombocytopenia.²⁴⁶

As these treatments carry risks for immune-related adverse events, we must consider the nuances of managing these types of toxicities in older adults. High-dose steroids for the management of immune-related toxicities must be used with caution in older patients as they may worsen other comorbidities or cognitive function. The NCCN Panel recommends that when steroids are being used for supportive care, careful



consideration must be given to the dose and duration of therapy, and for management of immunotherapy-related adverse events, lowest possible effective dose should be used.

Management of Side Effects in Older Adults Undergoing Cancer-Specific Treatment

In older patients undergoing chemotherapy, the most common complications include myelosuppression resulting in neutropenia, anemia, or thrombocytopenia; mucositis; renal toxicity; cardiac toxicity; and neurotoxicity. Older patients appear to be at special risk for severe and prolonged myelosuppression and mucositis, increased risk for cardiomyopathy, and increased risk for peripheral neuropathy. In addition, they are also at risk for infection (with or without neutropenia), dehydration, electrolyte disorders, and malnutrition either as a side effect of the chemotherapy or directly from the tumor. Chemotherapy can also affect cognition, function, balance, vision, hearing, continence, and mood.²⁴⁷ The combination of these complications enhances the risk of delirium and functional dependence. It is essential to detect and correct these complications (that may interfere with treatment) in order to achieve maximum benefit from chemotherapy. Prevention and/or amelioration of some of the common chemotherapy-related complications are discussed below.

Cardiovascular Toxicity

Anthracyclines are associated with increased cardiac toxicity resulting in LVD and CHF.^{248,249} Other antineoplastic drugs associated with significant cardiovascular complications include alkylating agents, antimetabolites, microtubule-stabilizing agents, and targeted therapies such as trastuzumab and immunotherapies. These drugs may have an additional effect on anthracycline-induced cardiovascular toxicity. Risk factors for anthracycline-induced cardiovascular toxicity include an existing or history of heart failure or cardiac dysfunction, hypertension, diabetes and CAD,

older age (independent of comorbidities and performance status), prior treatment with anthracyclines, higher cumulative doses, and short infusion duration.^{249,250}

Cardiac toxicity in older patients receiving trastuzumab remains a concern.²⁵¹⁻²⁵⁴ Increased incidence of cardiotoxicity are seen among older patients with breast cancer with a history of cardiac disease and/or diabetes treated with trastuzumab.²⁵⁴ In a large, population-based, retrospective study of older patients with stage I–III breast cancer (≥66 years; 9535 patients; 2203 patients received trastuzumab), the use of trastuzumab resulted in a CHF rate of 30%, which is substantially higher than that reported in clinical trials. Among patients treated with trastuzumab, older age (≥80 years), hypertension, CAD, cardiac comorbidities, and weekly administration of trastuzumab were associated with increased risk of CHF.²⁵⁵ In general, taxane-anti-HER2 combinations without anthracyclines and with close cardiac monitoring are recommended for older patients. Although investigated in the general population of lower-risk adjuvant breast cancer patients, the combination of paclitaxel and trastuzumab is associated with excellent outcomes and tolerability.²⁵⁶

Emerging data from clinical studies suggest that trastuzumab, when used in combination with non-anthracycline-based chemotherapy, has similar efficacy with lower rates of cardiac events in patients with early-stage as well as metastatic HER2-positive breast cancer.²⁵⁷⁻²⁵⁹ The subgroup analysis of the randomized trial that evaluated trastuzumab in combination with docetaxel and pertuzumab in patients with HER2-positive metastatic breast cancer (808 patients; 127 patients were ≥65 years) did not show any increase in the risk of cardiac dysfunction associated with trastuzumab, and there was also no evidence of late or cumulative cardiac toxicity.²⁵⁹ In addition, the results also showed no significant correlation between age and the development of left ventricular systolic dysfunction in



older patients. Additional data are needed regarding the tolerability of these regimens in older patients.

Cardiac toxicity from immunotherapy is rare but can include arrhythmias, myocarditis, and heart failure, which could lead to severe consequences including death. Prevalence is much higher in patients on combination immunotherapy.²⁶⁰

Renal Toxicity

The GFR decreases with age, which in turn delays elimination of many drugs. Delayed renal excretion may enhance the toxicity of medications whose parent compounds are excreted by the kidneys (ie, carboplatin, oxaliplatin, methotrexate, bleomycin) and drugs that are converted to active (ie, idarubicin, daunorubicin) or toxic metabolites (ie, high-dose cytarabine).⁵ Dose adjustment to the measured GFR should be considered for these drugs to decrease systemic toxicity.

Renal insufficiency is common in older patients with cancer, particularly in patients receiving nephrotoxic drugs, patients with genitourinary cancers, or patients with multiple myeloma. In patients with preexisting renal problems who are at a greater risk of renal impairment, the use of nephrotoxic drugs should be limited or avoided. Serum creatinine is not a good indicator of renal function in older adults. Calculation of creatinine clearance is recommended to assess renal function and adjust dose to reduce systemic toxicity.

Neurotoxicity

Neurotoxicity is also a dose-limiting toxicity associated with chemotherapy.²⁶¹ Vinca alkaloids, platinum-based therapies, and taxanes induce peripheral neurotoxicity. Methotrexate, cytarabine, and ifosfamide are associated with central neurotoxic side effect. Purine analogs (eg, fludarabine, cladribine, pentostatin) are associated with life-threatening neurotoxicity at significantly higher doses than the recommended clinical

dose.²⁶² High-dose cytarabine can cause an acute cerebellar syndrome. Patient's age (>60 years), drug dose and schedule, and renal and hepatic dysfunction are the most important risk factors for cytarabine-induced cerebellar toxicity.^{263,264}

Management of neurotoxicity mainly consists of dose reductions or lower dose intensities. Older patients are particularly susceptible to the toxicity of cytarabine-based regimens due to decreased renal excretion of the toxic metabolite ara-uridine, and increased vulnerability of the cerebellum. Particular attention should be paid to the use of cytarabine in high doses, especially in patients with renal insufficiency. Dose reductions are necessary in patients with reduced GFR. The Guidelines recommend monitoring for cerebellum function, hearing loss, and peripheral neuropathy. The risk of falls due to peripheral neuropathy is of particular concern in older patients.¹⁸⁵

Myelosuppression

Available data from various studies have shown that the risk of myelosuppression increases substantially by age 65 years.²⁶⁵⁻²⁶⁹ The risk of myelosuppression is decreased by 50% when using growth factors.²⁷⁰⁻²⁷² The use of growth factors in these circumstances does not appear to be associated with increased cost and may even be cost saving if it prevents lengthy hospitalizations from neutropenic infections in older persons.

Neutropenia

Neutropenia is the major dose-limiting toxicity associated with chemotherapy, especially in older patients. Among older patients with aggressive non-Hodgkin lymphoma treated with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) chemotherapy, the incidences of fever and neutropenia were significantly higher for patients aged greater than or equal to 70 years (42% vs. 8% for



patients aged 61–69 years; $P < .0001$).²⁷³ In patients 60 years or older receiving induction or consolidation chemotherapy for AML, the prophylactic use of hematopoietic growth factors results in faster recovery of neutrophil and shorter hospitalization, but it does not impact OS.^{274,275}

Meta-analysis of controlled clinical trials on the prophylactic use of recombinant granulocyte colony-stimulating factors (G-CSF) has confirmed their effectiveness in reducing the risk of febrile neutropenia.²⁷⁶ The use of growth factors appears to be the best established strategy to improve treatment in older patients.²⁷⁷ The EORTC has issued recommendations for the prophylactic use of G-CSF in older patients with cancer.²⁷⁸ The NCCN Guidelines for Myelodysplastic Syndrome available at www.NCCN.org address the use of G-CSFs in patients with solid tumors and non-myeloid malignancies.

Anemia

Anemia has been shown to be a risk factor for chemotherapy-related toxicity and is one of the factors responsible for the reduction in volume of distribution, which may result in increased peak concentration and increased toxicity of drugs.²⁷⁹ Anemia is also associated with cardiovascular disease, CHF, CAD, and dementia.²⁸⁰⁻²⁸³ In older patients of aged 65 years or more with cancer, anemia is significantly associated with multidimensional loss of function (eg, mobility limitations, impaired cognition) and higher rates of functional disability.^{284,285}

In patients with severe anemia, blood transfusions may be necessary to prevent serious clinical consequences. Although erythropoiesis-stimulating agents (ESAs) have been demonstrated to decrease the need for transfusion in patients receiving chemotherapy,²⁸⁶ randomized studies have reported decreased survival and poorer tumor control among patients with cancer receiving erythropoietic drugs for correction of anemia

and target hemoglobin levels 12 g/dL.²⁸⁷ The use of ESAs in patients with cancer is also associated with increased risks of venous thromboembolism and mortality.^{288,289} In July 2008, based on the results of these trials, the FDA strengthened its warnings to alert physicians of increased risk of tumor progression and shortened survival in patients with advanced breast, cervical and head and neck cancers, lymphoid neoplasms, and NSCLC. Physicians were advised to use the lowest dose necessary to avoid transfusion. In addition, the use of ESAs is restricted to the treatment of anemia specifically related to myelosuppressive chemotherapy without curative intent. ESAs should be discontinued once the course of chemotherapy has been completed and the anemia has resolved. Evaluation of deficiency in iron, B12 and folic acid should be conducted in the setting of anemia with initiation of the appropriate replacement therapy is recommended. The panel recommends that anemia in older patients with cancer should be managed as outlined in the NCCN Guidelines for Hematopoietic Growth Factors available at: www.NCCN.org.

Thrombocytopenia

Chemotherapy-induced thrombocytopenia (CIT) is a common hematologic toxicity associated with cytotoxic and myeloablative chemotherapy. Dose reductions and/or interruptions of chemotherapy regimens are necessary in patients with severe thrombocytopenia. While chemotherapy-induced anemia and neutropenia can be managed with hematopoietic growth factors, safe and effective treatment of CIT is still a significant problem. Recombinant interleukin-11 is the only currently approved treatment of CIT in patients with non-myeloid malignancies.²⁹⁰ However, it is toxic and of minimal clinical benefit. A phase II clinical trial demonstrated significant efficacy of thrombopoietin-like agents such as romiplostim and eltrombopag for the treatment of CIT; however, the settings for which these agents will provide clinical benefit are important and not yet fully defined in older patients.^{291,292} Current recommendations



include the management of CIT in older patients similar to the younger patient population.

Nausea and Vomiting

Chemotherapy-induced nausea and vomiting (CINV) is a debilitating side effect that can significantly affect a patient's QOL and compliance with treatment. In addition, older adults may be at higher risk for dehydration and other complications as a result of significant nausea and vomiting. Serotonin (5-HT₃)–receptor antagonists, neurokinin-1-receptor antagonists, and corticosteroids are the most effective antiemetic drugs used for the management of CINV.²⁹³ Older patients may have an increased risk of toxicity from antiemetic drugs due to age-related physiologic changes in drug absorption, distribution and excretion, drug interactions, and polypharmacy used to treat comorbidities.^{294,295}

Therefore, the selection of appropriate antiemetic therapy in older patients should be based on individual patient characteristics, prior history of CINV, the emetogenic potential of the specific chemotherapeutic agent, and most importantly the side effect profile of the antiemetic agent. For example, QTc prolongation has been reported as a class effect of 5-HT₃–receptor antagonists, especially dolasetron, tropisetron, and palonosetron, and these should be used with caution in older patients with cardiovascular complications.²⁹⁴ CINV should be managed as described in the NCCN Guidelines for Antiemesis and the NCCN Guidelines for Palliative Care available at www.NCCN.org.

Diarrhea

Diarrhea is a well-recognized side effect associated with a number of chemotherapeutic agents, particularly fluorouracil and irinotecan. Loss of fluids and electrolytes associated with persistent and severe diarrhea can lead to dehydration, renal insufficiency, and electrolyte imbalance.²⁹⁶ Furthermore, chemotherapy-induced diarrhea can lead to dose reductions, delay in therapy, or discontinuation of chemotherapy, which ultimately

affect clinical outcomes.²⁹⁷ Based on the results from various clinical trials, the ASCO guidelines for the comprehensive evaluation and management of cancer treatment-induced diarrhea recommend loperamide as the standard therapy for mild-to-moderate diarrhea.²⁹⁶ Octreotide (subcutaneous or intravenous if the patient is severely dehydrated) may be beneficial for patients with severe diarrhea or diarrhea that is refractory to loperamide therapy. Diphenoxylate/Atropine (oral opiate) therapy is also occasionally prescribed for cancer treatment-induced diarrhea with mild symptoms (although loperamide is preferred) and is used with extreme caution in patients with renal and/or liver failure.²⁹⁸

The NCCN Guidelines recommend early aggressive rehydration and management with octreotide (if oral treatments are ineffective) for older patients with chemotherapy-induced diarrhea.

Mucositis

Oral and GI mucositis are significant complications of radiotherapy and chemotherapy. The risk of mucositis increases with age, and its presence in older adults can lead to decreased oral intake, leading to dehydration and additional complications. In a phase III randomized study of 212 patients with hematologic cancers undergoing high-dose chemotherapy and total body irradiation followed by autologous HCT, palifermin (human keratinocyte growth factor) was associated with a significant reduction of oral mucositis compared to placebo (20% vs. 62%).²⁹⁹ Palifermin is approved for the treatment of oral mucositis in patients with hematologic malignancies receiving myeloablative therapy requiring hematopoietic stem cell support. A few studies have reported that palifermin is also well tolerated and effective in the prevention of oral mucositis in patients with metastatic CRC treated with fluorouracil-based chemotherapy and in patients with head and neck cancer treated with postoperative or definitive chemoradiation therapy.³⁰⁰⁻³⁰² The 2014 Multinational Association of Supportive Care in Cancer and International Society of Oral Oncology



have detailed recommendations for the management of mucositis secondary to cancer therapy.³⁰³ Once mucositis has occurred, patients should be kept well hydrated with intravenous fluids. Early hospitalization may be necessary for patients with mucositis who also develop dysphagia or diarrhea.

Insomnia

Insomnia is characterized by difficulty falling or staying asleep, waking up too early, or experiencing poor-quality nonrestorative sleep associated with daytime impairment (fatigue, poor concentration, daytime sleepiness, or concerns about sleep).³⁰⁴ The incidence of insomnia in patients with cancer has been reported to be three times higher than that reported in the general population and ranges from 25% to 69%, depending on the type of cancer.^{305,306} In a longitudinal study that assessed the prevalence and natural course of insomnia in patients with cancer during an 18-month period, Savard et al reported higher rates of insomnia in patients with breast (42%–69%) and gynecologic (33%–68%) cancer and lower rates among those with prostate cancer (25%–39%).³⁰⁶

Insomnia is more prevalent in older adults, and older patients with cancer should be screened for sleep disturbances prior to the initiation of treatment and at regular intervals during the course of treatment. The AGS has provided recommendations for the diagnosis, evaluation, and management of insomnia in older adults.³⁰⁴ The published Pan-Canadian practice guidelines also provide recommendations for the prevention, screening, assessment, and treatment of sleep disturbances in older patients with cancer.³⁰⁷

Cognitive behavioral therapy (CBT) and lifestyle modifications are the preferred first-line treatment options for the management of insomnia in older patients.^{304,307} The effectiveness of CBT with multicomponent interventions (stimulus control, sleep restriction, cognitive therapy, sleep hygiene, and fatigue management) for the management of insomnia in

patients with cancer has been demonstrated in randomized clinical trials.³⁰⁸⁻³¹¹ Adherence to CBT has been shown to yield greater sleep improvements among patients following primary treatment for breast cancer.³¹²

Pharmacologic therapy may be necessary for some patients until CBT takes effect.^{304,307} Benzodiazepines, non-benzodiazepines, and melatonin-receptor agonists are the FDA-approved classes of drugs for the treatment of insomnia.^{313,314} However, due to some of the severe adverse effects associated with benzodiazepines and non-benzodiazepines (eg, impaired postural stability, fractures, cognitive impairment),³¹³ these drugs are not recommended as first-line therapy for the treatment of insomnia in older adults.^{304,307} Patients should be cautioned that most over-the-counter sleep medications contain antihistamines that carry risk of toxicities in older adults and thus should be avoided if possible. If pharmacologic therapy is to be utilized, it is recommended only for short-term use, with the lowest dose that is safe and effective to address the particular type of sleep disturbance in an individual patient. The risks and benefits of the therapy should be discussed. The panel notes that if zolpidem is considered, the FDA has advised that the recommended dose of zolpidem for patients assigned female at birth should be lowered.³¹⁵

Adherence to Therapy

Adherence to the prescribed regimen, especially oral therapy, is essential to derive maximal clinical benefit. While older age per se is not a consistent risk factor for non-adherence, older adults are at an increased risk for non-adherence for a variety of reasons, including cognitive impairment, increased number of comorbid conditions, polypharmacy, higher risk of side effects adversely affecting comorbidities, increased likelihood of drug interactions, limited insurance coverage, social isolation, and inadequate social support.³¹⁶ Treatment-related adverse events,



complexity of regimens, and poor understanding of the need for treatment are some of the other common barriers to adherence.

Discontinuation and nonadherence to adjuvant hormonal and chemotherapies are well documented in patients with early-stage breast cancer. In studies that have evaluated adherence to adjuvant hormonal therapy (ie., tamoxifen) among older patients (≥ 55 years) diagnosed with early-stage breast cancer, the reported rates of nonadherence or discontinuation range from 15% to 49%.³¹⁷⁻³²¹ In the randomized study (CALGB 49907) that evaluated adjuvant chemotherapy with oral capecitabine versus standard chemotherapy in 161 patients (≥ 65 years) with early-stage breast cancer, 25% of the patients took fewer than 80% of the planned doses.³²² Adherence was not related to age, tumor stage, or hormone receptor status. However, in other studies, poor adherence to adjuvant chemotherapy was more frequent in older patients (≥ 65 –75 years).^{323,324} In the ADAGIO study, non-adherence was associated with poorer response to imatinib in patients with chronic myeloid leukemia (CML); non-adherence rates were significantly higher for patients with suboptimal response compared to those with optimal response to imatinib (23% and 7%, respectively).³²⁵ Marin and colleagues also identified adherence as the only independent predictor for achieving complete molecular response on standard-dose imatinib in patients with CML.³²⁶ Adherence to chemotherapy also significantly reduced the risk of cancer-related mortality in patients with stage III colon cancer with [RR], 0.79 (95% CI = 0.69 to 0.89), with greater non-adherence observed in those with cancer recurrence (for adjuvant therapy completion, [RR], 0.22, 95% CI = 0.14-0.31). The likelihood of completing the cancer treatment decreased with age, with those older than 75 years were less likely to complete adjuvant chemotherapy.³²⁷ In patients of age 66 years and older with local or regional head and neck cancer, adherence was more common in the patients receiving surgical procedures prior to radiotherapy

as compared to the patients who receive radiotherapy alone or in combination with chemotherapy.³²⁸

Few studies have determined the actual adherence to oral therapies in patients with cancer, but clinical trials in a variety of cancer types attribute reduced adherence in older patients to toxicity. A task force report from SIOG that reviewed the impact of age-related factors on adherence to oral therapy in older adults recommends careful patient selection (using CGA, mentioned above, or other geriatric screening tools) and close monitoring of adherence to oral therapy.³²⁹ The task force report summarizes all potential determinants of adherence in older adults as attributed to factors that may be patient-related, age-specific, socioeconomic, disease-related, therapy (toxicity)-related, or health care team-associated. Since non-adherence is a complex issue associated with increased mortality and health care costs, the task force has also compiled a corresponding set of health care-led and patient-driven intervention strategies to promote adherence and overcome the barriers to adherence.

In older patients with cancer, assessment of risk factors for non-adherence is recommended when considering a treatment regimen that will include an oral agent. Close monitoring of patient adherence; reduction of regimen complexity (if possible); interventions designed to educate older patients about the risks and benefits of oral therapy and the importance of adherence to therapy; adequate and appropriate management of side effects; and scheduling of follow-up visits at regular intervals to review side effects are some strategies that may be helpful to minimize non-adherence to therapy. In addition, prioritizing the clinical pharmacists' involvement in adherence management especially for patients receiving oral anti-cancer therapies is recommended.³³⁰ Muluneh et al executed an integrated, closed-loop, pharmacy-led oral chemotherapy management program within their institution to provide specialty pharmacy services to their patients to facilitate their copays, prior authorizations, clinical



education, refill follow-up via phone calls, dispensation, home delivery, etc. Their program also credentialed the clinical pharmacists in oncology to educate and counsel patients starting oral chemotherapy either via phone or in clinic, as well as assess the patient's adherence to medication.

Patient's understanding and assessment of adherence was evaluated via pre-tests, post-tests, and follow-up questions. The results showed an increase in comprehension of oral chemotherapy treatment from 43% to 95%. Adherence rates for the GI/breast and malignant hematology patient populations were 85% and 93.9%, respectively.³³⁰

Approach to Cancer Screening and Surveillance Testing

Cancer screening refers to screening for new primary cancers that are different than the cancer survivor's prior cancer. The older adults with cancer often have multiple chronic conditions that could decrease their life expectancy.³³¹ Although screening older adults could be beneficial in detecting cancers at early stages to allow for early intervention strategies, one major downside is overdiagnosis and treatment of cancers that might not have caused any symptoms during the patient's lifetime.³³² Harms of screening relevant to older adults include fatigue from tests, discomfort, side effects, harms of procedure after-care, and distracting/time consuming. Moreover, the direct benefits of cancer screening are less evident specifically for this population since the RCTs of screening rarely include older age groups.³³¹ There is some evidence to support routine screening for the following cancers (although evidence in older individuals is limited): breast, colorectal, and lung cancer. In a retrospective cohort study with 5186 patients with breast cancer aged 65 and older, mammogram screening of breast cancer was associated with reduction in risk of death for all patients with mild to moderate comorbidities; however, those with severe or multiple comorbidities showed no improvement in OS.³³³ The American Cancer Society recommends mammography in older patients who have a life expectancy of 10 years or more, as it is unlikely to benefit those with less than a 10-year life expectancy. Screening decisions

among patients aged 75 years and older should be made according to overall health and patient preferences.³³⁴ Several trials have shown benefits of CRC screening such as sigmoidoscopy, fecal occult blood testing, and CT colonography and/or colonoscopy in older patients in reducing CRC-specific mortality rates.³³⁵ However, colonoscopy was associated with serious adverse events in asymptomatic persons including perforations and bleeding and is not recommended for persons with less than a 10-year life expectancy or those aged 85 years and older. There is limited or no evidence to support screening for cervical cancer or prostate cancer in older people. False-positive of abnormal pap smear is common in older patients due to difficulty obtaining an adequate sample. Cervical cancer growth is slow and can take 10 to 30 years, and there is a possibility of spontaneous regression of low-grade cervical lesions in older adults.³³² In addition, pap smears are associated with high anxiety and psychological distress. Data are lacking to demonstrate any benefit in prostate cancer screening for patients older than 75 years. For patients aged 55 to 74 years, the U.S. PLCO trial of over 75,000 patients found no benefits,³³⁶ although younger patients with no comorbidities showed reduction in prostate cancer-specific mortality rates with screening.³³⁷

Hence, routine cancer screening should be performed on older adult patients after careful consideration of their overall life expectancy. If the patient's life expectancy is 10 years or less, the patient is unlikely to benefit from routine cancer screening and more likely to experience immediate harms and distress. Thus, cancer screening should be stopped for such patients. If the patient's life expectancy is greater or equal to 10 years, the patient's goals and values must be consistent with wanting treatment if the cancer is detected to warrant continuation of routine screening.³³²

“Surveillance screening” refers to routine screening (in the absence of symptoms or abnormal physical examination findings) for recurrence or



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new primary cancers of the same type as the cancer survivor's prior cancer(s) beyond routine history and physical examination. (Note that diagnostic evaluation is recommended for any patient with symptoms or signs suspicious for cancer recurrence on history or physical examination.) If the patient's life expectancy is 5 years or less, they are unlikely to benefit from routine surveillance testing. The NCCN Panel recommends stopping routine surveillance testing for these patients in the absence of symptoms or findings on physical examination. If the patient's life expectancy is greater than 5 years, the patient's goals and values must be consistent with wanting treatment should cancer recurrence be detected, the health status should be appropriate, and individualized, shared decision-making should be engaged when determining the need for routine surveillance testing.

The benefits of cancer screening and routine surveillance testing are likely to exceed the harms of screening if the patient's risk of cancer is higher than average (eg, genetic cancer syndrome, prior exposures such as radiation or chemotherapy) and if life expectancy is sufficient (>5 years). The harm of screening and surveillance testing will outweigh the benefit in the setting of significant comorbidities, which can limit the ability to conduct the test (eg, colonoscopy in the setting of significant cardiac or lung disease) or impact ability to treat cancer if detected. For example, patients with favorable-subtype breast cancers treated with endocrine therapy carry a lower risk of recurrence/new primaries compared to similar-aged patients with no history of breast cancer, and thus are not likely to benefit from routine surveillance testing.³³⁸

Summary

There are unique issues to consider when caring for an older adult with cancer. The physiologic changes associated with aging may impact an older adult's ability to tolerate cancer therapy and should be considered

in the treatment decision-making process. Nevertheless, advanced age alone should not be the only criterion to preclude a patient from receiving effective cancer treatment that could improve QOL or lead to a survival benefit. Treatment should be individualized based on the nature of the disease, the physiologic status of the patient, and the patient's preferences.

Appropriate use of geriatric screening tools and/or CGA enables physicians to develop a coordinated plan for cancer treatment as well as guide interventions tailored to the individual patient based on his/her functional status and physiologic age rather than chronologic age. The goal of the NCCN Guidelines for Older Adult Oncology is to assist clinicians in providing evidence-based oncology care that enhances treatment decision-making and improves QOL in older adults with cancer. The updated guidelines include a roadmap that could assist providers in tailoring a geriatric assessment that could be routinely used in their clinical practice as they provide care to this vulnerable patient population.

**References**

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. *CA Cancer J Clin* 2022;72:7-33. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/35020204>.
2. Howlander N NA, Krapcho M, Miller D, Brest A, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2018: National Cancer Institute. Bethesda, MD, based on November 2020 SEER data submission, posted to the SEER web site, April 2021. Available at: https://seer.cancer.gov/csr/1975_2018/.
3. Smith BD, Smith GL, Hurria A, et al. Future of cancer incidence in the United States: burdens upon an aging, changing nation. *J Clin Oncol* 2009;27:2758-2765. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/19403886>.
4. Talarico L, Chen G, Pazdur R. Enrollment of elderly patients in clinical trials for cancer drug registration: a 7-year experience by the US Food and Drug Administration. *J Clin Oncol* 2004;22:4626-4631. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/15542812>.
5. Balducci L. Management of cancer in the elderly. *Oncology (Williston Park)* 2006;20:135-143; discussion 144, 146, 151-132. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16562648>.
6. Saltzstein SL, Behling CA. 5- and 10-year survival in cancer patients aged 90 and older: a study of 37,318 patients from SEER. *J Surg Oncol* 2002;81:113-116; discussion 117. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/12407720>.
7. Extermann M. Management issues for elderly patients with breast cancer. *Curr Treat Options Oncol* 2004;5:161-169. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/14990210>.
8. Christman K, Muss HB, Case LD, Stanley V. Chemotherapy of metastatic breast cancer in the elderly. *The Piedmont Oncology Association experience* [see comment]. *JAMA* 1992;268:57-62. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/1608114>.
9. Sargent DJ, Goldberg RM, Jacobson SD, et al. A pooled analysis of adjuvant chemotherapy for resected colon cancer in elderly patients. *N Engl J Med* 2001;345:1091-1097. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/11596588>.
10. Chen H, Cantor A, Meyer J, et al. Can older cancer patients tolerate chemotherapy? A prospective pilot study. *Cancer* 2003;97:1107-1114. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/12569613>.
11. Wedding U, Honecker F, Bokemeyer C, et al. Tolerance to chemotherapy in elderly patients with cancer. *Cancer Control* 2007;14:44-56. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/17242670>.
12. Walter LC, Covinsky KE. Cancer screening in elderly patients: a framework for individualized decision making. *JAMA* 2001;285:2750-2756. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/11386931>.
13. Carey EC, Walter LC, Lindquist K, Covinsky KE. Development and validation of a functional morbidity index to predict mortality in community-dwelling elders. *J Gen Intern Med* 2004;19:1027-1033. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/15482555>.
14. Lee SJ, Lindquist K, Segal MR, Covinsky KE. Development and validation of a prognostic index for 4-year mortality in older adults. *JAMA* 2006;295:801-808. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16478903>.
15. Studenski S, Perera S, Patel K, et al. Gait speed and survival in older adults. *JAMA* 2011;305:50-58. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21205966>.
16. White DK, Neogi T, Nevitt MC, et al. Trajectories of gait speed predict mortality in well-functioning older adults: the Health, Aging and Body Composition study. *J Gerontol A Biol Sci Med Sci* 2013;68:456-464. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/23051974>.



17. Ostir GV, Berges I, Kuo YF, et al. Assessing gait speed in acutely ill older patients admitted to an acute care for elders hospital unit. *Arch Intern Med* 2012;172:353-358. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/22371922>.

18. Cho H, Klabunde CN, Yabroff KR, et al. Comorbidity-adjusted life expectancy: a new tool to inform recommendations for optimal screening strategies. *Ann Intern Med* 2013;159:667-676. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/24247672>.

19. Walter LC, Schonberg MA. Screening mammography in older women: a review. *JAMA* 2014;311:1336-1347. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/24691609>.

20. Harrington SE, Smith TJ. The role of chemotherapy at the end of life: "when is enough, enough?". *JAMA* 2008;299:2667-2678. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/18544726>.

21. Sessums LL, Zembruska H, Jackson JL. Does this patient have medical decision-making capacity? *JAMA* 2011;306:420-427. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/21791691>.

22. Balducci L, Extermann M. Management of cancer in the older person: a practical approach. *Oncologist* 2000;5:224-237. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/10884501>.

23. Ingram SS, Seo PH, Martell RE, et al. Comprehensive assessment of the elderly cancer patient: the feasibility of self-report methodology. *J Clin Oncol* 2002;20:770-775. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/11821460>.

24. Repetto L, Fratino L, Audisio RA, et al. Comprehensive geriatric assessment adds information to Eastern Cooperative Oncology Group performance status in elderly cancer patients: an Italian Group for Geriatric Oncology Study. *J Clin Oncol* 2002;20:494-502. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/11786579>.

25. Maione P, Perrone F, Gallo C, et al. Pretreatment quality of life and functional status assessment significantly predict survival of elderly

patients with advanced non-small-cell lung cancer receiving chemotherapy: a prognostic analysis of the multicenter Italian lung cancer in the elderly study. *J Clin Oncol* 2005;23:6865-6872. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16192578>.

26. Koroukian SM, Xu F, Bakaki PM, et al. Comorbidities, functional limitations, and geriatric syndromes in relation to treatment and survival patterns among elders with colorectal cancer. *J Gerontol A Biol Sci Med Sci* 2010;65:322-329. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/20018824>.

27. Winkelmann N, Petersen I, Kiehnopf M, et al. Results of comprehensive geriatric assessment effect survival in patients with malignant lymphoma. *J Cancer Res Clin Oncol* 2011;137:733-738. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20602238>.

28. Clough-Gorr KM, Thwin SS, Stuck AE, Silliman RA. Examining five- and ten-year survival in older women with breast cancer using cancer-specific geriatric assessment. *Eur J Cancer* 2012;48:805-812. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/21741826>.

29. Caillet P, Canoui-Poitrine F, Vouriot J, et al. Comprehensive geriatric assessment in the decision-making process in elderly patients with cancer: ELCAPA study. *J Clin Oncol* 2011;29:3636-3642. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/21709194>.

30. Soubeyran P, Fonck M, Blanc-Bisson C, et al. Predictors of early death risk in older patients treated with first-line chemotherapy for cancer. *J Clin Oncol* 2012;30:1829-1834. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/22508806>.

31. Aparicio T, Jouve JL, Teillet L, et al. Geriatric factors predict chemotherapy feasibility: ancillary results of FFCD 2001-02 phase III study in first-line chemotherapy for metastatic colorectal cancer in elderly patients. *J Clin Oncol* 2013;31:1464-1470. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/23460711>.

32. Klepin HD, Geiger AM, Tooze JA, et al. Geriatric assessment predicts survival for older adults receiving induction chemotherapy for



acute myelogenous leukemia. Blood 2013;121:4287-4294. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/23550038>.

33. Hamaker ME, Seynaeve C, Wymenga AN, et al. Baseline comprehensive geriatric assessment is associated with toxicity and survival in elderly metastatic breast cancer patients receiving single-agent chemotherapy: results from the OMEGA study of the Dutch breast cancer trialists' group. Breast 2014;23:81-87. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/24314824>.

34. Palumbo A, Brinthen S, Mateos MV, et al. Geriatric assessment predicts survival and toxicities in elderly myeloma patients: an International Myeloma Working Group report. Blood 2015;125:2068-2074. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25628469>.

35. Spina M, Balzarotti M, Uziel L, et al. Modulated chemotherapy according to modified comprehensive geriatric assessment in 100 consecutive elderly patients with diffuse large B-cell lymphoma. Oncologist 2012;17:838-846. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/22610154>.

36. Bellera CA, Rainfray M, Mathoulin-Pelissier S, et al. Screening older cancer patients: first evaluation of the G-8 geriatric screening tool. Ann Oncol 2012;23:2166-2172. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/22250183>.

37. Kenis C, Bron D, Libert Y, et al. Relevance of a systematic geriatric screening and assessment in older patients with cancer: results of a prospective multicentric study. Ann Oncol 2013;24:1306-1312. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/23293115>.

38. Martinez-Tapia C, Canoui-Poitrine F, Bastuji-Garin S, et al. Optimizing the G8 Screening Tool for Older Patients With Cancer: Diagnostic Performance and Validation of a Six-Item Version. Oncologist 2016;21:188-195. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26764250>.

39. Saliba D, Elliott M, Rubenstein LZ, et al. The Vulnerable Elders Survey: a tool for identifying vulnerable older people in the community. J

Am Geriatr Soc 2001;49:1691-1699. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/11844005>.

40. Mohile SG, Bylow K, Dale W, et al. A pilot study of the vulnerable elders survey-13 compared with the comprehensive geriatric assessment for identifying disability in older patients with prostate cancer who receive androgen ablation. Cancer 2007;109:802-810. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/17219443>.

41. Luciani A, Ascione G, Bertuzzi C, et al. Detecting disabilities in older patients with cancer: comparison between comprehensive geriatric assessment and vulnerable elders survey-13. J Clin Oncol 2010;28:2046-2050. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20308657>.

42. Owusu C, Koroukian SM, Schluchter M, et al. Screening older cancer patients for a Comprehensive Geriatric Assessment: A comparison of three instruments. J Geriatr Oncol 2011;2:121-129. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21927633>.

43. Decoster L, Van Puyvelde K, Mohile S, et al. Screening tools for multidimensional health problems warranting a geriatric assessment in older cancer patients: an update on SIOG recommendations. Ann Oncol 2015;26:288-300. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/24936581>.

44. Soubeyran P, Bellera C, Goyard J, et al. Screening for vulnerability in older cancer patients: the ONCODAGE Prospective Multicenter Cohort Study. PLoS One 2014;9:e115060. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25503576>.

45. Overcash JA, Beckstead J, Moody L, et al. The abbreviated comprehensive geriatric assessment (aCGA) for use in the older cancer patient as a prescreen: scoring and interpretation. Crit Rev Oncol Hematol 2006;59:205-210. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16904902>.

46. Kellen E, Bulens P, Deckx L, et al. Identifying an accurate pre-screening tool in geriatric oncology. Crit Rev Oncol Hematol



2010;75:243-248. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/20060313>.

47. Molina-Garrido MJ, Guillen-Ponce C. Comparison of two frailty screening tools in older women with early breast cancer. *Crit Rev Oncol Hematol* 2011;79:51-64. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/20663685>.

48. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56:M146-156. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/11253156>.

49. Biganzoli L, Boni L, Becheri D, et al. Evaluation of the cardiovascular health study (CHS) instrument and the Vulnerable Elders Survey-13 (VES-13) in elderly cancer patients. Are we still missing the right screening tool? *Ann Oncol* 2013;24:494-500. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/23045516>.

50. Lachs MS, Feinstein AR, Cooney LM, Jr., et al. A simple procedure for general screening for functional disability in elderly patients. *Ann Intern Med* 1990;112:699-706. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/2334082>.

51. Extermann M. Evaluation of the senior cancer patient: comprehensive geriatric assessment and screening tools for the elderly. In: Schrijvers D, Aapro M, Zakotnik B, et al., eds. *Handbook of Cancer in the Senior Patient*. New York, London, : Informa Healthcare; 2010:13-21.

52. Russo C, Giannotti C, Signori A, et al. Predictive values of two frailty screening tools in older patients with solid cancer: a comparison of SAOP2 and G8. *Oncotarget* 2018;9:35056-35068. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/30416679>.

53. Hamaker ME, Jonker JM, de Rooij SE, et al. Frailty screening methods for predicting outcome of a comprehensive geriatric assessment in elderly patients with cancer: a systematic review. *Lancet Oncol* 2012;13:e437-444. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/23026829>.

54. Deckx L, van den Akker M, Daniels L, et al. Geriatric screening tools are of limited value to predict decline in functional status and quality of life: results of a cohort study. *BMC Fam Pract* 2015;16:30. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/25888485>.

55. van Winden MEC, Garcovich S, Peris K, et al. Frailty screening in dermatology practice: a modified Delphi study and a systematic review of the literature. *J Eur Acad Dermatol Venereol* 2021;35:95-104. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/32403174>.

56. Pal SK, Katheria V, Hurria A. Evaluating the older patient with cancer: understanding frailty and the geriatric assessment. *CA Cancer J Clin* 2010;60:120-132. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/20173172>.

57. Wildiers H, Heeren P, Puts M, et al. International Society of Geriatric Oncology consensus on geriatric assessment in older patients with cancer. *J Clin Oncol* 2014;32:2595-2603. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/25071125>.

58. Mohile SG, Velarde C, Hurria A, et al. Geriatric Assessment-Guided Care Processes for Older Adults: A Delphi Consensus of Geriatric Oncology Experts. *J Natl Compr Canc Netw* 2015;13:1120-1130. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/26358796>.

59. Hurria A, Togawa K, Mohile SG, et al. Predicting chemotherapy toxicity in older adults with cancer: a prospective multicenter study. *J Clin Oncol* 2011;29:3457-3465. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/21810685>.

60. Hurria A, Mohile S, Gajra A, et al. Validation of a Prediction Tool for Chemotherapy Toxicity in Older Adults With Cancer. *J Clin Oncol* 2016;34:2366-2371. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/27185838>.

61. Extermann M, Boler I, Reich RR, et al. Predicting the risk of chemotherapy toxicity in older patients: the Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score. *Cancer*



2012;118:3377-3386. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/22072065>.

62. Mohile SG, Epstein RM, Hurria A, et al. Communication With Older Patients With Cancer Using Geriatric Assessment: A Cluster-Randomized Clinical Trial From the National Cancer Institute Community Oncology Research Program. *JAMA Oncol* 2020;6:196-204. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/31697365>.

63. Katz S, Ford AB, Moskowitz RW, et al. Studies of Illness in the Aged. The Index of Adl: A Standardized Measure of Biological and Psychosocial Function. *JAMA* 1963;185:914-919. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/14044222>.

64. Lawton MP. Scales to measure competence in everyday activities. *Psychopharmacol Bull* 1988;24:609-614. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/3074322>.

65. Freyer G, Geay JF, Touzet S, et al. Comprehensive geriatric assessment predicts tolerance to chemotherapy and survival in elderly patients with advanced ovarian carcinoma: a GINECO study. *Ann Oncol* 2005;16:1795-1800. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16093275>.

66. Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc* 1991;39:142-148. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/1991946>.

67. Pondal M, del Ser T. Normative data and determinants for the timed "up and go" test in a population-based sample of elderly individuals without gait disturbances. *J Geriatr Phys Ther* 2008;31:57-63. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/19856551>.

68. Shumway-Cook A, Brauer S, Woollacott M. Predicting the probability for falls in community-dwelling older adults using the Timed Up & Go Test. *Phys Ther* 2000;80:896-903. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/10960937>.

69. Overcash JA, Rivera HR, Jr. Physical performance evaluation of older cancer patients: a preliminary study. *Crit Rev Oncol Hematol* 2008;68:233-241. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/18789714>.

70. Luciani A, Jacobsen PB, Extermann M, et al. Fatigue and functional dependence in older cancer patients. *Am J Clin Oncol* 2008;31:424-430. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/18838877>.

71. Cesari M, Kritchevsky SB, Penninx BW, et al. Prognostic value of usual gait speed in well-functioning older people--results from the Health, Aging and Body Composition Study. *J Am Geriatr Soc* 2005;53:1675-1680. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16181165>.

72. Klepin HD, Geiger AM, Tooze JA, et al. Physical performance and subsequent disability and survival in older adults with malignancy: results from the health, aging and body composition study. *J Am Geriatr Soc* 2010;58:76-82. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20122042>.

73. Pamoukdjian F, Levy V, Sebbane G, et al. Slow Gait Speed Is an Independent Predictor of Early Death in Older Cancer Outpatients: Results from a Prospective Cohort Study. *J Nutr Health Aging* 2017;21:202-206. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28112777>.

74. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol* 1994;49:M85-94. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/8126356>.

75. Guralnik JM, Ferrucci L, Simonsick EM, et al. Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. *N Engl J Med* 1995;332:556-561. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/7838189>.

76. Vasunilashorn S, Coppin AK, Patel KV, et al. Use of the Short Physical Performance Battery Score to predict loss of ability to walk 400



meters: analysis from the InCHIANTI study. *J Gerontol A Biol Sci Med Sci* 2009;64:223-229. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/19182232>.

77. Pavasini R, Guralnik J, Brown JC, et al. Short Physical Performance Battery and all-cause mortality: systematic review and meta-analysis. *BMC Med* 2016;14:215. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/28003033>.

78. Perez-Zepeda MU, Belanger E, Zunzunegui MV, et al. Assessing the Validity of Self-Rated Health with the Short Physical Performance Battery: A Cross-Sectional Analysis of the International Mobility in Aging Study. *PLoS One* 2016;11:e0153855. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/27089219>.

79. Extermann M. Interaction between comorbidity and cancer. *Cancer Control* 2007;14:13-22. Available at:

<http://www.ncbi.nlm.nih.gov/pubmed/17242667>.

80. Pal SK, Hurria A. Impact of age, sex, and comorbidity on cancer therapy and disease progression. *J Clin Oncol* 2010;28:4086-4093. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20644100>.

81. Meyerhardt JA, Catalano PJ, Haller DG, et al. Impact of diabetes mellitus on outcomes in patients with colon cancer. *J Clin Oncol* 2003;21:433-440. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/12560431>.

82. Nanda A, Chen MH, Braccioforte MH, et al. Hormonal therapy use for prostate cancer and mortality in men with coronary artery disease-induced congestive heart failure or myocardial infarction. *JAMA* 2009;302:866-873. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/19706860>.

83. Srokowski TP, Fang S, Hortobagyi GN, Giordano SH. Impact of diabetes mellitus on complications and outcomes of adjuvant chemotherapy in older patients with breast cancer. *J Clin Oncol* 2009;27:2170-2176. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/19307509>.

84. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373-383. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/3558716>.

85. Linn BS, Linn MW, Gurel L. Cumulative illness rating scale. *J Am Geriatr Soc* 1968;16:622-626. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/5646906>.

86. Klepin HD, Pitcher BN, Ballman KV, et al. Comorbidity, chemotherapy toxicity, and outcomes among older women receiving adjuvant chemotherapy for breast cancer on a clinical trial: CALGB 49907 and CALGB 361004 (alliance). *J Oncol Pract* 2014;10:e285-292. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25074878>.

87. Williams GR, Deal AM, Lund JL, et al. Patient-Reported Comorbidity and Survival in Older Adults with Cancer. *Oncologist* 2018;23:433-439. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29242282>.

88. Fillenbaum GG, Smyer MA. The development, validity, and reliability of the OARS multidimensional functional assessment questionnaire. *J Gerontol* 1981;36:428-434. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/7252074>.

89. Frasci G, Lorusso V, Panza N, et al. Gemcitabine plus vinorelbine versus vinorelbine alone in elderly patients with advanced non-small-cell lung cancer. *J Clin Oncol* 2000;18:2529-2536. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/10893283>.

90. Gronberg BH, Sundstrom S, Kaasa S, et al. Influence of comorbidity on survival, toxicity and health-related quality of life in patients with advanced non-small-cell lung cancer receiving platinum-doublet chemotherapy. *Eur J Cancer* 2010;46:2225-2234. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/20471248>.

91. Ngeow J, Leong SS, Gao F, et al. Impact of comorbidities on clinical outcomes in non-small cell lung cancer patients who are elderly and/or have poor performance status. *Crit Rev Oncol Hematol* 2010;76:53-60. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/19939700>.



92. Sanabria A, Carvalho AL, Vartanian JG, et al. Comorbidity is a prognostic factor in elderly patients with head and neck cancer. *Ann Surg Oncol* 2007;14:1449-1457. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/17235712>.

93. Keller JW, Andreadis C, Damon LE, et al. Hematopoietic cell transplantation comorbidity index (HCT-CI) is predictive of adverse events and overall survival in older allogeneic transplant recipients. *J Geriatr Oncol* 2014;5:238-244. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/24894413>.

94. Tomaka J, Thompson S, Palacios R. The relation of social isolation, loneliness, and social support to disease outcomes among the elderly. *J Aging Health* 2006;18:359-384. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/16648391>.

95. Seeman TE, Kaplan GA, Knudsen L, et al. Social network ties and mortality among the elderly in the Alameda County Study. *Am J Epidemiol* 1987;126:714-723. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/3631060>.

96. Moser A, Stuck AE, Silliman RA, et al. The eight-item modified Medical Outcomes Study Social Support Survey: psychometric evaluation showed excellent performance. *J Clin Epidemiol* 2012;65:1107-1116. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/22818947>.

97. Sherbourne CD, Stewart AL. The MOS social support survey. *Soc Sci Med* 1991;32:705-714. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/2035047>.

98. Stilley CS, Bender CM, Dunbar-Jacob J, et al. The impact of cognitive function on medication management: three studies. *Health Psychol* 2010;29:50-55. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/20063935>.

99. Extermann M. Older patients, cognitive impairment, and cancer: an increasingly frequent triad. *J Natl Compr Canc Netw* 2005;3:593-596.

Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16038648>.

100. Petersen RC, Smith GE, Waring SC, et al. Mild cognitive impairment: clinical characterization and outcome. *Arch Neurol* 1999;56:303-308. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/10190820>.

101. Njegovan V, Hing MM, Mitchell SL, Molnar FJ. The hierarchy of functional loss associated with cognitive decline in older persons. *J Gerontol A Biol Sci Med Sci* 2001;56:M638-643. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/11584037>.

102. 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:

<https://www.ncbi.nlm.nih.gov/pubmed/1202204>.

103. Tombaugh TN, McIntyre NJ. The mini-mental state examination: a comprehensive review. *J Am Geriatr Soc* 1992;40:922-935. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/1512391>.

104. Crum RM, Anthony JC, Bassett SS, Folstein MF. Population-based norms for the Mini-Mental State Examination by age and educational level. *JAMA* 1993;269:2386-2391. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/8479064>.

105. Nasreddine ZS, Phillips NA, Bedirian V, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc* 2005;53:695-699. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/15817019>.

106. Borson S, Scanlan J, Brush M, et al. The mini-cog: a cognitive 'vital signs' measure for dementia screening in multi-lingual elderly. *Int J Geriatr Psychiatry* 2000;15:1021-1027. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/11113982>.

107. McCarten JR, Anderson P, Kuskowski MA, et al. Screening for cognitive impairment in an elderly veteran population: acceptability and results using different versions of the Mini-Cog. *J Am Geriatr Soc* 2011;59:309-313. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/21314650>.



108. Carpenter CR, Bassett ER, Fischer GM, et al. Four sensitive screening tools to detect cognitive dysfunction in geriatric emergency department patients: brief Alzheimer's Screen, Short Blessed Test, Ottawa 3DY, and the caregiver-completed AD8. *Acad Emerg Med* 2011;18:374-384. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/21496140>.

109. Ghosh A. Endocrine, metabolic, nutritional, and toxic disorders leading to dementia. *Ann Indian Acad Neurol* 2010;13:S63-68. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21369420>.

110. Chew ML, Mulsant BH, Pollock BG, et al. Anticholinergic activity of 107 medications commonly used by older adults. *J Am Geriatr Soc* 2008;56:1333-1341. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/18510583>.

111. Fox C, Richardson K, Maidment ID, et al. Anticholinergic medication use and cognitive impairment in the older population: the medical research council cognitive function and ageing study. *J Am Geriatr Soc* 2011;59:1477-1483. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/21707557>.

112. Pasina L, Djade CD, Lucca U, et al. Association of anticholinergic burden with cognitive and functional status in a cohort of hospitalized elderly: comparison of the anticholinergic cognitive burden scale and anticholinergic risk scale: results from the REPOSI study. *Drugs Aging* 2013;30:103-112. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/23239364>.

113. Schneider LS, Dagerman KS, Insel P. Risk of death with atypical antipsychotic drug treatment for dementia: meta-analysis of randomized placebo-controlled trials. *JAMA* 2005;294:1934-1943. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/16234500>.

114. Kales HC, Valenstein M, Kim HM, et al. Mortality risk in patients with dementia treated with antipsychotics versus other psychiatric medications. *Am J Psychiatry* 2007;164:1568-1576; quiz 1623. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/17898349>.

115. Rochon PA, Normand SL, Gomes T, et al. Antipsychotic therapy and short-term serious events in older adults with dementia. *Arch Intern Med* 2008;168:1090-1096. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/18504337>.

116. Hilmer SN, Mager DE, Simonsick EM, et al. A drug burden index to define the functional burden of medications in older people. *Arch Intern Med* 2007;167:781-787. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/17452540>.

117. Cordell CB, Borson S, Boustani M, et al. Alzheimer's Association recommendations for operationalizing the detection of cognitive impairment during the Medicare Annual Wellness Visit in a primary care setting. *Alzheimers Dement* 2013;9:141-150. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/23265826>.

118. Canoui-Poitrine F, Reinald N, Laurent M, et al. Geriatric assessment findings independently associated with clinical depression in 1092 older patients with cancer: the ELCAPA Cohort Study. *Psychooncology* 2016;25:104-111. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/26123351>.

119. Hurria A, Li D, Hansen K, et al. Distress in older patients with cancer. *J Clin Oncol* 2009;27:4346-4351. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/19652074>.

120. Beauplet B, Soulie O, Niemier JY, et al. Dealing with the lack of evidence to treat depression in older patients with cancer: French Societies of Geriatric Oncology (SOGOG) and PsychoOncology (SFFPO) position paper based on a systematic review. *Support Care Cancer* 2021;29:563-571. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/32870413>.

121. Yesavage JA, Brink TL, Rose TL, et al. Development and validation of a geriatric depression screening scale: a preliminary report. *J Psychiatr Res* 1982;17:37-49. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/7183759>.



122. D'Ath P, Katona P, Mullan E, et al. Screening, detection and management of depression in elderly primary care attenders. I: The acceptability and performance of the 15 item Geriatric Depression Scale (GDS15) and the development of short versions. *Fam Pract* 1994;11:260-266. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/7843514>.

123. Jongenelis K, Pot AM, Eisses AM, et al. Diagnostic accuracy of the original 30-item and shortened versions of the Geriatric Depression Scale in nursing home patients. *Int J Geriatr Psychiatry* 2005;20:1067-1074. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16250079>.

124. Jacobsen PB. Assessment of fatigue in cancer patients. *J Natl Cancer Inst Monogr* 2004:93-97. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/15263047>.

125. Jacobsen PB, Donovan KA, Weitzner MA. Distinguishing fatigue and depression in patients with cancer. *Semin Clin Neuropsychiatry* 2003;8:229-240. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/14613050>.

126. Respini D, Jacobsen PB, Thors C, et al. The prevalence and correlates of fatigue in older cancer patients. *Crit Rev Oncol Hematol* 2003;47:273-279. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/12962901>.

127. Levis B, Sun Y, He C, et al. Accuracy of the PHQ-2 Alone and in Combination With the PHQ-9 for Screening to Detect Major Depression: Systematic Review and Meta-analysis. *JAMA* 2020;323:2290-2300. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/32515813>.

128. Zabora J, BrintzenhofeSzoc K, Jacobsen P, et al. A new psychosocial screening instrument for use with cancer patients. *Psychosomatics* 2001;42:241-246. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/11351113>.

129. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67:361-370. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/6880820>.

130. Mitchell AJ. Pooled results from 38 analyses of the accuracy of distress thermometer and other ultra-short methods of detecting cancer-related mood disorders. *J Clin Oncol* 2007;25:4670-4681. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/17846453>.

131. Hoffman BM, Zevon MA, D'Arrigo MC, Cecchini TB. Screening for distress in cancer patients: the NCCN rapid-screening measure. *Psychooncology* 2004;13:792-799. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/15386639>.

132. Jacobsen PB, Donovan KA, Trask PC, et al. Screening for psychologic distress in ambulatory cancer patients. *Cancer* 2005;103:1494-1502. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/15726544>.

133. Alexandre J, Gross-Goupil M, Falissard B, et al. Evaluation of the nutritional and inflammatory status in cancer patients for the risk assessment of severe haematological toxicity following chemotherapy. *Ann Oncol* 2003;14:36-41. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/12488290>.

134. Pressoir M, Desne S, Berchery D, et al. Prevalence, risk factors and clinical implications of malnutrition in French Comprehensive Cancer Centres. *Br J Cancer* 2010;102:966-971. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20160725>.

135. Aaldriks AA, Maartense E, le Cessie S, et al. Predictive value of geriatric assessment for patients older than 70 years, treated with chemotherapy. *Crit Rev Oncol Hematol* 2011;79:205-212. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/20709565>.

136. Aaldriks AA, van der Geest LG, Giltay EJ, et al. Frailty and malnutrition predictive of mortality risk in older patients with advanced colorectal cancer receiving chemotherapy. *J Geriatr Oncol* 2013;4:218-226. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/24070460>.

137. Bullock AF, Greenley SL, McKenzie GAG, et al. Relationship between markers of malnutrition and clinical outcomes in older adults with cancer: systematic review, narrative synthesis and meta-analysis.



Eur J Clin Nutr 2020;74:1519-1535. Available at:
<https://www.ncbi.nlm.nih.gov/pubmed/32366995>.

138. Boleo-Tome C, Monteiro-Grillo I, Camilo M, Ravasco P. Validation of the Malnutrition Universal Screening Tool (MUST) in cancer. Br J Nutr 2012;108:343-348. Available at:
<https://www.ncbi.nlm.nih.gov/pubmed/22142968>.

139. Bjorkman MP, Sorva AJ, Risteli J, Tilvis RS. Low parathyroid hormone levels in bedridden geriatric patients with vitamin D deficiency. J Am Geriatr Soc 2009;57:1045-1050. Available at:
<https://www.ncbi.nlm.nih.gov/pubmed/19473453>.

140. Maggiore RJ, Gross CP, Hurria A. Polypharmacy in older adults with cancer. Oncologist 2010;15:507-522. Available at:
<https://www.ncbi.nlm.nih.gov/pubmed/20418534>.

141. Sokol KC, Knudsen JF, Li MM. Polypharmacy in older oncology patients and the need for an interdisciplinary approach to side-effect management. J Clin Pharm Ther 2007;32:169-175. Available at:
<https://www.ncbi.nlm.nih.gov/pubmed/17381667>.

142. Puts MT, Costa-Lima B, Monette J, et al. Medication problems in older, newly diagnosed cancer patients in Canada: How common are they? A prospective pilot study. Drugs Aging 2009;26:519-536. Available at:
<https://www.ncbi.nlm.nih.gov/pubmed/19591526>.

143. Lees J, Chan A. Polypharmacy in elderly patients with cancer: clinical implications and management. Lancet Oncol 2011;12:1249-1257. Available at:
<https://www.ncbi.nlm.nih.gov/pubmed/21741307>.

144. Riechelmann RP, Saad ED. A systematic review on drug interactions in oncology. Cancer Invest 2006;24:704-712. Available at:
<https://www.ncbi.nlm.nih.gov/pubmed/17118781>.

145. Riechelmann RP, Tannock IF, Wang L, et al. Potential drug interactions and duplicate prescriptions among cancer patients. J Natl Cancer Inst 2007;99:592-600. Available at:
<https://www.ncbi.nlm.nih.gov/pubmed/17440160>.

146. Riechelmann RP, Zimmermann C, Chin SN, et al. Potential drug interactions in cancer patients receiving supportive care exclusively. J Pain Symptom Manage 2008;35:535-543. Available at:
<https://www.ncbi.nlm.nih.gov/pubmed/18243638>.

147. Tam-McDevitt J. Polypharmacy, aging, and cancer. Oncology (Williston Park) 2008;22:1052-1055, discussion 1055, 1058, 1060. Available at:
<https://www.ncbi.nlm.nih.gov/pubmed/18777955>.

148. Popa MA, Wallace KJ, Brunello A, et al. Potential drug interactions and chemotoxicity in older patients with cancer receiving chemotherapy. J Geriatr Oncol 2014;5:307-314. Available at:
<https://www.ncbi.nlm.nih.gov/pubmed/24821377>.

149. Steinman MA, Landefeld CS, Rosenthal GE, et al. Polypharmacy and prescribing quality in older people. J Am Geriatr Soc 2006;54:1516-1523. Available at:
<https://www.ncbi.nlm.nih.gov/pubmed/17038068>.

150. Currow DC, Stevenson JP, Abernethy AP, et al. Prescribing in palliative care as death approaches. J Am Geriatr Soc 2007;55:590-595. Available at:
<https://www.ncbi.nlm.nih.gov/pubmed/17397439>.

151. Maggiore RJ, Dale W, Gross CP, et al. Polypharmacy and potentially inappropriate medication use in older adults with cancer undergoing chemotherapy: effect on chemotherapy-related toxicity and hospitalization during treatment. J Am Geriatr Soc 2014;62:1505-1512. Available at:
<https://www.ncbi.nlm.nih.gov/pubmed/25041361>.

152. Berdot S, Bertrand M, Dartigues JF, et al. Inappropriate medication use and risk of falls--a prospective study in a large community-dwelling elderly cohort. BMC Geriatr 2009;9:30. Available at:
<https://www.ncbi.nlm.nih.gov/pubmed/19627577>.

153. Woolcott JC, Richardson KJ, Wiens MO, et al. Meta-analysis of the impact of 9 medication classes on falls in elderly persons. Arch Intern Med 2009;169:1952-1960. Available at:
<https://www.ncbi.nlm.nih.gov/pubmed/19933955>.



154. Turner JP, Jamsen KM, Shakib S, et al. Polypharmacy cut-points in older people with cancer: how many medications are too many? Support Care Cancer 2016;24:1831-1840. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26449548>.

155. Beers MH. Explicit criteria for determining potentially inappropriate medication use by the elderly. An update. Arch Intern Med 1997;157:1531-1536. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/9236554>.

156. Fick DM, Cooper JW, Wade WE, et al. Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. Arch Intern Med 2003;163:2716-2724. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/14662625>.

157. Flood KL, Carroll MB, Le CV, Brown CJ. Polypharmacy in hospitalized older adult cancer patients: experience from a prospective, observational study of an oncology-acute care for elders unit. Am J Geriatr Pharmacother 2009;7:151-158. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/19616183>.

158. Lichtman SM, Boparai MK. Geriatric medication management: Evaluation of pharmacist interventions and potentially inappropriate medication (PIM) use in older (>=65 years) cancer patients. J Clin Oncol 2009;27:9507. Available at: <http://meeting.ascopubs.org/cgi/content/abstract/27/15S/9507>.

159. American Geriatrics Society Beers Criteria Update Expert P. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2012;60:616-631. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/22376048>.

160. Croke L. Beers Criteria for Inappropriate Medication Use in Older Patients: An Update from the AGS. Am Fam Physician 2020;101:56-57. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/31894929>.

161. Hanlon JT, Schmader KE, Samsa GP, et al. A method for assessing drug therapy appropriateness. J Clin Epidemiol 1992;45:1045-1051. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/1474400>.

162. Samsa GP, Hanlon JT, Schmader KE, et al. A summated score for the medication appropriateness index: development and assessment of clinimetric properties including content validity. J Clin Epidemiol 1994;47:891-896. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/7730892>.

163. Schmader K, Hanlon JT, Weinberger M, et al. Appropriateness of medication prescribing in ambulatory elderly patients. J Am Geriatr Soc 1994;42:1241-1247. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/7983285>.

164. Kassam R, Martin LG, Farris KB. Reliability of a modified medication appropriateness index in community pharmacies. Ann Pharmacother 2003;37:40-46. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/12503931>.

165. Hanlon JT, Artz MB, Pieper CF, et al. Inappropriate medication use among frail elderly inpatients. Ann Pharmacother 2004;38:9-14. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/14742785>.

166. Gallagher P, Baeyens JP, Topinkova E, et al. Inter-rater reliability of STOPP (Screening Tool of Older Persons' Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment) criteria amongst physicians in six European countries. Age Ageing 2009;38:603-606. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/19435757>.

167. Barry PJ, Gallagher P, Ryan C, O'Mahony D. START (screening tool to alert doctors to the right treatment)--an evidence-based screening tool to detect prescribing omissions in elderly patients. Age Ageing 2007;36:632-638. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/17881418>.

168. Gallagher P, O'Mahony D. STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions): application to acutely ill elderly patients and comparison with Beers' criteria. Age Ageing



2008;37:673-679. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/18829684>.

169. Gallagher PF, O'Connor MN, O'Mahony D. Prevention of potentially inappropriate prescribing for elderly patients: a randomized controlled trial using STOPP/START criteria. *Clin Pharmacol Ther* 2011;89:845-854. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21508941>.

170. Flood KL, Carroll MB, Le CV, et al. Geriatric syndromes in elderly patients admitted to an oncology-acute care for elders unit. *J Clin Oncol* 2006;24:2298-2303. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16710027>.

171. Mohile SG, Fan L, Reeve E, et al. Association of cancer with geriatric syndromes in older Medicare beneficiaries. *J Clin Oncol* 2011;29:1458-1464. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21402608>.

172. Giacalone A, Quitadamo D, Zanet E, et al. Cancer-related fatigue in the elderly. *Support Care Cancer* 2013;21:2899-2911. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/23852408>.

173. Rao AV, Seo PH, Cohen HJ. Geriatric assessment and comorbidity. *Semin Oncol* 2004;31:149-159. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/15112146>.

174. Minton O, Strasser F, Radbruch L, Stone P. Identification of factors associated with fatigue in advanced cancer: a subset analysis of the European palliative care research collaborative computerized symptom assessment data set. *J Pain Symptom Manage* 2012;43:226-235. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21839608>.

175. Vogelzang NJ, Breitbart W, Cella D, et al. Patient, caregiver, and oncologist perceptions of cancer-related fatigue: results of a tripart assessment survey. The Fatigue Coalition. *Semin Hematol* 1997;34:4-12. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/9253778>.

176. Demetri GD, Kris M, Wade J, et al. Quality-of-life benefit in chemotherapy patients treated with epoetin alfa is independent of

disease response or tumor type: results from a prospective community oncology study. Procrit Study Group. *J Clin Oncol* 1998;16:3412-3425. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/9779721>.

177. Berger AM, Farr L. The influence of daytime inactivity and nighttime restlessness on cancer-related fatigue. *Oncol Nurs Forum* 1999;26:1663-1671. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/10573683>.

178. Hardy SE, Studenski SA. Fatigue and function over 3 years among older adults. *J Gerontol A Biol Sci Med Sci* 2008;63:1389-1392. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/19126853>.

179. Hamerman D. Toward an understanding of frailty. *Ann Intern Med* 1999;130:945-950. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/10375351>.

180. Kirkhus L, Saltyte Benth J, Rostoft S, et al. Geriatric assessment is superior to oncologists' clinical judgement in identifying frailty. *Br J Cancer* 2017;117:470-477. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28664916>.

181. Kristjansson SR, Rønning B, Hurria A, et al. A comparison of two pre-operative frailty measures in older surgical cancer patients. *Journal of Geriatric Oncology* 2012;3:1-7. Available at: <http://www.sciencedirect.com/science/article/pii/S1879406811000622>.

182. Balducci L. Bone complications of cancer treatment in the elderly. *Oncology (Williston Park)* 2010;24:741-747. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20718254>.

183. Gralow JR, Biermann JS, Farooki A, et al. NCCN Task Force Report: Bone Health In Cancer Care. *J Natl Compr Canc Netw* 2013;11 Suppl 3:S1-50; quiz S51. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/23997241>.

184. Stone CA, Lawlor PG, Savva GM, et al. Prospective study of falls and risk factors for falls in adults with advanced cancer. *J Clin Oncol* 2012;30:2128-2133. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/22585687>.



185. Tofthagen C, Overcash J, Kip K. Falls in persons with chemotherapy-induced peripheral neuropathy. *Support Care Cancer* 2012;20:583-589. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/21380613>.

186. Puts MT, Monette J, Girre V, et al. The fall rate of older community-dwelling cancer patients. *Support Care Cancer* 2013;21:775-783.

Available at: <https://www.ncbi.nlm.nih.gov/pubmed/22941117>.

187. Vande Walle N, Kenis C, Heeren P, et al. Fall predictors in older cancer patients: a multicenter prospective study. *BMC Geriatr* 2014;14:135. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/25511244>.

188. Sattar S, Haase K, Kuster S, et al. Falls in older adults with cancer: an updated systematic review of prevalence, injurious falls, and impact on cancer treatment. *Support Care Cancer* 2021;29:21-33. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/32671565>.

189. Chang JT, Morton SC, Rubenstein LZ, et al. Interventions for the prevention of falls in older adults: systematic review and meta-analysis of randomised clinical trials. *BMJ* 2004;328:680. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/15031239>.

190. Campbell AJ, Robertson MC. Rethinking individual and community fall prevention strategies: a meta-regression comparing single and multifactorial interventions. *Age Ageing* 2007;36:656-662. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/18056731>.

191. Panel on Prevention of Falls in Older Persons AGS, British Geriatrics S. Summary of the Updated American Geriatrics Society/British Geriatrics Society clinical practice guideline for prevention of falls in older persons. *J Am Geriatr Soc* 2011;59:148-157. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/21226685>.

192. Murad MH, Elamin KB, Abu Elnour NO, et al. Clinical review: The effect of vitamin D on falls: a systematic review and meta-analysis. *J Clin Endocrinol Metab* 2011;96:2997-3006. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/21795448>.

193. Gillespie LD, Robertson MC, Gillespie WJ, et al. Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 2012;9:CD007146. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/22972103>.

194. Salonoja M, Salminen M, Vahlberg T, et al. Withdrawal of psychotropic drugs decreases the risk of falls requiring treatment. *Arch Gerontol Geriatr* 2012;54:160-167. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/21420744>.

195. Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. *Lancet* 2014;383:911-922. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/23992774>.

196. Bush SH, Bruera E. The assessment and management of delirium in cancer patients. *Oncologist* 2009;14:1039-1049. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/19808772>.

197. Edelstein A, Alici Y. Diagnosing and Managing Delirium in Cancer Patients. *Oncology (Williston Park)* 2017;31:686-692, III. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/29071696>.

198. Bush SH, Lawlor PG, Ryan K, et al. Delirium in adult cancer patients: ESMO Clinical Practice Guidelines. *Ann Oncol* 2018;29 Suppl 4:iv143-iv165. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/32169223>.

199. Inouye SK, van Dyck CH, Alessi CA, et al. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Ann Intern Med* 1990;113:941-948. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/2240918>.

200. Wei LA, Fearing MA, Sternberg EJ, Inouye SK. The Confusion Assessment Method: a systematic review of current usage. *J Am Geriatr Soc* 2008;56:823-830. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/18384586>.

201. Lawlor PG, Nekolaichuk C, Gagnon B, et al. Clinical utility, factor analysis, and further validation of the memorial delirium assessment



scale in patients with advanced cancer: Assessing delirium in advanced cancer. *Cancer* 2000;88:2859-2867. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/10870073>.

202. Gaudreau JD, Gagnon P, Harel F, et al. Fast, systematic, and continuous delirium assessment in hospitalized patients: the nursing delirium screening scale. *J Pain Symptom Manage* 2005;29:368-375. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/15857740>.

203. Gaudreau JD, Gagnon P, Harel F, et al. Psychoactive medications and risk of delirium in hospitalized cancer patients. *J Clin Oncol* 2005;23:6712-6718. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/16170179>.

204. Gaudreau JD, Gagnon P, Roy MA, et al. Opioid medications and longitudinal risk of delirium in hospitalized cancer patients. *Cancer* 2007;109:2365-2373. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/17469164>.

205. Chow WB, Rosenthal RA, Merkow RP, et al. Optimal preoperative assessment of the geriatric surgical patient: a best practices guideline from the American College of Surgeons National Surgical Quality Improvement Program and the American Geriatrics Society. *J Am Coll Surg* 2012;215:453-466. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/22917646>.

206. Korc-Grodzicki B, Downey RJ, Shahrokni A, et al. Surgical considerations in older adults with cancer. *J Clin Oncol* 2014;32:2647-2653. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/25071124>.

207. Ramesh HS, Pope D, Gennari R, Audisio RA. Optimising surgical management of elderly cancer patients. *World J Surg Oncol* 2005;3:17. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/15788092>.

208. Hornor MA, Ma M, Zhou L, et al. Enhancing the American College of Surgeons NSQIP Surgical Risk Calculator to Predict Geriatric Outcomes. *J Am Coll Surg* 2020;230:88-100 e101. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/31672676>.

209. American Geriatrics Society Expert Panel on Postoperative Delirium in Older A. American Geriatrics Society abstracted clinical practice guideline for postoperative delirium in older adults. *J Am Geriatr Soc* 2015;63:142-150. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/25495432>.

210. American Geriatrics Society Expert Panel on Postoperative Delirium in Older A. Postoperative delirium in older adults: best practice statement from the American Geriatrics Society. *J Am Coll Surg* 2015;220:136-148 e131. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/25535170>.

211. Zachariah B, Balducci L. Radiation therapy of the older patient. *Hematol Oncol Clin North Am* 2000;14:131-167. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/10680076>.

212. Smith GL, Smith BD. Radiation treatment in older patients: a framework for clinical decision making. *J Clin Oncol* 2014;32:2669-2678. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/25071132>.

213. Wasil T, Lichtman SM, Gupta V, Rush S. Radiation therapy in cancer patients 80 years of age and older. *Am J Clin Oncol* 2000;23:526-530. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/11039517>.

214. Kunkler IH, Audisio R, Belkacemi Y, et al. Review of current best practice and priorities for research in radiation oncology for elderly patients with cancer: the International Society of Geriatric Oncology (SIOG) task force. *Ann Oncol* 2014;25:2134-2146. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/24625455>.

215. Donato V, Valeriani M, Zurlo A. Short course radiation therapy for elderly cancer patients. Evidences from the literature review. *Crit Rev Oncol Hematol* 2003;45:305-311. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/12633841>.

216. Berkey FJ. Managing the adverse effects of radiation therapy. *Am Fam Physician* 2010;82:381-388, 394. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/20704169>.



217. Metri K, Bhargav H, Chowdhury P, Koka PS. Ayurveda for chemo-radiotherapy induced side effects in cancer patients. *J Stem Cells* 2013;8:115-129. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/24698988>.

218. Ibrahim NK, Frye DK, Buzdar AU, et al. Doxorubicin-based chemotherapy in elderly patients with metastatic breast cancer. Tolerance and outcome. *Arch Intern Med* 1996;156:882-888. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/8774207>.

219. Giovanazzi-Bannon S, Rademaker A, Lai G, Benson AB, 3rd. Treatment tolerance of elderly cancer patients entered onto phase II clinical trials: an Illinois Cancer Center study. *J Clin Oncol* 1994;12:2447-2452. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/7964962>.

220. Newcomb PA, Carbone PP. Cancer treatment and age: patient perspectives. *J Natl Cancer Inst* 1993;85:1580-1584. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/8411231>.

221. Lichtman SM, Wildiers H, Chatelut E, et al. International Society of Geriatric Oncology Chemotherapy Taskforce: evaluation of chemotherapy in older patients--an analysis of the medical literature. *J Clin Oncol* 2007;25:1832-1843. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/17488981>.

222. Hagiwara Y, Sawaki M, Uemura Y, et al. Impact of chemotherapy on cognitive functioning in older patients with HER2-positive breast cancer: a sub-study in the RESPECT trial. *Breast Cancer Res Treat* 2021;188:675-683. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/34080094>.

223. Kashiwabara K, Fujii S, Tsumura S, Sakamoto K. Overall survival of super-elderly (85 years or older) advanced non-small cell lung cancer patients with active epidermal growth factor receptor mutations receiving first-line gefitinib therapy: a single-institute retrospective study. *J Cancer Res Clin Oncol* 2021;147:287-293. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/32761377>.

224. Hurria A, Lichtman SM. Clinical pharmacology of cancer therapies in older adults. *Br J Cancer* 2008;98:517-522. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/18256586>.

225. Extermann M, Bonetti M, Sledge GW, et al. MAX2--a convenient index to estimate the average per patient risk for chemotherapy toxicity; validation in ECOG trials. *Eur J Cancer* 2004;40:1193-1198. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/15110883>.

226. Shayne M, Crawford J, Dale DC, et al. Predictors of reduced dose intensity in patients with early-stage breast cancer receiving adjuvant chemotherapy. *Breast Cancer Res Treat* 2006;100:255-262. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16705366>.

227. Hurria A, Brogan K, Panageas KS, et al. Patterns of toxicity in older patients with breast cancer receiving adjuvant chemotherapy. *Breast Cancer Res Treat* 2005;92:151-156. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/15986124>.

228. Fader AN, von Gruenigen V, Gibbons H, et al. Improved tolerance of primary chemotherapy with reduced-dose carboplatin and paclitaxel in elderly ovarian cancer patients. *Gynecol Oncol* 2008;109:33-38. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/18261784>.

229. Li D, Sun CL, Kim H, et al. Geriatric Assessment-Driven Intervention (GAIN) on Chemotherapy-Related Toxic Effects in Older Adults With Cancer: A Randomized Clinical Trial. *JAMA Oncol* 2021;7:e214158. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/34591080>.

230. Mohile SG, Mohamed MR, Xu H, et al. Evaluation of geriatric assessment and management on the toxic effects of cancer treatment (GAP70+): a cluster-randomised study. *Lancet* 2021;398:1894-1904. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/34741815>.

231. Agostara B, Carruba G, Usset A. The management of cancer in the elderly: targeted therapies in oncology. *Immun Ageing* 2008;5:16. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/19116012>.



232. Gonsalves W, Ganti AK. Targeted anti-cancer therapy in the elderly. *Crit Rev Oncol Hematol* 2011;78:227-242. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/20599391>.

233. Widakowich C, de Castro G, Jr., de Azambuja E, et al. Review: side effects of approved molecular targeted therapies in solid cancers. *Oncologist* 2007;12:1443-1455. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/18165622>.

234. Floyd JD, Nguyen DT, Lobins RL, et al. Cardiotoxicity of cancer therapy. *J Clin Oncol* 2005;23:7685-7696. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/16234530>.

235. Boehm S, Rothermundt C, Hess D, Joerger M. Antiangiogenic drugs in oncology: a focus on drug safety and the elderly - a mini-review. *Gerontology* 2010;56:303-309. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/19940466>.

236. Yeh ET, Bickford CL. Cardiovascular complications of cancer therapy: incidence, pathogenesis, diagnosis, and management. *J Am Coll Cardiol* 2009;53:2231-2247. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/19520246>.

237. Abdullah SE, Haigentz M, Jr., Piperdi B. Dermatologic Toxicities from Monoclonal Antibodies and Tyrosine Kinase Inhibitors against EGFR: Pathophysiology and Management. *Chemother Res Pract* 2012;2012:351210. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/22997576>.

238. Kanesvaran R, Cordoba R, Maggiore R. Immunotherapy in Older Adults With Advanced Cancers: Implications for Clinical Decision-Making and Future Research. *Am Soc Clin Oncol Educ Book* 2018;38:400-414. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/30231397>.

239. Kasherman L, Siu DHW, Lee KWC, et al. Efficacy of immune checkpoint inhibitors in older adults with advanced stage cancers: A meta-analysis. *J Geriatr Oncol* 2020;11:508-514. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/31129081>.

240. Yang F, Markovic SN, Molina JR, et al. Association of Sex, Age, and Eastern Cooperative Oncology Group Performance Status With Survival Benefit of Cancer Immunotherapy in Randomized Clinical Trials: A Systematic Review and Meta-analysis. *JAMA Netw Open* 2020;3:e2012534. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/32766800>.

241. Reck M, Rodriguez-Abreu D, Robinson AG, et al. Pembrolizumab versus Chemotherapy for PD-L1-Positive Non-Small-Cell Lung Cancer. *N Engl J Med* 2016;375:1823-1833. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/27718847>.

242. Kanesvaran R, Cordoba R, Maggiore R. Immunotherapy in Older Adults With Advanced Cancers: Implications for Clinical Decision-Making and Future Research. *Am Soc Clin Oncol Educ Book* 2018;38:400-414. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/30231397>.

243. Bellmunt J, de Wit R, Vaughn DJ, et al. Pembrolizumab as Second-Line Therapy for Advanced Urothelial Carcinoma. *N Engl J Med* 2017;376:1015-1026. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/28212060>.

244. Landre T, Des Guetz G, Chouahnia K, et al. Immune Checkpoint Inhibitors for Patients Aged ≥ 75 Years with Advanced Cancer in First- and Second-Line Settings: A Meta-Analysis. *Drugs Aging* 2020;37:747-754. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/32681403>.

245. Neelapu SS, Jacobson CA, Oluwole OO, et al. Outcomes of older patients in ZUMA-1, a pivotal study of axicabtagene ciloleucel in refractory large B-cell lymphoma. *Blood* 2020;135:2106-2109. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/32181801>.

246. Zettler ME, Feinberg BA, Phillips EG, Jr., et al. Real-world adverse events associated with CAR T-cell therapy among adults age ≥ 65 years. *J Geriatr Oncol* 2021;12:239-242. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/32798213>.

247. Naeim A, Reuben D. Geriatric syndromes and assessment in older cancer patients. *Oncology (Williston Park)* 2001;15:1567-1577, 1580;



discussion 1581, 1586, 1591. Available at:
<https://www.ncbi.nlm.nih.gov/pubmed/11780701>.

248. Hershman DL, McBride RB, Eisenberger A, et al. Doxorubicin, cardiac risk factors, and cardiac toxicity in elderly patients with diffuse B-cell non-Hodgkin's lymphoma. *J Clin Oncol* 2008;26:3159-3165. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/18591554>.

249. Pinder MC, Duan Z, Goodwin JS, et al. Congestive heart failure in older women treated with adjuvant anthracycline chemotherapy for breast cancer. *J Clin Oncol* 2007;25:3808-3815. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/17664460>.

250. Aapro M, Bernard-Marty C, Brain EG, et al. Anthracycline cardiotoxicity in the elderly cancer patient: a SIOG expert position paper. *Ann Oncol* 2011;22:257-267. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20956616>.

251. 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>.

252. Piccart-Gebhart MJ, Procter M, Leyland-Jones B, et al. Trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer. *N Engl J Med* 2005;353:1659-1672. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16236737>.

253. Romond EH, Perez EA, Bryant J, et al. Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer. *N Engl J Med* 2005;353:1673-1684. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16236738>.

254. Serrano C, Cortes J, De Mattos-Arruda L, et al. Trastuzumab-related cardiotoxicity in the elderly: a role for cardiovascular risk factors.

Ann Oncol 2012;23:897-902. Available at:
<https://www.ncbi.nlm.nih.gov/pubmed/21828361>.

255. Chavez-MacGregor M, Zhang N, Buchholz TA, et al. Trastuzumab-related cardiotoxicity among older patients with breast cancer. *J Clin Oncol* 2013;31:4222-4228. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/24127446>.

256. Tolaney SM, Barry WT, Dang CT, et al. Adjuvant paclitaxel and trastuzumab for node-negative, HER2-positive breast cancer. *N Engl J Med* 2015;372:134-141. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25564897>.

257. Valero V, Forbes J, Pegram MD, et al. Multicenter phase III randomized trial comparing docetaxel and trastuzumab with docetaxel, carboplatin, and trastuzumab as first-line chemotherapy for patients with HER2-gene-amplified metastatic breast cancer (BCIRG 007 study): two highly active therapeutic regimens. *J Clin Oncol* 2011;29:149-156. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21115860>.

258. Au HJ, Eiermann W, Robert NJ, et al. Health-related quality of life with adjuvant docetaxel- and trastuzumab-based regimens in patients with node-positive and high-risk node-negative, HER2-positive early breast cancer: results from the BCIRG 006 Study. *Oncologist* 2013;18:812-818. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/23814044>.

259. Miles D, Baselga J, Amadori D, et al. Treatment of older patients with HER2-positive metastatic breast cancer with pertuzumab, trastuzumab, and docetaxel: subgroup analyses from a randomized, double-blind, placebo-controlled phase III trial (CLEOPATRA). *Breast Cancer Res Treat* 2013;142:89-99. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/24129974>.

260. Upadhrasta S, Elias H, Patel K, Zheng L. Managing cardiotoxicity associated with immune checkpoint inhibitors. *Chronic Dis Transl Med* 2019;5:6-14. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/30993259>.



261. Sul JK, Deangelis LM. Neurologic complications of cancer chemotherapy. *Semin Oncol* 2006;33:324-332. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/16769421>.

262. Cheson BD, Vena DA, Foss FM, Sorensen JM. Neurotoxicity of purine analogs: a review. *J Clin Oncol* 1994;12:2216-2228. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/7931492>.

263. Smith GA, Damon LE, Rugo HS, et al. High-dose cytarabine dose modification reduces the incidence of neurotoxicity in patients with renal insufficiency. *J Clin Oncol* 1997;15:833-839. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/9053511>.

264. Rubin EH, Andersen JW, Berg DT, et al. Risk factors for high-dose cytarabine neurotoxicity: an analysis of a cancer and leukemia group B trial in patients with acute myeloid leukemia. *J Clin Oncol* 1992;10:948-953. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/1588374>.

265. Balducci L, Repetto L. Increased risk of myelotoxicity in elderly patients with non-Hodgkin lymphoma. *Cancer* 2004;100:6-11. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/14692018>.

266. Crivellari D. Results of adjuvant treatments in breast cancer patients over 70 years old: the IBCSG experience. *International Breast Cancer Study Group. Tumori* 2002;88:S81-82. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/11989935>.

267. Langer CJ, Manola J, Bernardo P, et al. Cisplatin-based therapy for elderly patients with advanced non-small-cell lung cancer: implications of Eastern Cooperative Oncology Group 5592, a randomized trial. *J Natl Cancer Inst* 2002;94:173-181. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/11830607>.

268. Rocha Lima CM, Herndon JE, 2nd, Kosty M, et al. Therapy choices among older patients with lung carcinoma: an evaluation of two trials of the Cancer and Leukemia Group B. *Cancer* 2002;94:181-187. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/11815975>.

269. Neubauer M, Schwartz J, Caracandas J, et al. Results of a phase II study of weekly paclitaxel plus carboplatin in patients with extensive small-cell lung cancer with Eastern Cooperative Oncology Group Performance Status of 2, or age > or = 70 years. *J Clin Oncol* 2004;22:1872-1877. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/15143079>.

270. Zinzani PL, Pavone E, Storti S, et al. Randomized trial with or without granulocyte colony-stimulating factor as adjunct to induction VNCOP-B treatment of elderly high-grade non-Hodgkin's lymphoma. *Blood* 1997;89:3974-3979. Available at:

<http://www.ncbi.nlm.nih.gov/pubmed/9166835>.

271. Doorduijn JK, van der Holt B, van Imhoff GW, et al. CHOP compared with CHOP plus granulocyte colony-stimulating factor in elderly patients with aggressive non-Hodgkin's lymphoma. *J Clin Oncol* 2003;21:3041-3050. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/12915593>.

272. Osby E, Hagberg H, Kvaloy S, et al. CHOP is superior to CNOP in elderly patients with aggressive lymphoma while outcome is unaffected by filgrastim treatment: results of a Nordic Lymphoma Group randomized trial. *Blood* 2003;101:3840-3848. Available at:

<http://www.ncbi.nlm.nih.gov/pubmed/12531794>.

273. Gomez H, Mas L, Casanova L, et al. Elderly patients with aggressive non-Hodgkin's lymphoma treated with CHOP chemotherapy plus granulocyte-macrophage colony-stimulating factor: identification of two age subgroups with differing hematologic toxicity. *J Clin Oncol* 1998;16:2352-2358. Available at:

<https://www.ncbi.nlm.nih.gov/pubmed/9667250>.

274. Amadori S, Suci S, Jehn U, et al. Use of glycosylated recombinant human G-CSF (lenograstim) during and/or after induction chemotherapy in patients 61 years of age and older with acute myeloid leukemia: final results of AML-13, a randomized phase-3 study. *Blood* 2005;106:27-34. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/15761020>.



275. Lowenberg B, van Putten W, Theobald M, et al. Effect of priming with granulocyte colony-stimulating factor on the outcome of chemotherapy for acute myeloid leukemia. *N Engl J Med* 2003;349:743-752. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/12930926>.

276. Lyman GH, Kuderer NM, Djulbegovic B. Prophylactic granulocyte colony-stimulating factor in patients receiving dose-intensive cancer chemotherapy: a meta-analysis. *Am J Med* 2002;112:406-411. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/11904116>.

277. Lyman GH, Kuderer N, Agboola O, Balducci L. Evidence-based use of colony-stimulating factors in elderly cancer patients. *Cancer Control* 2003;10:487-499. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/14652525>.

278. Repetto L, Biganzoli L, Koehne CH, et al. EORTC Cancer in the Elderly Task Force guidelines for the use of colony-stimulating factors in elderly patients with cancer. *Eur J Cancer* 2003;39:2264-2272. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/14556916>.

279. Pierelli L, Perillo A, Greggi S, et al. Erythropoietin addition to granulocyte colony-stimulating factor abrogates life-threatening neutropenia and increases peripheral-blood progenitor-cell mobilization after epirubicin, paclitaxel, and cisplatin combination chemotherapy: results of a randomized comparison. *J Clin Oncol* 1999;17:1288. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/10561191>.

280. Pickett JL, Theberge DC, Brown WS, et al. Normalizing hematocrit in dialysis patients improves brain function. *Am J Kidney Dis* 1999;33:1122-1130. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/10352201>.

281. Silverberg DS, Wexler D, Blum M, et al. The use of subcutaneous erythropoietin and intravenous iron for the treatment of the anemia of severe, resistant congestive heart failure improves cardiac and renal function and functional cardiac class, and markedly reduces hospitalizations. *J Am Coll Cardiol* 2000;35:1737-1744. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10841219>.

282. Metivier F, Marchais SJ, Guerin AP, et al. Pathophysiology of anaemia: focus on the heart and blood vessels. *Nephrol Dial Transplant* 2000;15 Suppl 3:14-18. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/11032352>.

283. Wu WC, Rathore SS, Wang Y, et al. Blood transfusion in elderly patients with acute myocardial infarction. *N Engl J Med* 2001;345:1230-1236. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/11680442>.

284. Zilinski J, Zillmann R, Becker I, et al. Prevalence of anemia among elderly inpatients and its association with multidimensional loss of function. *Ann Hematol* 2014;93:1645-1654. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/24870940>.

285. Owusu C, Cohen HJ, Feng T, et al. Anemia and Functional Disability in Older Adults With Cancer. *J Natl Compr Canc Netw* 2015;13:1233-1239. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26483063>.

286. Bohlius J, Wilson J, Seidenfeld J, et al. Recombinant human erythropoietins and cancer patients: updated meta-analysis of 57 studies including 9353 patients. *J Natl Cancer Inst* 2006;98:708-714. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16705125>.

287. Juneja V, Keegan P, Gootenberg JE, et al. Continuing reassessment of the risks of erythropoiesis-stimulating agents in patients with cancer. *Clin Cancer Res* 2008;14:3242-3247. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/18519748>.

288. Bennett CL, Silver SM, Djulbegovic B, et al. Venous thromboembolism and mortality associated with recombinant erythropoietin and darbepoetin administration for the treatment of cancer-associated anemia. *JAMA* 2008;299:914-924. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/18314434>.

289. Bohlius J, Schmidlin K, Brillant C, et al. Recombinant human erythropoiesis-stimulating agents and mortality in patients with cancer: a meta-analysis of randomised trials. *Lancet* 2009;373:1532-1542. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/19410717>.



290. Tepler I, Elias L, Smith JW, et al. A randomized placebo-controlled trial of recombinant human interleukin-11 in cancer patients with severe thrombocytopenia due to chemotherapy. *Blood* 1996;87:3607-3614. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/8611684>.

291. Winer ES, Safran H, Karaszewska B, et al. Eltrombopag for thrombocytopenia in patients with advanced solid tumors receiving gemcitabine-based chemotherapy: a randomized, placebo-controlled phase 2 study. *Int J Hematol* 2017;106:765-776. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28864871>.

292. Soff GA, Miao Y, Devlin SM, et al. Romiplostim for Chemotherapy-Induced Thrombocytopenia (CIT). Results of a Phase 2 Trial. *Blood* 2017;130:289-289. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6823892/>.

293. Feyer P, Jordan K. Update and new trends in antiemetic therapy: the continuing need for novel therapies. *Ann Oncol* 2011;22:30-38. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20947707>.

294. Aapro M, Johnson J. Chemotherapy-induced emesis in elderly cancer patients: the role of 5-HT₃-receptor antagonists in the first 24 hours. *Gerontology* 2005;51:287-296. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16110229>.

295. Jakobsen JN, Herrstedt J. Prevention of chemotherapy-induced nausea and vomiting in elderly cancer patients. *Crit Rev Oncol Hematol* 2009;71:214-221. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/19162507>.

296. Benson AB, 3rd, Ajani JA, Catalano RB, et al. Recommended guidelines for the treatment of cancer treatment-induced diarrhea. *J Clin Oncol* 2004;22:2918-2926. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/15254061>.

297. Arnold RJ, Gabrail N, Raut M, et al. Clinical implications of chemotherapy-induced diarrhea in patients with cancer. *J Support Oncol* 2005;3:227-232. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/15915825>.

298. Bergman L, Djarv L. A comparative study of loperamide and diphenoxylate in the treatment of chronic diarrhoea caused by intestinal resection. *Ann Clin Res* 1981;13:402-405. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/6753707>.

299. Spielberger R, Stiff P, Bensinger W, et al. Palifermin for oral mucositis after intensive therapy for hematologic cancers. *N Engl J Med* 2004;351:2590-2598. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/15602019>.

300. Rosen LS, Abdi E, Davis ID, et al. Palifermin reduces the incidence of oral mucositis in patients with metastatic colorectal cancer treated with fluorouracil-based chemotherapy. *J Clin Oncol* 2006;24:5194-5200. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/17075109>.

301. Le QT, Kim HE, Schneider CJ, et al. Palifermin reduces severe mucositis in definitive chemoradiotherapy of locally advanced head and neck cancer: a randomized, placebo-controlled study. *J Clin Oncol* 2011;29:2808-2814. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21670453>.

302. Henke M, Alfonsi M, Foa P, et al. Palifermin decreases severe oral mucositis of patients undergoing postoperative radiochemotherapy for head and neck cancer: a randomized, placebo-controlled trial. *J Clin Oncol* 2011;29:2815-2820. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21670447>.

303. Lalla RV, Bowen J, Barasch A, et al. MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. *Cancer* 2014;120:1453-1461. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/24615748>.

304. Bloom HG, Ahmed I, Alessi CA, et al. Evidence-based recommendations for the assessment and management of sleep disorders in older persons. *J Am Geriatr Soc* 2009;57:761-789. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/19484833>.

305. Palesh OG, Roscoe JA, Mustian KM, et al. Prevalence, demographics, and psychological associations of sleep disruption in



patients with cancer: University of Rochester Cancer Center-Community Clinical Oncology Program. J Clin Oncol 2010;28:292-298. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/19933917>.

306. Savard J, Ivers H, Villa J, et al. Natural course of insomnia comorbid with cancer: an 18-month longitudinal study. J Clin Oncol 2011;29:3580-3586. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21825267>.

307. Howell D, Oliver TK, Keller-Olaman S, et al. A Pan-Canadian practice guideline: prevention, screening, assessment, and treatment of sleep disturbances in adults with cancer. Support Care Cancer 2013;21:2695-2706. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/23708820>.

308. Savard J, Simard S, Ivers H, Morin CM. Randomized study on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer, part II: Immunologic effects. J Clin Oncol 2005;23:6097-6106. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16135476>.

309. 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: <https://www.ncbi.nlm.nih.gov/pubmed/17878117>.

310. 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>.

311. Fiorentino L, McQuaid JR, Liu L, et al. Individual cognitive behavioral therapy for insomnia in breast cancer survivors: a randomized controlled crossover pilot study. Nat Sci Sleep 2010;2:1-8. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/23616695>.

312. Matthews EE, Schmiege SJ, Cook PF, et al. Adherence to cognitive behavioral therapy for insomnia (CBTI) among women following primary

breast cancer treatment: a pilot study. Behav Sleep Med 2012;10:217-229. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22742439>.

313. Brandt NJ, Piechocki JM. Treatment of insomnia in older adults: re-evaluating the benefits and risks of sedative hypnotic agents. J Gerontol Nurs 2013;39:48-54. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/23445185>.

314. Minkel J, Krystal AD. Optimizing the Pharmacologic Treatment of Insomnia: Current Status and Future Horizons. Sleep Med Clin 2013;8:333-350. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/24015116>.

315. Available at: <https://www.fda.gov/drugs/drugsafety/ucm334041.htm>. Accessed July 12, 2022.

316. Maloney KW, Kagan SH. Adherence and oral agents with older patients. Semin Oncol Nurs 2011;27:154-160. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21514484>.

317. Hershman DL, Kushi LH, Shao T, et al. Early discontinuation and nonadherence to adjuvant hormonal therapy in a cohort of 8,769 early-stage breast cancer patients. J Clin Oncol 2010;28:4120-4128. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20585090>.

318. Demissie S, Silliman RA, Lash TL. Adjuvant tamoxifen: predictors of use, side effects, and discontinuation in older women. J Clin Oncol 2001;19:322-328. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/11208822>.

319. Fink AK, Gurwitz J, Rakowski W, et al. Patient beliefs and tamoxifen discontinuance in older women with estrogen receptor--positive breast cancer. J Clin Oncol 2004;22:3309-3315. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/15310774>.

320. Lash TL, Fox MP, Westrup JL, et al. Adherence to tamoxifen over the five-year course. Breast Cancer Res Treat 2006;99:215-220. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16541307>.



321. Owusu C, Buist DS, Field TS, et al. Predictors of tamoxifen discontinuation among older women with estrogen receptor-positive breast cancer. *J Clin Oncol* 2008;26:549-555. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/18071188>.

322. Partridge AH, Archer L, Kornblith AB, et al. Adherence and persistence with oral adjuvant chemotherapy in older women with early-stage breast cancer in CALGB 49907: adherence companion study 60104. *J Clin Oncol* 2010;28:2418-2422. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20368559>.

323. De Maio E, Gravina A, Pacilio C, et al. Compliance and toxicity of adjuvant CMF in elderly breast cancer patients: a single-center experience. *BMC Cancer* 2005;5:30. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/15790416>.

324. Barcenas CH, Zhang N, Zhao H, et al. Anthracycline regimen adherence in older patients with early breast cancer. *Oncologist* 2012;17:303-311. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/22371383>.

325. Noens L, van Lierde MA, De Bock R, et al. Prevalence, determinants, and outcomes of nonadherence to imatinib therapy in patients with chronic myeloid leukemia: the ADAGIO study. *Blood* 2009;113:5401-5411. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/19349618>.

326. Marin D, Bazeos A, Mahon F-X, et al. Adherence is the critical factor for achieving molecular responses in patients with chronic myeloid leukemia who achieve complete cytogenetic responses on imatinib. *J Clin Oncol* 2010;28:2381-2388. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/20385986>.

327. Dobie SA, Baldwin LM, Dornitz JA, et al. Completion of therapy by Medicare patients with stage III colon cancer. *J Natl Cancer Inst* 2006;98:610-619. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16670386>.

328. Fesinmeyer MD, Mehta V, Tock L, et al. Completion of radiotherapy for local and regional head and neck cancer in medicare. *Arch Otolaryngol Head Neck Surg* 2009;135:860-867. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/19770417>.

329. Mislav AR, Wildes TM, Kanesvaran R, et al. Adherence to oral cancer therapy in older adults: The International Society of Geriatric Oncology (SIOG) taskforce recommendations. *Cancer Treat Rev* 2017;57:58-66. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28550714>.

330. Muluneh B, Schneider M, Faso A, et al. Improved Adherence Rates and Clinical Outcomes of an Integrated, Closed-Loop, Pharmacist-Led Oral Chemotherapy Management Program. *J Oncol Pract* 2018;14:e324-e334. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29799768>.

331. Eckstrom E, Feeny DH, Walter LC, et al. Individualizing cancer screening in older adults: a narrative review and framework for future research. *J Gen Intern Med* 2013;28:292-298. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/23054920>.

332. Kotwal AA, Walter LC. Cancer Screening Among Older Adults: a Geriatrician's Perspective on Breast, Cervical, Colon, Prostate, and Lung Cancer Screening. *Curr Oncol Rep* 2020;22:108. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/32803486>.

333. McPherson CP, Swenson KK, Lee MW. The effects of mammographic detection and comorbidity on the survival of older women with breast cancer. *J Am Geriatr Soc* 2002;50:1061-1068. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/12110066>.

334. Biganzoli L, Battisti NML, Wildiers H, et al. Updated recommendations regarding the management of older patients with breast cancer: a joint paper from the European Society of Breast Cancer Specialists (EUSOMA) and the International Society of Geriatric Oncology (SIOG). *Lancet Oncol* 2021;22:e327-e340. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/34000244>.



335. Lin JS, Piper MA, Perdue LA, et al. Screening for Colorectal Cancer: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA 2016;315:2576-2594. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27305422>.

336. Andriole GL, Crawford ED, Grubb RL, 3rd, et al. Prostate cancer screening in the randomized Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial: mortality results after 13 years of follow-up. J Natl Cancer Inst 2012;104:125-132. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/22228146>.

337. Crawford ED, Grubb R, 3rd, Black A, et al. Comorbidity and mortality results from a randomized prostate cancer screening trial. J Clin Oncol 2011;29:355-361. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21041707>.

338. Freedman RA, Minami CA, Winer EP, et al. Individualizing Surveillance Mammography for Older Patients After Treatment for Early-Stage Breast Cancer: Multidisciplinary Expert Panel and International Society of Geriatric Oncology Consensus Statement. JAMA Oncol 2021;7:609-615. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/33507222>.

Discussion
update in
progress