National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Smoking Cessation

Version 1.2024 — April 30, 2024

NCCN.org

Continue

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2024
Smoking Cessation

NCCN Guidelines Index
Table of Contents
Discussion

***Peter G. Shields, MD/Chair †**
The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute

***Laura J. Bierut, MD/Vice Chair θ**
Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine

Douglas Arenberg, MD Ξ
University of Michigan Rogel Cancer Center

David Balis, MD Þ
UT Southwestern Simmons Comprehensive Cancer Center

Paul M. Cinciripini, PhD θ
The University of Texas MD Anderson Cancer Center

James M. Davis, MD Þ
Duke Cancer Institute

Donna Edmondson, MSN, AOCNP, CRNP Ξ
Fox Chase Cancer Center

Sarah Evers-Casey, MPH ¥
Abramson Cancer Center at the University of Pennsylvania

Joy Feliciano, MD †
The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

Brian Hitsman, PhD θ
Robert H. Lurie Comprehensive Cancer Center of Northwestern University

Karen S. Hudmon, DrPH, MS, BS, CTTS Σ
Indiana University Melvin and Bren Simon Comprehensive Cancer Center

Michael T. Jaklitsch, MD ¶
Dana-Farber/Brigham and Women`s Cancer Center | Mass General Cancer Center

Thomas Klingemann, PharmD Σ
Fred and Pamela Buffett Cancer Center

Pamela M. Ling, MD, MPH Þ
UCSF Helen Diller Family Comprehensive Cancer Center

Richard S. Matulewicz, MD, MS, MSCI ω
Memorial Sloan Kettering Cancer Center

Danielle E. McCarthy, PhD θ
University of Wisconsin Carbone Cancer Center

Michael K. Ong, MD, PhD Þ
UCLA Jonsson Comprehensive Cancer Center

Elyse R. Park, PhD θ
Dana-Farber/Brigham and Women`s Cancer Center | Mass General Cancer Center

Judith J. Prochaska PhD, MPH θ
Stanford Cancer Institute

A. Jossie Sandoval, MD Ξ
City of Hope National Medical Center

Christine E. Sheffer, PhD θ
Roswell Park Comprehensive Cancer Center

Sharon Spencer, MD §
O'Neal Comprehensive Cancer Center at UAB

Jamie L. Studts, PhD £
University of Colorado Cancer Center

Marcia M. Tan, PhD, MPH θ
The UChicago Medicine Comprehensive Cancer Center

Tawee Tanvetyanon, MD, MPH †
Moffitt Cancer Center

Hilary A. Tindle, MD, MPH Þ
Vanderbilt-Ingram Cancer Center

Elisa K. Tong, MD, MA Þ
UC Davis Comprehensive Cancer Center

Matthew Triplette, MD, MPH Ξ
Fred Hutchinson Cancer Center

James Urbanic, MD §
UC San Diego Moores Cancer Center

Gregory Videtic, MD §
Case Comprehensive Cancer Center/ University Hospitals Seidman Cancer Center and Cleveland Clinic Taussig Cancer Institute

David Warner, MD φ
Mayo Clinic Comprehensive Cancer Center

NCCN

Susan Darlow, PhD
Beth McCullough, RN, BS

NCCN Guidelines Panel Disclosures

Continue

φ Anesthesiology
Þ Internal medicine
† Medical oncology
# Nursing
¥ Patient advocacy
Σ Pharmacology/ Pharmacogenetics
θ Psychiatry/Psychology/ Behavioral science
Ξ Pulmonary medicine
§ Radiotherapy/Radiation oncology
¶ Surgery/Surgical oncology
£ Supportive/Palliative Care
ω Urology
* Discussion Writing Committee Member

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2024
Smoking Cessation

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

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

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

See NCCN Categories of Evidence and Consensus.

NCCN Categories of Preference: All recommendations are considered appropriate.

See NCCN Categories of Preference.

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2024
Smoking Cessation

NCCN Guidelines Index
Table of Contents
Discussion

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 Smoking Cessation from Version 2.2023 include:

General:
• The term provider was revised to health care professionals.

Intro
• Second paragraph revised: As a generalization, the principles for treating ~~nicotine~~ *tobacco* use disorder of any ~~nicotine-containing~~ *tobacco* products are similar. Therefore, the NCCN Guidelines for Smoking Cessation are directly applicable to not only *combustible tobacco products* (*eg,* cigarettes, *pipes, cigars, hookah, cigarillos*) but also *electronic cigarettes (e-cigarettes)/vaping and* smokeless tobacco *products* ~~and vaping~~.
• Third paragraph, last sentence revised: ~~Nicotine addiction~~ *Tobacco use disorder* is a chronic relapsing ~~disorder~~ *condition*.
• Clinical Recommendations:
  ▸ Second bullet revised: ...*All patients undergoing smoking treatment should be considered for lung cancer screening*.
  ▸ Third bullet revised: ...~~Providers~~ *Health care professionals*, ~~the health care team, and~~ *including* tobacco treatment specialists*,* should discuss this and provide guidance and support to encourage continued abstinence from smoking. Smoking slips are not necessarily an indication to try an alternative method. It may take more than one quit attempt with the same therapy to achieve long-term cessation. *Health care professionals should educate patients to take smoking treatment medications according to the prescribed regimen and for the full course of therapy.*
  ▸ Fourth bullet revised: Treatment for smoking ~~should be offered as~~ *is* an integral part of oncology treatment and *should be* continued throughout the entire oncology care continuum, ~~including surgery, radiation therapy (RT), systemic therapy~~ *from treatment, to survivorship,* ~~and~~ *to* end-of-life care...
• Footnote b added: For lung cancer screening recommendations, see NCCN Guidelines for Lung Cancer Screening. (Also page SC-1)

SC-1
• Initial Evaluation, third bullet revised: Have you ever or do you currently use other tobacco~~-containing~~ products (eg, pipes, cigars, *hookah, cigarillos,* e-cigarettes~~,~~ */vaping,* smokeless tobacco)?
• Footnotes revised:
  ▸ Footnote c: ...Patients with cancer should be encouraged to achieve and maintain abstinence from all combustible tobacco products (eg, cigarettes, *pipes,* cigars, hookah, *cigarillos*), *e-cigarettes/vaping,* and smokeless tobacco products. For information about e-cigarettes, see Principles of Alternative Approaches to Treatment of Smoking (SC-A).
  ▸ Footnote e: Initial evaluation and assessment of patient smoking may be completed by any member of the health care team, including physicians, nurses, medical assistants, health educators, pharmacists, *tobacco treatment specialists,* or other dedicated staff.
  ▸ Footnote h: Patients who use multiple tobacco products may ~~be more resistant to quitting~~ *have more difficulty achieving abstinence*.

Continued

UPDATES

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2024
Smoking Cessation

NCCN Guidelines Index
Table of Contents
Discussion

Updates in Version 1.2024 of the NCCN Guidelines for Smoking Cessation from Version 2.2023 include:

SC-2
- Evaluation:
  - First bullet revised: ~~Nicotine~~ *Tobacco* use:
    - First sub-bullet revised: How much do you currently smoke or use ~~nicotine~~ *tobacco* products (eg, cigarettes, pipes, cigars, *hookah, cigarillos,* e-cigarettes~~,~~ */vaping,* smokeless tobacco) per day?
    - Third sub-bullet revised: How soon do you smoke or use ~~nicotine~~ *tobacco* products after you wake up in the morning? (ie, within 30 minutes)
  - Second bullet:
    - Second sub-bullet, new tertiary bullet added for strategies for quit attempts: Which were unsuccessful and why? (eg, side effects, cost, continued cravings, did not work, inadequate behavioral support)
    - Fourth sub-bullet, second tertiary bullet revised: Medications (eg, varenicline, bupropion *long-acting*, NRT)
    - Last sub-bullet removed: Why were previous quit attempts unsuccessful? (eg, side effects, cost, continued cravings, did not work, inadequate behavioral support)
- Second column revised: ~~Engage patients in a personalized motivational dialogue about smoking cessation~~ *Advise patients to quit*
- Footnotes revised:
  - Footnote l: Smoking by other household members is an important predictor for not remaining abstinent~~,~~ and *exposes the patient to secondhand smoke*. *To benefit the patient,* individuals in the ~~patient's~~ household should be encouraged to abstain from smoking*; resources may be provided* ~~to benefit the patient~~.
  - Footnote m: ~~Providers and members of the health care team should discuss potential benefits of quitting with each patient. Readiness to quit is to be determined by both provider and patient.~~ *Brief advice of about 3 minutes by health care professionals is associated with a small but important increase in smoking abstinence rates.* (Also page SC-3)

SC-3
- Status, second pathway revised: Ready to *set a* quit *date*
- Management:
  - Top pathway, second bullet revised: Encourage *continued* abstinence from smoking ~~as soon as possible if cancer surgery is planned~~.
  - Middle pathway, bullet removed: Set quit date as soon as possible.
- Footnote p revised: ~~Providers, the health care team, and~~ *Health care professionals, including* tobacco treatment specialists*,* should discuss risks of relapse and slips and provide guidance and support to encourage continued abstinence from smoking. ~~While NRT may be used long-term to help individuals who quit maintain abstinence, methods other than NRT may be considered so as not to reintroduce an individual who used to smoke to nicotine.~~ See Principles of Behavioral Treatment ~~for~~ *of* Smoking (SC-E). (Also page SC-4)

Continued

Updates in Version 1.2024 of the NCCN Guidelines for Smoking Cessation from Version 2.2023 include:

SC-5

- Footnotes revised:
  - Footnote t: The use of cannabis, or other substances associated with smoking relapse*, including alcohol*, is discouraged for those attempting to quit smoking. *Lynch KL, et al. Nicotine Tob Res 2019;21:1058-1064*. (Also page SC-6)
  - Footnote u: Combination NRT or varenicline are the preferred pharmacotherapy options. However, bupropion *long-acting* ± NRT may be appropriate for select patients (eg, for those with depression or fatigue)... (Also page SC-6)
  - Footnote w: Four or more sessions of individual/group therapy is recommended, with additional sustained counseling as needed. Brief advice by ~~physicians and other~~ *health care* ~~providers~~ *professionals* is associated with a small but important increase in smoking abstinence rates. . . (Also page SC-6)
  - Footnote y: For those being treated with varenicline, the addition of NRT or bupropion *long-acting* can be considered as clinically indicated to maintain abstinence despite continued urges to smoke. (Also page SC-6)
  - Footnote z: *Most* ~~N~~*n*icotine withdrawal symptoms *manifest in the first 1–2 days,* ~~typically~~ peak *within the first week, and subside* within 2–*4* weeks of quitting. *Increased appetite, weight gain, and cravings may persist for several months. It is important to parse out perceived withdrawal symptoms from treatment side effects.* Encourage continued therapy through brief slips. *Hughes JR. Nicotine Tob Res 2007;9:315-327. Benowitz NL. Med Clin North Am 1992;76:415-437.* (Also page SC-6)
- Footnote cc added: Drug levels of certain medications may be altered when a person stops smoking; assess for drug interactions.

SC-A

- Heading revised: ~~Electronic Cigarettes ("~~E-Cigarettes~~")~~ or Vaping
  - First bullet, sub-bullet revised: The FDA may authorize the sale of select electronic nicotine delivery system (ENDS) products as modified risk tobacco products. ~~To date~~ *Currently*, none of these products are FDA-approved for the treatment of smoking.
  - Fourth bullet, first sub-bullet revised: For patients who use both e-cigarettes and combustible tobacco, ~~complete smoking cessation is recommended.~~ ~~D~~*d*ual use is strongly discouraged as it continues to pose a risk of *cancer and other* smoking-related diseases. ~~Smoking even a few cigarettes a day can be hazardous to one's health.~~ *Complete smoking abstinence is recommended*.
  - Fifth bullet revised: Vaping ~~THC (the active ingredient in cannabis)~~ products contaminated with vitamin E acetate ~~is~~ *are* associated with EVALI (e-cigarette or vaping product use-associated lung injury). Investigations are ongoing and ~~providers~~ *health care professionals* should be aware of *the* latest recommendations from the Centers for Disease Control and Prevention (https://www.cdc.gov/tobacco/basic_information/e-cigarettes/index.html)...
- Other Alternative Methods, new bullet added: There are multiple nicotine-mimicking and nicotine-containing products that are not FDA approved for smoking treatment.
- Reference removed: Blount BC, Karwowski MP, Shields PG, et al. Vitamin E acetate in bronchoalveolar-lavage fluid associated with EVALI. N Engl J Med 2020;382:697-705.

SC-B (1 of 2)

- Second bullet, sixth sub-bullet revised: *To benefit the patient, individuals in* ~~Encourage all members of~~ the household *should be encouraged* to abstain from smoking ~~for the benefit of the patient~~*; resources may be provided*.

SC-B (2 of 2)

- New reference 2 added: Park ER, Perez GK, Regan S, et al. Effect of sustained smoking cessation counseling and provision of medication vs shorter-term counseling and medication Advice on smoking abstinence in patients recently diagnosed with cancer: A randomized clinical trial. JAMA 2020;324:1406-1418.

Continued

Updates in Version 1.2024 of the NCCN Guidelines for Smoking Cessation from Version 2.2023 include:

SC-C (1 of 2)

- Cancer-Related Resources for Patients:
  - American Cancer Society (ACS), third bullet revised: Guide to quitting smoking: ~~http://www.cancer.org/healthy/ stayawayfromtobacco/ guidetoquittingsmoking/index~~ https://www.cancer.org/cancer/risk-prevention/tobacco/guide-quitting-smoking.html.
  - Smokefree.gov:
    - ◊ Fifth bullet revised: SmokeFree Text Messaging Programs (available for adults, teens, ~~moms~~ *pregnant persons*, and veterans, and ~~en español~~ *in Spanish*): https://smokefree.gov/smokefree-text-messaging-programs.
    - ◊ Bullet removed: Springboard Beyond Cancer: https://survivorship.cancer.gov
- General Resources for Patients:
  - Centers for Disease Control and Prevention (CDC) Office on Smoking and Health, new bullet added: SmokeFree Text Messaging Programs (state and national services available for adults): Text QUITNOW to 333888 or https://www.cdc.gov/tobacco/campaign/tips/ quit-smoking/national-texting-portal. html.
  - TRICARE and UCanQuit2 (Military and family), second bullet revised: Text support ~~(SmokefreeMIL)~~: https://www.ycq2.org/resources/smokefreemil.
  - New resource added: VA How to Quit, Website: https://www.mentalhealth.va.gov/quit-tobacco/how-to-quit.asp.
- Footnote a revised: Free or low-cost support is sometimes available for *patients who are* uninsured or underinsured ~~patients~~. Resources may vary by organization and location. Contact each organization to learn more about the availability of free and low-cost smoking cessation and treatment resources offered regionally.

SC-C (2 of 2)

- General Resources for Health Professionals:
  - American Thoracic Society, bullet revised: Initiating Pharmacologic Treatment in Tobacco-Dependent Adults ~~–~~: An Official ~~American Thoracic Society~~ *ATS* Clinical Practice Guideline *Implementation Tools*: https://www.thoracic.org/statements/guidelineimplementation-tools/pharmacologic-treatment-of-tobacco-dependence.php.
  - National Behavioral Health Network *for Tobacco & Cancer Control*
  - U.S. Preventive Services Task Force (USPSTF), bullet revised: Final ~~Update Summary~~ *Recommendation Statement*: Tobacco Smoking Cessation in Adults, Including Pregnant *Persons* ~~Women~~: ~~Behavioral and Pharmacotherapy~~ Interventions. U.S. Preventive Services Task Force. ~~September 2015~~ *January 2021*.

SC-D

- First bullet,
  - First sub-bullet, second tertiary bullet revised: If ≥7 days to surgery, either combination NRT (category 1) or varenicline (category 1) are options. *Smoking treatment should happen as soon as possible; ideally, the patient should be abstinent for 4 weeks or more, but this recommendation should not cause a delay in surgery.*
  - Second sub-bullet revised: *NRT is not a contraindication to surgery.* There is no evidence that NRT degrades the wound-healing benefits of abstinence from smoking in humans...
- Third bullet revised: Patients should be encouraged to quit smoking as soon as possible before surgery, regardless of how short the time is to surgery. *Even quitting on the day of surgery has a benefit*.
- New reference added: https://www.quitforsurgery.com/

Continued

Updates in Version 1.2024 of the NCCN Guidelines for Smoking Cessation from Version 2.2023 include:

SC-E (1 of 3)

- Second bullet revised: ...Behavior therapy, tailored to the patient's ~~nicotine~~ *tobacco* use and previous quit attempts, provides strategies for:
  - First sub-bullet revised: ...(Note: Nicotine withdrawal ~~S~~symptoms *manifest in the first 1–2 days,* ~~typically~~ peak ~~between 48–72 hours after quitting~~ *within the first week*, and ~~last about 2–3 weeks before subsiding~~ *subside within 2–4 weeks of quitting*. *Increased appetite, weight gain, and cravings may persist for several months. It is important to parse out perceived withdrawal symptoms from treatment side effects)*.
- Sixth bullet revised: Smoking by other household members is an important predictor for not remaining abstinent *and exposes the patient to secondhand smoke*. *To benefit the patient,* ~~and~~ individuals in the ~~patient's~~ household should be encouraged to abstain from smoking ~~to benefit the patient~~*; resources may be provided*.
- Seventh bullet, second sub-bullet revised: High rates of menthol cigarette use that may increase nicotine use in African-American *communities and other groups that have been historically marginalized* ~~communities~~.

SC-E (2 of 3)

- Behavior Therapy/Counseling Recommendations:
  - First bullet, sub-bullet revised: Brief advice of about 3 minutes by ~~physicians and other~~ *health care* ~~providers~~ *professionals* is associated with a small but important increase in smoking abstinence rates...
  - Second bullet, second sub-bullet revised: Refer to *evidence-based resources for quitting, such as* a smoking cessation quitline, in addition to providing brief counseling from a *health care* ~~provider~~ *professional*, if face-to-face or group intervention is not available. *See* ~~Patient/Provider~~ Smoking Cessation and Treatment Resources *for Patients/Health Care Professionals* (SC-C).
- Motivational Counseling, first bullet revised: Motivational counseling is beneficial for all patients *throughout treatment* but is essential for those not immediately ready to quit.

SC-E (3 of 3)

- Reference 3 revised: Treating Tobacco Use and Dependence. Content last reviewed April 2013. Agency for Healthcare Research and Quality, Rockville, MD. ~~http://www.ahrq.gov/ professionals/clinicians-providers/guidelines-recommendations/tobacco/clinicians/update/index.html~~ *https://www.ahrq.gov/prevention/guidelines/tobacco/clinicians/ update/index.html*.
- Reference 9 revised: Centers for Disease Control and Prevention: American Indian~~s~~*/* and Alaska Native~~s~~ *People* and *Commercial* Tobacco*:* ~~Use~~ *Health Disparities and Ways to Advance Health Equity* (~~https://www.cdc.gov/tobacco/disparities/american-indians/index.htm~~ *https://www.cdc.gov/tobacco/health-equity/aian/index.html*).
- Reference 16 revised: Lindson-Hawley N, *Thompson TP, Begh R* ~~et al~~. *Motivational interviewing for smoking cessation*. Cochrane Database of Syst~~ematic~~ Rev~~iews~~ 2015~~, Issue 3. Art. No.:~~*;*~~CD006936.~~
- New reference 8 added: Jabba SV, Erythropel HC, Anastas PT, et al. Synthetic cooling agent and other flavor additives in "non-menthol" cigarettes marketed in California and Massachusetts after menthol cigarette bans. JAMA 2023;330:1689-1691.

Continued

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2024
Smoking Cessation

NCCN Guidelines Index
Table of Contents
Discussion

Updates in Version 1.2024 of the NCCN Guidelines for Smoking Cessation from Version 2.2023 include:

SC-F (1 of 4)
- Second bullet:
  - First sub-bullet revised: Follow-up is recommended (in-person or by phone/telehealth) within 3 weeks (*within* 1 week preferred) after starting pharmacotherapy, but can be adjusted to coordinate with regularly scheduled oncology appointments as needed...
  - Second sub-bullet revised: *Most* ~~N~~*n*icotine withdrawal symptoms *manifest in the first 1–2 days,* ~~typically~~ peak within ~~2~~ *the first* week~~s of quitting~~ and ~~then~~ subside *within 2–4 weeks of quitting. Increased appetite, weight gain, and cravings may persist for several months. It is important to parse out perceived withdrawal symptoms from treatment side effects*...
  - New sub-bullet added: Health care professionals should educate patients to take smoking treatment medications according to the prescribed regimen and for the full course of therapy.
- Box at bottom of page removed: Note: In September 2021, one brand of varenicline was voluntarily recalled by the manufacturer due to nitrosamine levels. Generic varenicline may be substituted.

SC-F (2 of 4):
- Bullet removed: A multicenter randomized controlled trial (RCT) examined the neuropsychiatric safety of varenicline and bupropion in 2 cohorts of patients: those with diagnosed psychiatric disorders (n = 4074) and those without (n = 3984). Rates of neuropsychiatric adverse events in individuals receiving varenicline or bupropion were not significantly increased relative to those receiving nicotine patches or placebo in either cohort.
- Standard Dose/Administration:
  - Combination NRT (preferred)
    - ◊ Second bullet revised: Short-acting ~~NRT~~ *gum or lozenge*: 2 or 4 mg
      - – Second sub-bullet revised: Every 1–2 h (while awake *and as tolerated*), or more often as needed
    - ◊ New bullet added: Short-acting nasal spray
      - – New sub-bullets added:
        - 1 spray (0.5 mg) in each nostril
        - Start with 1 or 2 doses per hour, may be increased up to a maximum recommended dose of 40 mg (80 sprays)
  - Varenicline (preferred), fourth bullet, first sub-bullet revised: Consider increase to 3 mg per day (*1.5 mg twice daily* if tolerated) for those who cut back by ≥50% but have not quit at 6 wks
- Duration column revised: Minimum of ~~12 weeks~~ *3 months (6 months preferred)* of pharmacotherapy is recommended...
- Reference moved to new SC-F (4 of 4): Anthenelli RM, et al. Lancet 2016;387:2507-2520. (Also page SC-F 3 of 4)
- Footnote removed: Same dosing/administration when used in combination with other pharmacotherapy options.

SC-F (3 of 4)
- Second bullet revised: A multicenter *randomized controlled trial (*RCT*)* examined the neuropsychiatric safety of varenicline and bupropion *sustained release* in 2 cohorts of patients: those with diagnosed psychiatric disorders (n = 4074) and those without (n = 3984). Rates of neuropsychiatric adverse events in individuals receiving varenicline or bupropion *sustained release* were not significantly increased relative to those receiving nicotine patches or placebo in either cohort.
- Bupropion, Adverse Effects and Contraindications, third bullet revised: Bupropion is contraindicated for patients with seizure disorder, those taking monoamine oxidase inhibitors (MAOIs) (increased risk of hypertensive reactions), *those with* current diagnosis or history of anorexia or bulimia, or *those who have* abrupt discontinuation of alcohol, benzodiazepines, barbiturates, or antiepileptic drugs.

Continued

Updates in Version 1.2024 of the NCCN Guidelines for Smoking Cessation from Version 2.2023 include:

SC-F (4 of 4)

- Reference 1 revised: Anthenelli RM, *Benowitz NL, West R,* et al. *Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomized, placebo-controlled clinical trial.* Lancet 2016;387:2507-2520.
- New references added:
  - Reference 2: Lee JH, Jones PG, Bybee K, O'Keefe JH. A longer course of varenicline therapy improves smoking cessation rates. Prev Cardiol 2008;11:210-214.
  - Reference 3: Tonstad S, Tønnesen P, Hajek P, et al. Effect of maintenance therapy with varenicline on smoking cessation: a randomized controlled trial. JAMA 2006;296:64-71.
  - Reference 4: Evins AE, Cather C, Pratt SA, et al. Maintenance treatment with varenicline for smoking cessation in patients with schizophrenia and bipolar disorder: a randomized clinical trial. JAMA 2014;311:145-154.
  - Reference 5: Baker TB, Piper ME, Smith SS, et al. Effects of combined varenicline with nicotine patch and of extended treatment duration on smoking cessation: A randomized clinical trial. JAMA 2021;326:1485-1493.
  - Reference 6: Cahill K, Stevens S, Perera R, Lancaster T. Pharmacological interventions for smoking cessation: an overview and network meta-analysis. Cochrane Database Syst Rev 2013;2013:CD009329.
  - Reference 7: Howes S, Hartmann-Boyce J, Livingstone-Banks J, et al. Antidepressants for smoking cessation. Cochrane Database Syst Rev 2020;4:CD000031.
  - Reference 8: US Preventive Services Task Force, Krist AH, Davidson KW, et al. Interventions for tobacco smoking cessation in adults, including pregnant persons: US Preventive Services Task Force Recommendation Statement. JAMA 2021;325:265-279.

GENERAL PRINCIPLES OF THE SMOKING CESSATION GUIDELINES

The NCCN Panel recommends that treatment plans are offered for all people with cancer who smoke, regardless of readiness to quit. Treatment plans should include:

- **evidence-based motivational strategies and behavior therapy,**
- **evidence-based pharmacotherapy, and**
- **close follow-up with retreatment as needed.**

As a generalization, the principles for treating tobacco use disorder of any tobacco products are similar. Therefore, the NCCN Guidelines for Smoking Cessation are directly applicable to not only combustible tobacco products (eg, cigarettes, pipes, cigars, hookah, cigarillos) but also electronic cigarettes (e-cigarettes)/vaping and smokeless tobacco products.

These guidelines are focused on recommendations for the treatment of smoking for patients with cancer and cancer survivors. There are health benefits to smoking cessation even after a cancer diagnosis, regardless of site, stage, or prognosis, namely improvement in cancer treatment outcomes, primary cancer recurrence, and secondary cancers. It is never too late for patients with cancer to quit smoking and experience health benefits. Tobacco use disorder is a chronic relapsing condition.

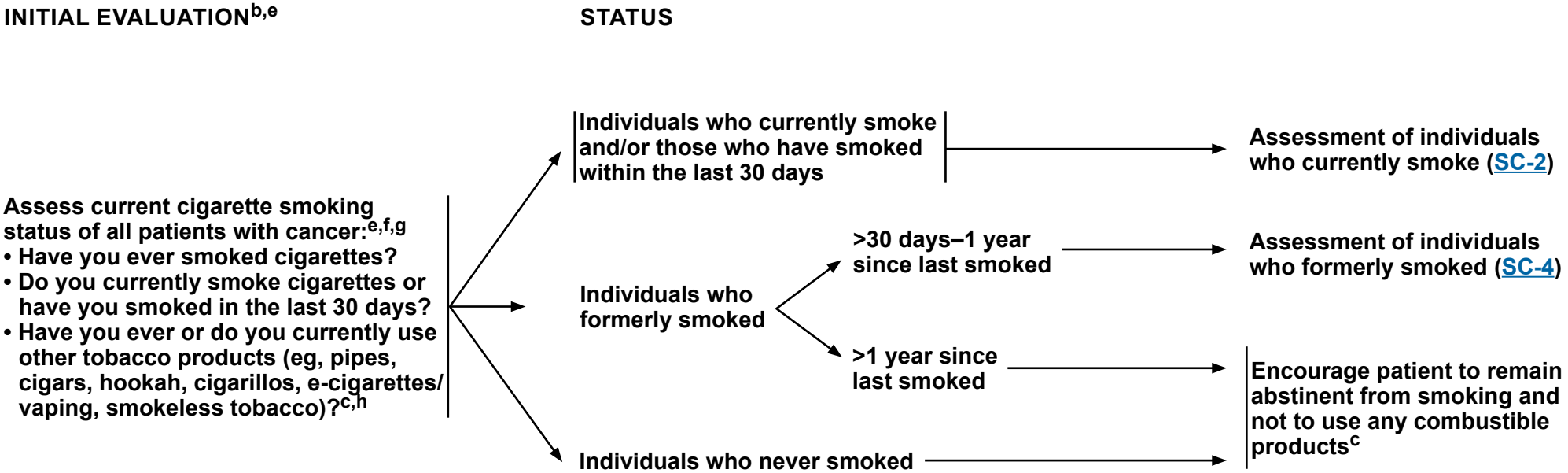
Clinical Recommendations:

- **Combining pharmacologic therapy and behavior therapy is the most effective approach for achieving and maintaining abstinence from smoking, or smoking reduction for those not ready to quit.**
  - **The most effective pharmacotherapy approaches are combination nicotine replacement therapy (NRT)[a] and/or varenicline.**
  - **Behavior therapy with multiple counseling sessions is most effective. At a minimum, brief counseling is needed. Quitlines are a source of brief behavioral counseling for quitting smoking and may have added value, especially in lower-resource settings.**
- **Smoking status should be documented in the patient health record. Patient health records should be updated at regular intervals to indicate changes in smoking status, quit attempts made, and interventions utilized. All patients undergoing smoking treatment should be considered for lung cancer screening.[b]**
- **Smoking relapse and brief slips are common and can be managed. Health care professionals, including tobacco treatment specialists, should discuss this and provide guidance and support to encourage continued abstinence from smoking. Smoking slips are not necessarily an indication to try an alternative method. It may take more than one quit attempt with the same therapy to achieve long-term cessation. Health care professionals should educate patients to take smoking treatment medications according to the prescribed regimen and for the full course of therapy.**
- **Treatment for smoking is an integral part of oncology treatment and should be continued throughout the entire oncology care continuum, from treatment, to survivorship, to end-of-life care. An emphasis should be put on patient preferences and values when considering the best approach to smoking treatment during end-of-life care.**
- **E-cigarettes are not FDA-approved for the treatment of smoking. Patients should be counseled toward the use of evidence-based smoking treatment approaches. For patients who choose to use e-cigarettes exclusively for smoking cessation, despite recommendations to use evidence-based pharmacotherapies, encourage behavioral counseling and abstinence from smoking.**

[a] Combination NRT = Long-acting NRT (nicotine patch) + short-acting NRT (ie, lozenge, gum, inhaler, nasal spray).
[b] For lung cancer screening recommendations, see NCCN Guidelines for Lung Cancer Screening.

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

EVALUATION AND ASSESSMENT OF PATIENT SMOKING[c,d]



[b] For lung cancer screening recommendations, see NCCN Guidelines for Lung Cancer Screening.
[c] The Smoking Cessation algorithms can be applied for any other tobacco product. Patients with cancer should be encouraged to achieve and maintain abstinence from all combustible tobacco products (eg, cigarettes, pipes, cigars, hookah, cigarillos), e-cigarettes/vaping, and smokeless tobacco products. For information about e-cigarettes, see Principles of Alternative Approaches to Treatment of Smoking (SC-A).
[d] General Principles of the Smoking Cessation Guidelines.
[e] Initial evaluation and assessment of patient smoking may be completed by any member of the health care team, including physicians, nurses, medical assistants, health educators, pharmacists, tobacco treatment specialists, or other dedicated staff.
[f] Smoking status of all tobacco products, including e-cigarettes, should be documented in the patient health record and assessment should be repeated at every visit.
[g] Treatment for smoking should be offered to all people with cancer who smoke regardless of cancer stage or prognosis. See Smoking-Associated Risks for Patients With Cancer (SC-B).
[h] Patients who use multiple tobacco products may have more difficulty achieving abstinence.

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.

INDIVIDUALS WHO CURRENTLY SMOKE (WITHIN LAST 30 DAYS)

EVALUATION

Assess and document in the patient health record:

- **Tobacco use:**
  - **How much do you currently smoke or use tobacco products (eg, cigarettes, pipes, cigars, hookah, cigarillos, e-cigarettes/vaping, smokeless tobacco) per day?**
  - **What is the typical amount?**
  - **How soon do you smoke or use tobacco products after you wake up in the morning? (ie, within 30 minutes)[i]**
- **History of quit attempts:**
  - **What is the longest period you have gone without smoking?**
  - **Which strategies were successful?**
    - ◊ **Which were unsuccessful and why? (eg, side effects, cost, continued cravings, did not work, inadequate behavioral support)**
  - **When was your last quit attempt?**
  - **Did you use anything to help you quit in the past? If so, what?**
    - ◊ **Unaided**
    - ◊ **Medications[j] (eg, varenicline, bupropion long-acting, NRT)**
    - ◊ **Support group**
    - ◊ **Behavior therapy**
    - ◊ **Quitlines, websites, smart phone apps, or other media**
    - ◊ **E-cigarettes[k]**
    - ◊ **Other**
- **Tobacco use of individuals within household[l]**

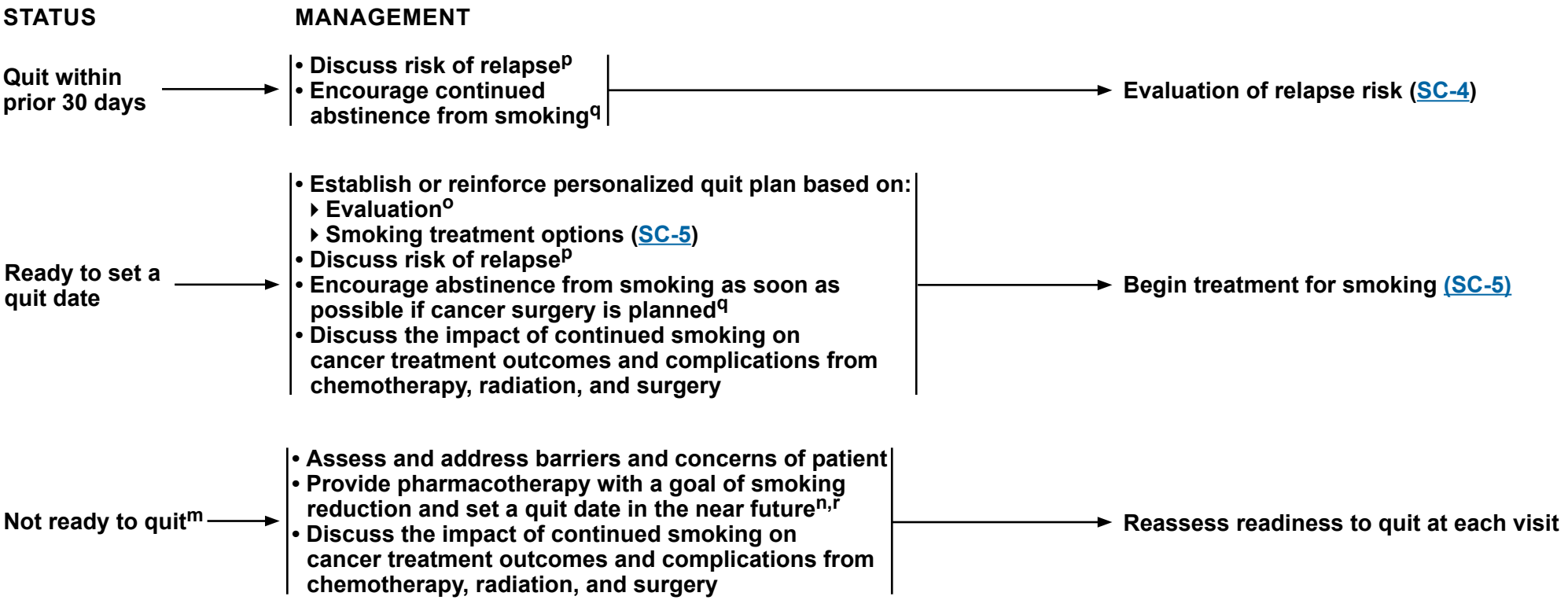
→ **Advise patients to quit[m]**
- **Review risks of smoking and benefits of quitting (Smoking-Associated Risks for Patients with Cancer [SC-B])**
- **Provide patient education resources (Smoking Cessation and Treatment Resources for Patients/Health Care Professionals, [SC-C])**
- **Assess patient readiness to quit[n]**

→ **Management (SC-3)**

[i] Time to first cigarette is used to select the strength of the nicotine gum and lozenge (2 mg, 4 mg).
[j] Document medication name, strength, dose, and duration of use during previous quit attempts. If medication was discontinued early during prior quit attempt(s), longer duration of use may improve efficacy.
[k] Principles of Alternative Approaches to Treatment of Smoking (SC-A).
[l] Smoking by other household members is an important predictor for not remaining abstinent and exposes the patient to secondhand smoke. To benefit the patient, individuals in the household should be encouraged to abstain from smoking; resources may be provided.
[m] Brief advice of about 3 minutes by health care professionals is associated with a small but important increase in smoking abstinence rates.
[n] Making an immediate quit attempt is recommended, but smoking reduction with pharmacotherapy and counseling may be considered with a goal of achieving and maintaining abstinence from smoking at a future quit date (ie, 1–3 mo).

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.

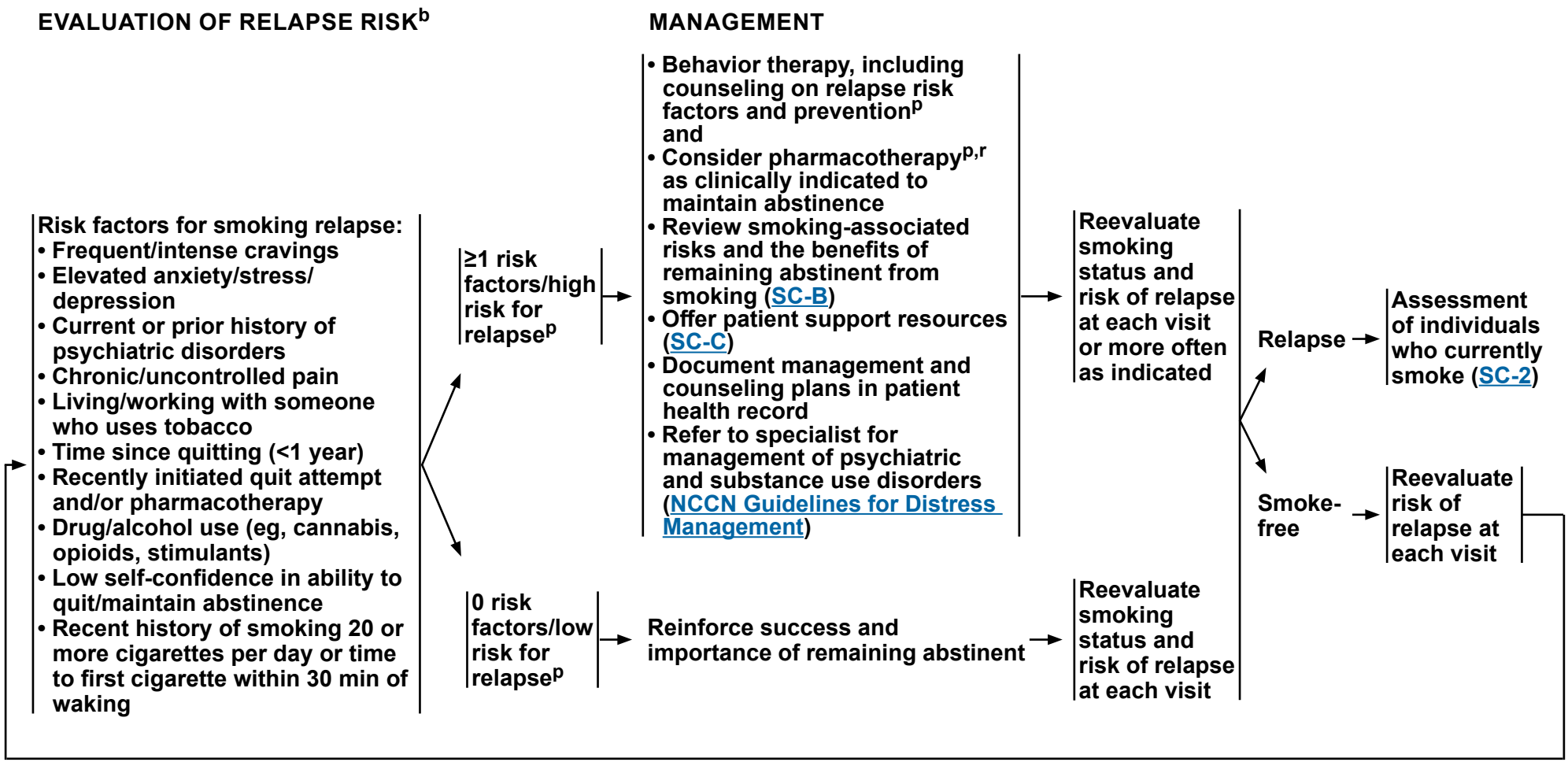
INDIVIDUALS WHO CURRENTLY SMOKE (WITHIN LAST 30 DAYS)



[m] Brief advice of about 3 minutes by health care professionals is associated with a small but important increase in smoking abstinence rates.
[n] Making an immediate quit attempt is recommended, but smoking reduction with pharmacotherapy and counseling may be considered with a goal of achieving and maintaining abstinence at a future quit date (ie, 1–3 mo).
[o] Adjustments to therapy length, intensity, and surveillance may be considered, as clinically indicated, for patients with high nicotine use and/or prior unsuccessful quit attempts.
[p] Health care professionals, including tobacco treatment specialists, should discuss risks of relapse and slips and provide guidance and support to encourage continued abstinence from smoking. See Principles of Behavioral Treatment of Smoking (SC-E).
[q] Longer periods of abstinence from smoking confer better surgical outcomes but should not delay appropriate timing of cancer resection. See Principles of Smoking Cessation and Cancer Surgery (SC-D).
[r] Principles of Pharmacotherapy for Smoking (SC-F).

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.

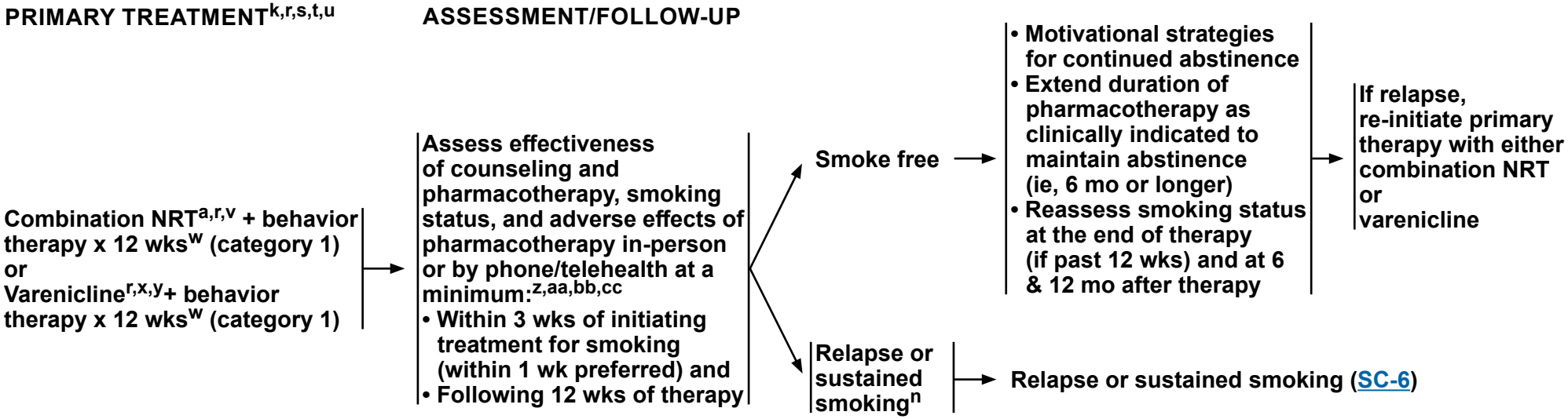
INDIVIDUALS WHO FORMERLY SMOKED (More than 30 Days Since Last Smoked)



[b] For lung cancer screening recommendations, see NCCN Guidelines for Lung Cancer Screening.
[p] Health care professionals, including tobacco treatment specialists, should discuss risks of relapse and slips and provide guidance and support to encourage continued abstinence from smoking. See Principles of Behavioral Treatment of Smoking (SC-E).
[r] Principles of Pharmacotherapy for Smoking (SC-F).

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

GENERAL APPROACH TO TREATMENT OF SMOKING FOR PATIENTS WITH CANCER AND SURVIVORS



[a] Combination NRT = Long-acting NRT (nicotine patch) + short-acting NRT (ie, lozenge, gum, inhaler, nasal spray).

[k] Principles of Alternative Approaches to Treatment of Smoking (SC-A).

[n] Making an immediate quit attempt is recommended, but smoking reduction with pharmacotherapy and counseling may be considered with a goal of achieving and maintaining abstinence at a future quit date (ie, 1–3 mo).

[r] Principles of Pharmacotherapy for Smoking (SC-F).

[s] Principles of Behavioral Treatment of Smoking (SC-E).

[t] The use of cannabis, or other substances associated with smoking relapse, including alcohol, is discouraged for those attempting to quit smoking. Lynch KL, et al. Nicotine Tob Res 2019;21:1058-1064.

[u] Combination NRT or varenicline are the preferred pharmacotherapy options. However, bupropion long-acting ± NRT may be appropriate for select patients (eg, for those with depression or fatigue). See SC-F.

[v] Patient assistance programs may be available.

[w] Four or more sessions of individual/group therapy is recommended, with additional sustained counseling as needed. Brief advice by health care professionals is associated with a small but important increase in smoking abstinence rates. Longer, more frequent sessions with trained counselors are associated with higher abstinence rates. See Principles of Behavioral Treatment of Smoking (SC-E).

[x] Nausea is a common side effect of varenicline and may need to be managed for patients with cancer, especially during chemotherapy.

[y] For those being treated with varenicline, the addition of NRT or bupropion long-acting can be considered as clinically indicated to maintain abstinence despite continued urges to smoke.

[z] Most nicotine withdrawal symptoms manifest in the first 1–2 days, peak within the first week, and subside within 2–4 weeks of quitting. Increased appetite, weight gain, and cravings may persist for several months. It is important to parse out perceived withdrawal symptoms from treatment side effects. Encourage continued therapy through brief slips. Hughes JR. Nicotine Tob Res 2007;9:315-327. Benowitz NL. Med Clin North Am 1992;76:415-437.

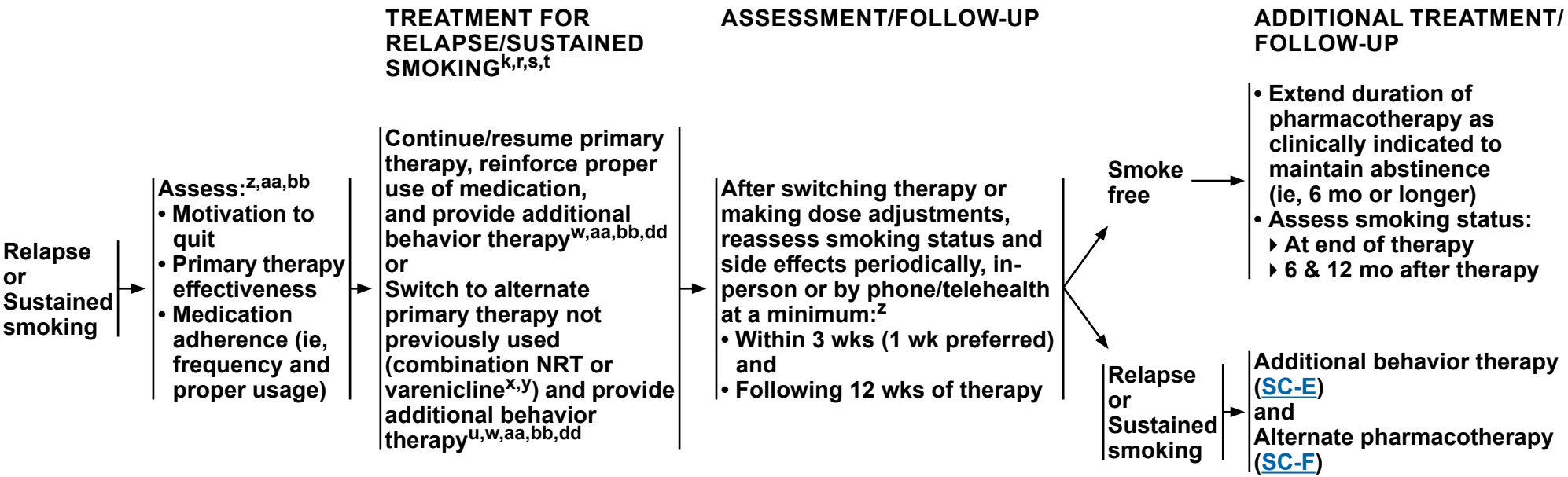
[aa] Adjust behavior therapy frequency as needed.

[bb] Pharmacotherapy dose adjustments can be considered as clinically indicated. Doses may be reduced for adverse effects or increased if risk of relapse is high. See Principles of Pharmacotherapy for Smoking (SC-F).

[cc] Drug levels of certain medications may be altered when a person stops smoking; assess for drug interactions.

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

GENERAL APPROACH TO TREATMENT OF SMOKING FOR PATIENTS WITH CANCER AND SURVIVORS
Relapse or Sustained Smoking



[k] Principles of Alternative Approaches to Treatment of Smoking (SC-A).
[r] Principles of Smoking Cessation Pharmacotherapy (SC-F).
[s] Principles of Behavioral Treatment of Smoking (SC-E).
[t] The use of cannabis, or other substances associated with smoking relapse, including alcohol, is discouraged for those attempting to quit smoking. Lynch KL, et al. Nicotine Tob Res 2019;21:1058-1064.
[u] Combination NRT or varenicline are the preferred pharmacotherapy options. However, bupropion long-acting ± NRT may be appropriate for select patients (eg, for those with depression or fatigue). See SC-F.
[w] Four or more sessions of individual/group therapy is recommended, with additional sustained counseling as needed. Brief advice by health care professionals results in a small but important increase in quit rates. Longer, more frequent sessions with trained counselors are linked to higher success rates. See Principles of Behavioral Treatment of Smoking (SC-E).
[x] Nausea is a common side effect of varenicline and may need to be managed for patients with cancer, especially during chemotherapy.
[y] For those being treated with varenicline, the addition of NRT or bupropion long-acting can be considered as clinically indicated to maintain abstinence despite continued urges to smoke.
[z] Most nicotine withdrawal symptoms manifest in the first 1–2 days, peak within the first week, and subside within 2–4 weeks of quitting. Increased appetite, weight gain, and cravings may persist for several months. It is important to parse out perceived withdrawal symptoms from treatment side effects. Encourage continued therapy through brief slips. Hughes JR. Nicotine Tob Res 2007;9:315-327. Benowitz NL. Med Clin North Am 1992;76:415-437.
[aa] Adjust behavior therapy frequency as needed.
[bb] Pharmacotherapy dose adjustments can be considered as clinically indicated. Doses may be reduced for adverse effects or increased if risk of relapse is high. See Principles of Pharmacotherapy for Smoking (SC-F).
[dd] Decision to continue or switch therapy should be based on prior cessation success, patient preference, toxicity, and/or a change in clinical status (eg, upcoming surgery).

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.

PRINCIPLES OF ALTERNATIVE APPROACHES TO TREATMENT OF SMOKING[1]

- **Offer motivational and behavioral support to all patients attempting to quit smoking, regardless of what smoking treatment method(s) is/are being used. See Principles of Behavioral Treatment of Smoking (SC-E).**
- **For patients who are unable or unwilling to quit, one potential strategy is smoking reduction with a goal of quitting (SC-2).**
- **Encourage the use of evidence-based approaches to avoid delays in achieving abstinence.**
- **For patients using alternative approaches, continue to provide support during quit attempts.**
- **Relapse and smoking slips are common. Remind patients that repeated attempts with evidence-based methods are frequently needed to achieve longer-term abstinence.**

E-Cigarettes or Vaping

- **E-cigarettes are not FDA-approved for the treatment of smoking.**
  - **The FDA may authorize the sale of select electronic nicotine delivery system (ENDS) products as modified risk tobacco products. Currently, none of these products are FDA-approved for the treatment of smoking.**
- **The use of e-cigarettes is often referred to as vaping.**
- **The most effective use of e-cigarettes is unknown, particularly when considering factors such as real-world use and the addition of behavior therapy. Efficacy of e-cigarette use in patients with cancer is also unknown. Thus, patients should be counseled toward the use of evidence-based smoking treatment approaches.**
- **For patients who choose to use e-cigarettes exclusively for smoking cessation, despite recommendations to use evidence-based pharmacotherapies, encourage abstinence from smoking and incorporate behavioral counseling.**
  - **For patients who use both e-cigarettes and combustible tobacco, dual use is strongly discouraged as it continues to pose a risk of cancer and other smoking-related diseases. Complete smoking abstinence is recommended.**
  - **If an individual has already quit using combustible tobacco and is solely using e-cigarettes, support continued non-smoking. If long-term abstinence with e-cigarettes is maintained, continue counseling and redirect to evidence-based methods in the event of relapse. As the patient becomes more confident about quitting combustible tobacco, encourage cessation of e-cigarettes, but not at the risk of relapse to smoking combustible products.**
- **Vaping products contaminated with vitamin E acetate are associated with EVALI (e-cigarette or vaping product use-associated lung injury). Investigations are ongoing and health care professionals should be aware of the latest recommendations from the Centers for Disease Control and Prevention (https://www.cdc.gov/tobacco/basic_information/e-cigarettes/index.html). Educate patients on the unknown risks of using e-cigarettes in lieu of evidence-based methods. Continue to provide support during any quit attempts.**

Other Alternative Methods

- **There is currently insufficient evidence to support the use of alternative methods (eg, hypnosis, acupuncture, nutritional supplements) when used alone or in combination with standard smoking treatment approaches.**
- **Prior unsuccessful quit attempts with conventional therapies do not justify the use of unproven alternative approaches, because multiple attempts with evidence-based methods may be necessary to achieve abstinence.**
- **There are very limited, low-quality data regarding the efficacy of exercise-based interventions.**
- **There are multiple nicotine-mimicking and nicotine-containing products that are not FDA approved for smoking treatment.**

[1] See Discussion for references.

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.

SMOKING-ASSOCIATED RISKS FOR PATIENTS WITH CANCER

- The 2014 Surgeon General's Report[1] stated that:
  - Sufficient evidence exists to support a causal relationship between smoking and adverse health outcomes, increased all-cause mortality and cancer-specific mortality, and increased risk for secondary primary cancers.
  - Existing evidence is suggestive of a link between smoking and increased risk of cancer recurrence, poor treatment response, and increased treatment-related toxicity.
- Health care professionals should:
  - Inform patients of the potential benefits of abstinence from smoking, including improved survival, treatment outcomes, and health-related quality of life, as well as decreased treatment-related toxicity, drug side effects, and surgical complications.
  - Educate patients on the specific risks of smoking during treatment for their particular cancer.
  - Encourage abstinence from smoking as far in advance as possible before initiating cancer treatment.
  - Consider patient smoking status prior to initiating treatment and when making decisions regarding treatment selection, dosage, and timing of initiation.
  - Discuss treatment for smoking with all patients who smoke. Patient satisfaction is enhanced when smoking treatment is offered by health care professionals.
  - To benefit the patient, individuals in the household should be encouraged to abstain from smoking; resources may be provided.[2]

Treatment-Specific Risks (see Discussion for additional information)

- Smoking can impact the metabolism of chemotherapy and targeted therapy.
  - Smoking effects on cytochrome P450 enzymes may include altered drug clearance time and plasma concentration, potentially impacting the efficacy of certain drugs. Health care professionals should consider whether patients are at risk for altered drug metabolism due to smoking and determine if medication or dose adjustments may be required. Drugs whose metabolisms are known to be affected include erlotinib, irinotecan, and bendamustine.[3-7]
- Smoking increases risk of RT-associated treatment complications during RT and may decrease treatment response.[8-10] Patients who receive RT and continue to smoke may also have an increased risk of developing a second primary cancer.[11-14]
- Smoking is associated with increased rates of postoperative complications and mortality after cancer surgery.
  - Compared with those who do not smoke, patients who smoke may experience decreased health-related quality of life after cancer surgery (eg, dyspnea, fatigue, pain).[15-17]
  - Smoking may impair wound healing following surgery for cancer.[18,19]
  - Increased infection rates, cardiovascular and pulmonary complications, and longer postoperative hospital stays are more commonly observed in patients who smoke.[20]
  - Postoperative mortality rates are higher among patients who smoke.[21]

Potential Nicotine Effects on Cancer and Cardiovascular Risks (see Discussion for additional information)

- Blood nicotine levels from NRT, including combination NRT, are significantly less than from smoking cigarettes. Therefore, health care professionals and people who smoke should not be dissuaded from using NRT to foster quitting and long-term abstinence.
- There is insufficient evidence that NRT causes cancer in humans.[22-26]
- There is insufficient evidence that NRT increases the risk of myocardial infarction or cardiovascular disease.[27]

References

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.

SMOKING-ASSOCIATED RISKS FOR PATIENTS WITH CANCER
REFERENCES

[1] The Health Consequences of Smoking-50 Years of Progress: A Report of the Surgeon General. Atlanta (GA); 2014. Available at: https://www.hhs.gov/sites/default/files/consequences-smoking-exec-summary.pdf. Accessed March 3, 2020.
[2] Park ER, Perez GK, Regan S, et al. Effect of sustained smoking cessation counseling and provision of medication vs shorter-term counseling and medication advice on smoking abstinence in patients recently diagnosed with cancer: A randomized clinical trial. JAMA 2020;324:1406-1418.
[3] Li H, Shi Q. Drugs and diseases interacting with cigarette smoking in US prescription drug labeling. Clin Pharmacokinet 2015;54:493-501.
[4] O'Malley M, King AN, Conte M, et al. Effects of cigarette smoking on metabolism and effectiveness of systemic therapy for lung cancer. J Thorac Oncol 2014;9:917-926.
[5] Hamilton M, Wolf JL, Rusk J, et al. Effects of smoking on the pharmacokinetics of erlotinib. Clin Cancer Res 2006;12:2166-2171.
[6] van der Bol JM, Mathijssen RH, Loos WJ, et al. Cigarette smoking and irinotecan treatment: pharmacokinetic interaction and effects on neutropenia. J Clin Oncol 2007;25:2719-2726.
[7] Darwish M, Bond M, Hellriegel E, et al. Pharmacokinetic and pharmacodynamic profile of bendamustine and its metabolites. Cancer Chemother Pharmacol 2015;75:1143-1154.
[8] Eifel PJ, Jhingran A, Bodurka DC, et al. Correlation of smoking history and other patient characteristics with major complications of pelvic radiation therapy for cervical cancer. J Clin Oncol 2002;20:3651-3657.
[9] Browman GP, Wong G, Hodson I, et al. Influence of cigarette smoking on the efficacy of radiation therapy in head and neck cancer. N Engl J Med 1993;328:159-163.
[10] Zevallos JP, Mallen MJ, Lam CY, et al. Complications of radiotherapy in laryngopharyngeal cancer: effects of a prospective smoking cessation program. Cancer 2009;115:4636-4644.
[11] Kaufman EL, Jacobson JS, Hershman DL, et al. Effect of breast cancer radiotherapy and cigarette smoking on risk of second primary lung cancer. J Clin Oncol 2008;26:392-398.
[12] Arnold M, Liu L, Kenter GG, et al. Second primary cancers in survivors of cervical cancer in The Netherlands: Implications for prevention and surveillance. Radiother Oncol 2014;111:374-381.
[13] Tucker MA, Murray N, Shaw EG, et al. Second primary cancers related to smoking and treatment of small-cell lung cancer. Lung Cancer Working Cadre. J Natl Cancer Inst 1997;89:1782-1788.
[14] Neugut AI, Murray T, Santos J, et al. Increased risk of lung cancer after breast cancer radiation therapy in cigarette smokers. Cancer 1994;73:1615-1620.
[15] Balduyck B, Sardari Nia P, Cogen A, et al. The effect of smoking cessation on quality of life after lung cancer surgery. Eur J Cardiothorac Surg 2011;40:1432-1437; discussion 1437-1438.
[16] Erhunmwunsee L, Onaitis MW. Smoking cessation and the success of lung cancer surgery. Curr Oncol Rep 2009;11:269-274.
[17] Mason DP, Subramanian S, Nowicki ER, et al. Impact of smoking cessation before resection of lung cancer: a Society of Thoracic Surgeons General Thoracic Surgery Database study. Ann Thorac Surg 2009;88:362-370; discussion 370-361.
[18] Chang DW, Reece GP, Wang B, et al. Effect of smoking on complications in patients undergoing free TRAM flap breast reconstruction. Plast Reconstr Surg 2000;105:2374-2380.
[19] Kuri M, Nakagawa M, Tanaka H, et al. Determination of the duration of preoperative smoking cessation to improve wound healing after head and neck surgery. Anesthesiology 2005;102:892-896.
[20] Ehlers SL, Gastineau DA, Patten CA, et al. The impact of smoking on outcomes among patients undergoing hematopoietic SCT for the treatment of acute leukemia. Bone Marrow Transplant 2011;46:285-290.
[21] Sharma A, Deeb AP, Iannuzzi JC, et al. Tobacco smoking and postoperative outcomes after colorectal surgery. Ann Surg 2013;258:296-300.
[22] Stepanov I, Carmella SG, Briggs A, et al. Presence of the carcinogen N'-nitrosonornicotine in the urine of some users of oral nicotine replacement therapy products. Cancer Res 2009;69:8236-8240.
[23] Murray RP, Connett JE, Zapawa LM. Does nicotine replacement therapy cause cancer? Evidence from the Lung Health Study. Nicotine Tob Res 2009;11:1076-1082.
[24] Murphy SE, von Weymarn LB, Schutten MM, et al. Chronic nicotine consumption does not influence 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone-induced lung tumorigenesis. Cancer Prev Res (Phila) 2011;4:1752-1760.

Continued

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.

SMOKING-ASSOCIATED RISKS FOR PATIENTS WITH CANCER
REFERENCES

[25] Maier CR, Hollander MC, Hobbs EA, et al. Nicotine does not enhance tumorigenesis in mutant K-ras-driven mouse models of lung cancer. Cancer Prev Res (Phila) 2011;4:1743-1751.
[26] Shields PG. Long-term nicotine replacement therapy: cancer risk in context. Cancer Prev Res (Phila) 2011;4:1719-1723.
[27] Mills EJ, Wu P, Lockhart I, et al. Adverse events associated with nicotine replacement therapy (NRT) for smoking cessation. A systematic review and meta-analysis of one hundred and twenty studies involving 177,390 individuals. Tob Induc Dis 2010;8:8.

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.

SMOKING CESSATION AND TREATMENT RESOURCES FOR PATIENTS

Cancer-Related Resources for Patients[a]

American Cancer Society (ACS)
- Website: https://www.cancer.org/healthy/stay-away-from-tobacco.html
- Phone: 1.800.227.2345
- Guide to quitting smoking: https://www.cancer.org/cancer/risk-prevention/tobacco/guide-quitting-smoking.html

American Society of Clinical Oncology (ASCO)
- Website: https://www.asco.org/news-initiatives/current-initiatives/prevention-survivorship/tobacco-cessation-control
- Resource: "Stopping Tobacco Use After a Cancer Diagnosis" https://www.asco.org/sites/new-www.asco.org/files/content-files/practice-and-guidelines/documents/stopping-tobacco-use-booklet.pdf

American Lung Association
- Website: http://www.lung.org/stop-smoking
- Lung Cancer Helpline: 1.844.252.5864
- Program: Freedom from Smoking®: http://www.lung.org/stop-smoking/join-freedom-from-smoking

Smokefree.gov
- Website: https://www.smokefree.gov
- NCI Quitline: 1.877.448.7848
- LiveHelp: https://livehelp.cancer.gov
- QuitGuide App: https://smokefree.gov/apps-quitguide
- SmokeFree Text Messaging Programs (available for adults, teens, pregnant persons, and veterans, and in Spanish): https://smokefree.gov/smokefree-text-messaging-programs
- "Clearing the Air: Quit Smoking Today": http://smokefree.gov/sites/default/files/pdf/clearing-the-air-accessible.pdf

General Resources for Patients[a]

American Heart Association
- https://www.heart.org/en/healthy-living

American Indian Commercial Tobacco Program
- Website: https://americanindian.quitlogix.org
- Phone: 1.855.372.0037

Asian Smokers' Quitline
- Website: http://www.asiansmokersquitline.org
- Mandarin/Cantonese: 1.800.838.8917; Korean: 1.800.556.5564; Vietnamese: 1.800.778.8440

Ex: A New Way To Think About Quitting Smoking
- Website: http://www.becomeanex.org
- ExCommunity: https://excommunity.becomeanex.org

Centers for Disease Control and Prevention (CDC) Office on Smoking and Health
- Website: https://www.cdc.gov/tobacco/quit_smoking/how_to_quit/index.htm
- English: 1.800.QUIT.NOW (1.800.784.8669)
- Spanish: 1.855.335.3569
- SmokeFree Text Messaging Programs (state and national services available for adults): Text QUITNOW to 333888 or https://www.cdc.gov/tobacco/campaign/tips/quit-smoking/national-texting-portal.html

TRICARE and UCanQuit2 (Military and family)
- Website: http://www.tricare.mil/HealthWellness/Tobacco.aspx
- Text support: https://www.ycq2.org/resources/smokefreemil

VA How to Quit
- Website: https://www.mentalhealth.va.gov/quit-tobacco/how-to-quit.asp

Pharmacies Providing Cessation Services
- https://www.QuitSmokingPharmacies.com

[a] Free or low-cost support is sometimes available for patients who are uninsured or underinsured. Resources may vary by organization and location. Contact each organization to learn more about the availability of free and low-cost smoking cessation and treatment resources offered regionally.

Continued

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.

SMOKING CESSATION AND TREATMENT RESOURCES FOR HEALTH CARE PROFESSIONALS

Cancer-Related Resources for Health Professionals

American Association for Cancer Research (AACR)
- Policy Statement: https://cancerres.aacrjournals.org/content/70/9/3419?ijkey=9980cf69559104118cb06580ca278aea35f5a899&keytype2=tf_ipsecsha

NCCN Guidelines for Lung Cancer Screening
- http://www.nccn.org/professionals/physician_gls/pdf/lung_screening.pdf

NCI- Physician Data Query (PDQ)
- https://www.cancer.gov/about-cancer/causes-prevention/risk/tobacco/quit-smoking-hp-pdq

American Society of Clinical Oncology (ASCO)
- Tobacco Cessation Guide for Oncology Providers: https://www.asco.org/sites/new-www.asco.org/files/content-files/blog-release/documents/tobacco-cessation-guide.pdf

NCCN Guidelines for Survivorship
- http://www.nccn.org/professionals/physician_gls/pdf/survivorship.pdf

U.S. Department of Health and Human Services, Public Health Service
- Treating Tobacco Use and Dependence: 2008 Update. Content last reviewed June 2015. Agency for Healthcare Research and Quality, Rockville, MD. http://www.ahrq.gov/professionals/clinicians-providers/guidelines-recommendations/tobacco/index.html

General Resources for Health Professionals

American Academy of Family Physicians (AAFP)
- Ask and Act Smoking Cessation Program: https://www.aafp.org/family-physician/patient-care/care-resources/tobacco-and-nicotine/ask-act.html

American Thoracic Society
- Initiating Pharmacologic Treatment in Tobacco-Dependent Adults: An Official ATS Clinical Practice Guideline Implementation Tools: https://www.thoracic.org/statements/guideline-implementation-tools/pharmacologic-treatment-of-tobacco-dependence.php

Million Hearts® 2022
- Tobacco Cessation Change Package: https://millionhearts.hhs.gov/tools-protocols/action-guides/tobacco-change-package/index.html

Rx for Change: Clinician-Assisted Tobacco Cessation
- http://rxforchange.ucsf.edu

Society for Research on Nicotine & Tobacco
- https://www.srnt.org

U.S. Department of Health and Human Services
- Surgeon General Reports: https://www.hhs.gov/surgeongeneral/reports-and-publications/tobacco/index.html

American College of Chest Physicians (ACCP)
- Toolkit: http://tobaccodependence.chestnet.org

Association for the Treatment of Tobacco Use and Dependence (ATTUD)/Council for Tobacco Treatment Training Programs (CTTTP)
- http://www.attud.org
- Accredited training programs: http://ctttp.org/accredited-programs

National Behavioral Health Network for Tobacco & Cancer Control
- https://www.bhthechange.org

Smokefree.gov
- http://smokefree.gov/health-care-professionals

U.S. Preventive Services Task Force (USPSTF)
- Final Recommendation Statement: Tobacco Smoking Cessation in Adults, Including Pregnant Persons Interventions. U.S. Preventive Services Task Force. January 2021. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/tobacco-use-in-adults-and-pregnant-women-counseling-and-interventions

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.

PRINCIPLES OF SMOKING CESSATION AND CANCER SURGERY

- **People who smoke who need surgery should be treated with evidence-based smoking treatment approaches, including pharmacotherapy, in order to improve surgical outcomes and long-term abstinence from smoking. Initial therapy with combination NRT or varenicline is recommended. There is substantial evidence that the combination of behavioral counseling and pharmacotherapy is more effective than either one alone.**
  - **For primary therapy and follow-up recommendations, see SC-4. Preoperative pharmacotherapy options depend on urgency of surgery, within one week or more than one week. Options include:**
    - **If <7 days to surgery, combination NRT is preferred (category 1) because guidelines for quitting with NRT include a quit date within 24 hours, while varenicline is typically 7 days. However, varenicline is an option; in some clinical situations the quit date for varenicline may be sooner.**
    - **If ≥7 days to surgery, either combination NRT (category 1) or varenicline (category 1) are options. Smoking treatment should happen as soon as possible; ideally, the patient should be abstinent for 4 weeks or more, but this recommendation should not cause a delay in surgery.[1]**
  - **NRT is not a contraindication to surgery. There is no evidence that NRT degrades the wound-healing benefits of abstinence from smoking in humans. NRT offers benefits over continued smoking. While some data from animal studies have suggested an association between nicotine and decreased wound healing, no such studies exist in humans.[2-4] NRT typically provides less nicotine than cigarettes, and nearly doubles the chance of smoking abstinence.**
- **Smoking increases the risk of pulmonary complications, surgical site infection, and poor wound healing in patients undergoing surgery. See Smoking-Associated Risks for Patients With Cancer (SC-B). Quitting smoking reduces these complications. There is no evidence that quitting smoking shortly before surgery increases the risks of any complications.**
- **Patients should be encouraged to quit smoking as soon as possible before surgery, regardless of how short the time is to surgery. Even quitting on the day of surgery has a benefit.**
- **Longer periods of abstinence from smoking confer better surgical outcomes but should not delay appropriate timing for cancer resection.**
- **There is insufficient evidence to support delaying a quit attempt at any time prior to surgery.**
- **Although quitting smoking reduces surgical risk, access to cancer surgery should not be restricted solely on the basis of continued smoking.**

[1] https://www.quitforsurgery.com.
[2] Nolan B, Warner O. Safety and efficacy of nicotine replacement therapy in the perioperative period: a narrative review. Mayo Clin Proc 2015;90:1553-1561.
[3] Sørensen LT. Wound healing and infection in surgery: the pathophysiological impact of smoking, smoking cessation, and nicotine replacement therapy: a systematic review. Ann Surg 2012;255:1069-1079.
[4] Stefan MS, Pack Q, Shieh MS, et al. The association of nicotine replacement therapy with outcomes among smokers hospitalized for a major surgical procedure. Chest 2020;157:1354-1361.

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.

PRINCIPLES OF BEHAVIORAL TREATMENT OF SMOKING

- Pharmacotherapy is most effective when combined with behavior therapy.[1] Brief counseling is better than no counseling.
  - While implementing evidence-based smoking cessation remains the responsibility of all health professionals, population-level studies of smoking treatment modalities indicate that counseling plus medication results in a significant improvement in cessation rates relative to no counseling or medication.[2] In addition to the benefits of enhancing motivation and knowledge of the addiction process, behavior therapy assists patients with medication use and strategies since adherence to tobacco treatment medication recommendations is often inadequate. Therefore, pharmacotherapy alone without some form of counseling may not be better than quitting unaided.
- Through behavior therapy, people who smoke learn coping skills and receive support and education. Behavior therapy, tailored to the patient's tobacco use and previous quit attempts, provides strategies for:[1-3]
  - Coping with nicotine withdrawal symptoms and cravings (Note: Nicotine withdrawal symptoms manifest in the first 1–2 days, peak within the first week, and subside within 2–4 weeks of quitting. Increased appetite, weight gain, and cravings may persist for several months. It is important to parse out perceived withdrawal symptoms from treatment side effects.)
  - Identifying what triggers them to smoke (eg, coffee, alcohol, social situations, stress)
  - Coping with stressful and difficult situations in which smoking is likely
  - Avoiding high-risk situations
  - Addressing other patient-specific barriers to and facilitators of smoking behavior change
  - Coping with obstacles such as pain, a desire to maintain personal control, second-hand smoke exposure, guilt over smoking, fear of stigmatization, and fatalism regarding disease
- Therapy should include skills training, social support, and motivational interviewing with print- or web-based patient education materials.
- Specialized treatment centers may consider providing treatment for smoking targeted specifically to patients with cancer (eg, individual therapy and group support that focus on challenges specific to cancer survival and treatment). Therapy should be performed by a Tobacco Treatment Specialist or a dedicated staff member (ie, nurse, medical assistant, health educator) trained in the evidence-based treatment of smoking.
- In people with cancer who smoke, there is a high incidence of depression, anxiety, and stress, all of which are common causes of relapse. Health care professionals should routinely assess for these symptoms among those who smoke throughout treatment for smoking. It may be optimal to enroll patients in a behavior therapy program with specific interventions designed to ameliorate these conditions and other cancer-related relapse challenges. This may require referral for appropriate evaluation and treatment as needed or to specialized smoking treatment programs that have staff trained to treat psychiatric and/or other substance use disorders.
- Smoking by other household members is an important predictor for not remaining abstinent and exposes the patient to secondhand smoke. To benefit the patient, individuals in the household should be encouraged to abstain from smoking; resources may be provided.
- Specific populations may have particular concerns to consider in treatment:
  - Increased relapse risk among patients living with HIV,[4] psychiatric disorders,[5] or other substance use disorders[6]
  - High rates of menthol cigarette use that may increase nicotine use in African-American communities and other groups that have been historically marginalized[7,8]
  - Preserving sacred use of tobacco while reducing commercial tobacco use in American Indian or Native American communities[9]
- For more information on behavior therapy for smoking cessation, see Discussion.

References
Continued

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.

PRINCIPLES OF BEHAVIORAL TREATMENT OF SMOKING

Behavior Therapy/Counseling Recommendations

- Four or more sessions are recommended during each course of pharmacotherapy, with additional sustained counseling as needed. The first session is recommended within 3 weeks of cessation (within 1 week preferred as a majority of people who smoke relapse in this time frame).[10]
  - Brief advice of about 3 minutes by health care professionals is associated with a small but important increase in smoking abstinence rates.[3] Longer, more frequent sessions are associated with higher abstinence rates.[11] The maximum benefit is with intensive and sustained counseling with trained counselors.[12]
- Individual or group therapy should take place in-person and/or by phone/telehealth, in coordination with a smoking treatment clinic if available.[13,14]
  - For those in active cancer treatment, behavior therapy can occur during scheduled oncology visits to avoid the need for additional appointments.
  - Refer to evidence-based resources for quitting, such as a smoking cessation quitline, in addition to providing brief counseling from a health care professional, if face-to-face or group intervention is not available. See Smoking Cessation and Treatment Resources for Patients/Health Care Professionals (SC-C).
    - ◊ Quitlines are a source of brief behavioral counseling for quitting smoking and may have added value, especially in lower-resource settings.

Motivational Counseling

- Motivational counseling is beneficial for all patients throughout treatment but is essential for those not immediately ready to quit.[3,15,16]
  - Motivational counseling involves first establishing a connection with the patient and then exploring feelings (eg, distress), beliefs (eg, fatalistic), and values (eg, importance of family) in order to help the patient address ambivalence or conflicting motivations. Clinicians use a guiding and empathetic style to help the patient: 1) understand their motivations; 2) understand the relation of these to their values and goals; and 3) build their confidence to achieve and maintain abstinence. To achieve this, clinicians ask open-ended questions, reflect patient emotions and concerns, affirm patient strengths, and summarize important points. Clinicians should express acceptance for the patient and validate the patient's worth, strengths, and independence.
  - Physicians and health professionals use four basic strategies, commonly referred to as OARS, for motivational interviewing: Open-ended questions; Affirmations; Reflective listening; and Summary statements.
  - For patients who struggle to identify reasons to quit, the clinician can also use the 5 R's strategy focusing on: the personal Relevance of quitting; personal Risks of continuing smoking; personal Rewards of quitting; identifying Roadblocks to quitting; and Repeating the message at every contact.[3]

References

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.

PRINCIPLES OF BEHAVIORAL TREATMENT OF SMOKING
REFERENCES

[1] Stead LF, Lancaster T. Combined pharmacotherapy and behavioural interventions for smoking cessation. Cochrane Database Syst Rev 2012;10:CD008286.
[2] Stead LF, Koilpillai P, Lancaster T. Additional behavioural support as an adjunct to pharmacotherapy for smoking cessation. Cochrane Database Syst Rev 2015;12:CD009670.
[3] Treating Tobacco Use and Dependence. Content last reviewed April 2013. Agency for Healthcare Research and Quality, Rockville, MD. https://www.ahrq.gov/prevention/guidelines/tobacco/clinicians/update/index.html.
[4] Vijayaraghavan M, Penko J, Vittinghoff E, et al. Smoking behaviors in a community-based cohort of HIV-infected indigent adults. AIDS Behav 2014;18:535-543.
[5] Cather C, Pachas GN, Cieslak KM, et al. Achieving smoking cessation in individuals with schizophrenia: Special considerations. CNS Drugs 2017;31:471-481.
[6] Reid MS, Jiang H, Fallon B, et al. Smoking cessation treatment among patients in community-based substance abuse rehabilitation programs: exploring predictors of outcome as clues toward treatment improvement. Am J Drug Alcohol Abuse 2011;37:472-478.
[7] Trinidad DR, Pérez-Stable EJ, Messer K, et al. Menthol cigarettes and smoking cessation among racial/ethnic groups in the United States. Addiction 2010;105:84-94.
[8] Jabba SV, Erythropel HC, Anastas PT, et al. Synthetic cooling agent and other flavor additives in "non-menthol" cigarettes marketed in California and Massachusetts after menthol cigarette bans. JAMA 2023;330:1689-1691.
[9] Centers for Disease Control and Prevention: American Indian and Alaska Native People and Commercial Tobacco: Health Disparities and Ways to Advance Health Equity (https://www.cdc.gov/tobacco/health-equity/aian/index.html).
[10] Herd N, Borland R. The natural history of quitting smoking: findings from the International Tobacco Control (ITC) Four Country Survey. Addiction 2009;104:2075-2087.
[11] Lai DT, Cahill K, Qin Y, et al. Motivational interviewing for smoking cessation. Cochrane Database Syst Rev 2010:CD006936.
[12] Park ER, Perez G, Regan S, et al. Effect of sustained smoking cessation counseling and provision of medication vs shorter-term counseling and medication advice on smoking abstinence in patients recently diagnosed with cancer: A randomized clinical trial. JAMA 2020;324:1406-1418.
[13] Cancer Center Cessation Initiative Telehealth Working Group. Telehealth delivery of tobacco cessation treatment in cancer care: An ongoing innovation accelerated by the COVID-19 pandemic. J Natl Compr Canc Netw 2021;19(Suppl_1):S21-S24.
[14] Kotsen C, Dilip D, Carter-Harris L, et al. Rapid scaling up of telehealth treatment for tobacco-dependent cancer patients during the COVID-19 outbreak in New York City. Telemed J E Health 2021;27:20-29.
[15] Miller WR, Rollnick S. Motivational interviewing: Helping people for change (3rd edition). New York, NY: Guilford Press; 2013.
[16] Lindson-Hawley N, Thompson TP, Begh R. Motivational interviewing for smoking cessation. Cochrane Database of Syst Rev 2015; CD006936.

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.

PRINCIPLES OF PHARMACOTHERAPY FOR SMOKING

- **Abstinence from smoking improves clinical outcomes for patients with cancer. Therefore, the included agents and methodologies should be made available to all patients with cancer who smoke.**
- **A minimum of 12 weeks of combination NRT or varenicline[a] is recommended for the initial quit attempt. Therapy may be extended to 6 months or longer, when clinically indicated, to promote continued abstinence.**
  - **Follow-up is recommended (in-person or by phone/telehealth) within 3 weeks (within 1 week preferred) after starting pharmacotherapy, but can be adjusted to coordinate with regularly scheduled oncology appointments as needed. Additional periodic follow-up during therapy (at a minimum of 12-week intervals), and after completion of therapy, is recommended.**
  - **Most nicotine withdrawal symptoms manifest in the first 1–2 days, peak within the first week, and subside within 2–4 weeks of quitting. Increased appetite, weight gain, and cravings may persist for several months. It is important to parse out perceived withdrawal symptoms from treatment side effects. Encourage continued therapy through brief slips. Patients who do not quit immediately may quit at some later point after withdrawal symptoms subside.**
  - **Health care professionals should educate patients to take smoking treatment medications according to the prescribed regimen and for the full course of therapy.**
  - **Pharmacotherapy dose adjustments may be considered as clinically indicated.**
- **Track attempts at smoking reduction. If reduction efforts stall, or reaching total abstinence seems unlikely, consider switching to a different pharmacotherapy.**
- **As patients progress through multiple lines of treatment, behavior therapy should be progressively intensified with referral to specialty care (eg, psychiatrist, psychologist) as indicated.**
- **When considering pharmacotherapy options, consider cultural and contextual factors including cost, ability to pay, insurance coverage, ability to adhere to the treatment regimen, and patient preferences.**

Pharmacotherapy Options[a]

Preferred Regimens	Other Recommended Regimens
Combination NRT: Long-acting NRT (nicotine patch) + short-acting NRT (lozenge/gum/inhaler/nasal spray) **or** **Varenicline[b]** **or** **Switch to alternate preferred primary therapy option not previously used (combination NRT or varenicline)[a]**	**Varenicline[b] + NRT[c]** **or** **Bupropion (long-acting)[d] ± NRT[c] (eg, for patients with depression or fatigue)[a]** **or** **Varenicline + bupropion (long-acting)[b]**

[a] Decision to continue or switch therapy should be based on prior cessation success, patient preference, toxicity, and/or a change in clinical status (eg, upcoming surgery).
[b] Nausea is a common side effect of varenicline and may need to be managed for patients with cancer, especially during chemotherapy. Varenicline should be used with caution for those with seizure risk.
[c] Any form of NRT or combination NRT (nicotine patch + short-acting NRT) may be used. Studies evaluating the efficacy of varenicline combined with NRT utilized the nicotine patch (Koegelenberg CF, et al. JAMA 2014;312:155-161).
[d] Bupropion (long-acting) should be avoided in patients with seizure risk, including those with brain metastases or primary brain tumors.

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

Continued

PRINCIPLES OF PHARMACOTHERAPY FOR SMOKING

- **In most circumstances, the side effects related to preferred smoking treatment medications are minimal and are considered an acceptable risk compared to smoking. Serious side effects are extremely rare. Refer to manufacturer inserts for exhaustive lists of potential side effects and warnings.**

	Standard Dose/Administration[f,g,h]	Duration
Combination NRT (preferred)	• Begin with 21-mg patch + short-acting NRT ▸ If 21-mg patch is not effective, consider using more than one patch to increase the dose to 35 or 42 mg • Short-acting gum or lozenge: 2 or 4 mg ▸ 2 mg preferred if time to first cigarette is >30 minutes after waking; or 4 mg preferred if time to first cigarette is ≤30 minutes after waking ▸ Every 1–2 h (while awake and as tolerated), or more often as needed • Short-acting nasal spray ▸ 1 spray (0.5 mg) in each nostril ▸ Start with 1 or 2 doses per hour, may be increased up to a maximum recommended dose of 40 mg (80 sprays)	Minimum of 3 months (6 months preferred) of pharmacotherapy is recommended.[2-8] However, therapy may be substantially extended to promote continued abstinence.
Varenicline (preferred)	• Initiate dosing 1–5 wks prior to quitting • Days 1–3: 0.5 mg orally, once daily • Days 4–7: 0.5 mg orally, twice daily • Day 8 to end of treatment: 1 mg orally, twice daily (if tolerated) ▸ Consider increase to 3 mg per day (1.5 mg twice daily if tolerated) for those who cut back by ≥50% but have not quit at 6 wks ▸ If severe renal impairment (estimated creatinine clearance <30 mL/min): Begin with 0.5 mg once daily and titrate to 0.5 mg twice daily ▸ For patients with end-stage renal disease undergoing hemodialysis, 0.5 mg maximum daily, if tolerated	
Bupropion	• Initiate dosing 1–2 wks prior to quitting • Days 1–3: 150 mg orally, once daily • Day 4 – end of treatment: ▸ Sustained release: 150 mg orally, twice daily, if tolerated; or ▸ Extended release: 300 mg, once daily, if tolerated • Maximum 300 mg per day • Adjust dose or frequency for: ▸ Renal impairment[g] ▸ Hepatic impairment: Maximum dose 150 mg every other day for moderate/severe hepatic impairment (Child-Pugh score 7–15); For mild hepatic impairment (Child-Pugh score 5–6), consider reducing the dose and/or frequency adjustment	

Adverse Effects and Contraindications

[f] Dose adjustments may be considered if clinically indicated.
[g] See drug labels and full prescribing information for varenicline, bupropion (long-acting), and NRT products.
[h] Gradually decrease dose over 10 weeks or more. Dose reduction may not be appropriate for patients with limited life expectancy.

References

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.

PRINCIPLES OF PHARMACOTHERAPY FOR SMOKING

- **In most circumstances, the side effects related to preferred smoking treatment medications are minimal and are considered an acceptable risk compared to smoking. Serious side effects are extremely rare. Refer to manufacturer inserts for exhaustive lists of potential side effects and warnings.**
- **A multicenter randomized controlled trial (RCT) examined the neuropsychiatric safety of varenicline and bupropion sustained release in 2 cohorts of patients: those with diagnosed psychiatric disorders (n = 4074) and those without (n = 3984). Rates of neuropsychiatric adverse events in individuals receiving varenicline or bupropion sustained release were not significantly increased relative to those receiving nicotine patches or placebo in either cohort.[g,1]**

	Adverse Effects and Contraindications[g,1]
Combination NRT (preferred)	Blood nicotine levels from NRT, including combination NRT, are significantly less than from smoking cigarettes. NRT is well tolerated and nicotine toxicity is rare and transient, even when used with smoking. Patients commonly underdose when using combination NRT. Significant nicotine toxicity is rare, but possible and usually short-lived.
Varenicline (preferred)	• Nausea is a common side effect of varenicline and may need to be managed for patients with cancer, especially during chemotherapy. ▸ Take varenicline after eating and with a full glass of water to minimize nausea risk. • Although these side effects are uncommon, health care professionals should monitor for the development or worsening of serious neuropsychiatric issues (ie, depression and suicidal ideation/behavior), including for patients without a previous history, and discontinue use if these signs occur. • Use with caution in patients with a history of seizure disorder or at risk for seizures.
Bupropion	• Although these side effects are uncommon, health care professionals should monitor for the development or worsening of serious neuropsychiatric issues (ie, depression and suicidal ideation/behavior), including for patients without a previous history, and discontinue use if these signs occur. • Bupropion should be avoided in patients with seizure risk, including those with brain metastases or primary brain tumors. • Bupropion is contraindicated for patients with seizure disorder, those taking monoamine oxidase inhibitors (MAOIs) (increased risk of hypertensive reactions), those with current diagnosis or history of anorexia or bulimia, or those who have abrupt discontinuation of alcohol, benzodiazepines, barbiturates, or antiepileptic drugs. • Bupropion inhibits CYP2D6 and can increase concentrations of antidepressants, antipsychotics, beta-blockers, tamoxifen, and type 1C antiarrhythmics. Consider dose reduction when using with bupropion. Dose bupropion with caution when used with drugs that lower seizure threshold. Central nervous system (CNS) toxicity can occur when bupropion is used concomitantly with dopaminergic drugs.

[g] See drug labels and full prescribing information for varenicline, bupropion (long-acting), and NRT products.

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.

References

PRINCIPLES OF PHARMACOTHERAPY FOR SMOKING
REFERENCES

[1] Anthenelli RM, Benowitz NL, West R, et al. Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomized, placebo-controlled clinical trial. Lancet 2016;387:2507-2520.
[2] Lee JH, Jones PG, Bybee K, O'Keefe JH. A longer course of varenicline therapy improves smoking cessation rates. Prev Cardiol 2008;11:210-214.
[3] Tonstad S, Tønnesen P, Hajek P, et al. Effect of maintenance therapy with varenicline on smoking cessation: a randomized controlled trial. JAMA 2006;296:64-71.
[4] Evins AE, Cather C, Pratt SA, et al. Maintenance treatment with varenicline for smoking cessation in patients with schizophrenia and bipolar disorder: a randomized clinical trial. JAMA 2014;311:145-154.
[5] Baker TB, Piper ME, Smith SS, et al. Effects of combined varenicline with nicotine patch and of extended treatment duration on smoking cessation: A randomized clinical trial. JAMA 2021;326:1485-1493.
[6] Cahill K, Stevens S, Perera R, Lancaster T. Pharmacological interventions for smoking cessation: an overview and network meta-analysis. Cochrane Database Syst Rev 2013;2013:CD009329.
[7] Howes S, Hartmann-Boyce J, Livingstone-Banks J, et al. Antidepressants for smoking cessation. Cochrane Database Syst Rev 2020;4:CD000031.
[8] US Preventive Services Task Force; Krist AH, Davidson KW, Mangione CM, et al. Interventions for tobacco smoking cessation in adults, including pregnant persons: US Preventive Services Task Force Recommendation Statement. JAMA 2021;325:265-279.

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

CNS	**central nervous system**
ENDS	**electronic nicotine delivery system**
EVALI	**e-cigarette or vaping product use-associated lung injury**
NRT	**nicotine replacement therapy**
RCT	**randomized controlled trial**

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 Categories of Preference	
Preferred intervention	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
Other recommended intervention	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.
Useful in certain circumstances	Other interventions that may be used for selected patient populations (defined with recommendation).

All recommendations are considered appropriate.

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2024
Smoking Cessation

Discussion

This discussion corresponds to the NCCN Guidelines for Smoking Cessation. Last updated: September 15, 2023.

Table of Contents

Overview

Tobacco smoking has been implicated in causing cancers of the lungs, mouth, lips, nose, sinuses, larynx, pharynx, esophagus, stomach, pancreas, kidney, bladder, uterus, cervix, colon/rectum, and ovary, and myeloid leukemia.[1] Cancers linked to tobacco use comprise 40% of all cancer diagnoses, and cigarette smoking is linked to 30% of all cancer-related deaths nationwide.[2] State-level data suggest that cigarette smoking is responsible for as high as 40% of cancer-related deaths in some geographic regions.[3] Lung cancer is the leading cause of cancer-related death in both males and females.[4]

Smoking tobacco after a cancer diagnosis decreases the efficacy of cancer treatments, increases the side effects of cancer treatment, increases the risk of death from all causes, and adds to treatment complexities and the cost of cancer care, as well as the probability of new or worsening comorbidities.[5-8] Smoking cessation at any time after a cancer diagnosis is associated with improved cancer outcomes, enhanced quality of life, and reduced disease among cancer survivors.[9-14] Yet, 29.2% of cancer survivors aged 18 to 44 years smoke cigarettes, which is double the national prevalence of smoking in the United States.[9]

A life-threatening cancer diagnosis should be a strong incentive to quit smoking; however, cancer survivors face unique challenges. Nonetheless, the benefits of cessation are exceptionally compelling for cancer survivors. For these reasons, the NCCN has developed these guidelines to emphasize the importance of smoking cessation in all patients with cancer and seek to establish evidence-based recommendations tailored to the unique needs and concerns of patients with cancer. The recommendations contained herein describe interventions for cessation of all combustible tobacco products (eg, cigarettes, cigars, hookah), including smokeless tobacco products. However, recommendations are based on studies of cigarette smoking.

Smoking Prevalence in Patients with Cancer

Smoking often persists beyond cancer diagnosis and treatment and well into survivorship. Results from the 2020 National Health Interview Survey showed that 48.7% of patients with cancer reported ever having smoked cigarettes, with 12.2% reporting that they currently smoke.[15] Results from this survey also showed that patients with cancer who are age ≥65 years are less likely to report current smoking (7.4%), compared to patients who are aged 18 to 44 years (21.3%). In the Cancer Care Outcomes Research and Surveillance (CanCORS) cohort of patients with lung and colorectal cancers, at time of diagnosis, 39% of those with lung and 14% of those with colorectal cancer reported current smoking, and, of these individuals, 14% of patients with lung and 9% of patients with colorectal cancer continued to smoke at 5 months post-diagnosis.[16] Another study revealed smoking prevalence to be highest among survivors of bladder, lung, and ovarian cancers.[17] Finally, other studies have found a high prevalence of continued smoking in survivors of cervical cancers.[18]

Health Care Community Response

Given the adverse health effects and prevalence of smoking in patients with cancer and survivors, several leading national organizations have called upon the oncology community for improved smoking cessation efforts. In 2013, the American Association for Cancer Research (AACR) released a policy statement calling for provision of evidence-based smoking cessation assistance to all patients with cancer, outlining the following objectives:

- “Universal assessment and documentation of tobacco use by cancer patients in all clinical settings;

- Development of universal standards for measurement of tobacco use and exposure in clinical and research settings;
- Incorporation of evidence-based tobacco interventions into review criteria used by research and health care quality and accreditation bodies; and
- Recognition and support of the value of tobacco cessation interventions by health systems, payers, and research funders through provision of appropriate incentives for infrastructure development and intervention delivery."[19]

Additionally, American Society of Clinical Oncology (ASCO) has called upon oncology professionals to treat nicotine use disorder as aggressively and compassionately as cancer and to advocate for the wide availability of tobacco cessation services.[20]

More than 80% of oncology care-providing hospitals offer smoking cessation programs, with nationally designated cancer centers being more likely to offer programs.[21] However, despite general consensus on the importance of smoking cessation, particularly for patients with cancer, many cancer centers and oncology practices report that they fall short of providing consistent, high-quality smoking cessation services. In a survey of 58 National Cancer Institute (NCI)-designated cancer centers, 20% reported offering no smoking cessation services for their patients, 38% did not routinely provide tobacco educational materials to patients, and only half reported that they effectively identified tobacco use in their patients.[22] The AACR Task Force on Tobacco and Cancer found that few cancer care institutions utilize systematic and consistent mechanisms to foster cessation among patients with cancer.[19] Several studies have linked increased patient satisfaction to the delivery of smoking cessation advice or intervention.[23,24] Data from large surveys of oncologists practicing in academic medical centers, non-academic hospitals, and oncology practices depict generally high rates of smoking assessment and providing initial advice to quit.[25-28] However, smoking assessment rates were weaker outside of the academic/university setting (ie, for those practicing in a hospital-based, non-academic, or private setting).[28] Regardless of work setting, only 30% to 44% of respondents reported discussing specific interventions or providing subsequent follow-up. Moreover, the majority of respondents reported inadequate training and/or a lack of confidence in ability to provide effective smoking cessation counseling and intervention.[25-28] A dearth of smoking assessment and documentation has also been demonstrated in oncology trials.[29,30]

Issues regarding insurance coverage and provider reimbursement for smoking cessation assessment, counseling, and cessation aids have also presented a challenge for the oncology community in the past. However, implementation of the Affordable Care Act has led to changes designed to increase access to smoking cessation interventions.[31] An intervention study conducted at an NCCN Member Institution showed that use of electronic health record (EHR) functionality can be used to ensure that tobacco use is assessed and addressed in health care settings.[32]

The NCI states that smoking cessation treatment can be incorporated into every step of the cancer care continuum (screening, diagnosis, treatment, and survivorship).[15] They have identified the following strategies to support the dissemination, adoption, and reach of smoking cessation treatment programs in cancer care clinical settings:

- "Establish an evidence-based standard of smoking cessation care across cancer clinical delivery systems that includes tobacco user identification, advice to quit, provision of or referral to evidence-based tobacco treatment, and patient follow-up.
- Measure and report the delivery of smoking cessation treatment as performance metrics for clinicians, hospitals, and health care system leadership.

- Emphasize the delivery of smoking cessation treatment as an important evaluation criterion for oncologists and cancer clinics by professional oncology organizations.
- Implement changes in health care systems, such as using electronic health record tools and other workflow adaptations that facilitate the consistent delivery of smoking cessation interventions in cancer care.
- Develop resources that enable universal implementation of smoking cessation treatment programs in cancer care settings, including strategies that: reduce clinician burden; enhance clinical workflow integration; and provide patients with easy access to multiple treatment options."

Smoking Cessation in Patients with Cancer

Given the complexity of smoking cessation interventions for patients with cancer, there is a great need for resources that provide guidance on smoking cessation specifically for this patient population. The NCCN Clinical Practice Guidelines (NCCN Guidelines®) for Smoking Cessation have been created to establish recommendations for smoking cessation in patients with cancer. The NCCN Guidelines Panel has developed these guidelines in order to facilitate implementation of this standard, to allow for quality control monitoring, to fill a gap among existing treatment guidelines, and ultimately, to improve the health and outcomes for patients with cancer.

Smoking cessation in this patient population presents a number of challenges. Patients may have limited awareness about the harms associated with continued smoking upon a diagnosis of cancer. A survey assessed knowledge of the harms of continued smoking in 1118 patients who currently or formerly smoked and had a cancer diagnosis.[33] Across the board, 38% to 62% of the respondents were unaware of the negative impact that smoking can have on chemotherapy, radiation therapy (RT), surgery, overall treatment efficacy, survival, and development of second primary cancers. Lack of awareness was associated with current smoking at time of diagnosis.

In the general population, individuals who smoke report a number of different barriers to quitting, including stress; dependence; home, work, and social environmental factors; and lack of resources and support for quitting.[34] Importantly, patients and providers in the oncology setting face additional life challenges that can amplify the magnitude of these barriers. However, pain, desire to maintain personal control, second-hand smoke exposure, guilt over smoking, fear of stigmatization, and fatalism regarding disease also represent obstacles unique to oncology patients, particularly those with advanced disease.[35-41] A study that examined whether cancer-related disease factors adversely affected engagement with smoking cessation treatment with varenicline and behavior counseling showed that disease factors such as tumor site, cancer treatment, and time since diagnosis were not associated with medication adherence, counseling adherence, or abstinence.[42] Although health-related quality of life (HRQOL) was predictive of medication adherence, abstinence rates were not impacted. Use of multiple tobacco products is associated with more smoking and greater nicotine dependence.[43,44]

In a population-based analysis of individuals recently diagnosed with cancer who actively smoked, health professional-provided cessation counseling was provided to only 52% of individuals over the course of 12 months.[45] Surveys of oncology providers have identified common themes among barriers to smoking cessation for patients with cancer. In a large survey, medical and radiation oncologists reported a preference for smoking cessation interventions to be managed by other members of the health care team.[46] Inadequate provider training, lack of time, and perceived patient harm/benefit are often cited by oncology providers as

barriers to successful intervention.[26,47] Providers have also cited patient-related factors such as inability to quit, lack of motivation, or resistance to treatment.[25,26] Several groups have described interventions to improve referral to smoking cessation services for patients with cancer by successfully integrating smoking cessation treatment into the cancer care plan.[48-51]

Notably, clinical trial research on smoking cessation for patients with cancer is limited, particularly for patients thought to have non-tobacco–related cancers. Barriers that limit or prevent enrollment in smoking cessation trials include smoking rate, medical history, contraindicated medications, lack of interest, and language barriers.[52] A study describing outcomes from the tobacco treatment program at MD Anderson Cancer Center reported 3-, 6-, and 9-month self-reported abstinence rates of 45.1%, 45.8%, and 43.7%, respectively.[53] Ongoing randomized controlled trials (RCTs) are examining smoking cessation interventions designed specifically for patients with cancer (eg, NCT02816697).

Guidelines Update Methodology

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

Literature Search Criteria and Guidelines Update Methodology

Prior to the update of this version of the NCCN Guidelines® for Smoking Cessation, an electronic search of the PubMed database was performed to obtain key literature in thyroid cancers published since the previous Guidelines update, using the following search terms: ("Smoking Cessation") OR "Tobacco") AND "Neoplasms". The PubMed database was chosen because it remains the most widely used resource for medical literature and indexes peer-reviewed biomedical literature.

The search results were narrowed by selecting studies in humans published in English. Results were confined to the following article types: Clinical Trial, Phase III; Clinical Trial, Phase IV; Guideline; Practice Guidelines; Randomized Controlled Trial; Meta-Analysis; Systematic Reviews; and Validation Studies. The data from key PubMed articles as well as articles from additional sources deemed as relevant to these guidelines as discussed by the panel during the Guidelines update 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.

Sensitive/Inclusive Language Usage

NCCN Guidelines strive to use language that advances the goals of equity, inclusion, and representation. NCCN Guidelines endeavor to use language that is person-first; not stigmatizing; anti-racist, anti-classist, anti-misogynist, anti-ageist, anti-ableist, and anti-weight-biased; and inclusive of individuals of all sexual orientations and gender identities. NCCN Guidelines incorporate non-gendered language, instead focusing on organ-specific recommendations. This language is both more accurate and more inclusive and can help fully address the needs of individuals of all sexual orientations and gender identities. NCCN Guidelines will continue to use the terms men, women, female, and male when citing statistics, recommendations, or data from organizations or sources that do not use inclusive terms. Most studies do not report how sex and gender data are collected and use these terms interchangeably or inconsistently. If sources do not differentiate gender from sex assigned at birth or organs present, the information is presumed to predominantly represent cisgender individuals. NCCN encourages researchers to collect more specific data in future studies and organizations to use more inclusive and accurate language in their future analyses.

General Principles of the Smoking Cessation Guidelines

The NCCN Guidelines for Smoking Cessation can be applied to any tobacco product, including cigarettes, smokeless tobacco, and vaping. As a generalization, the principles for treating nicotine use disorder of any nicotine-containing products are similar. All patients, regardless of stage or treatment modalities, should be encouraged to achieve and maintain abstinence from all combustible tobacco products (eg, cigarettes, cigars, hookah) and smokeless tobacco products. Smoking cessation has health benefits even after a cancer diagnosis, regardless of site, stage, or prognosis—namely improvement in cancer treatment outcomes, primary cancer recurrence, and secondary cancers. Importantly, a diagnosis of cancer may present a teachable moment and valuable opportunity for providers to encourage smoking cessation.[42,54-56] It is the view of the NCCN Guidelines Panel that it is never too late for patients with cancer at any stage to stop smoking and experience health benefits.

The panel recommends a multimodal approach to cessation therapy. The panel recommends that treatment plans for all patients with cancer who smoke include the following three concurrent methods: 1) evidence-based motivational strategies and behavior therapy (counseling), which can be brief; 2) evidence-based pharmacotherapy; and 3) close follow-up with retreatment as needed.

The panel asserts that a smoking cessation approach combining pharmacologic therapy and behavior therapy is the most effective and leads to the best results for achieving and maintaining abstinence from smoking, or smoking reduction for those not ready to quit. The two most effective pharmacotherapies are combination nicotine replacement therapy (NRT) (combined long- and short-acting NRT) and varenicline. There is a dose-response relationship for the success of counseling; high-intensity behavior therapy with multiple counseling sessions is most effective, but at least a minimum of brief counseling is needed.[57-60]

Quitlines are a source of brief behavioral counseling for quitting smoking and may have added value, especially in lower-resource settings.[61,62]

The panel also emphasizes the importance of documenting smoking status and treatment plans in the patient health record. Patient health records should be updated at regular intervals to indicate changes in smoking status, quit attempts made, and interventions utilized.

The panel emphasizes that smoking relapse and brief slips are common and can be managed. Providers, the health care team, and tobacco treatment specialists should discuss this with patients and provide guidance and support to encourage continued abstinence from smoking. Additionally, providers should be aware that smoking slips do not necessarily indicate a need for an alternative intervention. More than one quit attempt with the same therapy may be necessary to achieve long-term cessation.

Treatment for smoking should be offered as an integral part of oncology treatment and continued throughout the oncology care continuum, including surgery, RT, systemic therapy, and end-of-life care. Emphasis on patient preferences and values is important when considering the best approach to smoking treatment in that setting. Cultural context is also important. For example, American Indians and Alaska Natives may use traditional tobacco for ceremonial or medicinal purposes.[63] Smoking cessation efforts in this population should target reduction of commercial tobacco use, not use of sacred tobacco.

E-cigarettes are not U.S. Food and Drug Administration (FDA)-approved for the treatment of smoking. Patients should be counseled toward the use of evidence-based smoking treatment approaches. For patients who choose to use e-cigarettes exclusively for smoking cessation, despite recommendations to use evidence-based pharmacotherapies, encourage behavioral counseling and abstinence from smoking, working with the

patient as they continue to use e-cigarettes. As the patient becomes more confident about quitting smoking, encourage cessation of e-cigarettes, but not at the risk of relapse to smoking combustible products. For a full discussion, see the section on *Electronic Cigarettes ("E-Cigarettes")/Vaping*, below.

Smoking-Associated Risks for Patients with Cancer

Exposing cancer cells to cigarette smoke has been shown to promote a more malignant phenotype through its effects on angiogenesis and cell proliferation, migration, invasion, and survival. For a review of the preclinical data, see Sobus and Warren (2014).[64] These data have been corroborated by clinical studies. The 2020 Surgeon General's Report[65] confirms that smoking cessation reduces cumulative exposure to tobacco smoke across the life course and therefore supports the conclusion that smoking cessation reduces the risk of cancers that have been causally linked to cigarette smoking. Additionally, existing evidence is suggestive of a link between smoking and increased risk of cancer recurrence, poor treatment response, and increased treatment-related toxicity.

NCCN recommends that providers should inform patients of the potential benefits of abstinence from smoking, including improved survival, treatment outcomes, and HRQOL, as well as decreased treatment-related toxicity, drug side effects, and surgical complications. Patients should receive education on the specific risks of smoking during treatment for their particular cancer and should be encouraged to abstain from smoking as far in advance as possible before initiating cancer treatment. All members in the household who smoke should be encouraged to abstain from smoking for the benefit of the patient. Prior to initiating treatment, when making decisions regarding treatment selection, dosage, and timing of initiation, providers should consider patient smoking status and potential smoking-related effects.

Overall Survival and Mortality

Smoking has been linked not only to the development of disease in tobacco-related cancers, but also to prognosis upon diagnosis and risk of death during treatment. Evidence suggests that current smoking increases risk of death and negatively impacts survival for patients with cancer in a variety of disease sites, including bladder,[66-70] breast,[6,71-73] cervix,[74,75] colon/rectum,[76-79] endometrium,[80] esophagus,[81,82] head and neck,[83-87] kidney,[88-90] lung,[5,10,11,79,91,92] thyroid,[87] ovary,[93] pancreas,[94,95] and prostate,[87,96,97] as well as hematologic malignancies[98] and brain metastases.[99]

A number of studies of smoking at cancer diagnosis offer insight into the negative effects of smoking on overall survival (OS), disease-specific mortality (DSM), and all cause mortality (ACM). A recent population-based, cross-sectional study using data from the National Health and Nutrition Examination Survey found that in 255,100 person-years of follow-up, the risk of ACM increases according to the number of cigarettes smoked per day (non-daily, <20 cigarettes per day, 20–40 cigarettes per day, and ≥40 cigarettes per day). [100] In the 2020 Surgeon General's Report, the findings of 10,975 patients from 10 studies (7 prospective cohort and 3 retrospective cohort studies) were analyzed.[65] Three prospective cohort studies compared continued smoking and smoking cessation to never smoking. Continued smoking after a cancer diagnosis significantly increased the risk of mortality compared to never smoking. The risk of ACM for those who continued to smoke was greater than for those who quit.[6,86,101] An additional three studies reported that compared to persistent smoking, quitting was significantly associated with reduced ACM in patients with either non-small cell lung cancer (NSCLC) or small cell lung cancer.[102-104] Lastly, four studies similarly reported increased ACM in disease sites including lung, colorectal, bladder, and other cancers with continued smoking relative to quitting.[5,12,101,105] The 2020 Surgeon General's Report therefore concluded that smoking cessation after a

cancer diagnosis can significantly reduce ACM relative to continued smoking.[65] The quality and quantity of evidence presented was consistent with knowledge of a reduction in ACM with smoking cessation in the general population.

Risk of Recurrence or Secondary Primary Tumor

A number of studies have linked cigarette smoking and heightened risk of recurrence (ie, recurrent cancer in the same anatomic location as the original primary cancer). The 2014 Surgeon General's Report identified a positive association between smoking and risk of recurrence in 82% of the reviewed studies (42/51), with 53% of studies revealing significantly increased risk.[7] Among the studies that compared relative risk (RR) of recurrence between patients who never smoked, patients who formerly smoked, and patients who currently smoke, the median RR was 1.42 and 1.15 for current and former smoking, respectively.[7]

Disease sites with data linking current patient smoking to increased risk of recurrence include the anus,[106] bladder,[66,107,108] breast,[109] lung,[10,110] stomach,[111] and prostate.[96,97,112-115]

Studies have also examined the impact of continued smoking in patients with cancer on the risk of second primary tumor formation. The 2014 Surgeon General's Report identified a positive association between smoking and risk of second primary tumor in all studies examined (n = 26). The association was strongest when considering the effects of smoking on RR of developing a smoking-related second primary cancer (eg, lung cancer). Among five studies classifying smoking status into "never," "former," and "current," the median elevated RR of a second primary tumor was 1.20 and 2.20 for former and current smoking, respectively. Data from a large retrospective series and pooled data analyses have continued to provide support for smoking and increased risk of second primary malignancy, especially smoking-associated cancers.[116,117] Additionally, data also suggest that smoking interacts synergistically with RT to elevate the risk of second primary cancers.[7,118,119]

Smoking cessation is linked to reduced risk of recurrence and second primary tumor formation. Data from patients with lung and head and neck cancers showed that rates of second primary cancers were lower for patients who quit smoking than for those who continued to smoke after diagnosis.[120-122] In a cohort of patients with colon cancer, current smoking was associated with significantly greater risk for baseline metastasis, but interestingly, rates among those who formerly smoked and never smoked were similar and significantly less in comparison.[123]

Smoking-Related Effects on Treatment Efficacy, Side Effects, and Outcomes

A majority of the existing data establishes and supports the detrimental impact of persistent smoking during cancer treatment. In a 2014 report from the Surgeon General, 80% of the evaluated studies (66/82) demonstrated a statistically significant association between smoking and increased anticancer treatment-related toxicity.[7] Smoking has implications across the spectrum of cancer treatment, including surgical outcomes, RT efficacy and toxicity, chemotherapy metabolism and side effects, and overall symptom burden. This discussion also addresses the developing evidence base for the benefits of abstinence from smoking after receiving a cancer diagnosis.

Smoking-Associated Risks

Surgery

Smoking negatively impacts outcomes from cancer surgery, affecting postoperative complications, quality of life, length of hospital stay, and mortality risk.

The adverse effects of smoking on postoperative outcomes were examined in more than 20,000 patients with gastrointestinal (n = 12,432), lung (n = 4490), and urinary tract cancers (n = 3491) using the Veteran's Health Administration Surgical Quality Improvement Program (VASQIP) database from 2002 through 2008.[124] Surgical complications examined included surgical site infections, vascular complications (ie, venous thromboembolism, stroke/cerebrovascular accident, myocardial infarction), and composite pulmonary outcomes (CPO: pneumonia, failure to wean from ventilator >48 hours, or re-intubation for cardio-respiratory failure). Compared with patients who formerly smoked, patients in the gastrointestinal cancer cohort who smoke had higher postoperative rates of pneumonia, failure to wean from ventilator, reintubation, and CPO. In the lung cancer cohort, patients who smoke had higher rates of pneumonia, failure to wean from the ventilator, reintubation, CPO, and return to surgery compared with patients who formerly smoked. Current smoking status was associated with an increased length of hospital stay across all cancer sites when compared with patients who never smoked; patients who never smoked and patients who formerly smoked did not differ on this measure.

Similar findings have been reported by other groups for patients who had surgery for lung cancer, bladder cancer, and gastric cancer, and in patients with leukemia undergoing hematopoietic cell transplantation (HCT).[125-131]

Postsurgical outcomes (ie, incisional infections, infectious and major complications, mortality at 30 days) were compared between cohorts of patients who never smoked, formerly smoked, and currently smoke using data from more than 26,000 patients with colorectal cancer in the American College of Surgeons National Surgical Quality Improvement Program database (2005–2010). Postoperative morbidity and mortality rates were higher among patients who smoke, and a significant dose-dependent effect was observed when stratifying risk of major complications by pack-years of smoking.[132] Similarly, a retrospective analysis of 5715 patients from the Veterans Affairs Surgical Quality Improvement Program database found that patients who smoke had a 48% higher likelihood of suffering a pulmonary complication (95% CI, 1.03–2.14; P = .035) and 72% higher likelihood of suffering multiple complications (95% CI, 1.07–2.76; P = .035), compared to patients who recently quit smoking.[133] For patients aged >70 years, a retrospective analysis of the American College of Surgeons National Surgical Quality Improvement Program database from 2011 to 2017 found that the risk of a major complication increased from 17.8% in patients who don't smoke to 21.7% in patients who smoke (P < .001).[134]

Smoking can also impair wound healing and predispose patients to surgical complications if undergoing reconstructive surgeries after cancer treatment. Among patients with breast cancer or head and neck cancers, smoking was associated with significantly higher risk of flap complications and delayed healing,[135-138] and evidence suggested that complication risk may be reduced by preoperative smoking cessation.[135,138] A systematic review including 19 studies (all retrospective except for one prospective study) of the impact of smoking on head and neck reconstructive surgery with free vascularized tissue flap showed that smoking was not significantly associated with flap failure but was associated with increased risk of hematoma and overall surgical complications.[139]

Radiation

Studies have shown that former smoking and current smoking during RT may decrease treatment response and increase complication rates, particularly in patients with head and neck cancers, but also in patients with cervical, lung, breast, or prostate cancers. Patients who receive RT and smoke may also have an increased risk of developing a second

primary cancer. Smoking amplified the risk of second primary cancer associated with RT for initial breast, lung, or cervical cancers.[140-143]

In patients with head and neck cancer receiving RT, current smoking was associated with poorer rates of locoregional control.[84,144] In another cohort, patients with head and neck cancer who smoked during RT had lower rates of complete response and worse survival times than patients who never smoked or those who quit prior to treatment.[145] Smoking during RT in patients with head and neck cancer has also been shown to increase the rates of treatment-related complications. In patients with laryngopharyngeal cancers, smoking during treatment was associated with significantly elevated incidence of osteoradionecrosis and hospitalization during treatment.[146] Another study demonstrated a significantly greater decline in several HRQOL measures in patients who smoked during therapy compared with patients who quit beforehand.[147]

Among 3489 patients receiving RT as part of treatment for stage I or II cervical cancer, heavy smoking (defined as ≥1 pack/day) was the strongest independent factor for predicting long-term major bladder, rectal, or small bowel complications, with even light/moderate smoking (<1 pack/day) predisposing patients to small bowel complications, compared to patients who did not smoke.[148] In another study of 565 patients with cervical cancer who were receiving primary RT, patients who smoked during treatment had lower cure rates, higher frequency of RT side effects, and higher rates of severe, irreversible complications, compared to patients who did not smoke.[149]

Smoking during RT for NSCLC was associated with significantly decreased locoregional control.[150] Smoking may also decrease the efficacy of RT for prostate cancers and increase the prevalence of long-lasting treatment-related effects on the bowel and anal sphincter.[151-153] Concurrent smoking and RT increased the risk of cardiovascular disease in 4414 10-year survivors of breast cancer.[154]

Systemic Therapy

Data on the impact of smoking on chemotherapy are much more limited than that for surgery and RT, in part because smoking quantity during treatment is often left out of the medical record.[29] Many of the purported effects of smoking during chemotherapy are extrapolated from what is known about the impact of chemotherapy and smoking as individual health factors. Smoking has the potential to exacerbate the risk of anticancer drug-related pulmonary and cardiac toxicities such as cardiomyopathy and pulmonary fibrosis.[155] Combining neoplastic agents with RT while smoking may lead to further toxicity. Additionally, cancer drug side effects such as weight loss, cachexia, and fatigue may also be increased by smoking during treatment.[155,156]

Many systemic anticancer agents result in some degree of immune suppression/compromise, and smoking during chemotherapy may further compromise immune function in an already vulnerable patient population.[29,155] Preclinical and clinical studies suggest that smoking and nicotine exposure can be detrimental to the function of both the adaptive[157-160] and innate immune system.[161-165] Similarly, cigarette smoking may increase the incidence of infection, particularly for smoking-related infectious diseases such as pneumonia and influenza.[166]

Preclinical studies also suggest a potential link between nicotine exposure and the development of chemoresistance, [167-171] although no clinical data are currently available to support these findings. This should not be a consideration in the decision to prescribe NRT, given the poor outcomes associated with cigarette smoking specifically.

Smoking can also impact the metabolism of certain cytotoxic chemotherapies and other systemic therapy. Smoking effects on cytochrome P450 enzymes may alter drug clearance time and plasma concentration, potentially impacting the efficacy of certain drugs for patients who smoke.[172] Providers should consider whether patients are at

risk for altered drug metabolism due to smoking and determine if medication or dose adjustments may be required.

Drugs with metabolisms that are known to be affected by smoking include erlotinib and irinotecan. Rapid drug clearance has been observed in patients who smoke who were receiving erlotinib therapy, such that higher doses may be required to achieve equivalent systemic exposure to standard dosing in patients who never smoke.[173,174] Similarly, smoking increases the clearance time of irinotecan, potentially lessening systemic exposure.[173,175] Given the narrow therapeutic index of systemic therapy for lung cancer, small changes in drug exposure due to smoking could affect treatment efficacy and patient outcomes.[173] Bendamustine metabolism is also likely to be impacted by smoking, resulting in decreased drug plasma concentration and increased concentration of its active metabolites.[176] However, smoking does not appear to alter the pharmacokinetic properties of taxane chemotherapeutics (eg, docetaxel, paclitaxel) despite its paradoxical protective effects on drug-induced neutropenia and leukopenia.[177]

Symptom Burden

Analysis from the US FDA Population Assessment of Tobacco and Health Study, including 1409 adults diagnosed with cancer, showed that both cigarette smoking and vaping were associated with greater cancer symptom burden (fatigue, pain, and emotional problems).[178] However, cigarette smoking in adults with cancer was associated with worse QOL, while vaping was not significantly associated. In a study of 947 patients who were undergoing chemotherapy and/or RT, smoking during treatment was linked to a higher overall burden of symptoms commonly experienced among patients with cancer. In analyses that controlled for age, gender, race, education, occupation, treatment, cancer site, and Karnofsky performance score, patients who smoke had a significantly higher symptom burden compared with patients who never smoke, both during treatment and 6 months afterward.[179] Smoking in patients with advanced lung cancer was associated with greater symptom burden on diagnosis and poorer HRQOL post-diagnosis.[180] Additional studies suggest that patients with cancer who smoke may experience more severe or frequent pain than nonsmoking counterparts.[181-185]

Benefits of Smoking Cessation for Patients with a Cancer Diagnosis

For many who smoke, the benefits of smoking cessation can be appreciated immediately through reduced blood carbon monoxide levels, decreased irritative respiratory symptoms (eg, cough, shortness of breath), and improved lung function. In the long term, cessation is associated with reduced risk of smoking-related disease, development of malignancy, and smoking-related mortality.[186] Although the deleterious effects of smoking after a cancer diagnosis are well documented and understood, research on the benefits of cessation post-diagnosis is much more limited.[19,187] For patients with cancer, the potential benefits and risk reductions associated with cessation are of critical importance.

Studies have evaluated the impact of abstaining from smoking at or near the time of a cancer diagnosis by comparing outcomes of patients who smoke during cancer treatment to those who quit prior to treatment. Studies generally show that patients who recently quit have survival outcomes intermediate to that of patients who never smoke and those who smoke, suggesting a measurable benefit of cessation post-diagnosis. The data to support this survival pattern are derived primarily from retrospective cohorts of patients with lung or head and neck cancers,[10,11,92,105,122,145,188-192] but similar patterns have been observed for colorectal, bladder, and kidney cancers, as well as various other disease sites.[11,68,193,194]

Retrospective studies have estimated a roughly 25% reduction in risk of mortality between those who smoke and those who used to smoke who were diagnosed with NSCLC and bladder cancers.[69,189]

A study of cancer registry data from Japan (n = 30,658) compared the risk of ACM in patients who never smoke, who formerly smoked (>3 years), who recently quit (≤3 years; 85% within the past year), and who currently smoke.[195] When combined results were weighted by disease site prevalence, risk of death in patients who recently quit was reduced by 11% compared with patients who currently smoke (hazard ratio [HR], 0.89; 95% CI, 0.81–0.97). Risk of death in patients who never/formerly smoked was found to be 15% to 16% lower than in patients who currently smoke. Over the course of 10 years, adjusted survival rates were consistently higher among those who recently quit, formerly smoked, and never smoked. When comparing patients who recently quit smoking to those who currently smoke, a small but significant difference in survival rate was observed in those who recently quit (+1.8% to 2.9% over 5 years).[195]

A prospective longitudinal study examined the impact of smoking at diagnosis in 5185 patients with cancer across 13 disease sites over the course of at least 12 years.[11] In this study, patients who recently quit were examined as a specific subset of those who quit within 1 year of the study's structured smoking assessment, allowing for comparisons to individuals who continued to smoke during cancer treatment. For disease sites with larger recent quit cohorts (ie, lung, head/neck cancers), those who recently quit had lower overall mortality risk compared with those who continued to smoke (current smoking vs. recent quitting: lung cancer HR, 1.38–1.42; head/neck cancer HR, 2.11–2.15).[11] Similarly, two systematic reviews including studies of patients with lung cancer showed that quitting smoking was associated with a survival benefit.[10,191]

In a longitudinal prospective cohort study including 517 people who smoked with early stage (IA–IIIA) lung cancer, patients who quit smoking after diagnosis were compared to patients who continued to smoke.[13] Median OS (6.6 vs. 4.8 years, respectively; *P* = .001), 5-year OS (60.6% vs. 48.6%, respectively; *P* = .001), and 5-year progression-free survival (PFS) (54.4% vs. 43.8%, respectively; *P* = .004) were higher for patients who quit smoking, compared to patients who continued to smoke. In patients who quit smoking, a 33% decrease in overall mortality risk and a 25% decrease in cancer-specific mortality risk were observed over a mean 7-year follow-up. The benefits of smoking cessation were significant, regardless of cancer stage, pack-years smoked, and treatment received.

Abstaining from smoking at or near cancer diagnosis appears to reduce treatment-related complications compared to patients who continued smoking. In patients undergoing lung cancer resection, studies suggest that preoperative abstinence mitigates the risk of pulmonary complications and in-hospital mortality.[127,129] In one study, risk-adjusted odds ratios (ORs) for mortality and pulmonary complications decreased as preoperative cessation time increased from 14 days to 1 month, to 1 to 12 months, and to more than 12 months.[129] A larger retrospective study comparing preoperative cessation intervals of increasing lengths suggested that longer periods of preoperative cessation may be more effective than shorter periods for reducing risk of postoperative complications, although cessation for any amount of time prior to surgery significantly reduced risk.[127] A retrospective study of 188 patients undergoing reconstructive surgery after treatment for head and neck cancer revealed that preoperative smoking cessation of at least 3 weeks led to lower incidence of wound healing complications than patients who continued smoking.[196] In a study of 107 older adult males with lung cancer who underwent elective thoracoscopic radical lung resection, smoking cessation at least 3 weeks before surgery was associated with better pain outcomes than smoking cessation less than 3 weeks before surgery.[197]

Abstinence has been shown to lead to improvements in various measures of general health and well-being for patients with cancer. Smoking abstinence improved performance status at 6 and 12 months post-lung cancer diagnosis over that of continued smoking when adjusting for

disease stage, patient demographics, therapy, and comorbidity.[14] Additionally, patients with cancer who quit smoking benefited from lower rates of smoking-related cardiovascular and pulmonary disease.[198]

Evaluation and Assessment of Patient Smoking

These Guidelines highlight the importance of evaluating and assessing smoking status and history in patients with cancer. The AACR emphasized in a policy statement the need for universal assessment and documentation of tobacco use by patients with cancer both in the standard clinical setting and in oncology clinical trials.[19] The NCI-AACR Cancer Patient Tobacco Use Assessment Task Force published proposed core and extension items to be used for the assessment of tobacco use in patients with cancer enrolled in research trials.[199] Current practice is suboptimal, as inadequate or inconsistent assessment and documentation of smoking status has been reported both in the care setting and in the context of cancer registries and clinical trials.[22,30,200]

Despite the demonstrated adverse effects of smoking during cancer treatment, a large proportion of cancer clinical trials do not collect adequate, up-to-date information regarding patient smoking status and history, particularly for malignancies other than well-known tobacco-related cancers (eg, lung, head and neck cancers).[29,30] Such assessments are needed to make evidence-based determinations of the impact of smoking on patients, treatment efficacy, and side effects.

In a large study conducted at an NCCN member institution, a smoking assessment questionnaire was integrated into the EHRs in order to automatically identify and refer appropriate candidates for onsite cessation services.[201] The smoking assessment items incorporated into the EHR were refined based on analysis of responses from an initial patient screen containing 23 items. Response analysis revealed that the most effective questions for generating referrals included whether 1) patients smoked cigarettes every day, some days, or not at all; and 2) if/what other types of tobacco products were used. For patients who formerly smoked, it was important to assess the last time a patient smoked a cigarette, “even a puff,” and for established enrollees to the cessation program, what type(s) of cessation aids were being used. The study revealed that just three assessment questions made it possible to efficiently and accurately identify the vast majority (>98%) of patients who currently smoke or those at risk for smoking relapse. These questions are as follows: 1) Have you smoked at least 100 cigarettes in your entire life? (yes, no); 2) Do you now smoke cigarettes every day, some days, or not at all?; and 3) Do you currently use any other tobacco products, such as cigars, pipes, chewing tobacco, snuff, dip, snus, clove cigarettes, kreteks, or bidis? (Every day/some days/not at all).

Determining Smoking Status

The NCCN Guidelines for Smoking Cessation advocate for smoking status to be updated in the patient’s health record at regular intervals to indicate any status changes or quit attempts. To do so, the panel recommends the providers initially ascertain: 1) whether the patient has ever smoked, and if so, then regularly assess; 2) whether the patient currently smokes; and 3) whether the patient has smoked within the past 30 days (as an arbitrary number to identify patients at very high risk of relapse). All information regarding smoking status of all tobacco products (including pipes, cigars, e-cigarettes, and smokeless tobacco) should be recorded in the medical record. As a follow-up to the initial evaluation, these guidelines direct providers to a tailored patient assessment based on smoking status and history. Specific algorithms for patients who currently smoke (patient smoked within the last 30 days) and formerly smoked who recently quit (more than 30 days to 1 year prior) are included. For patients who never smoked or those who quit more than 1 year prior, providers should urge patients to remain abstinent from smoking, explaining the benefits of remaining abstinent. For recommendations regarding lung cancer

screening for current/former smoking, see the NCCN Guidelines for Lung Cancer Screening (available at www.NCCN.org).

Assessment of Current Smoking

In patients who currently smoke or use nicotine products (or those who have smoked in the last 30 days), providers should assess nicotine use to understand the chances for success and risk of relapse and document the findings in the patient's health record. To assess nicotine use, providers should query patients regarding the amount currently smoked per day (including cigarettes, pipes, cigars, e-cigarettes, and smokeless tobacco), the typical amount smoked or used, and how soon the patient smokes or uses nicotine products after waking up in the morning (ie, within 30 minutes). Though smoking within 5 minutes of waking is indicative of greater dependence,[202] time to first cigarette is used to determine the appropriate strength of nicotine gum and lozenge (2 or 4 mg). The Fagerstrom Test for Nicotine Dependence is an alternative standardized tool for assessing nicotine dependence.[203] However, the panel has opted to recommend a more streamlined assessment for use in the oncology setting.

To best tailor treatment, providers should also gather information regarding the patient's history of quit attempts and why they were or were not successful. Specifically, providers should ascertain the longest period of abstinence achieved, the date of the most recent quit attempt, what cessation aids were used, and why these failed. It is important to document the patient's previous experience with smoking cessation aids, including any medications, behavior therapy, e-cigarettes, quitlines, websites, smart phone apps, or other media aids. The patient's reasons for why these aids were unsuccessful are important pieces of information. For example, the patient may have experienced side effects and/or continued cravings with medication, and this may indicate a need for alternative or complementary treatment. If the medication seemed to be ineffective, then duration of use should be noted, as it is possible that it was discontinued too soon. In this discussion, the provider should avoid discouragement by normalizing previous failed attempts by counseling the patient that it is the norm to undergo multiple attempts before quitting permanently and that, with each try, something new is learned.

Providers are encouraged to engage patients in a personalized motivational dialogue about smoking and to ensure patients are aware of the disease-specific risks of smoking and benefits of quitting, and to do so in a manner that does not blame the patient.[35] Educational resources should be provided. The panel recommends that clinicians provide patients with reasons and ideas for smoking cessation, emphasizing the importance of both encouragement and directness with patients who smoke. When incorporating motivational interviewing (MI) to promote willingness to quit, the panel emphasized the importance of the following general principles: 1) express empathy, 2) develop discrepancy (ie, ask patients to identify conflicts between their values/priorities and current tobacco use), 3) roll with resistance, and 4) support self-efficacy.[204,205] For a summary of the methods and data on MI for smoking cessation, see the *Principles of Behavior Treatment of Smoking* section below.

Patient readiness to quit should be assessed jointly with the patient and provider. If patients are not ready to quit, providers should assess and address patient-reported barriers and concerns regarding cessation. When possible, providers should work with patients to set a near future quit date (ie, 1–3 months, or longer for patients who may take longer to move from precontemplation to contemplating quitting[206]) and/or consider smoking reduction with pharmacotherapy and counseling with the goal of achieving and maintaining abstinence from smoking in the future.[207] Providers should discuss the impact of continued smoking on cancer treatment outcomes and complications from chemotherapy, radiation, and surgery. Starting pharmacotherapy prior to having a quit date is also appropriate in

these patients.[208] A meta-analysis of 10 randomized trials in 3760 patients with cancer found quit rates to be comparable when comparing abrupt cessation to gradual smoking reduction.[209] Therefore, both options can be used after discussions with the patient. Trial data since then have continued to mirror this trend of comparable success rates with abrupt cessation and gradual reduction.[210] At each visit, providers should reassess readiness to quit and engage in motivational dialogue as indicated.

Assessment of Former Smoking

Providers should evaluate and document the risk of relapse for patients with more than 30 days' abstinence. The panel suggests the following characteristics to identify patients at high risk for relapse: frequent/intense cravings; elevated anxiety, stress, or depression; current or prior history of psychiatric disorders[211]; cohabitating or working with someone who uses tobacco; quitting within the past year; recently initiated smoking cessation pharmacotherapy or other nicotine delivery mechanisms; drug/alcohol use or misuse[212]; recent history of nicotine use disorder; and/or low self-confidence in ability to quit/maintain abstinence. Patients with poor pain control may also be at increased risk for smoking relapse.[213] There is also an increased risk of relapse among patients living with HIV.[214] The panel considers patients demonstrating at least one of these characteristics to be at higher risk for relapse and recommends a management plan tailored to prevent relapse. Providers should discuss risk of relapse with patients and provide guidance and support to promote continued smoking cessation attempts. As indicated, providers may refer patients with psychiatric and substance use disorders to a specialist (see the NCCN Guidelines for Distress Management, available at www.NCCN.org).

Treatment of patients who demonstrate an elevated risk of relapse includes behavior therapy with counseling on relapse risk factors (eg, identification of triggers for smoking urges or living with someone who smokes) and relapse prevention. Pharmacotherapy can be considered to promote maintenance of abstinence. While NRT may be used long-term to help maintain abstinence, methods other than NRT may be considered to avoid reintroducing nicotine to patients who have been nicotine-free for an extended period of time (ie, ≥30 days). Providers should review smoking-associated risks for patients with cancer as well as the health benefits of abstinence. All management plans and counseling should be documented in the patient health record. For patients deemed to be at low risk for relapse, providers should reinforce success and highlight the importance of continued abstinence.

It is important to regularly reevaluate patients' smoking status and risk of relapse. If relapse occurs, patients should be evaluated per the recommendations for current smoking. Additionally, providers should remain aware that patient self-report of smoking status might underestimate the rate of current smoking among patients with cancer, as is evidenced by research comparing self-reported and objective measures.[215-217] Patients who remain abstinent should regularly undergo reevaluation (ie, at each visit) with documentation of any risk factor changes.

Treatment of Smoking During or After Cancer Treatment

The following recommendations are appropriate for patients who are currently undergoing cancer treatment as well as cancer survivors.

Devising a Treatment Plan

Following assessments, providers should establish a personalized quit plan for each patient that takes into account the patient's nicotine dependency, prior quit attempts and any cessation aids used, and smoking treatment options. Providers should work with patients to set a quit date as soon as possible. Risks of relapse and slips should be

discussed with the patient along with guidance and support for continued abstinence from smoking.

Smoking Cessation and Cancer Surgery

Smoking has been shown to increase the risk of pulmonary and cardiovascular complications, surgical site infection, and poor wound healing in patients undergoing surgery. For an overview of the data, see the section on *Smoking-Related Effects on Treatment Efficacy, Side Effects, and Outcomes* in this Discussion. Preoperative pharmacotherapy options for patients within 1 week of surgery include combination NRT (preferred; category 1) or varenicline. NRT is listed as preferred in this setting because guidelines for its use include a quit date within 24 hours, while varenicline quit dates are typically 7 days from initiation of therapy. However, in some clinical situations, varenicline has been used with an earlier quit date. If there is 1 week or more until scheduled surgery, combination NRT or varenicline are both category 1 recommendations.

Some surgeons may not allow perioperative NRT use in their patients. This practice may be due to findings in animal studies regarding an association between nicotine and decreased wound healing. However, no similar data in humans exist, and NRT typically provides a lower overall dose of nicotine compared with cigarettes, while nearly doubling the chance of achieving smoking abstinence.[218] NRT at the normal doses has not been shown to negatively affect acute wound healing,[219,220] and offers benefits over continued smoking.

Preoperative smoking cessation reduces postoperative complications. In randomized trials of smoking cessation or reduction interventions, postoperative complications from orthopedic surgery were significantly decreased in patients who quit compared with patients who continued smoking.[221,222] Study findings also support the benefits of preoperative smoking cessation in patients with cancer, which has been shown to reduce postoperative morbidity for various cancer types.[126,127,129,223,224] The optimal timeframe for abstinence from smoking to achieve full benefit is not yet clear, but longer periods of time are likely to be more effective for reducing postoperative complications.[126,127]

Patients who smoke who need surgery should be treated with evidence-based approaches, including pharmacotherapy and behavior therapy, in order to improve surgical outcomes and long-term cessation rates.[221,222,225,226] For patients with planned cancer surgery, abstinence from smoking should occur as soon as possible before surgery, regardless of how soon surgery will be occurring. There is no evidence to support a harmful effect of a quit attempt at any point in time before surgery. Although longer periods of preoperative abstinence from smoking may confer better surgical outcomes,[126,127,224,227] the panel emphasizes that patient smoking should not delay appropriate timing for cancer resection, and access to cancer surgery should not be restricted solely on the basis of continued smoking.[228]

Elective procedures, such as plastic surgery reconstruction, may be associated with benefit from delaying surgery for a period of time after smoking cessation. At this time, consensus on an optimal time period of preoperative cessation has not been demonstrated through the existing literature.[227] Providing surgery-specific resources and advice for smoking cessation may facilitate smoking reduction or cessation in patients undergoing elective (non-cancer) surgery.[229,230]

Primary Treatment

Based on clinical trial data of smoking cessation in patients with cancer, the panel recommends a combination frontline approach including pharmacotherapy and behavior therapy for smoking cessation for patients with cancer. Population studies and meta-analyses of randomized or quasi-randomized trial data support the addition of behavior therapy to pharmacotherapy to enhance the rate of success.[231-234]

Preferred primary therapy options in these Guidelines are combination NRT (category 1) that uses long-acting NRT (nicotine patch) plus a short-acting NRT, such as nicotine gum, lozenge, inhaler, or nasal spray. An alternate option is oral varenicline (category 1). Patients commonly underdose when using combination NRT.[235-237] Patients should be advised that, as with any medication, adverse events may occur with nicotine replacement pharmacotherapy, but these are typically mild and short-lived and can be managed by their provider by changing the dose or product. For discussion of the evidence for and safety of individual pharmacotherapeutic regimens, see the section below on *Principles of Pharmacotherapy*.

Follow-up

Assessment of effectiveness of counseling and pharmacotherapy, smoking status, and adverse effects of pharmacotherapy should be performed in person or by phone/telehealth at a minimum of: within 3 weeks of initiating treatment for smoking (within 1 week preferred, if possible), and following 12 weeks of therapy. Assessment should continue on a periodic basis moving forward, including within about 12 weeks following completion of pharmacotherapy. Nicotine withdrawal symptoms typically peak 48 to 72 hours after quitting and last about 2 to 3 weeks before subsiding. Slips also commonly happen in the first week of abstinence. Patients who do not quit immediately may quit at a later point. Therefore, providers should encourage continued treatment adherence through and beyond brief slips, with adjustments to dose or behavior therapy frequency as indicated.[238] Adverse effects may also warrant dose adjustments.

When possible, in-person follow-up during planned clinical visits or individual/group therapy sessions is preferred. To minimize the burden on patients in active cancer therapy, behavior therapy can be provided by a trained member of the health care team during oncology visits. Alternatives include phone or telehealth. During follow-up, providers should assess risk of relapse and as indicated, consider adjusting the dose and or type of pharmacotherapy. Patients may slip or relapse, which is expected and can be managed. Maintain close follow-up through the duration of therapy. At 12 weeks, assessment of smoking status should be made in person or by phone/telehealth. For pharmacotherapy courses exceeding 12 weeks duration, assessment should be repeated at the end of the course of therapy.

For patients who remain abstinent, additional follow-up should take place at 6 and 12 months, either in person or by phone/telehealth. Motivational strategies should be used to promote continued abstinence. Duration of pharmacotherapy can be extended beyond 6 months if clinically indicated to maintain abstinence. For patients who experience smoking relapse, treatment with either combination NRT or varenicline should be re-initiated.

Treatment for Relapse or Sustained Smoking

For patients who continue to smoke or experience relapse, assess effectiveness or prior pharmacotherapies and medical adherence (ie, frequency and proper usage). The panel recommends one of two options in this setting. The first option is to continue or resume primary therapy, reinforce proper use of medication, and provide additional behavior therapy. The second option is switching to the alternate preferred option (combination NRT or varenicline). The panel recommends that these regimens be paired with additional behavior therapy. In most circumstances, both preferred primary therapy approaches (combination NRT and varenicline) should be tried before proceeding to any other pharmacotherapy options. However, bupropion with or without NRT may be appropriate in earlier treatment settings for select patients (eg, those with symptoms of depression or fatigue). For those being treated with varenicline, the addition of NRT or bupropion can be considered as

clinically indicated to maintain abstinence despite continued urges to smoke. The decision to continue or switch therapy should be based on prior cessation success, patient preference, toxicity, cost and/or coverage, and/or a change in clinical status (eg, upcoming surgery).

After switching therapy or adjusting the dose of an existing regimen, follow-up should occur within 3 weeks (within 1 week preferred) and after 12 weeks of therapy. Smoking status should be re-evaluated. For patients who remain abstinent, the course of pharmacotherapy can be extended as clinically indicated. Additional follow-up at 6 and 12 months after successful quitting is recommended. For further relapse or sustained smoking, extended duration of pharmacotherapy or switching to an alternate regimen can be considered. Additional or more intensive behavior therapy is also an option.

Principles of Pharmacotherapy

General

A minimum of 12 weeks of pharmacotherapy, but typically longer, is recommended for the initial quit attempt. Duration of therapy can be substantially extended to promote continued abstinence, for example a year or more.[239] Research suggests that longer courses of certain cessation regimens may be associated with higher rates of abstinence.[240]

Follow-up is recommended within 3 weeks of starting pharmacotherapy to coordinate with scheduled oncology appointments, though follow-up within 1 week is preferred. For relapse or sustained smoking, options include continuation of the initial agent or a switch to the alternative preferred agent. Dose adjustments should be considered as clinically indicated. Attempts at smoking reduction should be tracked. If reduction efforts stall or if complete abstinence seems unlikely, providers should consider an alternative pharmacotherapy regimen.

In most circumstances, the side effects related to primary smoking treatment medications, which often peak in the first 1 to 2 weeks of administration, are minimal and are considered an acceptable risk compared to smoking. A review of post-marketing case reports on adverse neuropsychiatric effects from smoking treatment medications has generated some safety concerns in the past,[241] but large-scale analyses of the data support the safety of these regimens.[242,243] Although serious side effects of primary treatment approaches are extremely rare, providers should refer to manufacturer inserts for exhaustive lists of potential side effects and warnings.

Adherence to pharmacotherapy is important to promote optimal outcomes and success, and numerous studies have tested interventions designed to promote and improve medication adherence.[238,244] Nonadherence is associated with perceiving that cessation aids are not needed, adverse effects, forgetfulness, and limited finances.[245,246]

Below, data from various clinical trials are discussed. Included in this discussion are findings from a Cochrane network meta-analysis that included data on pharmacologic interventions across 267 individual studies in 101,804 participants.[247] The authors characterized positive treatment outcome as continuous or prolonged abstinence at least 6 months from the start of smoking treatment. Harm outcomes were measured by the incidence of serious adverse events associated with treatment.

Pharmacotherapy Options

For patients with cancer, the Guidelines recommend primary therapy with either combination NRT (long-acting patch plus a short-acting formulation) or varenicline, paired with behavior therapy. If smoking is sustained or relapse occurs while a patient is on an initial primary therapy regimen, providers should continue therapy with that initial regimen or switch to the

alternate primary therapy option. Both preferred primary therapy options (combination NRT or varenicline) should be used before trying other pharmacotherapy options. Bupropion with or without NRT may be appropriate for select patients (eg, those with symptoms of depression or fatigue). For those being treated with varenicline, the addition of NRT or bupropion can be considered as clinically indicated to maintain abstinence despite continued urges to smoke. Data supporting the recommended pharmacotherapy options are described below.

Varenicline

Efficacy

Varenicline is a non-nicotinic partial agonist of the alpha4beta2 subtype of the nicotinic acetylcholine receptor. Varenicline partially mimics the effects of nicotine in the brain's reward center and competitively inhibits the binding of nicotine from cigarettes.[248]

Systematic reviews/meta-analyses have identified varenicline as the most effective single pharmacotherapy option for smoking cessation.[247,249,250] However, medication adherence is an important factor in cessation success.[238] Cochrane network meta-analysis data report that varenicline increases the odds of smoking cessation by almost three-fold compared with placebo (OR, 2.88; 95% CI, 2.40–3.47).[247] Direct comparison of the cumulative data suggest that varenicline was more efficacious than bupropion (OR, 1.59; 95% CI, 1.29–1.96) and single forms of NRT such as nicotine patch, nicotine gum, and other formulations (OR, 1.57; 95% CI, 1.29–1.91).[247] Varenicline appeared to be equally as likely to promote smoking cessation as combined treatment with more than one form of NRT (OR, 1.06; 95% CI, 0.75–1.48), so that both may be offered depending on patient circumstances.[247] An analysis from a Cochrane review including 11 studies showed that varenicline prevents relapse in those who abstain from smoking, based on moderate-certainty evidence (RR, 1.23; 95% CI, 1.08–1.41).[251]

Results published from the double-blind EAGLES RCT (n = 8144) revealed that patients treated with varenicline achieved higher abstinence than patients receiving placebo (OR, 3.61; 95% CI, 3.07–4.24), nicotine patch (OR, 1.68; 95% CI, 1.46–1.93), or bupropion (OR, 1.75; 95% CI, 1.52–2.01).[252] A study that investigated the efficacy of varenicline specifically for patients with cancer revealed 84% retention and 40% abstinence at 12 weeks. Side effect profiles mimicked those observed in the general population, and abstinence improved cognitive function and reduced negative effect over time.[253]

Varenicline may also be efficacious for smoking reduction in those not ready to quit. A clinical trial enrolling 1510 individuals revealed that a 24-week course of varenicline effectively promoted smoking cessation in patients who were unwilling to quit but willing to gradually reduce cigarette consumption.[254] Therefore, this agent provides an alternative for patients who cannot or will not attempt abrupt cessation. A clinical trial in 1236 individuals who smoke showed that an additional 12 weeks of varenicline maintenance therapy helped to sustain continued abstinence in those who successfully quit during initial treatment.[255] A 2021 clinical trial among 1251 treatment-seeking individuals found that extended therapy of varenicline for 24 (vs. 12) weeks did not produce higher abstinence rates. Taken together, results of these trials suggest that tailoring extended varenicline therapy to individuals at high risk of relapse may be the most appropriate approach.[256] Additionally, another RCT showed that varenicline was effective and well tolerated for retreating patients who had previously received this agent (n = 498).[257]

Several studies have also suggested that varenicline dose increases beyond the standard 2 mg/day may boost treatment efficacy in patients who had a low or no response to standard dosing.[258-260] A double-blind RCT of 503 patients who smoke found no evidence to suggest that gradual dose titration beyond the standard 2-mg dose (up to a maximum 5

mg/day) lessened frequency of urges and nicotine withdrawal symptoms, or increased cessation rates.[258] However, dose increases did exacerbate adverse effects such as nausea and vomiting for some individuals.[258,260] A propensity score-matched analysis including 214 patients who reduced smoking by 50% but were unable to quit showed that patients who received an increased dosage of varenicline (3 mg/day; n = 72) reported greater 7-day abstinence, compared to patients who maintained the standard dose (2 mg/day; n = 142) at 3- (RR, 2.9; 95% CI, 1.1–4.7; *P* = .004), 6- (RR, 2.5; 95% CI, 1.1–5.2; *P* = .02), and 9-month follow-up (RR, 2.7; 95% CI, 1.2–5.2; *P* = .008), based on models adjusted for imputation and propensity score matching.[259] In patients who have reduced smoking but not yet quit, a dosage increase to 3 mg/day may be considered, if tolerated.

Safety

Varenicline safety has been extensively examined to determine the risk of adverse effects, particularly serious cardiovascular events and neuropsychiatric changes. Initial phase III studies found varenicline to be safe and generally well tolerated compared with bupropion or placebo; common side effects included nausea, insomnia, and abnormal dreams with rates of approximately 28% to 29%, 14%, and 10% to 13%, respectively.[261,262]

Concerns regarding neuropsychiatric adverse effects of varenicline have been extensively investigated in patients who smoke and have comorbid psychiatric disorders.[247] Despite reviews of case reports that raised concern,[241] a 2015 systematic review and meta-analysis of 39 randomized controlled smoking cessation trials identified no evidence to suggest that varenicline increases risk of suicide or suicide attempts, suicidal ideation, depression, or death.[243] Another trial showed that varenicline increased smoking cessation rates without exacerbating anxiety and depression symptoms in adults with stably treated current or past depression.[263] Results were published from a large double-blind RCT (EAGLES trial) that enrolled two cohorts: individuals with psychiatric disorders (n = 4116) and those without psychiatric disorders (n = 4028). No significant increase in neuropsychiatric events was observed for varenicline relative to nicotine patch or placebo. Varenicline was associated with significantly higher abstinence than bupropion plus nicotine patch, as well as placebo.[252]

Cardiovascular risks have also been examined. Importantly, systematic reviews and meta-analyses of RCT data have not identified a significant link between varenicline and increased risk of serious cardiovascular adverse events.[247,264-266] However, the cardiovascular safety of varenicline has remained a topic of interest and concern,[267-269] although the cardiovascular risks of continued smoking has been extensively documented.[65]

In a 2015 retrospective review of 164,766 individuals who received pharmacotherapy for smoking cessation (varenicline, n = 51,450; NRT, n = 106,759; bupropion, n = 6557), neither varenicline nor bupropion posed an elevated risk of cardiovascular or neuropsychiatric (ie, depression, self-harm) events compared with NRT.[270] Based on the current evidence base for safety risks, the panel considers varenicline to be safe and to have a favorable risk/benefit ratio for use in patients with cancer who smoke.

Although rare, elevated seizure risk can be a concern in certain individuals receiving varenicline therapy.[271,272] In patients with a history or seizure disorder or at risk for seizures (eg, patients with brain metastases or primary brain tumors), varenicline should be used with caution. Dose reduction is indicated if there is renal impairment.

In September 2021, one brand of varenicline was voluntarily recalled by the manufacturer due to nitrosamine levels. Generic varenicline is now the only form of varenicline currently available and may be substituted.

Combination Nicotine Replacement Therapy

Efficacy

NRT offers an alternative nicotine delivery method and can be used to ameliorate nicotine withdrawal symptoms during cessation attempts. Combination NRT incorporating long-term and short-acting NRT offers the greatest potential benefits for those who smoke.[225,247,251,273,274] Multiple Cochrane reviews show that, compared with single forms of NRT, combination NRT using a patch plus short-acting NRT improved the odds of quitting.[232,247,251,275] Data show that all forms of NRT are superior to placebo,[276] but people who smoke using combination NRT were almost three times as likely to succeed (OR, 2.73; 95% CI, 2.07–3.65).[247] Regarding duration of use, a 2015 study of 525 individuals seeking treatment for smoking found that NRT duration of 24 weeks was more efficacious that 8 weeks; however, NRT use beyond 24 weeks was safe but did not result in greater efficacy.[239] This study focused on NRT monotherapy and did not vary in duration of dual-use preparations.

The success of NRT is bolstered by concurrent behavior therapy to support cessation. In a large population study, over-the-counter NRT resulted in similar rates of cessation to those who used no aid.[231] The addition of behavior therapy to NRT increased the odds of success nearly three-fold.

Safety

The safety of combination NRT for use in humans, including long-term use, has been demonstrated and benefits are considered to outweigh potential risks.[277] Importantly, providers should be aware that blood nicotine levels from NRT, including combination NRT, are significantly less than that from smoking cigarettes.[278-280] In fact, patients commonly underdose when using combination NRT,[235-237] and although significant nicotine toxicity is possible, it is rare and usually short-lived. Therefore, providers and patients who smoke should not be dissuaded from using NRT to foster quitting and long-term abstinence. Reviews of the data suggest that NRT is not linked to increased serious cardiovascular adverse events when used for smoking cessation.[266,281] While myocardial infarction has rarely been reported in patients who use NRT, there is insufficient evidence that NRT increases the risk of myocardial infarction or cardiovascular disease.[275,276,281,282] Data from large case series have not shown elevated risk with the use of NRT in patients with acute coronary syndromes.[283,284]

In the past, the safety of NRT has been evaluated in light of the bioactivity of nicotine and evidence that this drug can promote cell growth in certain types of cancer cells.[285] Some in vitro data suggested that nicotine increased the malignant potential of small cell lung cancer cells[286]; induced chemoresistance in models using lung cancer cells[167-169] and nasal epithelial cells[170]; and promoted chemoresistance and metastasis in pancreatic cancer cell and mouse models.[171] However, other studies suggested no effects of physiological levels of nicotine exposure on tumorigenesis in mouse lung cancer models.[287,288] Moreover, there is no evidence from human studies that NRT causes cancer in humans.[287-291] Evaluation of data from 3320 participants in the Lung Health Study, which recorded in-study NRT use and smoking exposure, found that NRT was not a significant predictor of lung cancer, while smoking was.[290]

Varenicline + NRT

A study in 435 individuals who smoke found that the addition of nicotine patch to varenicline therapy significantly increased the cessation rates at the end of treatment (12 weeks), at 24 weeks, and at 6-month follow-up.[292] No significant differences were noted for side effect incidence between varenicline/NRT and varenicline/placebo with the exception of skin reactions, which were increased with combination therapy (14.4% vs. 7.8%; $P = .03$). However, one RCT of 341 individuals who smoke did not find enhanced cessation rates at 12- and 24-week follow-up among

individuals receiving a combination of varenicline and nicotine patch, versus varenicline alone.[293] The addition of nicotine patch to varenicline did not cause significant changes in side effect profiles. Similarly, a trial in 117 participants did not find evidence that the addition of nicotine patch to varenicline increased abstinence at 1, 4, or 12 weeks after the targeted quit date, and no between-group differences in adverse effects were found.[294] Based on the evidence, varenicline combined with NRT may be considered as a pharmacotherapy option. Though the studies described above specifically examined the nicotine patch,[292,293] any form of NRT or combination NRT (ie, nicotine patch + short-acting NRT) may be used.

Bupropion + NRT

A large trial in the United Kingdom (n = 1071) examined the efficacy of NRT alone, bupropion alone, and NRT plus bupropion.[295] All participants received 7 weeks of behavior therapy support in addition to the pharmacologic interventions. Abstinence at 6-month follow-up ranged from 24.2% to 27.9% and did not differ significantly between cohorts. Several unwanted side effects were more common with bupropion than NRT (eg, disturbed sleep, dry mouth, headaches, nausea), and side effects of combination therapy were not significantly different versus bupropion alone. Five serious adverse events occurred in the bupropion group, including allergic reaction (n = 3), neuropsychiatric symptoms (n = 1), and chest pain (n = 1). A trend toward improved efficacy of bupropion in patients with a history of depression was noted ($\chi^2 = 2.86$; $P = .091$).

A double-blind RCT compared bupropion + NRT, bupropion alone, nicotine patch alone, and placebo in 893 individuals who smoked at least 15 cigarettes per day. At 12 months, the highest abstinence rates were observed for the bupropion + NRT group (35.5%) and bupropion only group (30.3%), although these groups did not differ significantly.[296] A smaller RCT studying the addition of bupropion to combination NRT and behavior therapy in patients with schizophrenia suggested that combination pharmacotherapy promoted smoking reduction and cessation, but also demonstrated a high relapse rate after discontinuation of treatment.[297] A 2014 meta-analysis of 12 trials examining this combination revealed a nonsignificant trend in improved cessation with the addition of NRT to bupropion.[298]

Bupropion

Bupropion was first approved to treat depression but its efficacy as a cessation aid also became apparent. In addition to its effects on the dopaminergic and adrenergic systems, this agent also acts as an inhibitor of nicotinic acetylcholine receptors. A 2014 Cochrane review of 44 trials examined bupropion efficacy, revealing an RR of 1.62 (95% CI, 1.49–1.76).[298] Results from the EAGLES trial (n = 8144) revealed that patients receiving bupropion achieved superior abstinence compared with placebo (OR, 2.07; 95% CI, 1.75–2.45).[252] Efficacy was similar to nicotine patch but less than that for varenicline. Some evidence suggests that bupropion may be particularly beneficial as a smoking cessation agent for persons with depression.[295,299] Additionally, longer duration of bupropion treatment may help to prevent relapse in those who have successfully quit.[300]

Bupropion is a CYP2B6 inhibitor and may increase the concentration of drugs that metabolize or that also inhibit CYP2B6 (ie, certain antidepressants, antipsychotics, beta-blockers, and Type 1C antiarrhythmics).[301] Dose reduction of these agents may be considered when used concurrently with bupropion. The selective estrogen receptor modulator tamoxifen requires metabolic activation by CYP2D6 and may be less effective when used concurrently with a CYP2B6 inhibitor such as bupropion.[302] Bupropion reduces the seizure threshold, and meta-analyses of trial data have found a 0.1% seizure risk among those receiving the drug for smoking cessation.[298] In patients with seizure risk (eg, patients with brain metastases or primary brain tumors who have a history or elevated risk of seizure), bupropion should be avoided. Bupropion is

contraindicated for those taking monoamine oxidase inhibitors (MAOIs), those with a current diagnosis or history of anorexia or bulimia, or in cases of abrupt discontinuation of alcohol, benzodiazepines, barbiturates, or antiepileptic drugs. Bupropion is a norepinephrine-dopamine reuptake inhibitor; central nervous system (CNS) toxicity may occur when used concurrently with other dopaminergic drugs.

Neuropsychiatric effects have also been identified as a safety concern with bupropion, although to a lesser extent than with varenicline.[241] However, systematic reviews of the data have found that serious neuropsychiatric adverse events were rarely associated with bupropion prescribed for smoking cessation, including studies of bupropion in patients with mental illness.[247,303] In the EAGLES trial, no significant increase in neuropsychiatric events was observed for bupropion relative to nicotine patch or placebo.[252]

Regarding risk of serious adverse cardiovascular effects, meta-analyses do not show elevated risk as a result of bupropion use for smoking cessation.[247,266,298] Dose adjustments/reductions are indicated in the event of renal or hepatic impairment.[301]

Varenicline + Bupropion

In an RCT of individuals who smoke who demonstrated an inadequate response to front-line nicotine patch treatment (n = 222), combination therapy with varenicline and bupropion appeared to be more efficacious than varenicline alone as a second-line therapy option.[304] This observation was more pronounced among males and those with a high level of nicotine dependency. Although no significant differences in side effects were observed between varenicline and bupropion versus varenicline alone, dose reductions were required for 11.5% and 24.8% of patients, respectively. Common side effects were vivid dreams, change in taste perception, thirst, insomnia, and irritability. In a follow-up to this study, males who smoke (*N* = 174) were randomized to receive combination varenicline + bupropion or varenicline alone.[305] Like the previous study, the combination therapy was more efficacious than varenicline alone in those with a higher baseline level of nicotine dependence (n = 63; OR, 3.14; 95% CI, 1.11–8.92; *P* [one-tailed] = .016). Another study of varenicline + bupropion therapy versus varenicline alone (n = 316) demonstrated that combination therapy increased prolonged abstinence but did not affect 7-day point prevalence at 12- and 26-week follow-up, and no significant differences were observed between the groups at 52 weeks.[306] In this study, anxiety (7.2% vs. 3.1%; *P* = .04) and depressive symptoms (3.6% vs. 0.8%; *P* = .03) occurred more frequently in patients receiving combination therapy versus varenicline alone. In an RCT (n = 385), the addition of bupropion to varenicline did not improve prolonged abstinence at 12 months compared with varenicline alone, although both regimens were superior to placebo.[307] The diversity in populations used for these studies makes it difficult to draw conclusions about the efficacy of combination varenicline and bupropion, and this regimen is not commonly used as a first-line approach.

Principles of Behavioral Treatment of Smoking

General Principles

The Guidelines provide the following guiding principles on behavior therapy, which have been developed in consideration of the existing evidence base, clinical practice guidelines, and expert consensus.[232,233,277]

The panel recommends a combination of behavior therapy with pharmacotherapy for best outcomes. In fact, studies suggest that counseling for smoking cessation may enhance patient satisfaction.[23,24] A 2012 systematic review of 41 studies provided support for the efficacy of this approach.[232] The “real world effectiveness” of adding a behavior therapy component to smoking cessation therapy was further supported by a large population study published in 2014.[231] Additionally, a 2016 meta-analysis of data from 1239 patients with head and neck cancer

showed improved smoking cessation rates with the addition of counseling to usual care (NRT).[308] A systematic review published in 2023, which included 17 RCTs and 19 non-RCT studies, also supported a combined behavioral and pharmacologic approach, but the ability to draw firm conclusions in this area is limited by study flaws, such as absence of biochemical verification of abstinence.[234]

Behavior therapy may enhance motivation and support optimal medication strategies and adherence to pharmacotherapy. When possible, therapy should be provided by a tobacco treatment specialist or dedicated staff member (ie, nurse, medical assistant, health educator) with training in evidence-based treatment of smoking.

As a general principle, the panel recommends more intensive and sustained behavior therapy over brief advice or counseling.[233,309,310] However, brief counseling is better than no counseling. The evidence supports a measurable dose-response effect of behavior therapy with more numerous and/or longer sessions delivering improved cessation rates.[233,311,312] An RCT published in 2020 including 303 patients with cancer who also smoke cigarettes showed that those randomized to receive intensive treatment (free FDA-approved cessation medication and four weekly telephone counseling sessions, followed by 4 biweekly telephone sessions and 3 monthly booster sessions) were more likely to have quit smoking at 6-month follow-up (biochemically confirmed) than patients who received standard treatment (medication advice and 4 weekly telephone counseling sessions) (35% vs. 17%, respectively; OR, 2.15; 95% CI, 1.14–4.05; $P = .02$).[310] Among patients in the intensive treatment group, completion of more counseling sessions, but not medication use, was significantly associated with likelihood of quitting.

The panel recommends that the first counseling session occur within 3 weeks of cessation, but preferably within 1 week as a majority of people who smoke relapse during this period.[313] The panel defines intensive behavior therapy as at least four sessions of at least 10 minutes (in person and/or by phone/telehealth; group or individual), ideally. As described above, longer, more frequent sessions are associated with higher abstinence rates.[309] If intensive therapy is not feasible, brief counseling of about 3 minutes should still be given. Studies have demonstrated a small but significant increase in smoking abstinence rates with brief counseling lasting only a few minutes.[57,58,314,315] As patients progress through multiple lines of pharmacotherapy, behavior therapy should be progressively intensified with referral to specialty care (eg, tobacco treatment specialist, psychologist) as indicated. Studies have also demonstrated additional benefit for relapse prevention of extending behavior therapy for 6 months or more.[316-318]

The most successful behavior therapy strategies use practical counseling in which patients learn coping skills and receive support and education. Optimally, behavior therapy plans should take into account the presence of a nicotine use disorder, previous quit attempts, and cessation aids utilized. In doing so, patients can be equipped with tailored strategies to cope with nicotine withdrawal symptoms, environmental smoking triggers (eg, coffee, alcohol, social situations), and stressful situations. For instance, the addition of a cognitive behavior therapy program designed to improve stress management improved cessation rates over controls receiving standard smoking cessation therapy.[319] The presence of other household members who smoke is a predictor of relapse or sustained smoking,[320,321] and there is no risk-free level of secondhand smoke exposure among those who don't smoke by causing lung cancer, heart disease, and acute respiratory effects.[7] Therefore, individuals in the patient's household who smoke should also be encouraged to abstain from smoking to benefit the patient. Providers should prepare patients for nicotine withdrawal symptoms and cravings, which typically peak 48 to 72 hours after quitting and last about 2 to 3 weeks before gradually subsiding.[322-324]

A number of modalities can be used to deliver behavior therapy to patients. Counseling can take place in a variety of settings such as in person, remotely by phone or telehealth,[61,325,326] or through web-based interventions.[327,328] Effective in-person counseling can occur as an individual session or in the group therapy setting.[329,330] Additionally, print materials[331] and mobile telephone "apps"[332-334] can be used to deliver behavior therapy. However, providers should be aware that media-based behavioral interventions, particularly those using mobile telephones, might vary in the degree to which they comply with clinical practice guidelines.[335] Digital resources such as the NCI's smokefree.gov provide free, evidence-based cessation support through mobile-optimized websites, text messaging programs, and two mobile applications. A study revealed that approximately 7 to 8 million people accessed smokefree.gov resources in 2018 alone and that people do take advantage of the full range of technology tools.[336]

A study investigating preferences for the provision of smoking cessation information among Canadian patients with cancer showed that patients most often preferred print materials (45%), followed by telephone support (39%), speaking with a clinician (29%), website-based information (15%), and support groups (11%). Patients ≤45 years were more likely to prefer cessation advice via telephone, while patients ≥46 years preferred print materials.[337] Selection of a particular modality or modalities should be guided by patient preference, medical history, and resource availability. A meta-analysis including 21 RCTs targeting smoking cessation in cancer survivors showed larger effects with interventions delivered by nurses, compared to interventions delivered by others (eg, research team, doctor, educator, counselor/therapist).[338]

For patients who are unable to quit, referral to a smoking cessation specialist is encouraged when available. If specialized resources are limited, effective behavior counseling can still be provided. For instance, brief counseling by providers has been shown to generate a small but important increase in quit rates.[57-59] Additionally, quitlines can provide essential behavioral support in the absence of in-person counseling resources.[61] For instance, the addition of combination NRT to quitline counseling improved cessation outcomes.[339]

Tailoring Behavior Therapy for Patients with Cancer

As resources allow, specialized treatment centers should provide tailored treatment for smoking that address the unique needs of patients with cancer, or refer to external resources (eg, quitlines) that provide such specialized services. For patients in active cancer treatment, behavior therapy can be provided during scheduled oncology visits to obviate the need for additional appointments. Interventions initiated during hospital stays have also been successful. Intensive behavioral interventions provided during hospitalization, with at least 1 month of subsequent follow-up upon discharge, increased smoking cessation rates.[311] Beneficial services might include individual and group therapy focusing on the challenges specific to cancer treatment and survival, which would ideally be provided by clinicians experienced in working with patients with cancer. One study suggested age-based differences in preferences for smoking cessation resources.[337]

The prevalence of psychiatric disorders or serious emotional concerns in patients with cancer is high, with several large studies reporting rates between 30% and 40%.[340-342] The high rates of anxiety, depression, and stress can present a significant challenge for patients with cancer who attempt to quit smoking in the face of these common smoking/relapse triggers. Providers should routinely assess for these symptoms among those who smoke throughout treatment for smoking. Patients with cancer, particularly those experiencing psychiatric comorbidity, may benefit significantly from behavior therapy programs tailored to manage cancer-related issues that predispose patients to relapse. Referral for appropriate

evaluation and treatment as needed or to specialized smoking treatment programs may be necessary so that these patients have access to staff trained to treat psychiatric and/or substance use disorders.

Motivational Enhancement

All patients with and survivors of cancer should be encouraged to quit. Strategies to enhance motivation to quit are beneficial for all patients, including those who are currently ambivalent or unwilling to quit. MI is one evidence-based approach to foster motivation to quit in which a clinician offers empathy as the patient explores ambivalence regarding quitting smoking. Clinicians reflect, validate, and summarize patient emotions and concerns and help patients identify discrepancies between smoking and core values/goals (eg, health, parenting) and support patient confidence to achieve and maintain abstinence.[36,204,205]

A 2015 Cochrane database review of 28 studies examined the efficacy of MI for smoking cessation, revealing a modest but significant increase in chance of quitting with MI versus brief advice or usual care.[343] MI by a primary care physician appeared to be somewhat more successful than that administered by counselors, although both were effective. Notably, one-time short MI sessions of less than 20 minutes had demonstrated efficacy.[343] One systematic review summarized the evidence to support MI for behavioral change, including smoking cessation, in patients with cancer.[344]

In order to promote willingness to quit smoking, the US Preventive Services Task Force (USPSTF) recommends a model of MI that uses the "5 R's" of the personal Relevance of quitting; personal Risks of continuing smoking; personal Rewards of quitting; identifying Roadblocks to quitting; and Repeating the message at every contact.[277] This model encourages that motivational information be relevant to the individual patient, and that clinicians and patients work together to identify personalized risks of smoking and potential rewards of cessation. By having the patient identify perceived roadblocks to quitting, providers can suggest tailored treatments to address patient-reported concerns. Finally, this model recommends repetition of MI at each patient visit, coupled with reminders that repeated quit attempts may be necessary to achieve long-term cessation.

Alternative Treatment Approaches

The panel has reviewed the available evidence for several alternative smoking cessation treatment approaches. With any approach, it is critical to continue to provide motivational and behavioral support to all patients during quit attempts, regardless of what smoking cessation methods are being used. At the current time, e-cigarettes are not an FDA-approved method for smoking treatment, but its potential as a smoking cessation aid continues to be considered by the panel. Particular attention has been paid to the discussion of e-cigarettes for smoking treatment given increasing popularity and widespread use, and not fostering dual use with cigarettes. Limited data are available on the safety and efficacy of these approaches, specifically for patients with cancer; data have been drawn primarily from studies in the general population.

The panel has found insufficient evidence to recommend the use of alternative therapies alone or in combination with standard smoking treatment approaches, and use of alternative therapies is not recommended. The guidelines recommend that patients use evidence-based cessation methods to avoid any delay in achieving smoking abstinence. Smoking slips and relapses are common, and prior unsuccessful quit attempts with conventional therapies do not justify the use of unproven alternative approaches. When discussing alternative therapies, providers should counsel patients on potential interactions with evidence-based cessation methods and/or cancer treatments.

Electronic Cigarettes ("E-Cigarettes")/Vaping

The popularity of electronic cigarettes, also known as e-cigarettes or vaping, is a recent phenomenon, and, as such, the available literature is new and relatively limited, particularly within specific subpopulations such as patients with cancer. As stated above, e-cigarettes are currently not FDA-approved for the treatment of smoking. The FDA may authorize the sale of select electronic nicotine delivery system products as modified-risk tobacco products. Below is a discussion of the current data and expert opinions on e-cigarettes for smoking cessation.

Several health care organizations have released similar policy statements concerning e-cigarettes, highlighting the urgent need for research on the safety of these devices and efficacy as a cessation aid. The American Heart Association, American Cancer Society (ACS), AACR, and ASCO recognize the potential for e-cigarettes to alter existing smoking behaviors, as well as the lack of definitive data regarding associated benefits and harms.[345,346] Experts in the field generally acknowledge that e-cigarettes may offer an attractive approach for smoking cessation in certain populations. However, these policy statements also highlight the unknown potential for e-cigarettes to affect symptoms associated with nicotine use disorder, combustible tobacco product use, and renormalization of smoking behaviors. Concurrent use of both e-cigarettes and combustible cigarettes is strongly discouraged by the ACS.[347] In their 2021 statement, the USPSTF concluded that the current evidence is insufficient to recommend e-cigarettes for tobacco cessation and that smoking treatment efforts should continue to focus on behavioral counseling and pharmacotherapy.[348] Dual use of smoking cigarettes and e-cigarettes is associated with high exposure to tobacco toxicants.[349,350]

Efficacy and Effectiveness in the General Population

In the first head-to-head comparison, an RCT (n = 886) compared e-cigarettes to NRT (combination NRT allowed), paired with at least 4 weeks of behavioral support.[351] Abstinence rates at 1 year were 18% and 9.9% for e-cigarettes and NRT, respectively (RR, 1.83; 95% CI, 1.30–2.58; $P < .001$). However, prolonged e-cigarette use extended beyond the initial treatment period, particularly among abstainers, with unclear health implications.[351] In a real-world setting, people who smoke who reported dual use of e-cigarettes were more likely to report abstinence at 6 months, but this pattern was no longer present at 12 or 18 months.[352] A 2022 Cochrane review found better abstinence from smoking rates with nicotine e-cigarettes, compared to NRT, with high certainty (RR, 1.63; 95% CI, 1.30–2.04).[353] However, this difference is most likely due to dose; specifically, e-cigarette use provides an on-demand continuous supply of nicotine, with some doses equivalent to that for cigarette smoking.

Initiation of e-cigarette use may lead to long-term use and the continued dual use of both e-cigarettes and cigarettes, which has greater health risk concerns. Although individuals using e-cigarettes alone or NRT alone had lower levels of toxins than those using combustible cigarettes only, toxicant exposure was greatest among those who use both e-cigarette and combustible cigarettes.[350,354] A prospective cohort study compared e-cigarette use, tobacco use, and dual use with longer-term follow-up. At 24 months, those who used only e-cigarettes were more likely to remain abstinent from other tobacco products than those who used only tobacco or those who used both e-cigarettes and tobacco (abstinence rates of 61.1%, 23.1%, and 26.0%, respectively).[355] Analyses of adults who used e-cigarettes and enrolled in the Population Assessment of Tobacco and Health Study (n = 2835), an ongoing longitudinal cohort study, showed that 48.8% had quit both e-cigarettes and combustible cigarettes over a 1-year period (2013–2014 and 2014–2015), while 11.4% decreased their frequency of e-cigarette use.[356] However, it is important to note that there are now more potent e-cigarette products available. Therefore, these results may not be generalizable to the present day. The same study showed that, among baseline dual users (n = 2036), 87.8% reported

continued smoking of combustible cigarettes at the time of follow-up assessment. Among those who smoked solely e-cigarettes at baseline (n = 869), 43.4% continued to smoke e-cigarettes after 1 year, while 30.9% had quit smoking e-cigarettes. Non-daily e-cigarette use at baseline was associated with discontinued e-cigarette use at the time of follow-up assessment. However, those who used e-cigarettes daily at baseline were more likely to report having quit combustible cigarettes after 1 year, compared to those with non-daily use. Similar associations were found in a large cohort study of individuals who smoke initially not using e-cigarettes and with no plans to ever quit smoking.[357] Abstinence rates of cigarettes after 12 months were higher in those who used e-cigarettes daily, compared to those who did not (28.0% vs. 5.8%, respectively; OR, 8.11; 95% CI, 3.14–20.97). However, non-daily e-cigarette use was not associated with abstinence from cigarettes (OR, 0.53; 95% CI, 0.08–3.35).

Several systematic reviews and meta-analyses have reported somewhat divergent findings. A meta-analysis of 20 controlled studies (2 trials, 15 cohort studies, and 3 cross-sectional studies) by Kalkhoran and Glantz (2016) calculated that individuals using e-cigarettes were 28% less likely to achieve smoking cessation (OR, 0.72; 95% CI, 0.57–0.91).[358] Similarly, a 2020 systematic review including 13 studies suggested that e-cigarettes were not significantly associated with increased smoking cessation among individuals who smoke cigarettes.[359] Two additional meta-analyses published in 2016 concluded that, based on low- or very-low-quality evidence, e-cigarettes may be helpful for smoking reduction and possibly cessation for some who smoke.[360,361] A more recent and comprehensive Cochrane review published in 2021, which included 61 total studies, showed that quitting cigarettes for 6 months or longer was more likely in those who used nicotine-containing e-cigarettes, compared to NRT (four studies with moderate certainty; RR, 1.53; 95% CI, 1.21–1.93), nicotine-free e-cigarettes (five studies with moderate certainty; RR, 1.94; 95% CI, 1.21–3.13), and behavioral or no treatment (six studies with very low certainty; RR, 2.61; 95% CI, 1.44–4.74).[362]

A large cross-sectional survey of 5863 adults in the United Kingdom assessed the “real-world effectiveness” of e-cigarettes for smoking cessation compared to NRT and unaided quitting, revealing that those who use e-cigarettes were more likely to self-report abstinence from cigarettes compared with the other cohorts (e-cigarettes vs. NRT: OR, 2.23; 95% CI, 1.70–2.93; e-cigarettes vs. no aid: OR, 1.38; 95% CI, 1.08–1.76).[363] However, it is important to note that e-cigarettes in the U.K. are different than those in the U.S., which lags in product regulation in the real-world marketplace.

Federal, state, and local health departments investigated e-cigarette or vaping use-associated lung injury (EVALI). EVALI is associated with respiratory, constitutional, and gastrointestinal symptoms,[364] with about half of patients experiencing EVALI requiring intensive care for respiratory failure.[365] Factors correlated with EVALI-associated death include age ≥35 years, obesity, and the presence of a chronic medical condition (ie, chronic respiratory disease and cardiac disease).[366] An analysis of bronchoalveolar lavage (BAL) fluid in 51 patients with EVALI and 99 patients without EVALI (including patients who never smoke, patients who smoke combustible cigarettes, and patients who smoke e-cigarettes) showed that vitamin E acetate was found in 94% of patients with EVALI and in none of the comparators, making it the likely causative agent.[367] Vitamin E acetate is often added to THC (the active ingredient in cannabis) vaping liquids as a diluting or thickening agent. Limonene and coconut oil were found in the BAL fluid of two patients with EVALI (1 patient each), but no other potentially toxic substances (eg, plant oil, petroleum distillates) were found. The reporting structure for these events has been officially closed.

Studies in Patients with Cancer

One study examined e-cigarette use in 1074 patients with cancer who enrolled in a tobacco treatment program at a comprehensive cancer center.[368] The study revealed a marked increase in e-cigarette use from 10.6% to 38.5% between 2012 and 2013. Patients who use e-cigarettes, most often diagnosed with thoracic or head and neck cancers, were more nicotine dependent and had greater numbers of prior quit attempts. At follow-up (6–12 months after intake), patients who use e-cigarettes were no more likely to have quit than patients who did not use e-cigarettes (OR, 1.0; 95% CI, 0.5–1.7), calling into question the potential benefits of e-cigarettes as a cessation agent for patients with cancer. Two cross-sectional studies of cancer survivors in the United States showed that e-cigarette use was highest among patients who currently smoke cigarettes, compared with patients who formerly smoked or who never smoked cigarettes.[369,370] Two other cross-sectional studies including cancer survivors showed that e-cigarette use was associated with current cigarette smoking.[371,372] Collectively, these studies highlight the importance of screening and addressing e-cigarette usage by patients with cancer and cancer survivors.

E-cigarette use did not decrease cigarette smoking in a cross-sectional study in 106 patients with head and neck cancers seeking to quit. Those who abstained from using e-cigarettes had a significantly greater rate of cessation compared with patients who use e-cigarettes (72% vs. 39%; P = .0057).[373] Another cross-sectional study surveyed 121 patients with cancer who were currently using e-cigarettes.[374] Eighty-one percent of these surveyed patients who use e-cigarettes reported smoking cessation as their motivation for initiating e-cigarette use, but 51% also reported dual use of combustible cigarettes with e-cigarettes. Additionally, more than 70% reported that they had not discussed their e-cigarette use with their oncology care providers.

NCCN Recommendations

At the current time, e-cigarettes are not an FDA-approved method for smoking treatment. It is not yet clear how factors such as real-world use or the addition of behavior therapy may influence the efficacy, safety, and effectiveness of e-cigarettes. Patients should be counseled toward the use of evidence-based smoking treatment approaches. For patients who choose to use e-cigarettes for smoking cessation, despite recommendations to use evidence-based methods, encourage smoking abstinence even if this is by the use of e-cigarettes, and incorporate behavioral counseling, given the harm to one's health that is associated with smoking combustible cigarettes. For patients who use both e-cigarettes and combustible tobacco, complete smoking cessation is recommended. Dual use is strongly discouraged, as it continues to pose a risk of smoking-related diseases.[375-377] When the patient develops more confidence about not smoking, cessation of e-cigarettes should be encouraged, but not at the risk of relapse to smoking combustible products.

Other Alternative Approaches

Very limited data exist to support exercise-based interventions; small study size, inadequate controls, and insufficient exercise intensity limit the ability to make conclusions based on the existing evidence.[378] Sufficient efficacy data are also lacking to support the use of alternative therapies such as acupuncture, hypnosis, and nutritional supplements. A 2014 systematic review of the data on acupuncture, acupressure, and laser therapy revealed no consistent, bias-free evidence to support these methods for smoking cessation, although pooled evidence was suggestive of possible short-term benefits.[379] Acupuncture was less effective than NRT and there was no evidence to support electrostimulation for smoking cessation. Similarly, systematic reviews of the data on hypnosis for smoking cessation revealed inadequate high-quality evidence to support this approach.[380,381] Claims of efficacy data for hypnosis from several

studies were not substantiated by the review of RCT data. Controlled studies are needed to provide higher quality evidence on these interventions both in the general population and among patients with cancer.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. CA Cancer J Clin 2019;69:7-34. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30620402.

2. Cancer and tobacco use. CDC Vital Signs. Atlanta: Centers for Disease Control and Prevention; 2016. Available at: https://www.cdc.gov/vitalsigns/pdf/2016-11-vitalsigns.pdf.

3. Lortet-Tieulent J, Goding Sauer A, Siegel RL, et al. State-level cancer mortality attributable to cigarette smoking in the United States. JAMA Intern Med 2016;176:1792-1798. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27775761.

4. 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.

5. Tao L, Wang R, Gao YT, Yuan JM. Impact of postdiagnosis smoking on long-term survival of cancer patients: the Shanghai cohort study. Cancer Epidemiol Biomarkers Prev 2013;22:2404-2411. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24319070.

6. Passarelli MN, Newcomb PA, Hampton JM, et al. Cigarette smoking before and after breast cancer diagnosis: Mortality from breast cancer and smoking-related diseases. J Clin Oncol 2016;34:1315-1322. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26811527.

7. The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services 2014. Available at: https://www.ncbi.nlm.nih.gov/books/NBK179276/pdf/Bookshelf_NBK179276.pdf.

8. Warren GW, Cartmell KB, Garrett-Mayer E, et al. Attributable failure of first-line cancer treatment and incremental costs associated with smoking by patients with cancer. JAMA Netw Open 2019;2:e191703. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30951159.

9. Underwood JM, Townsend JS, Tai E, et al. Persistent cigarette smoking and other tobacco use after a tobacco-related cancer diagnosis. J Cancer Surviv 2012;6:333-344. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22706885.

10. Parsons A, Daley A, Begh R, Aveyard P. Influence of smoking cessation after diagnosis of early stage lung cancer on prognosis: systematic review of observational studies with meta-analysis. BMJ 2010;340:b5569. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20093278.

11. Warren GW, Kasza KA, Reid ME, et al. Smoking at diagnosis and survival in cancer patients. Int J Cancer 2013;132:401-410. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22539012.

12. Dobson Amato KA, Hyland A, Reed R, et al. Tobacco cessation may improve lung cancer patient survival. J Thorac Oncol 2015;10:1014-1019. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26102442.

13. Sheikh M, Mukeriya A, Shangina O, et al. Postdiagnosis smoking cessation and reduced risk for lung cancer progression and mortality: a prospective cohort study. Ann Intern Med 2021;174:1232-1239. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34310171.

14. Baser S, Shannon VR, Eapen GA, et al. Smoking cessation after diagnosis of lung cancer is associated with a beneficial effect on performance status. Chest 2006;130:1784-1790. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17166997.

15. Treating Smoking in Cancer Patients: An Essential Component of Cancer Care. In: U.S. Department of Health and Human Services NIoH, National Cancer Institute ed. National Cancer Institute Tobacco Control Monograph 23. Bethesda, MD; 2022. Available at: https://cancercontrol.cancer.gov/brp/tcrb/monographs/monograph-23#:~:text=Monograph%2023%20Treating%20Smoking%20in,Essential%20Component%20of%20Cancer%20Care&text=Smoking%20adversely%20impacts%20oncologic%20and,experience%20multiple%20benefits%20by%20quitting.

16. Park ER, Japuntich SJ, Rigotti NA, et al. A snapshot of smokers after lung and colorectal cancer diagnosis. Cancer 2012;118:3153-3164. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22271645.

17. Westmaas JL, Alcaraz KI, Berg CJ, Stein KD. Prevalence and correlates of smoking and cessation-related behavior among survivors of ten cancers: findings from a nationwide survey nine years after diagnosis. Cancer Epidemiol Biomarkers Prev 2014;23:1783-1792. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25100826.

18. Mayer DK, Carlson J. Smoking patterns in cancer survivors. Nicotine Tob Res 2011;13:34-40. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21097514.

19. Toll BA, Brandon TH, Gritz ER, et al. Assessing tobacco use by cancer patients and facilitating cessation: an American Association for Cancer Research policy statement. Clin Cancer Res 2013;19:1941-1948. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23570694.

20. Hanna N, Mulshine J, Wollins DS, et al. Tobacco cessation and control a decade later: American society of clinical oncology policy statement update. J Clin Oncol 2013;31:3147-3157. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23897958.

21. Gallaway MS, Tai E, Rohan EA. Smoking cessation treatment programs offered at hospitals providing oncology services. J Smok Cessat 2019;14:65-71. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30057648.

22. Goldstein AO, Ripley-Moffitt CE, Pathman DE, Patsakham KM. Tobacco use treatment at the U.S. National Cancer Institute's designated Cancer Centers. Nicotine Tob Res 2013;15:52-58. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22499079.

23. Barzilai DA, Goodwin MA, Zyzanski SJ, Stange KC. Does health habit counseling affect patient satisfaction? Prev Med 2001;33:595-599. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11716655.

24. Conroy MB, Majchrzak NE, Regan S, et al. The association between patient-reported receipt of tobacco intervention at a primary care visit and smokers' satisfaction with their health care. Nicotine Tob Res 2005;7 Suppl 1:S29-34. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16036267.

25. Weaver KE, Danhauer SC, Tooze JA, et al. Smoking cessation counseling beliefs and behaviors of outpatient oncology providers. Oncologist 2012;17:455-462. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22334454.

26. Warren GW, Marshall JR, Cummings KM, et al. Addressing tobacco use in patients with cancer: a survey of American Society of Clinical Oncology members. J Oncol Pract 2013;9:258-262. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23943904.

27. Warren GW, Marshall JR, Cummings KM, et al. Practice patterns and perceptions of thoracic oncology providers on tobacco use and cessation in cancer patients. J Thorac Oncol 2013;8:543-548. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23529191.

28. Warren GW, Dibaj S, Hutson A, et al. Identifying targeted strategies to improve smoking cessation support for cancer patients. J Thorac Oncol 2015;10:1532-1537. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26317914.

29. Gritz ER, Dresler C, Sarna L. Smoking, the missing drug interaction in clinical trials: ignoring the obvious. Cancer Epidemiol Biomarkers Prev 2005;14:2287-2293. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16214906.

30. Peters EN, Torres E, Toll BA, et al. Tobacco assessment in actively accruing National Cancer Institute Cooperative Group Program Clinical Trials. J Clin Oncol 2012;30:2869-2875. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22689794.

31. McAfee T, Babb S, McNabb S, Fiore MC. Helping smokers quit--opportunities created by the Affordable Care Act. N Engl J Med

2015;372:5-7. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25409263.

32. Ramsey AT, Chiu A, Baker T, et al. Care-paradigm shift promoting smoking cessation treatment among cancer center patients via a low-burden strategy, electronic health record-enabled evidence-based smoking cessation treatment. Transl Behav Med 2020;10:1504-1514. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31313808.

33. Eng L, Alton D, Song Y, et al. Awareness of the harms of continued smoking among cancer survivors. Support Care Cancer 2020;28:3409-3419. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31781945.

34. Twyman L, Bonevski B, Paul C, Bryant J. Perceived barriers to smoking cessation in selected vulnerable groups: a systematic review of the qualitative and quantitative literature. BMJ Open 2014;4:e006414. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25534212.

35. Chapple A, Ziebland S, McPherson A. Stigma, shame, and blame experienced by patients with lung cancer: qualitative study. BMJ 2004;328:1470. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15194599.

36. Schnoll RA, Malstrom M, James C, et al. Correlates of tobacco use among smokers and recent quitters diagnosed with cancer. Patient Educ Couns 2002;46:137-145. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11867244.

37. Morgan G, Schnoll RA, Alfano CM, et al. National cancer institute conference on treating tobacco dependence at cancer centers. J Oncol Pract 2011;7:178-182. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21886500.

38. Mazza R, Lina M, Boffi R, et al. Taking care of smoker cancer patients: a review and some recommendations. Ann Oncol 2010;21:1404-1409. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20089563.

39. Aigner CJ, Cinciripini PM, Anderson KO, et al. The association of pain with smoking and quit attempts in an electronic diary study of cancer patients trying to quit. Nicotine Tob Res 2016;18:1449-1455. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26038362.

40. Eng L, Qiu X, Su J, et al. The role of second-hand smoke exposure on smoking cessation in non-tobacco-related cancers. Cancer 2015;121:2655-2663. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25877384.

41. Wells M, Aitchison P, Harris F, et al. Barriers and facilitators to smoking cessation in a cancer context: A qualitative study of patient, family and professional views. BMC Cancer 2017;17:348. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28526000.

42. Carroll AJ, Veluz-Wilkins AK, Blazekovic S, et al. Cancer-related disease factors and smoking cessation treatment: Analysis of an ongoing clinical trial. Psychooncology 2018;27:471-476. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28636795.

43. Guydish J, Tajima B, Pramod S, et al. Use of multiple tobacco products in a national sample of persons enrolled in addiction treatment. Drug Alcohol Depend 2016;166:93-99. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27449271.

44. Huh Y, Min Lee C, Cho HJ. Comparison of nicotine dependence between single and multiple tobacco product users among South Korean adults. Tob Induc Dis 2022;20:22. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35291560.

45. Ramaswamy AT, Toll BA, Chagpar AB, Judson BL. Smoking, cessation, and cessation counseling in patients with cancer: A population-based analysis. Cancer 2016;122:1247-1253. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26881851.

46. Day FL, Sherwood E, Chen TY, et al. Oncologist provision of smoking cessation support: A national survey of Australian medical and radiation oncologists. Asia Pac J Clin Oncol 2018;14:431-438. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29706029.

47. Conlon K, Pattinson L, Hutton D. Attitudes of oncology healthcare practitioners towards smoking cessation: A systematic review of the facilitators, barriers and recommendations for delivery of advice and support to cancer patients. Radiography (Lond) 2017;23:256-263. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28687295.

48. Nolan M, Ridgeway JL, Ghosh K, et al. Design, implementation, and evaluation of an intervention to improve referral to smoking cessation services in breast cancer patients. Support Care Cancer 2019;6:2153-2158. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30284040.

49. Japuntich SJ, Luberto CM, Streck JM, et al. Integrating tobacco treatment into thoracic oncology settings: Lessons learned. J Health Psychol 2016;21:2813-2823. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26044717.

50. Ramsey AT, Baker TB, Stoneking F, et al. Increased reach and effectiveness with a low-burden point-of-care tobacco treatment program in cancer clinics. J Natl Compr Canc Netw 2022;20:488-495 e484. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35545172.

51. Jenssen BP, Schnoll R, Beidas RS, et al. Cluster randomized pragmatic clinical trial testing behavioral economic implementation strategies to improve tobacco treatment for patients with cancer who smoke. J Clin Oncol 2023:JCO2300355. Available at: https://www.ncbi.nlm.nih.gov/pubmed/37467454.

52. Martinez E, Tatum KL, Weber DM, et al. Issues related to implementing a smoking cessation clinical trial for cancer patients. Cancer Causes Control 2009;20:97-104. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18758971.

53. Cinciripini PM, Karam-Hage M, Kypriotakis G, et al. Association of a comprehensive smoking cessation program with smoking abstinence among patients with cancer. JAMA Netw Open 2019;2:e1912251. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31560387.

54. Gritz ER, Fingeret MC, Vidrine DJ, et al. Successes and failures of the teachable moment: smoking cessation in cancer patients. Cancer 2006;106:17-27. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16311986.

55. Westmaas JL, Newton CC, Stevens VL, et al. Does a recent cancer diagnosis predict smoking cessation? An analysis from a large prospective US cohort. J Clin Oncol 2015;33:1647-1652. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25897151.

56. Tang MW, Oakley R, Dale C, et al. A surgeon led smoking cessation intervention in a head and neck cancer centre. BMC Health Serv Res 2014;14:636. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25527115.

57. Stead LF, Buitrago D, Preciado N, et al. Physician advice for smoking cessation. Cochrane Database Syst Rev 2013;5:CD000165. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23728631.

58. Coleman T. ABC of smoking cessation. Use of simple advice and behavioural support. BMJ 2004;328:397-399. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14962878.

59. Aveyard P, Begh R, Parsons A, West R. Brief opportunistic smoking cessation interventions: a systematic review and meta-analysis to compare advice to quit and offer of assistance. Addiction 2012;107:1066-1073. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22175545.

60. Lee SM, Landry J, Jones PM, et al. The effectiveness of a perioperative smoking cessation program: a randomized clinical trial. Anesth Analg 2013;117:605-613. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23868890.

61. Stead LF, Hartmann-Boyce J, Perera R, Lancaster T. Telephone counselling for smoking cessation. Cochrane Database Syst Rev 2013;8:CD002850. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23934971.

62. Lichtenstein E, Zhu SH, Tedeschi GJ. Smoking cessation quitlines: an underrecognized intervention success story. Am Psychol 2010;65:252-261. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20455619.

63. American Indians/Alaska Natives and Tobacco Use: Centers of Disease Control and Prevention; 2019. Available at: https://www.cdc.gov/healthytribes/native-american-smoking.html.

64. Sobus SL, Warren GW. The biologic effects of cigarette smoke on cancer cells. Cancer 2014;120:3617-3626. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25043526.

65. Smoking Cessation: A Report of the Surgeon General. Rockville, MD: U.S. Department of Health and Human Services; 2020. Available at: https://www.cdc.gov/tobacco/sgr/2020-smoking-cessation/index.html.

66. Rink M, Zabor EC, Furberg H, et al. Impact of smoking and smoking cessation on outcomes in bladder cancer patients treated with radical cystectomy. Eur Urol 2013;64:456-464. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23206854.

67. Ehdaie B, Furberg H, Zabor EC, et al. Impact of smoking status at diagnosis on disease recurrence and death in upper tract urothelial carcinoma. BJU Int 2013;111:589-595. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22642265.

68. Cumberbatch MG, Rota M, Catto JW, La Vecchia C. The role of tobacco smoke in bladder and kidney carcinogenesis: A comparison of exposures and meta-analysis of incidence and mortality risks. Eur Urol 2016;70:458-466. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26149669.

69. Liss MA, White M, Natarajan L, Parsons JK. Exercise decreases and smoking increases bladder cancer mortality. Clin Genitourin Cancer 2017;15:391-395. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28007367.

70. Cacciamani GE, Ghodoussipour S, Mari A, et al. Association between smoking exposure, neoadjuvant chemotherapy response and survival outcomes following radical cystectomy: systematic review and meta-analysis. J Urol 2020;204:649-660. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32105187.

71. Braithwaite D, Izano M, Moore DH, et al. Smoking and survival after breast cancer diagnosis: a prospective observational study and systematic review. Breast Cancer Res Treat 2012;136:521-533. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23053660.

72. Boone SD, Baumgartner KB, Baumgartner RN, et al. Active and passive cigarette smoking and mortality among Hispanic and non-Hispanic white women diagnosed with invasive breast cancer. Ann Epidemiol 2015;25:824-831. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26387598.

73. Darmon S, Park A, Lovejoy LA, et al. Relationship between cigarette smoking and cancer characteristics and survival among breast cancer patients. Int J Environ Res Public Health 2022;19:4084. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35409765.

74. Waggoner SE, Darcy KM, Fuhrman B, et al. Association between cigarette smoking and prognosis in locally advanced cervical carcinoma treated with chemoradiation: a Gynecologic Oncology Group study. Gynecol Oncol 2006;103:853-858. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16815535.

75. Gillison ML, Zhang Q, Jordan R, et al. Tobacco smoking and increased risk of death and progression for patients with p16-positive and p16-negative oropharyngeal cancer. J Clin Oncol 2012;30:2102-2111. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22565003.

76. Walter V, Jansen L, Hoffmeister M, Brenner H. Smoking and survival of colorectal cancer patients: systematic review and meta-analysis. Ann Oncol 2014;25:1517-1525. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24692581.

77. Walter V, Jansen L, Hoffmeister M, et al. Smoking and survival of colorectal cancer patients: population-based study from Germany. Int J Cancer 2015;137:1433-1445. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25758762.

78. Sharp L, McDevitt J, Brown C, Comber H. Smoking at diagnosis significantly decreases 5-year cancer-specific survival in a population-

based cohort of 18 166 colon cancer patients. Aliment Pharmacol Ther 2017;45:788-800. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28176335.

79. Japuntich SJ, Kumar P, Pendergast JF, et al. Smoking status and survival among a national cohort of lung and colorectal cancer patients. Nicotine Tob Res 2019;21:497-504. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29351659.

80. Modesitt SC, Huang B, Shelton BJ, Wyatt S. Endometrial cancer in Kentucky: the impact of age, smoking status, and rural residence. Gynecol Oncol 2006;103:300-306. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16631234.

81. Kountourakis P, Correa AM, Hofstetter WL, et al. Combined modality therapy of cT2N0M0 esophageal cancer: the University of Texas M. D. Anderson Cancer Center experience. Cancer 2011;117:925-930. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20960497.

82. Zheng Y, Cao X, Wen J, et al. Smoking affects treatment outcome in patients with resected esophageal squamous cell carcinoma who received chemotherapy. PLoS One 2015;10:e0123246. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25874561.

83. Platek AJ, Jayaprakash V, Merzianu M, et al. Smoking cessation is associated with improved survival in oropharynx cancer treated by chemoradiation. Laryngoscope 2016;126:2733-2738. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27346612.

84. Hoff CM, Grau C, Overgaard J. Effect of smoking on oxygen delivery and outcome in patients treated with radiotherapy for head and neck squamous cell carcinoma--a prospective study. Radiother Oncol 2012;103:38-44. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22385797.

85. Sharp L, McDevitt J, Carsin AE, et al. Smoking at diagnosis is an independent prognostic factor for cancer-specific survival in head and neck cancer: findings from a large, population-based study. Cancer Epidemiol Biomarkers Prev 2014;23:2579-2590. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25128401.

86. Choi SH, Terrell JE, Bradford CR, et al. Does quitting smoking make a difference among newly diagnosed head and neck cancer patients? Nicotine Tob Res 2016;18:2216-2224. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27613928.

87. Stang A, Knowlton R, Rekowski J, et al. Smoking cessation potential among newly diagnosed cancer patients: a population-based study of the ten most common cancers in Massachusetts, USA, 2008-2013. Ann Epidemiol 2021;56:55-60 e11. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33189878.

88. Ehdaie B, Furberg H, Zabor EC, et al. Comprehensive assessment of the impact of cigarette smoking on survival of clear cell kidney cancer. J Urol 2014;191:597-602. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24018238.

89. Keizman D, Gottfried M, Ish-Shalom M, et al. Active smoking may negatively affect response rate, progression-free survival, and overall survival of patients with metastatic renal cell carcinoma treated with sunitinib. Oncologist 2014;19:51-60. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24309979.

90. Fajkovic H, Shariat SF, Klatte T, et al. Impact of smoking status on survival after cytoreductive nephrectomy for metastatic renal cell carcinoma. World J Urol 2016;34:1411-1419. Available at: https://pubmed.ncbi.nlm.nih.gov/26879416/.

91. Tammemagi CM, Neslund-Dudas C, Simoff M, Kvale P. Smoking and lung cancer survival: the role of comorbidity and treatment. Chest 2004;125:27-37. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14718417.

92. Wang X, Romero-Gutierrez CW, Kothari J, et al. Prediagnosis smoking cessation and overall survival among patients with non-small cell lung cancer. JAMA Netw Open 2023;6:e2311966. Available at: https://www.ncbi.nlm.nih.gov/pubmed/37145597.

93. Kelemen LE, Warren GW, Koziak JM, et al. Smoking may modify the association between neoadjuvant chemotherapy and survival from ovarian cancer. Gynecol Oncol 2016;140:124-130. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26549109.

94. Lin Y, Yagyu K, Ueda J, et al. Active and passive smoking and risk of death from pancreatic cancer: findings from the Japan Collaborative Cohort Study. Pancreatology 2013;13:279-284. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23719601.

95. Yuan C, Morales-Oyarvide V, Babic A, et al. Cigarette smoking and pancreatic cancer survival [abstract]. J Clin Oncol 2017;35:1822-1828. Available at: http://ascopubs.org/doi/abs/10.1200/JCO.2016.71.2026.

96. Kenfield SA, Stampfer MJ, Chan JM, Giovannucci E. Smoking and prostate cancer survival and recurrence. JAMA 2011;305:2548-2555. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21693743.

97. Darcey E, Boyle T. Tobacco smoking and survival after a prostate cancer diagnosis: A systematic review and meta-analysis. Cancer Treat Rev 2018;70:30-40. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30055462.

98. Chelghoum Y, Danaila C, Belhabri A, et al. Influence of cigarette smoking on the presentation and course of acute myeloid leukemia. Ann Oncol 2002;13:1621-1627. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12377652.

99. Shenker RF, McTyre ER, Ruiz J, et al. The effects of smoking status and smoking history on patients with brain metastases from lung cancer. Cancer Med 2017;6:944-952. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28401684.

100. Zhu D, Zhao G, Wang X. Association of smoking and smoking cessation with overall and cause-specific mortality. Am J Prev Med 2021;60:504-512. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33745522.

101. Al-Mamgani A, van Rooij PH, Mehilal R, et al. Radiotherapy for T1a glottic cancer: the influence of smoking cessation and fractionation schedule of radiotherapy. Eur Arch Otorhinolaryngol 2014;271:125-132. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23797970.

102. Sandoval M, Font R, Manos M, et al. The role of vegetable and fruit consumption and other habits on survival following the diagnosis of oral cancer: a prospective study in Spain. Int J Oral Maxillofac Surg 2009;38:31-39. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18951763.

103. Sardari Nia P, Weyler J, Colpaert C, et al. Prognostic value of smoking status in operated non-small cell lung cancer. Lung Cancer 2005;47:351-359. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15713518.

104. Chen J, Jiang R, Garces YI, et al. Prognostic factors for limited-stage small cell lung cancer: a study of 284 patients. Lung Cancer 2010;67:221-226. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19497635.

105. Roach MC, Rehman S, DeWees TA, et al. It's never too late: Smoking cessation after stereotactic body radiation therapy for non-small cell lung carcinoma improves overall survival. Pract Radiat Oncol 2016;6:12-18. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26598909.

106. Ramamoorthy S, Luo L, Luo E, Carethers JM. Tobacco smoking and risk of recurrence for squamous cell cancer of the anus. Cancer Detect Prev 2008;32:116-120. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18639388.

107. Wyszynski A, Tanyos SA, Rees JR, et al. Body mass and smoking are modifiable risk factors for recurrent bladder cancer. Cancer 2014;120:408-414. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24122218.

108. Ogihara K, Kikuchi E, Yuge K, et al. Refraining from smoking for 15 years or more reduced the risk of tumor recurrence in non-muscle invasive

bladder cancer patients. Ann Surg Oncol 2016;23:1752-1759. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26671037.

109. Bishop JD, Killelea BK, Chagpar AB, et al. Smoking and breast cancer recurrence after breast conservation therapy. Int J Breast Cancer 2014;2014:327081. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24693439.

110. Aredo JV, Luo SJ, Gardner RM, et al. Tobacco smoking and risk of second primary lung cancer. J Thorac Oncol 2021;16:968-979. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33722709.

111. Han MA, Kim YW, Choi IJ, et al. Association of smoking history with cancer recurrence and survival in stage III-IV male gastric cancer patients. Cancer Epidemiol Biomarkers Prev 2013;22:1805-1812. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23904463.

112. Joshu CE, Mondul AM, Meinhold CL, et al. Cigarette smoking and prostate cancer recurrence after prostatectomy. J Natl Cancer Inst 2011;103:835-838. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21498781.

113. Moreira DM, Aronson WJ, Terris MK, et al. Cigarette smoking is associated with an increased risk of biochemical disease recurrence, metastasis, castration-resistant prostate cancer, and mortality after radical prostatectomy: results from the SEARCH database. Cancer 2014;120:197-204. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24127391.

114. Rieken M, Shariat SF, Kluth LA, et al. Association of cigarette smoking and smoking cessation with biochemical recurrence of prostate cancer in patients treated with radical prostatectomy. Eur Urol 2015;68:949-956. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26050111.

115. Khan S, Thakkar S, Drake B. Smoking history, intensity, and duration and risk of prostate cancer recurrence among men with prostate cancer who received definitive treatment. Ann Epidemiol 2019;38:4-10. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31563295.

116. Boyle JM, Tandberg DJ, Chino JP, et al. Smoking history predicts for increased risk of second primary lung cancer: a comprehensive analysis. Cancer 2015;121:598-604. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25283893.

117. Shiels MS, Gibson T, Sampson J, et al. Cigarette smoking prior to first cancer and risk of second smoking-associated cancers among survivors of bladder, kidney, head and neck, and stage I lung cancers. J Clin Oncol 2014;32:3989-3995. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25385740.

118. Ford MB, Sigurdson AJ, Petrulis ES, et al. Effects of smoking and radiotherapy on lung carcinoma in breast carcinoma survivors. Cancer 2003;98:1457-1464. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14508833.

119. van Leeuwen FE, Klokman WJ, Stovall M, et al. Roles of radiotherapy and smoking in lung cancer following Hodgkin's disease. J Natl Cancer Inst 1995;87:1530-1537. Available at: http://www.ncbi.nlm.nih.gov/pubmed/7563187.

120. Richardson GE, Tucker MA, Venzon DJ, et al. Smoking cessation after successful treatment of small-cell lung cancer is associated with fewer smoking-related second primary cancers. Ann Intern Med 1993;119:383-390. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8393311.

121. Garces YI, Schroeder DR, Nirelli LM, et al. Second primary tumors following tobacco dependence treatments among head and neck cancer patients. Am J Clin Oncol 2007;30:531-539. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17921716.

122. Khuri FR, Kim ES, Lee JJ, et al. The impact of smoking status, disease stage, and index tumor site on second primary tumor incidence and tumor recurrence in the head and neck retinoid chemoprevention trial. Cancer Epidemiol Biomarkers Prev 2001;10:823-829. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11489748.

123. Amri R, Bordeianou LG, Sylla P, Berger DL. Does active smoking induce hematogenous metastatic spread in colon cancer? Am J Surg 2015;210:930-932. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26251219.

124. Gajdos C, Hawn MT, Campagna EJ, et al. Adverse effects of smoking on postoperative outcomes in cancer patients. Ann Surg Oncol 2012;19:1430-1438. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22065194.

125. Balduyck B, Sardari Nia P, Cogen A, et al. The effect of smoking cessation on quality of life after lung cancer surgery. Eur J Cardiothorac Surg 2011;40:1432-1437; discussion 1437-1438. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21498082.

126. Lugg ST, Tikka T, Agostini PJ, et al. Smoking and timing of cessation on postoperative pulmonary complications after curative-intent lung cancer surgery. J Cardiothorac Surg 2017;12:52. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28629433.

127. Fukui M, Suzuki K, Matsunaga T, et al. Importance of smoking cessation on surgical outcome in primary lung cancer. Ann Thorac Surg 2019;107:1005-1009. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30610851.

128. Ehlers SL, Gastineau DA, Patten CA, et al. The impact of smoking on outcomes among patients undergoing hematopoietic SCT for the treatment of acute leukemia. Bone Marrow Transplant 2011;46:285-290. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20479707.

129. Mason DP, Subramanian S, Nowicki ER, et al. Impact of smoking cessation before resection of lung cancer: a Society of Thoracic Surgeons General Thoracic Surgery Database study. Ann Thorac Surg 2009;88:362-370; discussion 370-361. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19632374.

130. Quan H, Ouyang L, Zhou H, et al. The effect of preoperative smoking cessation and smoking dose on postoperative complications following radical gastrectomy for gastric cancer: a retrospective study of 2469 patients. World J Surg Oncol 2019;17:61. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30940207.

131. Kadomatsu Y, Sugiyama T, Sato K, et al. Relationship of smoking cessation period with the incidence of complications in lung cancer surgery. Eur J Cardiothorac Surg 2022;62. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35266529.

132. Sharma A, Deeb AP, Iannuzzi JC, et al. Tobacco smoking and postoperative outcomes after colorectal surgery. Ann Surg 2013;258:296-300. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23059503.

133. Napolitano MA, Rosenfeld ES, Chen SW, et al. Impact of timing of smoking cessation on 30-day outcomes in veterans undergoing lobectomy for cancer. Semin Thorac Cardiovasc Surg 2021;33:860-868. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33207278.

134. Haeuser L, Marchese M, Schrag D, et al. The impact of smoking on radical cystectomy complications increases in elderly patients. Cancer 2021;127:1387-1394. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33351967.

135. Chang DW, Reece GP, Wang B, et al. Effect of smoking on complications in patients undergoing free TRAM flap breast reconstruction. Plast Reconstr Surg 2000;105:2374-2380. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10845289.

136. Spear SL, Ducic I, Cuoco F, Hannan C. The effect of smoking on flap and donor-site complications in pedicled TRAM breast reconstruction. Plast Reconstr Surg 2005;116:1873-1880. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16327598.

137. Marin VP, Pytynia KB, Langstein HN, et al. Serum cotinine concentration and wound complications in head and neck reconstruction. Plast Reconstr Surg 2008;121:451-457. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18300961.

138. Crippen MM, Patel N, Filimonov A, et al. Association of smoking tobacco with complications in head and neck microvascular reconstructive

surgery. JAMA Facial Plast Surg 2019;21:20-26. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30347003.

139. Garip M, Van Dessel J, Grosjean L, et al. The impact of smoking on surgical complications after head and neck reconstructive surgery with a free vascularised tissue flap: a systematic review and meta-analysis. Br J Oral Maxillofac Surg 2021;59:e79-e98. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33546845.

140. Neugut AI, Murray T, Santos J, et al. Increased risk of lung cancer after breast cancer radiation therapy in cigarette smokers. Cancer 1994;73:1615-1620. Available at: https://www.ncbi.nlm.nih.gov/pubmed/8156488.

141. Tucker MA, Murray N, Shaw EG, et al. Second primary cancers related to smoking and treatment of small-cell lung cancer. Lung Cancer Working Cadre. J Natl Cancer Inst 1997;89:1782-1788. Available at: https://www.ncbi.nlm.nih.gov/pubmed/9392619.

142. Arnold M, Liu L, Kenter GG, et al. Second primary cancers in survivors of cervical cancer in The Netherlands: Implications for prevention and surveillance. Radiother Oncol 2014;111:374-381. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24833558.

143. Kaufman EL, Jacobson JS, Hershman DL, et al. Effect of breast cancer radiotherapy and cigarette smoking on risk of second primary lung cancer. J Clin Oncol 2008;26:392-398. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18202415.

144. Chen AM, Chen LM, Vaughan A, et al. Tobacco smoking during radiation therapy for head-and-neck cancer is associated with unfavorable outcome. Int J Radiat Oncol Biol Phys 2011;79:414-419. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20399030.

145. Browman GP, Wong G, Hodson I, et al. Influence of cigarette smoking on the efficacy of radiation therapy in head and neck cancer. N Engl J Med 1993;328:159-163. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8417381.

146. Zevallos JP, Mallen MJ, Lam CY, et al. Complications of radiotherapy in laryngopharyngeal cancer: effects of a prospective smoking cessation program. Cancer 2009;115:4636-4644. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19569250.

147. Egestad H, Emaus N. Changes in health related quality of life in women and men undergoing radiation treatment for head and neck cancer and the impact of smoking status in the radiation treatment period. Eur J Oncol Nurs 2014;18:339-346. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24877857.

148. Eifel PJ, Jhingran A, Bodurka DC, et al. Correlation of smoking history and other patient characteristics with major complications of pelvic radiation therapy for cervical cancer. J Clin Oncol 2002;20:3651-3657. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12202666.

149. Kucera H, Enzelsberger H, Eppel W, Weghaupt K. The influence of nicotine abuse and diabetes mellitus on the results of primary irradiation in the treatment of carcinoma of the cervix. Cancer 1987;60:1-4. Available at: http://www.ncbi.nlm.nih.gov/pubmed/3581022.

150. Rades D, Setter C, Schild SE, Dunst J. Effect of smoking during radiotherapy, respiratory insufficiency, and hemoglobin levels on outcome in patients irradiated for non-small-cell lung cancer. Int J Radiat Oncol Biol Phys 2008;71:1134-1142. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18258387.

151. Alsadius D, Hedelin M, Johansson KA, et al. Tobacco smoking and long-lasting symptoms from the bowel and the anal-sphincter region after radiotherapy for prostate cancer. Radiother Oncol 2011;101:495-501. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21737169.

152. Steinberger E, Kollmeier M, McBride S, et al. Cigarette smoking during external beam radiation therapy for prostate cancer is associated with an increased risk of prostate cancer-specific mortality and treatment-related toxicity. BJU Int 2015;116:596-603. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25345838.

153. Pickles T, Liu M, Berthelet E, et al. The effect of smoking on outcome following external radiation for localized prostate cancer. J Urol 2004;171:1543-1546. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15017216.

154. Hooning MJ, Botma A, Aleman BM, et al. Long-term risk of cardiovascular disease in 10-year survivors of breast cancer. J Natl Cancer Inst 2007;99:365-375. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17341728.

155. Tyc VL, Hudson MM, Hinds P, et al. Tobacco use among pediatric cancer patients: recommendations for developing clinical smoking interventions. J Clin Oncol 1997;15:2194-2204. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9196131.

156. Tobacco Use During Cancer Treatment. American Society for Clinical Oncology; 2012. Available at: http://www.cancer.net/navigating-cancer-care/prevention-and-healthy-living/tobacco-use/tobacco-use-during-cancer-treatment. Accessed September 23, 2015.

157. Geng Y, Savage SM, Razani-Boroujerdi S, Sopori ML. Effects of nicotine on the immune response. II. Chronic nicotine treatment induces T cell anergy. J Immunol 1996;156:2384-2390. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8786295.

158. Kalra R, Singh SP, Savage SM, et al. Effects of cigarette smoke on immune response: chronic exposure to cigarette smoke impairs antigen-mediated signaling in T cells and depletes IP3-sensitive Ca(2+) stores. J Pharmacol Exp Ther 2000;293:166-171. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10734166.

159. Geng Y, Savage SM, Johnson LJ, et al. Effects of nicotine on the immune response. I. Chronic exposure to nicotine impairs antigen receptor-mediated signal transduction in lymphocytes. Toxicol Appl Pharmacol 1995;135:268-278. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8545837.

160. Singh SP, Kalra R, Puttfarcken P, et al. Acute and chronic nicotine exposures modulate the immune system through different pathways. Toxicol Appl Pharmacol 2000;164:65-72. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10739745.

161. Birrell MA, Wong S, Catley MC, Belvisi MG. Impact of tobacco-smoke on key signaling pathways in the innate immune response in lung macrophages. J Cell Physiol 2008;214:27-37. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17541958.

162. Mehta H, Nazzal K, Sadikot RT. Cigarette smoking and innate immunity. Inflamm Res 2008;57:497-503. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19109742.

163. Kimura T, Shibata Y, Yamauchi K, et al. Oxidized phospholipid, 1-palmitoyl-2-(9'-oxo-nonanoyl)-glycerophosphocholine (PON-GPC), produced in the lung due to cigarette smoking, impairs immune function in macrophages. Lung 2012;190:169-182. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21986851.

164. Ferson M, Edwards A, Lind A, et al. Low natural killer-cell activity and immunoglobulin levels associated with smoking in human subjects. Int J Cancer 1979;23:603-609. Available at: http://www.ncbi.nlm.nih.gov/pubmed/457307.

165. Tollerud DJ, Clark JW, Brown LM, et al. Association of cigarette smoking with decreased numbers of circulating natural killer cells. Am Rev Respir Dis 1989;139:194-198. Available at: http://www.ncbi.nlm.nih.gov/pubmed/2912340.

166. Arcavi L, Benowitz NL. Cigarette smoking and infection. Arch Intern Med 2004;164:2206-2216. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15534156.

167. Nishioka T, Luo LY, Shen L, et al. Nicotine increases the resistance of lung cancer cells to cisplatin through enhancing Bcl-2 stability. Br J Cancer 2014;110:1785-1792. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24548862.

168. Zhang J, Kamdar O, Le W, et al. Nicotine induces resistance to chemotherapy by modulating mitochondrial signaling in lung cancer. Am J

Respir Cell Mol Biol 2009;40:135-146. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18676776.

169. Zhao J, Xin M, Wang T, et al. Nicotine enhances the antiapoptotic function of Mcl-1 through phosphorylation. Mol Cancer Res 2009;7:1954-1961. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19903766.

170. Shen T, Le W, Yee A, et al. Nicotine induces resistance to chemotherapy in nasal epithelial cancer. Am J Rhinol Allergy 2010;24:e73-77. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20338106.

171. Trevino JG, Pillai S, Kunigal S, et al. Nicotine induces inhibitor of differentiation-1 in a Src-dependent pathway promoting metastasis and chemoresistance in pancreatic adenocarcinoma. Neoplasia 2012;14:1102-1114. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23308043.

172. Li H, Shi Q. Drugs and diseases interacting with cigarette smoking in US prescription drug labelling. Clin Pharmacokinet 2015;54:493-501. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25701380.

173. O'Malley M, King AN, Conte M, et al. Effects of cigarette smoking on metabolism and effectiveness of systemic therapy for lung cancer. J Thorac Oncol 2014;9:917-926. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24926542.

174. Hamilton M, Wolf JL, Rusk J, et al. Effects of smoking on the pharmacokinetics of erlotinib. Clin Cancer Res 2006;12:2166-2171. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16609030.

175. van der Bol JM, Mathijssen RH, Loos WJ, et al. Cigarette smoking and irinotecan treatment: pharmacokinetic interaction and effects on neutropenia. J Clin Oncol 2007;25:2719-2726. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17563393.

176. Darwish M, Bond M, Hellriegel E, et al. Pharmacokinetic and pharmacodynamic profile of bendamustine and its metabolites. Cancer Chemother Pharmacol 2015;75:1143-1154. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25829094.

177. de Graan AJ, Loos WJ, Friberg LE, et al. Influence of smoking on the pharmacokinetics and toxicity profiles of taxane therapy. Clin Cancer Res 2012;18:4425-4432. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22645049.

178. Price SN, Palmer AM, Fucito LM, et al. Tobacco use and cancer-related symptom burden: Analysis of the US Population Assessment of Tobacco and Health Study. Cancer 2023;129:2385-2394. Available at: https://www.ncbi.nlm.nih.gov/pubmed/37211959.

179. Peppone LJ, Mustian KM, Morrow GR, et al. The effect of cigarette smoking on cancer treatment-related side effects. Oncologist 2011;16:1784-1792. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22135122.

180. Danson SJ, Rowland C, Rowe R, et al. The relationship between smoking and quality of life in advanced lung cancer patients: a prospective longitudinal study. Support Care Cancer 2016;24:1507-1516. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26364190.

181. Ditre JW, Gonzalez BD, Simmons VN, et al. Associations between pain and current smoking status among cancer patients. Pain 2011;152:60-65. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21168758.

182. Gonzalez A, Japuntich S, Keating NL, et al. Pain experiences among a population-based cohort of current, former, and never regular smokers with lung and colorectal cancer. Cancer 2014;120:3554-3561. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25043285.

183. Logan HL, Fillingim RB, Bartoshuk LM, et al. Smoking status and pain level among head and neck cancer patients. J Pain 2010;11:528-534. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20015696.

184. Novy DM, Lam C, Gritz ER, et al. Distinguishing features of cancer patients who smoke: pain, symptom burden, and risk for opioid misuse. J Pain 2012;13:1058-1067. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23010143.

185. Taniguchi C, Narisada A, Tanaka H, et al. Smoking cessation after cancer diagnosis reduces the risk of severe cancer pain: a longitudinal cohort study. PLoS One 2022;17:e0272779. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35944029.

186. The Health Benefits of Smoking Cessation: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services 1990. Available at: http://profiles.nlm.nih.gov/NN/B/B/C/T/.

187. Sitas F, Weber MF, Egger S, et al. Smoking cessation after cancer. J Clin Oncol 2014;32:3593-3595. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25267760.

188. Johnston-Early A, Cohen MH, Minna JD, et al. Smoking abstinence and small cell lung cancer survival. An association. JAMA 1980;244:2175-2179. Available at: http://www.ncbi.nlm.nih.gov/pubmed/6252357.

189. Gemine RE, Ghosal R, Collier G, et al. Longitudinal study to assess impact of smoking at diagnosis and quitting on 1-year survival for people with non-small cell lung cancer. Lung Cancer 2019;129:1-7. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30797485.

190. Koshiaris C, Aveyard P, Oke J, et al. Smoking cessation and survival in lung, upper aero-digestive tract and bladder cancer: cohort study. Br J Cancer 2017;117:1224-1232. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28898236.

191. Caini S, Del Riccio M, Vettori V, et al. Quitting smoking at or around diagnosis improves the overall survival of lung cancer patients: a systematic review and meta-analysis. J Thorac Oncol 2022;17:623-636. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34995798.

192. Lee JJW, Kunaratnam V, Kim CJH, et al. Cigarette smoking cessation, duration of smoking abstinence, and head and neck squamous cell carcinoma prognosis. Cancer 2023;129:867-877. Available at: https://www.ncbi.nlm.nih.gov/pubmed/36653915.

193. Fleshner N, Garland J, Moadel A, et al. Influence of smoking status on the disease-related outcomes of patients with tobacco-associated superficial transitional cell carcinoma of the bladder. Cancer 1999;86:2337-2345. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10590376.

194. Ordonez-Mena JM, Walter V, Schottker B, et al. Impact of prediagnostic smoking and smoking cessation on colorectal cancer prognosis: a meta-analysis of individual patient data from cohorts within the CHANCES consortium. Ann Oncol 2018;29:472-483. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29244072.

195. Tabuchi T, Goto A, Ito Y, et al. Smoking at the time of diagnosis and mortality in cancer patients: What benefit does the quitter gain? Int J Cancer 2017;140:1789-1795. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28073149.

196. Kuri M, Nakagawa M, Tanaka H, et al. Determination of the duration of preoperative smoking cessation to improve wound healing after head and neck surgery. Anesthesiology 2005;102:892-896. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15851873.

197. Zhao S, Chen F, Wang D, et al. Effect of preoperative smoking cessation on postoperative pain outcomes in elderly patients with high nicotine dependence. Medicine (Baltimore) 2019;98:e14209. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30653178.

198. Garces YI, Hays JT. Tobacco dependence: why should an oncologist care? J Clin Oncol 2003;21:1884-1886. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12721267.

199. Land SR, Toll BA, Moinpour CM, et al. Research priorities, measures, and recommendations for assessment of tobacco use in clinical cancer research. Clin Cancer Res 2016;22:1907-1913. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26888828.

200. Siegel DA, Henley SJ, Wike JM, et al. Capture of tobacco use among population-based registries: findings from 10 National Program of Cancer Registries states. Cancer 2018;124:2381-2389. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29579317.

201. Warren GW, Marshall JR, Cummings KM, et al. Automated tobacco assessment and cessation support for cancer patients. Cancer 2014;120:562-569. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24496870.

202. Transdisciplinary Tobacco Use Research Center Tobacco D, Baker TB, Piper ME, et al. Time to first cigarette in the morning as an index of ability to quit smoking: implications for nicotine dependence. Nicotine Tob Res 2007;9 Suppl 4:S555-570. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18067032.

203. Heatherton TF, Kozlowski LT, Frecker RC, Fagerstrom KO. The Fagerstrom Test for Nicotine Dependence: a revision of the Fagerstrom Tolerance Questionnaire. Br J Addict 1991;86:1119-1127. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1932883.

204. Miller WR, Rollnick S. Motivational Interviewing: Preparing People for Change (ed 3). New York, NY: The Guilford Press; 2012.

205. Rollnick S, Miller WR, Butler CC. Motivational Interviewing in Health Care: Helping Patients Change Behavior (ed 1). New York, NY: The Guilford Press; 2007.

206. Prochaska JO, Velicer WF. The transtheoretical model of health behavior change. Am J Health Promot 1997;12:38-48. Available at: https://www.ncbi.nlm.nih.gov/pubmed/10170434.

207. Lindson-Hawley N, Hartmann-Boyce J, Fanshawe TR, et al. Interventions to reduce harm from continued tobacco use. Cochrane Database Syst Rev 2016;10:CD005231. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27734465.

208. Leone FT, Zhang Y, Evers-Casey S, et al. Initiating pharmacologic treatment in tobacco-dependent adults. An Official American Thoracic Society Clinical Practice Guideline. Am J Respir Crit Care Med 2020;202:e5-e31. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32663106.

209. Lindson-Hawley N, Aveyard P, Hughes JR. Gradual reduction vs abrupt cessation as a smoking cessation strategy in smokers who want to quit. JAMA 2013;310:91-92. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23821093.

210. Ostroff JS, Burkhalter JE, Cinciripini PM, et al. Randomized trial of a presurgical scheduled reduced smoking intervention for patients newly diagnosed with cancer. Health Psychol 2014;33:737-747. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23895203.

211. Cather C, Pachas GN, Cieslak KM, Evins AE. Achieving smoking cessation in individuals with schizophrenia: special considerations. CNS Drugs 2017;31:471-481. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28550660.

212. Reid MS, Jiang H, Fallon B, et al. Smoking cessation treatment among patients in community-based substance abuse rehabilitation programs: exploring predictors of outcome as clues toward treatment improvement. Am J Drug Alcohol Abuse 2011;37:472-478. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21854292.

213. Ditre JW, Heckman BW, LaRowe LR, Powers JM. Pain status as a predictor of smoking cessation initiation, lapse, and relapse. Nicotine Tob Res 2021;23:186-194. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32594124.

214. Vijayaraghavan M, Penko J, Vittinghoff E, et al. Smoking behaviors in a community-based cohort of HIV-infected indigent adults. AIDS Behav 2014;18:535-543. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23918243.

215. Ehlers SL, Bronars CA, Patten CA, et al. Accuracy of self-reported tobacco use status among hematopoietic SCT patients. Bone Marrow Transplant 2014;49:961-965. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24732958.

216. Hald J, Overgaard J, Grau C. Evaluation of objective measures of smoking status--a prospective clinical study in a group of head and neck

cancer patients treated with radiotherapy. Acta Oncol 2003;42:154-159. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12801134.

217. Warren GW, Arnold SM, Valentino JP, et al. Accuracy of self-reported tobacco assessments in a head and neck cancer treatment population. Radiother Oncol 2012;103:45-48. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22119370.

218. Nolan MB, Warner DO. Safety and efficacy of nicotine replacement therapy in the perioperative period: A narrative review. Mayo Clin Proc 2015;90:1553-1561. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26455889.

219. Sorensen LT. Wound healing and infection in surgery: the pathophysiological impact of smoking, smoking cessation, and nicotine replacement therapy: a systematic review. Ann Surg 2012;255:1069-1079. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22566015.

220. Stefan MS, Pack Q, Shieh MS, et al. The association of nicotine replacement therapy with outcomes among smokers hospitalized for a major surgical procedure. Chest 2020;157:1354-1361. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31790653.

221. Moller AM, Villebro N, Pedersen T, Tonnesen H. Effect of preoperative smoking intervention on postoperative complications: a randomised clinical trial. Lancet 2002;359:114-117. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11809253.

222. Lindstrom D, Sadr Azodi O, Wladis A, et al. Effects of a perioperative smoking cessation intervention on postoperative complications: a randomized trial. Ann Surg 2008;248:739-745. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18948800.

223. Jung KH, Kim SM, Choi MG, et al. Preoperative smoking cessation can reduce postoperative complications in gastric cancer surgery. Gastric Cancer 2015;18:683-690. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25139298.

224. Yoshida N, Baba Y, Hiyoshi Y, et al. Duration of Smoking Cessation and Postoperative Morbidity After Esophagectomy for Esophageal Cancer: How Long Should Patients Stop Smoking Before Surgery? World J Surg 2016;40:142-147. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26330238.

225. Thomsen T, Villebro N, Moller AM. Interventions for preoperative smoking cessation. Cochrane Database Syst Rev 2014;3:CD002294. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24671929.

226. Wong J, Abrishami A, Yang Y, et al. A perioperative smoking cessation intervention with varenicline: a double-blind, randomized, placebo-controlled trial. Anesthesiology 2012;117:755-764. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22890119.

227. Theadom A, Cropley M. Effects of preoperative smoking cessation on the incidence and risk of intraoperative and postoperative complications in adult smokers: a systematic review. Tob Control 2006;15:352-358. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16998168.

228. Maiga AW, Deppen SA, Pinkerman R, et al. Timeliness of care and lung cancer tumor-stage progression: How long can we wait? Ann Thorac Surg 2017;104:1791-1797. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29033012.

229. Bottorff JL, Seaton CL, Viney N, et al. The Stop Smoking Before Surgery Program: impact on awareness of smoking-related perioperative complications and smoking behavior in Northern Canadian communities. J Prim Care Community Health 2016;7:16-23. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26385995.

230. Cropley M, Theadom A, Pravettoni G, Webb G. The effectiveness of smoking cessation interventions prior to surgery: a systematic review. Nicotine Tob Res 2008;10:407-412. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18324557.

231. Kotz D, Brown J, West R. 'Real-world' effectiveness of smoking cessation treatments: a population study. Addiction 2014;109:491-499. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24372901.

232. Stead LF, Lancaster T. Combined pharmacotherapy and behavioural interventions for smoking cessation. Cochrane Database Syst Rev 2012;10:CD008286. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23076944.

233. Stead LF, Koilpillai P, Lancaster T. Additional behavioural support as an adjunct to pharmacotherapy for smoking cessation. Cochrane Database Syst Rev 2015:CD009670. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26457723.

234. Yingst JM, Carrillo M, Chan KH, et al. Effectiveness of smoking cessation interventions among persons with cancer: a systematic review. Psychooncology 2023;32:1147-1162. Available at: https://www.ncbi.nlm.nih.gov/pubmed/37226331.

235. Ferguson SG, Shiffman S, Gitchell JG. Nicotine replacement therapies: patient safety and persistence. Patient Relat Outcome Meas 2011;2:111-117. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22915971.

236. Leyro TM, Hall SM, Hickman N, et al. Clinical management of tobacco dependence in inpatient psychiatry: provider practices and patient utilization. Psychiatr Serv 2013;64:1161-1165. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24185538.

237. Shiffman S. Use of more nicotine lozenges leads to better success in quitting smoking. Addiction 2007;102:809-814. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17493108.

238. Crawford G, Weisbrot J, Bastian J, et al. Predictors of varenicline adherence among cancer patients treated for tobacco dependence and its association with smoking cessation. Nicotine Tob Res 2019;21:1135-1139. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29955828.

239. Schnoll RA, Goelz PM, Veluz-Wilkins A, et al. Long-term nicotine replacement therapy: a randomized clinical trial. JAMA Intern Med 2015;175:504-511. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25705872.

240. Hughes JR. Dependence potential and abuse liability of nicotine replacement therapies. Biomed Pharmacother 1989;43:11-17. Available at: http://www.ncbi.nlm.nih.gov/pubmed/2659095.

241. Moore TJ, Furberg CD, Glenmullen J, et al. Suicidal behavior and depression in smoking cessation treatments. PLoS One 2011;6:e27016. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22073240.

242. Thomas KH, Martin RM, Davies NM, et al. Smoking cessation treatment and risk of depression, suicide, and self harm in the Clinical Practice Research Datalink: prospective cohort study. BMJ 2013;347:f5704. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24124105.

243. Thomas KH, Martin RM, Knipe DW, et al. Risk of neuropsychiatric adverse events associated with varenicline: systematic review and meta-analysis. BMJ 2015;350:h1109. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25767129.

244. Hollands GJ, McDermott MS, Lindson-Hawley N, et al. Interventions to increase adherence to medications for tobacco dependence. Cochrane Database Syst Rev 2015;2:CD009164. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25914910.

245. Pacek LR, McClernon FJ, Bosworth HB. Adherence to pharmacological smoking cessation interventions: a literature review and synthesis of correlates and barriers. Nicotine Tob Res 2018;20:1163-1172. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29059394.

246. Peng AR, Swardfager W, Benowitz NL, et al. Impact of early nausea on varenicline adherence and smoking cessation. Addiction 2020;115:134-144. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31502736.

247. Cahill K, Stevens S, Perera R, Lancaster T. Pharmacological interventions for smoking cessation: an overview and network meta-analysis. Cochrane Database Syst Rev 2013;5:CD009329. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23728690.

248. Coe JW, Brooks PR, Vetelino MG, et al. Varenicline: an alpha4beta2 nicotinic receptor partial agonist for smoking cessation. J Med Chem 2005;48:3474-3477. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15887955.

249. Mills EJ, Wu P, Lockhart I, et al. Comparisons of high-dose and combination nicotine replacement therapy, varenicline, and bupropion for smoking cessation: a systematic review and multiple treatment meta-analysis. Ann Med 2012;44:588-597. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22860882.

250. Cahill K, Stead LF, Lancaster T. Nicotine receptor partial agonists for smoking cessation. Cochrane Database Syst Rev 2012;4:CD006103. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22513936.

251. Livingstone-Banks J, Lindson N, Hartmann-Boyce J, Aveyard P. Effects of interventions to combat tobacco addiction: Cochrane update of 2019 and 2020 reviews. Addiction 2022;117:1573-1588. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34859525.

252. Anthenelli RM, Benowitz NL, West R, et al. Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial. Lancet 2016;387:2507-2520. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27116918.

253. Price S, Hitsman B, Veluz-Wilkins A, et al. The use of varenicline to treat nicotine dependence among patients with cancer. Psychooncology 2017;26:1526-1534. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27218657.

254. Ebbert JO, Hughes JR, West RJ, et al. Effect of varenicline on smoking cessation through smoking reduction: a randomized clinical trial. JAMA 2015;313:687-694. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25688780.

255. Tonstad S, Tonnesen P, Hajek P, et al. Effect of maintenance therapy with varenicline on smoking cessation: a randomized controlled trial. JAMA 2006;296:64-71. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16820548.

256. Baker TB, Piper ME, Smith SS, et al. Effects of combined varenicline with nicotine patch and of extended treatment duration on smoking cessation: a randomized clinical trial. JAMA 2021;326:1485-1493. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34665204.

257. Gonzales D, Hajek P, Pliamm L, et al. Retreatment with varenicline for smoking cessation in smokers who have previously taken varenicline: a randomized, placebo-controlled trial. Clin Pharmacol Ther 2014;96:390-396. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24911368.

258. Hajek P, McRobbie H, Myers Smith K, et al. Increasing varenicline dose in smokers who do not respond to the standard dosage: a randomized clinical trial. JAMA Intern Med 2015;175:266-271. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25545858.

259. Karam-Hage M, Kypriotakis G, Robinson JD, et al. Improvement of smoking abstinence rates with increased varenicline dosage: A propensity score-matched analysis. J Clin Psychopharmacol 2018;38:34-41. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29232312.

260. Jimenez-Ruiz CA, Barrios M, Pena S, et al. Increasing the dose of varenicline in patients who do not respond to the standard dose. Mayo Clin Proc 2013;88:1443-1445. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24290118.

261. Jorenby DE, Hays JT, Rigotti NA, et al. Efficacy of varenicline, an alpha4beta2 nicotinic acetylcholine receptor partial agonist, vs placebo or sustained-release bupropion for smoking cessation: a randomized controlled trial. JAMA 2006;296:56-63. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16820547.

262. Williams KE, Reeves KR, Billing CB, Jr., et al. A double-blind study evaluating the long-term safety of varenicline for smoking cessation. Curr Med Res Opin 2007;23:793-801. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17407636.

263. Anthenelli RM, Morris C, Ramey TS, et al. Effects of varenicline on smoking cessation in adults with stably treated current or past major depression: a randomized trial. Ann Intern Med 2013;159:390-400. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24042367.

264. Prochaska JJ, Hilton JF. Risk of cardiovascular serious adverse events associated with varenicline use for tobacco cessation: systematic review and meta-analysis. BMJ 2012;344:e2856. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22563098.

265. Svanstrom H, Pasternak B, Hviid A. Use of varenicline for smoking cessation and risk of serious cardiovascular events: nationwide cohort study. BMJ 2012;345:e7176. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23138033.

266. Mills EJ, Thorlund K, Eapen S, et al. Cardiovascular events associated with smoking cessation pharmacotherapies: a network meta-analysis. Circulation 2014;129:28-41. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24323793.

267. Sharma A, Thakar S, Lavie CJ, et al. Cardiovascular adverse events associated with smoking-cessation pharmacotherapies. Curr Cardiol Rep 2015;17:554. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25410148.

268. Chelladurai Y, Singh S. Varenicline and cardiovascular adverse events: a perspective review. Ther Adv Drug Saf 2014;5:167-172. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25083271.

269. Singh S, Loke YK, Spangler JG, Furberg CD. Risk of serious adverse cardiovascular events associated with varenicline: a systematic review and meta-analysis. CMAJ 2011;183:1359-1366. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21727225.

270. Kotz D, Viechtbauer W, Simpson C, et al. Cardiovascular and neuropsychiatric risks of varenicline: a retrospective cohort study. Lancet Respir Med 2015;3:761-768. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26355008.

271. FDA updates label for stop smoking drug Chantix (varenicline) to include potential alcohol interaction, rare risk of seizures, and studies of side effects on mood, behavior, or thinking. FDA Drug Safety Communication. Silver Spring, MD: U.S. Food and Drug Administration; 2015. Available at: http://www.fda.gov/Drugs/DrugSafety/ucm436494.htm.

272. Serafini A, Crespel A, Velizara R, Gelisse P. Varenicline-induced grand mal seizure. Epileptic Disord 2010;12:338. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21287775.

273. Smith SS, McCarthy DE, Japuntich SJ, et al. Comparative effectiveness of 5 smoking cessation pharmacotherapies in primary care clinics. Arch Intern Med 2009;169:2148-2155. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20008701.

274. Cahill K, Stevens S, Lancaster T. Pharmacological treatments for smoking cessation. JAMA 2014;311:193-194. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24399558.

275. Stead LF, Perera R, Bullen C, et al. Nicotine replacement therapy for smoking cessation. Cochrane Database Syst Rev 2012;11:CD000146. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23152200.

276. Hartmann-Boyce J, Chepkin SC, Ye W, et al. Nicotine replacement therapy versus control for smoking cessation. Cochrane Database Syst Rev 2018;5:CD000146. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29852054.

277. Fiore MC, Jaen CR, Baker TB. Treating Tobacco Use and Dependence: 2008 Update. In: Panel TUaDG ed. A Public Health Service-Sponsored Clinical Practice Guideline. Rockville, MD; 2008. Available at: http://www.ncbi.nlm.nih.gov/books/NBK63952/.

278. Benowitz NL, Jacob P, 3rd, Fong I, Gupta S. Nicotine metabolic profile in man: comparison of cigarette smoking and transdermal nicotine. J Pharmacol Exp Ther 1994;268:296-303. Available at: https://www.ncbi.nlm.nih.gov/pubmed/8301571.

279. Benowitz NL, Porchet H, Sheiner L, Jacob P, 3rd. Nicotine absorption and cardiovascular effects with smokeless tobacco use: comparison with cigarettes and nicotine gum. Clin Pharmacol Ther 1988;44:23-28. Available at: https://www.ncbi.nlm.nih.gov/pubmed/3391001.

280. Benowitz NL, Jacob P, 3rd, Savanapridi C. Determinants of nicotine intake while chewing nicotine polacrilex gum. Clin Pharmacol Ther 1987;41:467-473. Available at: https://www.ncbi.nlm.nih.gov/pubmed/3829583.

281. Mills EJ, Wu P, Lockhart I, et al. Adverse events associated with nicotine replacement therapy (NRT) for smoking cessation. A systematic review and meta-analysis of one hundred and twenty studies involving 177,390 individuals. Tob Induc Dis 2010;8:8. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20626883.

282. Kimmel SE, Berlin JA, Miles C, et al. Risk of acute first myocardial infarction and use of nicotine patches in a general population. J Am Coll Cardiol 2001;37:1297-1302. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11300438.

283. Hubbard R, Lewis S, Smith C, et al. Use of nicotine replacement therapy and the risk of acute myocardial infarction, stroke, and death. Tob Control 2005;14:416-421. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16319366.

284. Meine TJ, Patel MR, Washam JB, et al. Safety and effectiveness of transdermal nicotine patch in smokers admitted with acute coronary syndromes. Am J Cardiol 2005;95:976-978. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15820167.

285. Warren GW, Singh AK. Nicotine and lung cancer. J Carcinog 2013;12:1. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23599683.

286. Martinez-Garcia E, Irigoyen M, Gonzalez-Moreno O, et al. Repetitive nicotine exposure leads to a more malignant and metastasis-prone phenotype of SCLC: a molecular insight into the importance of quitting smoking during treatment. Toxicol Sci 2010;116:467-476. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20457658.

287. Maier CR, Hollander MC, Hobbs EA, et al. Nicotine does not enhance tumorigenesis in mutant K-ras-driven mouse models of lung cancer. Cancer Prev Res (Phila) 2011;4:1743-1751. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22027685.

288. Murphy SE, von Weymarn LB, Schutten MM, et al. Chronic nicotine consumption does not influence 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone-induced lung tumorigenesis. Cancer Prev Res (Phila) 2011;4:1752-1760. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22027684.

289. Stepanov I, Carmella SG, Briggs A, et al. Presence of the carcinogen N'-nitrosonornicotine in the urine of some users of oral nicotine replacement therapy products. Cancer Res 2009;69:8236-8240. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19843845.

290. Murray RP, Connett JE, Zapawa LM. Does nicotine replacement therapy cause cancer? Evidence from the Lung Health Study. Nicotine Tob Res 2009;11:1076-1082. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19571249.

291. Shields PG. Long-term nicotine replacement therapy: cancer risk in context. Cancer Prev Res (Phila) 2011;4:1719-1723. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22052338.

292. Koegelenberg CF, Noor F, Bateman ED, et al. Efficacy of varenicline combined with nicotine replacement therapy vs varenicline alone for smoking cessation: a randomized clinical trial. JAMA 2014;312:155-161. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25005652.

293. Ramon JM, Morchon S, Baena A, Masuet-Aumatell C. Combining varenicline and nicotine patches: a randomized controlled trial study in smoking cessation. BMC Med 2014;12:172. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25296623.

294. Hajek P, Smith KM, Dhanji AR, McRobbie H. Is a combination of varenicline and nicotine patch more effective in helping smokers quit than varenicline alone? A randomised controlled trial. BMC Med 2013;11:140. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23718718.

295. Stapleton J, West R, Hajek P, et al. Randomized trial of nicotine replacement therapy (NRT), bupropion and NRT plus bupropion for smoking cessation: effectiveness in clinical practice. Addiction 2013;108:2193-2201. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23859696.

296. Jorenby DE, Leischow SJ, Nides MA, et al. A controlled trial of sustained-release bupropion, a nicotine patch, or both for smoking cessation. N Engl J Med 1999;340:685-691. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10053177.

297. Evins AE, Cather C, Culhane MA, et al. A 12-week double-blind, placebo-controlled study of bupropion sr added to high-dose dual nicotine replacement therapy for smoking cessation or reduction in schizophrenia. J Clin Psychopharmacol 2007;27:380-386. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17632223.

298. Hughes JR, Stead LF, Hartmann-Boyce J, et al. Antidepressants for smoking cessation. Cochrane Database Syst Rev 2014;1:CD000031. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24402784.

299. van der Meer RM, Willemsen MC, Smit F, Cuijpers P. Smoking cessation interventions for smokers with current or past depression. Cochrane Database Syst Rev 2013;8:CD006102. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23963776.

300. Hays JT, Hurt RD, Rigotti NA, et al. Sustained-release bupropion for pharmacologic relapse prevention after smoking cessation. a randomized, controlled trial. Ann Intern Med 2001;135:423-433. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11560455.

301. Prescribing information for bupropion hydrochloride sustained-release tablets, for oral use. 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/020358s064lbl.pdf. Accessed May 5, 2022.

302. Binkhorst L, Mathijssen RH, van Herk-Sukel MP, et al. Unjustified prescribing of CYP2D6 inhibiting SSRIs in women treated with tamoxifen. Breast Cancer Res Treat 2013;139:923-929. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23760858.

303. Englisch S, Morgen K, Meyer-Lindenberg A, Zink M. Risks and benefits of bupropion treatment in schizophrenia: a systematic review of the current literature. Clin Neuropharmacol 2013;36:203-215. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24201231.

304. Rose JE, Behm FM. Combination treatment with varenicline and bupropion in an adaptive smoking cessation paradigm. Am J Psychiatry 2014;171:1199-1205. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24934962.

305. Rose JE, Behm FM. Combination varenicline/bupropion treatment benefits highly dependent smokers in an adaptive smoking cessation paradigm. Nicotine Tob Res 2017;19:999-1002. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29054128.

306. Ebbert JO, Hatsukami DK, Croghan IT, et al. Combination varenicline and bupropion SR for tobacco-dependence treatment in cigarette smokers: a randomized trial. JAMA 2014;311:155-163. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24399554.

307. Cinciripini PM, Minnix JA, Green CE, et al. An RCT with the combination of varenicline and bupropion for smoking cessation: clinical implications for front line use. Addiction 2018. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29679432.

308. Klemp I, Steffenssen M, Bakholdt V, et al. Counseling is effective for smoking cessation in head and neck cancer patients - a systematic review and meta-analysis. J Oral Maxillofac Surg 2016;74:1687-1694. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26973223.

309. Lai DT, Cahill K, Qin Y, Tang JL. Motivational interviewing for smoking cessation. Cochrane Database Syst Rev 2010:CD006936. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20091612

310. Park ER, Perez GK, Regan S, et al. Effect of sustained smoking cessation counseling and provision of medication vs shorter-term counseling and medication advice on smoking abstinence in patients recently diagnosed with cancer. JAMA 2020;324:1406-1418. Available at: https://pubmed.ncbi.nlm.nih.gov/33048154/.

311. Rigotti NA, Clair C, Munafo MR, Stead LF. Interventions for smoking cessation in hospitalised patients. Cochrane Database Syst Rev 2012:CD001837. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22592676.

312. Siu AL, Force USPST. Behavioral and pharmacotherapy interventions for tobacco smoking cessation in adults, including pregnant women: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2015;163:622-634. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26389730.

313. Herd N, Borland R. The natural history of quitting smoking: findings from the International Tobacco Control (ITC) Four Country Survey. Addiction 2009;104:2075-2087. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19922573.

314. Wang MP, Li WH, Cheung YT, et al. Brief advice on smoking reduction versus abrupt quitting for smoking cessation in Chinese smokers: A cluster randomized controlled trial. Nicotine Tob Res 2017;20:67-72. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28182243.

315. Li WHC, Wang MP, Ho KY, et al. Helping cancer patients quit smoking using brief advice based on risk communication: A randomized controlled trial. Sci Rep 2018;8:2712. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29426956.

316. Hall SM, Humfleet GL, Munoz RF, et al. Using extended cognitive behavioral treatment and medication to treat dependent smokers. Am J Public Health 2011;101:2349-2356. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21653904.

317. Hall SM, Humfleet GL, Munoz RF, et al. Extended treatment of older cigarette smokers. Addiction 2009;104:1043-1052. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19392908.

318. Killen JD, Fortmann SP, Schatzberg AF, et al. Extended cognitive behavior therapy for cigarette smoking cessation. Addiction 2008;103:1381-1390. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18855829.

319. Yalcin BM, Unal M, Pirdal H, Karahan TF. Effects of an anger management and stress control program on smoking cessation: a randomized controlled trial. J Am Board Fam Med 2014;27:645-660. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25201934.

320. Matheny KB, Weatherman KE. Predictors of smoking cessation and maintenance. J Clin Psychol 1998;54:223-235. Available at: https://www.ncbi.nlm.nih.gov/pubmed/9467767.

321. Senore C, Battista RN, Shapiro SH, et al. Predictors of smoking cessation following physicians' counseling. Prev Med 1998;27:412-421. Available at: https://www.ncbi.nlm.nih.gov/pubmed/9612831.

322. Hughes JR. Effects of abstinence from tobacco: valid symptoms and time course. Nicotine Tob Res 2007;9:315-327. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17365764.

323. McLaughlin I, Dani JA, De Biasi M. Nicotine withdrawal. Curr Top Behav Neurosci 2015;24:99-123. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25638335.

324. Shiffman S, Patten C, Gwaltney C, et al. Natural history of nicotine withdrawal. Addiction 2006;101:1822-1832. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17156182.

325. Liebmann EP, Preacher KJ, Richter KP, et al. Identifying pathways to quitting smoking via telemedicine-delivered care. Health Psychol 2019;38:638-647. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31021123.

326. Kotsen C, Dilip D, Carter-Harris L, et al. Rapid scaling up of telehealth treatment for tobacco-dependent cancer patients during the COVID-19 outbreak in New York City. Telemed J E Health 2021;27:20-29. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32649266.

327. Civljak M, Stead LF, Hartmann-Boyce J, et al. Internet-based interventions for smoking cessation. Cochrane Database Syst Rev 2013;7:CD007078. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23839868.

328. Bricker JB, Mull KE, McClure JB, et al. Improving quit rates of web-delivered interventions for smoking cessation: full-scale randomized trial of WebQuit.org versus Smokefree.gov. Addiction 2018;113:914-923. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29235186.

329. Stead LF, Lancaster T. Group behaviour therapy programmes for smoking cessation. Cochrane Database Syst Rev 2005:CD001007. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15846610.

330. Lancaster T, Stead LF. Individual behavioural counselling for smoking cessation. Cochrane Database Syst Rev 2005:CD001292. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15846616.

331. Hartmann-Boyce J, Lancaster T, Stead LF. Print-based self-help interventions for smoking cessation. Cochrane Database Syst Rev 2014;6:CD001118. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24888233.

332. Whittaker R, McRobbie H, Bullen C, et al. Mobile phone-based interventions for smoking cessation. Cochrane Database Syst Rev 2012;11:CD006611. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23152238.

333. Free C, Knight R, Robertson S, et al. Smoking cessation support delivered via mobile phone text messaging (txt2stop): a single-blind, randomised trial. Lancet 2011;378:49-55. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21722952.

334. Abroms LC, Boal AL, Simmens SJ, et al. A randomized trial of Text2Quit: a text messaging program for smoking cessation. Am J Prev Med 2014;47:242-250. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24913220.

335. Abroms LC, Padmanabhan N, Thaweethai L, Phillips T. iPhone apps for smoking cessation: a content analysis. Am J Prev Med 2011;40:279-285. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21335258.

336. Prutzman YM, Wiseman KP, Grady MA, et al. Using digital technologies to reach tobacco users who want to quit: evidence from the National Cancer Institute's Smokefree.gov initiative. Am J Prev Med 2021;60:S172-S184. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33663705.

337. Sampson L, Papadakos J, Milne V, et al. Preferences for the provision of smoking cessation education among cancer patients. J Cancer Educ 2016;33:7-11. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27075196.

338. Sheeran P, Jones K, Avishai A, et al. What works in smoking cessation interventions for cancer survivors? A meta-analysis. Health Psychol 2019;38:855-865. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31259596.

339. Smith SS, Keller PA, Kobinsky KH, et al. Enhancing tobacco quitline effectiveness: identifying a superior pharmacotherapy adjuvant. Nicotine Tob Res 2013;15:718-728. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22992296.

340. Mehnert A, Kuhnt S, Brahler E, et al. Twelve-month prevalence of mental disorders in cancer patients across major tumor entities [abstract]. ASCO Meeting Abstracts 2015;33:9552. Available at: http://meeting.ascopubs.org/cgi/content/abstract/33/15_suppl/9552.

341. Singer S, Das-Munshi J, Brahler E. Prevalence of mental health conditions in cancer patients in acute care--a meta-analysis. Ann Oncol 2010;21:925-930. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19887467.

342. Mehnert A, Brahler E, Faller H, et al. Four-week prevalence of mental disorders in patients with cancer across major tumor entities. J Clin Oncol 2014;32:3540-3546. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25287821.

343. Lindson-Hawley N, Thompson TP, Begh R. Motivational interviewing for smoking cessation. Cochrane Database Syst Rev 2015;3:CD006936. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25726920.

344. Spencer JC, Wheeler SB. A systematic review of Motivational Interviewing interventions in cancer patients and survivors. Patient Educ Couns 2016;99:1099-1105. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26879805.

345. Bhatnagar A, Whitsel LP, Ribisl KM, et al. Electronic cigarettes: a policy statement from the American Heart Association. Circulation 2014;130:1418-1436. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25156991.

346. Herbst RS, Hatsukami D, Acton D, et al. Electronic nicotine delivery systems: an updated policy statement from the American Association for Cancer Research and the American Society of Clinical Oncology. J Clin Oncol 2022;40:4144-4155. Available at: https://www.ncbi.nlm.nih.gov/pubmed/36287017.

347. American Cancer Society Position Statement on Electronic Cigarettes: American Cancer Society; 2018. Available at: https://www.cancer.org/healthy/stay-away-from-tobacco/e-cigarette-position-statement.html.

348. U. S. Preventive Services Task Force, Krist AH, Davidson KW, et al. Interventions for tobacco smoking cessation in adults, including pregnant persons: US Preventive Services Task Force recommendation statement. JAMA 2021;325:265-279. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33464343.

349. Smith DM, Christensen C, van Bemmel D, et al. Exposure to nicotine and toxicants among dual users of tobacco cigarettes and e-cigarettes: Population Assessment of Tobacco and Health (PATH) Study, 2013-2014. Nicotine Tob Res 2021;23:790-797. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33590857.

350. Goniewicz ML, Smith DM, Edwards KC, et al. Comparison of nicotine and toxicant exposure in users of electronic cigarettes and combustible cigarettes. JAMA Netw Open 2018;1:e185937. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30646298.

351. Hajek P, Phillips-Waller A, Przulj D, et al. A randomized trial of E-cigarettes versus nicotine-replacement therapy. N Engl J Med 2019;380:629-637. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30699054.

352. Sweet L, Brasky TM, Cooper S, et al. Quitting behaviors among dual cigarette and E-cigarette users and cigarette smokers enrolled in the tobacco user adult cohort. Nicotine Tob Res 2019;21:278-284. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30346585.

353. Hartmann-Boyce J, Lindson N, Butler AR, et al. Electronic cigarettes for smoking cessation. Cochrane Database Syst Rev 2022;11:CD010216. Available at: https://www.ncbi.nlm.nih.gov/pubmed/36384212.

354. Shahab L, Goniewicz ML, Blount BC, et al. Nicotine, carcinogen, and toxin exposure in long-term E-cigarette and nicotine replacement therapy users: A cross-sectional study. Ann Intern Med 2017;166:390-400. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28166548.

355. Manzoli L, Flacco ME, Ferrante M, et al. Cohort study of electronic cigarette use: effectiveness and safety at 24 months. Tob Control 2017;26:284-292. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27272748.

356. Coleman B, Rostron B, Johnson SE, et al. Transitions in electronic cigarette use among adults in the Population Assessment of Tobacco and Health (PATH) Study, Waves 1 and 2 (2013-2015). Tob Control 2019;28:50-59. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29695458.

357. Kasza KA, Edwards KC, Kimmel HL, et al. Association of e-cigarette use with discontinuation of cigarette smoking among adult smokers who were initially never planning to quit. JAMA Netw Open 2021;4:e2140880. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34962556.

358. Kalkhoran S, Glantz SA. E-cigarettes and smoking cessation in real-world and clinical settings: a systematic review and meta-analysis. Lancet Respir Med 2016;4:116-128. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26776875.

359. Patil S, Arakeri G, Patil S, et al. Are electronic nicotine delivery systems (ENDs) helping cigarette smokers quit?-current evidence. J Oral Pathol Med 2020;49:181-189. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31642553.

360. Malas M, van der Tempel J, Schwartz R, et al. Electronic cigarettes for smoking cessation: A systematic review. Nicotine Tob Res 2016;18:1926-1936. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27113014.

361. Hartmann-Boyce J, McRobbie H, Bullen C, et al. Electronic cigarettes for smoking cessation. Cochrane Database Syst Rev 2016;9:CD010216. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27622384.

362. Hartmann-Boyce J, McRobbie H, Lindson N, et al. Electronic cigarettes for smoking cessation. Cochrane Database Syst Rev 2021;4:CD010216. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33913154.

363. Brown J, Beard E, Kotz D, et al. Real-world effectiveness of e-cigarettes when used to aid smoking cessation: a cross-sectional population study. Addiction 2014;109:1531-1540. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24846453.

364. E-cigarette or vaping use-associated lung injury (EVALI): American Lung Association; 2020. Available at: https://www.lung.org/lung-health-diseases/lung-disease-lookup/evali.

365. Layden JE, Ghinai I, Pray I, et al. Pulmonary illness related to e-cigarette use in Illinois and Wisconsin - final report. N Engl J Med 2020;382:903-916. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31491072.

366. Werner AK, Koumans EH, Chatham-Stephens K, et al. Hospitalizations and deaths associated with EVALI. N Engl J Med 2020;382:1589-1598. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32320569.

367. Blount BC, Karwowski MP, Shields PG, et al. Vitamin E acetate in bronchoalveolar-lavage fluid associated with EVALI. N Engl J Med 2020;382:697-705. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31860793.

368. Borderud SP, Li Y, Burkhalter JE, et al. Electronic cigarette use among patients with cancer: characteristics of electronic cigarette users and their smoking cessation outcomes. Cancer 2014;120:3527-3535. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25252116.

369. Salloum RG, Getz KR, Tan AS, et al. Use of electronic cigarettes among cancer survivors in the U.S. Am J Prev Med 2016;51:762-766. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27242079.

370. Fahey MC, Bursac Z, Ebbert JO, et al. Prevalence and correlates of dual tobacco use in cancer survivors. Cancer Causes Control 2019;30:217-223. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30671688.

371. Little MA, Klesges RC, Bursac Z, et al. Correlates of smoking status in cancer survivors. J Cancer Surviv 2018;12:828-834. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30343442.

372. Akinboro O, Nwabudike S, Elias R, et al. Electronic cigarette use among survivors of smoking-related cancers in the United States. Cancer Epidemiol Biomarkers Prev 2019;28:2087-2094. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31501150.

373. McQueen N, Partington EJ, Harrington KF, et al. Smoking cessation and electronic cigarette use among head and neck cancer patients. Otolaryngol Head Neck Surg 2016;154:73-79. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26519457.

374. Correa JB, Brandon KO, Meltzer LR, et al. Electronic cigarette use among patients with cancer: Reasons for use, beliefs, and patient-provider communication. Psychooncology 2018;27:1757-1764. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29671928.

375. Osei AD, Mirbolouk M, Orimoloye OA, et al. Association between e-cigarette use and cardiovascular disease among never and current combustible-cigarette smokers. Am J Med 2019;132:949-954 e942. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30853474.

376. Cardenas VM, Ali MM, Fischbach LA, Nembhard WN. Dual use of cigarettes and electronic nicotine delivery systems during pregnancy and the risk of small for gestational age neonates. Ann Epidemiol 2020;52:86-92 e82. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32805398.

377. Kim T, Kang J. Association between dual use of e-cigarette and cigarette and chronic obstructive pulmonary disease: an analysis of a nationwide representative sample from 2013 to 2018. BMC Pulm Med 2021;21:231. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34256746.

378. Ussher MH, Taylor AH, Faulkner GE. Exercise interventions for smoking cessation. Cochrane Database Syst Rev 2014;8:CD002295. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25170798.

379. White AR, Rampes H, Liu JP, et al. Acupuncture and related interventions for smoking cessation. Cochrane Database Syst Rev 2014;1:CD000009. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24459016.

380. Abbot NC, Stead LF, White AR, et al. Hypnotherapy for smoking cessation. Cochrane Database Syst Rev 2000:CD001008. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10796583.

381. Barnes J, Dong CY, McRobbie H, et al. Hypnotherapy for smoking cessation. Cochrane Database Syst Rev 2010:CD001008. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20927723.