

Interventions for Tobacco Smoking Cessation in Adults, Including Pregnant Persons

US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

IMPORTANCE Tobacco use is the leading preventable cause of disease, disability, and death in the US. In 2014, it was estimated that 480 000 deaths annually are attributed to cigarette smoking, including second hand smoke exposure. Smoking during pregnancy can increase the risk of numerous adverse pregnancy outcomes (eg, miscarriage and congenital anomalies) and complications in the offspring (including sudden infant death syndrome and impaired lung function in childhood). In 2019, an estimated 50.6 million US adults (20.8% of the adult population) used tobacco; 14.0% of the US adult population currently smoked cigarettes and 4.5% of the adult population used electronic cigarettes (e-cigarettes). Among pregnant US women who gave birth in 2016, 7.2% reported smoking cigarettes while pregnant.






OBJECTIVE To update its 2015 recommendation, the USPSTF commissioned a review to evaluate the benefits and harms of primary care interventions on tobacco use cessation in adults, including pregnant persons.

POPULATION This recommendation statement applies to adults 18 years or older, including pregnant persons.

EVIDENCE ASSESSMENT The USPSTF concludes with high certainty that the net benefit of behavioral interventions and US Food and Drug Administration (FDA)-approved pharmacotherapy for tobacco smoking cessation, alone or combined, in nonpregnant adults who smoke is substantial. The USPSTF concludes with high certainty that the net benefit of behavioral interventions for tobacco smoking cessation on perinatal outcomes and smoking cessation in pregnant persons is substantial. The USPSTF concludes that the evidence on pharmacotherapy interventions for tobacco smoking cessation in pregnant persons is insufficient because few studies are available, and the balance of benefits and harms cannot be determined. The USPSTF concludes that the evidence on the use of e-cigarettes for tobacco smoking cessation in adults, including pregnant persons, is insufficient, and the balance of benefits and harms cannot be determined. The USPSTF has identified the lack of well-designed, randomized clinical trials on e-cigarettes that report smoking abstinence or adverse events as a critical gap in the evidence.

RECOMMENDATIONS The USPSTF recommends that clinicians ask all adults about tobacco use, advise them to stop using tobacco, and provide behavioral interventions and FDA-approved pharmacotherapy for cessation to nonpregnant adults who use tobacco. (A recommendation) The USPSTF recommends that clinicians ask all pregnant persons about tobacco use, advise them to stop using tobacco, and provide behavioral interventions for cessation to pregnant persons who use tobacco. (A recommendation) The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of pharmacotherapy interventions for tobacco cessation in pregnant persons. (I statement) The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of e-cigarettes for tobacco cessation in adults, including pregnant persons. The USPSTF recommends that clinicians direct patients who use tobacco to other tobacco cessation interventions with proven effectiveness and established safety. (I statement)

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Summary of Recommendations

The USPSTF recommends that clinicians ask all adults about tobacco use, advise them to stop using tobacco, and provide behavioral interventions and US Food and Drug Administration (FDA)-approved pharmacotherapy for cessation to nonpregnant adults who use tobacco.	A
The USPSTF recommends that clinicians ask all pregnant persons about tobacco use, advise them to stop using tobacco, and provide behavioral interventions for cessation to pregnant persons who use tobacco.	A
The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of pharmacotherapy interventions for tobacco cessation in pregnant persons .	I
The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of electronic cigarettes (e-cigarettes) for tobacco cessation in adults, including pregnant persons. The USPSTF recommends that clinicians direct patients who use tobacco to other tobacco cessation interventions with proven effectiveness and established safety.	I

See the Figure for a more detailed summary of the recommendations for clinicians. See the Practice Considerations section for more information on recommended behavioral interventions and pharmacotherapy and for suggestions for practice regarding the I statements. USPSTF indicates US Preventive Services Task Force.

Tobacco use is the leading preventable cause of disease, disability, and death in the US. In 2014, it was estimated that 480 000 deaths annually are attributed to cigarette smoking, including second hand smoke.¹ Smoking during pregnancy can increase the risk for miscarriage, congenital anomalies, stillbirth, fetal growth restriction, preterm birth, placental abruption, and complications in the offspring, including sudden infant death syndrome and impaired lung function in childhood.¹⁻⁴ In 2019 (the most recent data currently available), an estimated 50.6 million US adults (20.8% of the adult population) used tobacco; 14.0% of the US adult population currently smoked cigarettes; and 4.5% of the US adult population used electronic cigarettes (e-cigarettes).⁵ According to data from the National Vital Statistics System, in 2016, 7.2% of women who gave birth smoked cigarettes during pregnancy.⁶ There are disparities in smoking behaviors associated with certain sociodemographic factors: smoking rates are particularly high in non-Hispanic American Indian/Alaska Native persons; lesbian, gay, or bisexual adults; adults whose highest level of educational attainment is a General Educational Development certificate; persons who are uninsured and those with Medicaid; adults with a disability; and persons with mild, moderate, or severe generalized anxiety symptoms.⁵ According to the 2015 National Health Interview Survey, which reported responses from 33,672 adults, 68% of adults who smoked reported that they wanted to stop smoking and 55% attempted quitting in the past year⁷; only 7% reported having recently quit smoking and 31% reported having used cessation counseling, medication, or both when trying to quit.⁷

USPSTF Assessment of Magnitude of Net Benefit

The USPSTF concludes with high certainty that the net benefit of behavioral interventions and US Food and Drug Administration (FDA)-approved pharmacotherapy for tobacco smoking cessation, alone or combined, in nonpregnant adults who smoke is **substantial**.

The USPSTF concludes with high certainty that the net benefit of behavioral interventions for tobacco smoking cessation on perinatal outcomes and smoking cessation in pregnant persons is **substantial**.

The USPSTF concludes that the evidence on pharmacotherapy interventions for tobacco smoking cessation in pregnant persons is **insufficient** because few studies are available, and the balance of benefits and harms cannot be determined.

The USPSTF concludes that the evidence on the use of e-cigarettes for tobacco smoking cessation in adults, including pregnant persons, is **insufficient**, and the balance of benefits and harms cannot be determined. The USPSTF has identified the lack of well-designed, randomized clinical trials (RCTs) on e-cigarettes that report smoking abstinence or adverse events as a critical gap in the evidence.

See the **Figure**, **Table 1**, and the eFigure in the Supplement for more information on the USPSTF recommendation rationale and assessment. For more details on the methods the USPSTF uses to determine net benefit, see the USPSTF Procedure Manual.⁸

Practice Considerations

Patient Population Under Consideration

This recommendation applies to adults 18 years or older, including pregnant persons. The USPSTF has issued a separate recommendation statement on primary care interventions for the prevention and cessation of tobacco use in children and adolescents.⁹

Definitions

Key definitions related to tobacco use are reported in the **Box**. Although tobacco use refers broadly to the use of any tobacco product, cigarette smoking has historically been the most prevalent form of tobacco use in the US, and most of the evidence surrounding cessation of tobacco products relates to quitting combustible cigarette smoking. Thus, the current USPSTF recommendations focus on interventions for tobacco smoking cessation. Additionally, although e-cigarettes are considered a tobacco product that should also be the focus of tobacco prevention and cessation efforts, for this recommendation statement, the evidence on e-cigarettes as a potential cessation aid for cigarette smoking was also evaluated.

Figure. Clinician Summary: Interventions for Tobacco Smoking Cessation in Adults, Including Pregnant Persons

What does the USPSTF recommend?	<p>Nonpregnant adults:</p> <ul style="list-style-type: none"> • Ask about tobacco use • Provide behavioral interventions and pharmacotherapy for cessation to those who use tobacco <p>Grade A</p>
	<p>Pregnant persons:</p> <ul style="list-style-type: none"> • Ask about tobacco use • Provide behavioral interventions for cessation to those who use tobacco <p>Grade A</p>
	<p>Pregnant persons who use tobacco:</p> <ul style="list-style-type: none"> • The evidence is insufficient to assess the balance of benefits and harms of pharmacotherapy for tobacco cessation <p>I statement</p>
	<p>Adults and pregnant persons who use tobacco:</p> <ul style="list-style-type: none"> • The evidence is insufficient to assess the balance of benefits and harms of using e-cigarettes for tobacco cessation. Clinicians should direct patients to other cessation interventions with proven effectiveness and established safety <p>I statement</p>
To whom does this recommendation apply?	Adults 18 years or older, including pregnant persons.
What's new?	This recommendation is consistent with the 2015 USPSTF recommendation. This recommendation incorporates newer evidence and language in the field of tobacco cessation, including new evidence on the harms of e-cigarettes (ie, vaping).
How to implement this recommendation?	<ol style="list-style-type: none"> 1. Ask all adults, including pregnant persons, about tobacco use, using methods such as <ul style="list-style-type: none"> • "5 As": Ask, Advise, Assess, Assist, Arrange follow-up • "Ask, Advise, Refer" • "Vital Sign": Treat smoking status as a vital sign 2. Provide cessation interventions to persons who use tobacco <ul style="list-style-type: none"> • For nonpregnant adults who use tobacco, provide behavioral counseling and pharmacotherapy for cessation <ul style="list-style-type: none"> ◦ Effective behavioral counseling interventions include physician advice, nurse advice, individual counseling, group behavioral interventions, telephone counseling, and mobile phone-based interventions ◦ FDA-approved pharmacotherapy for cessation includes nicotine replacement therapy, bupropion sustained-release, and varenicline ◦ Combined behavioral counseling and pharmacotherapy includes at least 4 or more behavioral counseling sessions with 90 to 300 minutes of total contact time • For pregnant persons who use tobacco, provide behavioral counseling for cessation <ul style="list-style-type: none"> ◦ Effective behavioral counseling includes cognitive behavioral, motivational, and supportive therapies such as counseling, health education, feedback, financial incentives, and social support
What are other relevant USPSTF recommendations?	The USPSTF has made a recommendation on primary care interventions for prevention and cessation of tobacco use in children and adolescents. This recommendation is available at https://www.uspreventiveservicestaskforce.org
Where to read the full recommendation statement?	Visit the USPSTF website to read the full recommendation statement. This includes more details on the rationale of the recommendation, including benefits and harms; supporting evidence; and recommendations of others.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision-making to the specific patient or situation.

USPSTF indicates US Preventive Services Task Force.

Assessment of Tobacco Use

All patients should be asked about their tobacco use, whether or not risk factors for use are present, and encouraged to stop using tobacco. When smoking is identified, all patients should be provided interventions to quit smoking. Higher smoking prevalence has been observed in men; persons younger than 65 years; non-Hispanic American Indian/Alaska Native persons; persons who are lesbian, gay, or bisexual; persons whose highest level of educational attainment is a General Educational Development certificate; persons with an annual household income less than \$35 000; persons with a disability; and persons with mild, moderate, or severe anxiety symptoms.⁵

Common approaches for clinicians to assess patients' tobacco use include the following.

- The 5 As: (1) Ask about tobacco use; (2) Advise to quit through clear, personalized messages; (3) Assess willingness to quit; (4) Assist in quitting; and (5) Arrange follow-up and support.¹²
- "Ask, Advise, Refer," which encourages clinicians to ask patients about tobacco use, advise them to quit, and refer them to telephone quit lines, other evidence-based cessation interventions, or both.¹²
- Vital Sign: Treating smoking status as a vital sign and recording smoking status at every health visit are also frequently used to assess smoking status.¹²
Because many pregnant women who smoke do not report it, using multiple choice questions to assess smoking status in this group may improve disclosure.¹²

Table 1. Summary of USPSTF Rationale

Rationale	Nonpregnant adults	Pregnant persons
Benefits of intervention	<ul style="list-style-type: none"> • Convincing evidence that the benefit of behavioral interventions (including physician and nurse advice, individual and group counseling, and telephone and mobile phone-based interventions), alone or combined with pharmacotherapy, to increase achievement of tobacco smoking cessation in nonpregnant adults who smoke is substantial. • Convincing evidence that the benefit of pharmacotherapy interventions, including nicotine replacement therapy (NRT), bupropion hydrochloride sustained-release (bupropion SR), and varenicline—with or without behavioral counseling interventions—to achieve tobacco smoking cessation in nonpregnant adults is substantial. • Convincing evidence that using 2 types of NRT (fast-acting plus patch) moderately increases tobacco smoking cessation rates over using 1 type, and that addition of NRT to treatment with bupropion SR provides additional benefit over use of bupropion SR alone. • Inadequate evidence to determine the effect of electronic cigarettes (e-cigarettes) on achievement of tobacco smoking cessation. 	<ul style="list-style-type: none"> • Convincing evidence that the benefit of behavioral interventions to achieve tobacco smoking cessation in pregnant persons, and prevent infant low birth weight, is substantial. • Inadequate evidence on pharmacotherapy because of few available studies on the benefits of NRT and no studies reporting on the benefits of bupropion SR, varenicline, or e-cigarettes to achieve tobacco smoking cessation in pregnant persons or to improve infant outcomes.
Harms of intervention	<ul style="list-style-type: none"> • Adequate evidence to bound the magnitude of harms of behavioral interventions for tobacco smoking cessation in nonpregnant adults as small to none, based on the nature of the interventions, the low likelihood of serious harms, and the available information from studies reporting few harms. When direct evidence is limited, absent, or restricted to select populations or clinical scenarios, the USPSTF may place conceptual upper or lower bounds on the magnitude of benefit or harms. • Adequate evidence that the harms of pharmacotherapy interventions for tobacco smoking cessation in adults with NRT, bupropion SR, or varenicline are small. • Harms of NRT include irritation at nicotine exposure site, chest pain, arrhythmia, and minor cardiovascular events such as palpitations and bradycardia. • A statistically nonsignificant increase in severe adverse events was found with bupropion SR, but no difference in study withdrawals due to adverse events was seen and no increase risk of cardiovascular events (any or major) was seen with bupropion SR. • Use of varenicline was not associated with cardiovascular or neuropsychiatric adverse events but may be associated with an increased risk of general severe adverse events. • Inadequate evidence to determine the harms of e-cigarettes as a tobacco smoking cessation tool. 	<ul style="list-style-type: none"> • Adequate evidence to bound the magnitude of harms of behavioral interventions for tobacco smoking cessation in pregnant persons who smoke as small to none based on the nature of the intervention, the low likelihood of serious harms, and the available information from studies reporting few harms. When direct evidence is limited, absent, or restricted to select populations or clinical scenarios, the USPSTF may place conceptual upper or lower bounds on the magnitude of benefit or harms. • Inadequate evidence on the harms of pharmacotherapy interventions because of few available studies on NRT and no studies reporting on the harms of bupropion SR, varenicline, or e-cigarettes for tobacco smoking cessation in pregnant persons who smoke.
USPSTF assessment	<ul style="list-style-type: none"> • High certainty that the net benefit of behavioral interventions and US Food and Drug Administration–approved pharmacotherapy interventions for tobacco smoking cessation, alone or combined, in nonpregnant adults who smoke is substantial. • Insufficient evidence on the use of e-cigarettes for tobacco smoking cessation in adults, and the balance of benefits and harms cannot be determined. There is a critical gap in the evidence due to a lack of well-designed, randomized clinical trials on e-cigarettes for cessation that report smoking abstinence or adverse events. 	<ul style="list-style-type: none"> • High certainty that the net benefit of behavioral interventions for tobacco smoking cessation on perinatal outcomes and smoking cessation in pregnant persons is substantial. • Insufficient evidence on pharmacotherapy interventions for tobacco smoking cessation in pregnant persons because of a lack of studies, and the balance of benefits and harms cannot be determined. • Insufficient evidence on the use of e-cigarettes for tobacco smoking cessation in pregnant persons, and the balance of benefits and harms cannot be determined. Evidence is lacking.

Abbreviations: NRT, nicotine replacement therapy; SR, sustained release; USPSTF, US Preventive Services Task Force.

Interventions for Tobacco Cessation and Implementation Considerations

Nonpregnant Adults

Effective tobacco smoking cessation interventions for nonpregnant adults include behavioral counseling and pharmacotherapy, either individually or in combination.^{13,14}

Combined Behavioral Counseling Interventions and Pharmacotherapy

Combining behavioral and pharmacotherapy interventions has been shown to increase tobacco smoking cessation rates compared with either usual care/brief cessation interventions alone or pharmacotherapy alone.¹³ Most combination interventions include behavioral counseling involving several sessions (≥ 4), with planned total contact time usually ranging from 90 to 300 minutes.¹³ The largest effect was found in interventions that

provided 8 or more sessions, although the difference in effect among the number of sessions was not significant.¹³

Behavioral Counseling Interventions | Many behavioral counseling interventions are available to increase tobacco smoking cessation in adults. These interventions can be delivered in the primary care setting or can be referred to community settings with feedback to the primary care clinician. Effective behavioral interventions include physician advice, nurse advice, individual counseling with a cessation specialist, group behavioral interventions, telephone counseling, and mobile phone-based interventions.¹³ Behavioral counseling interventions used in studies typically targeted individuals who were motivated to quit tobacco smoking.¹³ For additional information about behavioral counseling interventions in nonpregnant adults, see Table 2.

Pharmacotherapy | The current pharmacotherapy interventions approved by the FDA for the treatment of tobacco smoking dependence in adults are nicotine replacement therapy (NRT) (including nicotine transdermal patches, lozenges, gum, inhalers, or nasal spray), bupropion hydrochloride sustained-release (SR), and varenicline.⁴⁶ All 3 types of pharmacotherapy increase tobacco smoking cessation rates. Using a combination of NRT products (in particular, combining short-acting plus long-acting forms of NRT) has been found to be more effective than using a single form of NRT.¹³ Based on a smaller number of studies, varenicline appears to be more effective than NRT or bupropion SR.¹³ Information on dosing regimens is available in the package inserts of individual medications or in the 2020 Surgeon General Report on Smoking Cessation.⁴⁷

Pregnant Persons

Behavioral Counseling Interventions | Providing any psychosocial intervention to pregnant persons who smoke tobacco can increase smoking cessation. The behavioral counseling intervention type most often studied in pregnant persons who smoke was counseling. Behavioral interventions were more effective when they provided more intensive counseling, were augmented with messages and self-help materials tailored for pregnant persons, and included messages about the effects of smoking on both maternal and fetal health and strong advice to quit as soon as possible.^{12,13} Although smoking cessation at any point during pregnancy yields substantial health benefits for the expectant mother and infant, quitting early in pregnancy provides the greatest benefit to the fetus.^{12,13} Other interventions included feedback, incentives, health education, and social support, although provision of health education alone, without counseling, was not found to be effective. For additional information about behavioral counseling interventions in pregnant persons, see Table 2.

Additional Resources

Primary care clinicians may find the following resources useful in talking with adults and pregnant persons about tobacco smoking cessation.

- Centers for Disease Control and Prevention
 - Health care clinician resources for treatment of tobacco use and dependence
<https://www.cdc.gov/tobaccoHCP>
 - Tips From Former Smokers
<https://www.cdc.gov/tobacco/campaign/tips/partners/health/index.html>
- US Department of Health and Human Services
 - SmokeFree.Gov Health Professionals Page
<https://smokefree.gov/help-others-quit/health-professionals>
 - SmokeFreeWomen
<http://women.smokefree.gov/pregnancy-motherhood>

In addition, the following resources may be useful to primary care clinicians and practices trying to implement interventions for tobacco smoking cessation.
- Million Hearts tools for clinicians for tobacco cessation
<https://millionhearts.hhs.gov/tools-protocols/tools/tobacco-use.html>
- Centers for Disease Control and Prevention state and community resources for tobacco control programs
<https://www.cdc.gov/tobacco/stateandcommunity/index.htm>

Box. Key Definitions Related to Tobacco Use

Tobacco Use

Tobacco use refers to use of any tobacco product. As defined by the US Food and Drug Administration, tobacco products include any product made or derived from tobacco intended for human consumption (except products that meet the definition of drugs), including, but not limited to, cigarettes, cigars (including cigarillos and little cigars), dissolvables, hookah tobacco, nicotine gels, pipe tobacco, roll-your-own tobacco, smokeless tobacco products (including dip, snuff, snus, and chewing tobacco), vapes, electronic cigarettes (e-cigarettes), hookah pens, and other electronic nicotine delivery systems.¹⁰

Smoking

Smoking generally refers to the inhaling and exhaling of smoke produced by combustible tobacco products such as cigarettes, cigars, and pipes.

Vaping

Vaping refers to the inhaling and exhaling of aerosols produced by e-cigarettes.¹¹ Vaping products (ie, e-cigarettes) usually contain nicotine, which is the addictive ingredient in tobacco. Substances other than tobacco can also be used to smoke or vape. While the 2015 USPSTF recommendation statement used the term "electronic nicotine delivery systems" or "ENDS," the USPSTF recognizes that the field has shifted to using the term "e-cigarettes" (or "e-cigs") and uses the term e-cigarettes in the current recommendation statement. e-Cigarettes can come in many shapes and sizes, but generally they heat a liquid that contains nicotine (the addictive drug in tobacco) to produce an aerosol (or "vapor") that is inhaled ("vaped") by users.¹¹

USPSTF indicates US preventive Services Task Force.

- The US Department of Veterans Affairs (VA) Primary Care & Tobacco Cessation Handbook
https://www.mentalhealth.va.gov/quit-tobacco/docs/IB_10-565-Primary-Care-Smoking-Handbook-PROVIDERS-508.pdf
- World Health Organization's toolkit for delivering brief smoking interventions in primary care
http://www.who.int/tobacco/publications/smoking_cessation/9789241506953/en/

In 2020, the Surgeon General issued a Report on Smoking Cessation.⁴⁷ The report's findings were largely similar to that of the USPSTF. The Surgeon General's report issued some additional findings regarding internet-based interventions for cessation and describes some suggestive but not sufficient evidence about specific e-cigarette use behaviors and increased cessation. Overall, the Surgeon General's report found that there is inadequate evidence to conclude that e-cigarettes increase smoking cessation. More information on the Surgeon General's Report on Smoking Cessation is available at https://www.cdc.gov/tobacco/data_statistics/sgr/2020-smoking-cessation/#fact-sheets.

Suggestions for Practice Regarding the I Statements

Pharmacotherapy for Pregnant Persons

According to data from the National Vital Statistics System, in 2016, 7.2% of women who gave birth smoked cigarettes during pregnancy,⁶ and among 1071 pregnant women aged 18 to 44 years, 3.6% reported using e-cigarettes.⁴⁸ Smoking during pregnancy reduces fetal growth, increases the risk of preterm birth, and doubles

Table 2. Tobacco Cessation Behavioral Counseling Interventions*

Intervention type		Individual or group-based counseling	Telephone and mobile phone-based interventions	Psychosocial intervention in pregnant persons
Intervention recipient	Physician or nurse advice Adult smokers motivated to quit	Adult smokers, regardless of motivation to quit	<ul style="list-style-type: none"> Adult smokers motivated to quit Most mobile phone-based interventions targeted adults younger than 45 y 	Pregnant smokers
Behavior change goals and techniques	<ul style="list-style-type: none"> Specific “advice” varied but generally included a verbal “stop smoking” message Most often, advice was given along with print materials, additional advice from health care staff, or a referral to a cessation clinic 	<ul style="list-style-type: none"> Typically included review of smoking history and motivation to quit, help in the identification of high-risk situations and the generation for problem solving strategies, and nonspecific support and encouragement Many group-based sessions included cognitive behavioral therapy. Initial sessions focused on discussion of motivation for quitting, health benefits, and strategies for planning a quit attempt 	<p>Telephone counseling and mobile phone-based interventions were generally tailored to participants’ smoking history and readiness to quit and focused on increasing motivation and likelihood of quitting</p> <ul style="list-style-type: none"> Cognitive behavioral, motivational and supportive therapies that include counseling, health education, feedback, financial incentives, and social support 	
Intervention intensity	Often a single session lasting less than 20 min (with or without print materials) plus up to 1 follow-up visit between 1 wk and 3 mo later	<ul style="list-style-type: none"> Often 1 face-to-face session with follow-up over 1 week to 4 months later Individual-based counseling given during 1 face-to-face session with multiple follow-up sessions in person or via telephone Group-based counseling delivered over 6 to 8 sessions 	<p>Varied from 2 wk to 1 y, with most taking place over 3 to 4 mo</p> <ul style="list-style-type: none"> Telephone counseling: <ul style="list-style-type: none"> 1 to 12 calls 10 to 20 minutes per call, although the first calls were often longer Occurred during scheduled telephone calls that began after smokers had first called a smoking quitline Mobile phone-based: <ul style="list-style-type: none"> Fewer than 2 messages per day every day over the course of the intervention Used text messaging 	<ul style="list-style-type: none"> Recruited during first prenatal visit or during second-trimester visit and continued through late pregnancy Frequency and intensity varied. Counseling ranged from a single session <5 min to several sessions up to 4 h per session and has been increasing over time
Interventionist	Physicians (eg, general practitioners, family practice) or nursing staff	Smoking cessation specialists, often with backgrounds in social work, psychology, psychiatry, health education, and nursing	<ul style="list-style-type: none"> Telephone counseling provided by professional counselors or trained health care professionals Text messages were developed and administered through computer expert-generated systems 	Varied
Practice settings	Primary care or hospital settings	Hospital or smoking cessation clinic settings	Virtual via telephone or mobile phone; a few studies provided face-to-face support	Women’s health clinic or smoking cessation clinic
Examples of interventions and materials used in studies ^{b,c}	<p>Intervention: Morgan et al,¹⁵ 1996</p> <p>Material used: Clear Horizons: A Quit Smoking Guide Especially for Those 50 and Over (Orleans et al,¹⁶ 1989)</p> <p>Intervention: Canga et al,¹⁷ 2000</p> <p>Materials used: Based on How to Help Your Patients Stop Smoking: A National Cancer Institute Manual for Physicians¹⁸ and the orientation of the Mayo Nicotine Dependence Center¹⁹</p>	<p>Intervention: Weisfeld et al,²⁰ 1991</p> <p>Material used: Clearing the Air: How to Quit Smoking and Quit for Keeps (National Cancer Institute,²¹ 1987)</p> <p>Other interventions: Fiore et al,²² 2004; Glasgow et al,²³ 2000</p>	<p>Intervention: Bock et al,²⁴ 2013</p> <p>Material used: American Lung Association guide (Stretchler et al,²⁵ 1989)</p> <p>Intervention: Orleans et al,²⁶ 1991</p> <p>Material used: A Lifetime of Freedom From Smoking (American Lung Association,²⁷ 1980)</p> <p>Intervention: McBride et al,²⁸ 1999</p> <p>Material used: Clearing The Air: Quit Smoking Today (National Cancer Institute, 2008 [https://www.cancer.gov/publications/patient-education/clearing-the-air])</p> <p>Other interventions: Curry et al,²⁹ 1995; Ellerbeck et al,³⁰ 2009; McClure et al,³¹ 2005</p>	<p>Intervention: Rigotti et al,³² 2006</p> <p>Material used: Solomon and Quinn,³³ 2004</p> <p>Intervention: Windsor et al,³⁴ 2011</p> <p>Materials used: Ask-Advise-Assess-Arrange SCRIPT,^{12,35-37} including a video,³⁸ guide to quit smoking,³⁹ and a ≤10-minute counseling session⁴⁰</p> <p>Other interventions: Bullock et al,⁴¹ 2009; Lee et al,⁴² 2015; Pollak et al,⁴³ 2013; Stotts et al,⁴⁴ 2009</p>

(continued)

Table 2. Tobacco Cessation Behavioral Counseling Interventions^a (continued)

Intervention type	Individual or group-based counseling	Telephone and mobile phone-based interventions	Psychosocial intervention in pregnant persons
<p>Physician or nurse advice</p> <p>Increases the rate of smoking cessation at 6 mo or more</p> <ul style="list-style-type: none"> Physician advice: RR, 1.76 (95% CI, 1.58-1.96). Some evidence suggests that providing additional follow-up is more effective Nurse advice: 1.29 (95% CI, 1.21-1.38) 	<p>Increases the rate of smoking cessation at 6 mo or more</p> <ul style="list-style-type: none"> Individual counseling: RR, 1.48 (95% CI, 1.34-1.64) Group-based therapy: RR, 1.88 (95% CI, 1.52-2.33) 	<p>Increases the rate of smoking cessation at 6 mo or more</p> <ul style="list-style-type: none"> Telephone counseling (provided after smoker calls quitline): RR, 1.38 (95% CI, 1.19-1.61) Telephone counseling (other settings): RR, 1.25 (95% CI, 1.15-1.35) Mobile phone-based interventions: RR, 1.54 (95% CI, 1.19-2.00) <p>Some evidence that interventions were more effective for smokers who were motivated to quit</p>	<ul style="list-style-type: none"> Increases smoking cessation in late pregnancy: RR, 1.35 (95% CI, 1.23-1.48) Interventions more effective when counseling was more intensive, augmented with messages and self-help materials tailored for pregnant women, and included messages about the effects of smoking on both maternal and fetal health with strong advice to quit as soon as possible Health education, without counseling, was not effective

Abbreviation: RR, risk ratio.

^a Adapted from Appendix H Table 1 in Patnode et al¹³ and a modified Template for Intervention Description and Replication (TIDieR) checklist.⁴⁵

^b Example interventions are those that demonstrated a positive direction of effect on smoking cessation, were at low risk of bias, and took place in the United States in primary care or a primary care-applicable setting among an unselected sample of adults (ie, those not selected based on having smoking-related disease or other

comorbid conditions). Inclusion of studies and materials is for example purposes only and does not indicate endorsement by the USPSTF.

^c Materials provided for practice include materials or protocols that were noted within the source study and that were able to be located.

^d Demonstrated benefit of intervention type is based on comparison of that intervention type with a given control and should not be used to compare the effectiveness of one intervention type with another.

the risk for delivering an infant with low birth weight. It also increases the relative risk for stillbirth death by 25% to 50%.^{1,2} Quitting smoking early in pregnancy can reduce or eliminate the adverse effects of smoking on fetal growth.⁴⁷ For pregnant persons for whom behavioral counseling alone does not work, evidence to support other options to increase smoking cessation during pregnancy are limited. Few clinical trials have evaluated the effectiveness of NRT for smoking cessation in pregnant women. Although most studies were in the direction of benefit, no statistically significant increase in cessation was seen.¹³ There is limited evidence on harms of NRT from trials in pregnant persons. Potential adverse maternal events reported in studies of NRT include slightly increased diastolic blood pressure and skin reactions to the patch.¹³ Potential adverse events reported in nonpregnant adults include higher rates of low-risk cardiovascular events, such as tachycardia.¹³ It has been suggested that NRT may be safer than smoking during pregnancy given that cigarette smoke contains harmful substances in addition to nicotine. The USPSTF identified no studies on bupropion SR or varenicline pharmacotherapy for tobacco smoking cessation during pregnancy.

In the absence of clear evidence on the balance of benefits and harms of pharmacotherapy in pregnant women, clinicians are encouraged to consider the severity of tobacco dependence in each patient and engage in shared decision-making to determine the best individual treatment course.

e-Cigarettes in Nonpregnant Adults and Pregnant Persons

No tobacco product use is risk-free, including the use of e-cigarettes. Tobacco smoking cessation can be difficult for many individuals; thus, having a variety of tools available to help persons quit smoking would potentially be helpful. Findings from small surveys and qualitative data report mixed findings on whether physicians are recommending e-cigarettes to patients to help them quit smoking.^{13,49-51} Few randomized trials have evaluated the effectiveness of e-cigarettes to increase tobacco smoking cessation in nonpregnant adults, and no trials have evaluated e-cigarettes for tobacco smoking cessation in pregnant persons.¹³ Overall, results were mixed on whether smoking cessation increased with e-cigarettes; however, continued e-cigarette use after the intervention phase of trials remained high, indicating continued nicotine dependence. Trial evidence on harms of e-cigarettes used for smoking cessation is also limited. The most commonly reported adverse effects from e-cigarette use reported in trials included coughing, nausea, throat irritation, and sleep disruption.¹³ Generally, no significant difference in short-term serious adverse events associated with e-cigarette use was reported.¹³ Evidence on potential harms of e-cigarette use in general (whether for tobacco smoking cessation or not) has been reviewed in the National Academies of Science, Engineering, and Medicine report Public Health Consequences of E-Cigarettes.⁵² For example, the report found conclusive evidence that in addition to nicotine, most e-cigarette products contain and emit numerous potentially toxic substances. Additionally, an outbreak of e-cigarette, or vaping product, use-associated lung injury (EVALI) that occurred in the US in late 2019 also suggests potential harms of e-cigarette use. The vast majority of cases have been associated with tetrahydrocannabinol (THC)-containing e-cigarettes.⁵³

Given the high rates of e-cigarette use in children and adolescents currently in the US,⁵⁴ the USPSTF recognizes that an overall

public health question remains on whether the potential use of e-cigarettes as a tobacco smoking cessation aid (if ever proven effective) could be balanced with the high rates of e-cigarette use in youth as a driver for increasing overall tobacco use. The USPSTF has issued a separate recommendation statement on the prevention of tobacco use, including e-cigarettes, in children and adolescents.⁹ The current USPSTF recommendation statement for adults evaluated the evidence on the benefits and harms of e-cigarettes to increase tobacco cessation; the USPSTF found this evidence to be insufficient. Given the proven effectiveness of behavioral counseling interventions in both nonpregnant and pregnant adults, and of pharmacotherapy in nonpregnant adults, the USPSTF recommends that clinicians focus on offering behavioral counseling and pharmacotherapy to increase smoking cessation in nonpregnant adults, and behavioral counseling to increase smoking cessation in pregnant persons.

Other Related USPSTF Recommendations

In 2020, the USPSTF recommended that primary care clinicians provide interventions, including education or brief counseling, to prevent the initiation of tobacco use (including e-cigarettes) in school-aged children and adolescents.⁹ The USPSTF found the evidence on primary care interventions for the cessation of tobacco use in youth to be insufficient.

Update of Previous USPSTF Recommendation

This recommendation statement replaces the 2015 USPSTF recommendation statement on behavioral and pharmacotherapy interventions for tobacco smoking cessation in adults, including pregnant women.⁵⁵ The current recommendation statement has been updated to reflect newer evidence and language in the field of tobacco cessation and includes a description of the 2019 EVALI outbreak in the US. However, the recommendations on the services primary care clinicians should provide for tobacco cessation are the same as in 2015.

Supporting Evidence

Scope of Review

The USPSTF commissioned a systematic review to evaluate the benefits and harms of primary care interventions on tobacco use cessation in adults, including pregnant persons.^{13,14} The USPSTF considered evidence on the benefits and harms of behavioral counseling interventions, pharmacotherapy interventions, and e-cigarettes in nonpregnant adults and pregnant persons. The vast majority of evidence identified focused on cigarette smoking cessation.

Benefits of Tobacco Cessation Interventions

Nonpregnant Adults

Behavioral Counseling Interventions | The USPSTF reviewed evidence on the benefits of behavioral counseling interventions on tobacco use cessation in general adults primarily from 20 systematic reviews that covered approximately 830 RCTs and more than 500 000 participants.¹³ The evidence almost exclusively evaluated interventions for cessation of cigarette smoking. Physician ad-

vice, nurse advice, individual counseling with a cessation specialist, group behavioral interventions, telephone counseling, and mobile phone-based interventions have all been found to be effective to increase cessation of cigarette smoking.¹³

Based on a 2013 systematic review that pooled 26 trials (n = 22 239), rates of smoking cessation at 6 months or more were an average of 8.0% in groups that received physician advice compared with 4.8% in groups that received no advice or usual care (risk ratio [RR], 1.76 [95% CI, 1.58-1.96]).^{13,56} When stratified by intensity level, both minimal advice (defined as a single session lasting <20 minutes with ≤1 follow-up sessions) and intensive advice (defined as a single session lasting ≥20 minutes or >1 follow-up session) from a physician was associated with significantly increased cessation rates compared with no advice. Although not definitive, some subgroup analyses suggest that more intensive physician counseling (>20 minutes for initial consult, use of additional materials, or >1 follow-up visit) may be associated with an increase in cessation rates, particularly in patients who have smoking-related disease.^{13,56}

Based on a 2017 systematic review that pooled 44 trials evaluating nurse advice, 14.2% of participants who received interventions from nurses achieved smoking cessation at 6 months or more compared with 12.2% of those who received usual care or minimal intervention (RR, 1.29 [95% CI, 1.21-1.38]).^{13,57} No evidence of effect modification was found when comparing higher- or lower-intensity counseling provided by nurses.

A systematic review from 2017 that pooled 33 trials (n = 13 762) found that an average of 11.4% of participants who received individual counseling with a cessation specialist achieved smoking cessation, compared with 7.7% of those who received minimal contact of less than 15 minutes of advice (RR, 1.48 [95% CI, 1.34-1.64]).^{13,58} The review found some evidence suggesting that more intensive counseling was associated with higher cessation rates. Another systematic review published in 2017 that pooled 13 trials (n = 4395) also found that participants receiving group behavioral interventions had higher cessation rates compared with those who received a self-help program (10.4% cessation rate in intervention group vs 5.8% cessation rate in control group; RR, 1.88 [95% CI, 1.52-2.33]).^{13,59}

A 2019 review on telephone counseling interventions found that proactive telephone counseling (where telephone counselors called participants directly either to initiate counseling or in response to a participant calling a quitline) was associated with increased cessation rates.^{13,60} If the telephone counseling was a "cold call" from telephone counselors to initiate counseling, smoking cessation rates were 11.0% in control participants and 13.9% in telephone counseling recipients (RR, 1.25 [95% CI, 1.15-1.35]; 65 trials; n = 41 233).^{13,60} If telephone counseling occurred in response to a participant contacting a quitline, cessation rates were 7.8% in control participants and 10.8% in intervention recipients (RR, 1.38 [95% CI, 1.19-1.61]; 14 trials; n = 32 484).^{13,60}

A 2019 review that pooled 13 trials (n = 14 133) found higher cessation rates associated with mobile phone-based interventions.^{13,61} All studies primarily used text messaging as the main intervention component, although a limited number of studies looked at individual mobile phone applications. Smoking cessation rates were an average of 5.6% in participants receiving usual or minimal care and 9.5% in those receiving mobile phone-based interventions (RR, 1.54 [95% CI, 1.19-2.00]).

The USPSTF considered evidence on other behavioral counseling interventions such as print-based, nontailored self-help materials, internet-based interventions, motivational interviewing, biofeedback, exercise, acupuncture, and hypnotherapy¹³; however, limited evidence was available on these interventions.

Pharmacotherapy | The USPSTF reviewed evidence from 4 systematic reviews on pharmacotherapy that reported smoking cessation at 6 months or more.¹³

A 2018 review on NRT (133 studies; n = 64 640)⁶² found that 16.9% of participants taking any form of NRT achieved smoking abstinence at 6 months or more compared with 10.5% of participants receiving placebo or taking no NRT (RR, 1.55 [95% CI, 1.49-1.61]). All forms of NRT (patch, gum, inhaler, intranasal, and tablets) were found to be effective. Another review found that using combination NRT (patch plus a fast-acting form) was associated with higher smoking cessation rates than using a single form of NRT (16.9% vs 13.9%; RR, 1.25 [95% CI, 1.15-1.36]).⁶³

A 2020 systematic review on the use of antidepressants for smoking cessation (46 studies; n = 17 866) found that bupropion SR was associated with a significantly higher rate of smoking abstinence at 6 months or more than placebo or no bupropion SR (19.0% vs 11.0%; RR, 1.64 [95% CI, 1.52-1.77]).⁶⁴

Based on pooled analyses of 27 studies (n = 12 625), a 2016 systematic review found that varenicline was associated with higher rates of smoking cessation over placebo (25.6% vs 11.1%; RR, 2.24 [95% CI, 2.06-2.43]).⁶⁵

Smaller subsets of studies from these reviews directly compared types of pharmacotherapy for smoking cessation. Eight studies (n = 6264) compared varenicline and NRT and found that varenicline was associated with a greater smoking cessation rate over any form of NRT.⁶⁵ Six studies (n = 6286) evaluated varenicline vs bupropion SR and found that varenicline was associated with a higher cessation rate.^{64,65} Smoking cessation rates among participants using NRT vs bupropion SR at 6 months or more did not significantly differ (10 studies; n = 9230).⁶⁴

Combined Behavioral Counseling Interventions and

Pharmacotherapy | Combinations of behavioral counseling and pharmacotherapy for smoking cessation were also effective, and potentially more effective than behavioral counseling or pharmacotherapy alone.¹³ A 2016 systematic review (52 studies; n = 19 488)⁶⁶ found that participants who received combination pharmacotherapy and intensive behavioral counseling had a higher abstinence rate at 6 months or more compared with control participants who received usual care, self-help materials, or brief advice on quitting (which was less intensive than the counseling or support given to the intervention groups) (15.2% vs 8.6%; RR, 1.83 [95% CI, 1.68-1.98]). These combination interventions often have behavioral components delivered by specialized smoking cessation counselors or trained staff; however, no difference in effectiveness was seen in studies in which a non-specialist provided the counseling.¹³ Most studies used NRT as the pharmacotherapy. The intensity and format of the behavioral counseling component of the intervention varied greatly, with the majority of studies offering at least 4 behavioral counseling sessions, with a total planned contact time generally ranging from 90 to 300 minutes. Most of the behavioral counseling was delivered by a specialized smoking cessation counselor or trained trial staff.

Another systematic review,⁶⁷ which pooled analyses of 65 studies (n = 23 331), found that cessation rates at 6 months or more were modestly higher in participants who received behavioral support as an adjunct to pharmacotherapy than in those who received pharmacotherapy alone. Most studies offered NRT as the pharmacotherapy. Participants in the control group may have also received some counseling or support, but it was less intensive than in the intervention group. The addition of behavioral support to pharmacotherapy was associated with significantly higher cessation rates, approximately 17% in persons using pharmacotherapy alone vs 20% in those using a combination of pharmacotherapy and behavioral support (RR, 1.15 [95% CI, 1.08-1.22]).¹³

Pregnant Persons

For benefits of tobacco use cessation interventions in pregnant persons, the USPSTF reviewed evidence from an existing systematic review on behavioral counseling interventions⁶⁸ and from primary studies of pharmacotherapy. As with the evidence base in nonpregnant adults, the available evidence primarily addressed smoking cessation.

Behavioral Counseling Interventions | Based on a systematic review from 2017,⁶⁸ the USPSTF found that behavioral counseling interventions in pregnant women were effective at improving rates of smoking cessation as well as some perinatal health outcomes. Pooled analyses from 97 studies (n = 26 637) found that use of any psychosocial intervention was associated with higher smoking cessation rates in late pregnancy relative to control groups (an average quit rate of 12.2% in control groups and 16.4% in intervention groups) (RR, 1.35 [95% CI, 1.23-1.48]). The majority of studies used counseling interventions, and analyses of only counseling interventions (51 studies; n = 18 276) found a significant increase in smoking cessation rates late in pregnancy, from 10.8% in control groups to 14.5% in intervention groups (RR, 1.31 [95% CI, 1.16-1.47]). Studies of other intervention types (health education, feedback, incentives, social support, and exercise) were much fewer, with fewer total participants. Findings of smoking cessation effectiveness by intervention type were all in the direction of benefit, although not all were statistically significant. No subgroup differences by intervention type were found. The same systematic review also assessed the association of behavioral counseling interventions with perinatal outcomes and found lower rates of low birth weight (RR, 0.83 [95% CI, 0.72-0.94]; 18 trials; n = 9402) and increased mean birth weight (mean difference, 55.6 g [95% CI, 29.82-81.38]; 26 trials; n = 11 338). No statistically significant difference in rates of preterm births or stillbirths was found.

Pharmacotherapy | The USPSTF identified 5 placebo-controlled trials on NRT during pregnancy.¹³ All 5 trials included behavioral counseling or support in addition to NRT. One trial used NRT gum as the intervention, one used an inhaler, while the other 3 trials used a NRT patch. Adherence to NRT in studies was low (<10% in 1 study). Findings of the 5 trials were all generally in the direction of benefit with NRT; however, none of the studies, either individually or when pooled, found a statistically significant difference in smoking cessation (11.9% in NRT intervention groups vs 10.1% in control groups; RR, 1.11 [95% CI, 0.79-1.56]; 5 trials; n = 2033).¹³ Seven trials (the 5 placebo-controlled trials previously mentioned plus 2 additional non-

placebo-controlled trials) reported on perinatal and health outcomes with NRT during pregnancy¹³; findings were inconsistent and imprecise. No studies on bupropion SR or varenicline for smoking cessation during pregnancy were identified.

e-Cigarettes in Nonpregnant Adults and Pregnant Persons

The FDA classifies e-cigarettes as a tobacco product and to date, no e-cigarettes have been approved as a smoking cessation aid. Approximately 4.5% of adults^{5,69} and 3.6% of pregnant women⁴⁸ report using e-cigarettes. Higher e-cigarette use is reported among young adults aged 18 to 24 years (7.6%)⁷⁰ and has been increasing in recent years.⁷⁰ In addition to young adults, e-cigarette use among adults is higher in men; non-Hispanic White adults and other non-Hispanic adults; lesbian, gay, or bisexual⁵ persons; and persons with chronic illnesses (such as cardiovascular disease, diabetes, cancer, asthma, chronic obstructive pulmonary disease, chronic kidney disease, and depression).^{13,71} Most adult e-cigarette users report that quitting smoking and health improvement are major reasons why they started using e-cigarettes.^{72,73} This is in contrast to youth, where it has been found that e-cigarette use increases risk of ever smoking cigarettes.⁵² Nineteen percent of tobacco users use 2 or more tobacco products, the most common combination being cigarettes and e-cigarettes.⁷⁴

The USPSTF identified 5 RCTs (n = 3117) on e-cigarettes for smoking cessation in nonpregnant adults^{13,75-80} and no studies in pregnant persons.¹³ All 5 studies were conducted outside of the US (2 in New Zealand, 1 in Italy, 1 in Korea, and 1 in the UK). Four of the studies included participants who either wanted to stop smoking or were attending a stop smoking service. The type of e-cigarette interventions (nicotine content, whether NRT was also given, nicotine cartridge vs e-liquid, and whether behavioral support was also provided) and control interventions (NRT vs nonnicotine e-cigarette) varied across studies, making comparisons difficult. Only 3 of the e-cigarettes used in the studies are currently available in the US. Study size ranged from 150 to 1124 participants.

Reported trial findings were mixed. The 2 largest and most recent trials reported a statistically significant increase in smoking cessation at 6 months; 1 study reported smoking cessation rates of 4% in control groups vs 7%⁷⁹ in intervention groups; the second trial reported smoking cessation rates of 25% in control groups vs 35%⁷⁸ in intervention groups. The 3 remaining trials reported no statistically significant differences in smoking cessation rates. Three of the studies reported on continued e-cigarette use after achievement of smoking cessation in intervention groups at 6 months to 1 year, with continued e-cigarette use ranging from 38% to 80%. One study reported that 26.9% of all study participants were using e-cigarettes at 1 year.⁷⁷

Harms of Tobacco Cessation Interventions

Nonpregnant Adults

Behavioral Counseling Interventions | The USPSTF identified limited evidence on harms from behavioral counseling interventions for tobacco cessation. Three systematic reviews (1 on internet-based interventions, another on incentives, and 1 on hypnotherapy) did not find evidence of serious adverse events associated with interventions.¹³

Pharmacotherapy | The USPSTF identified 4 systematic reviews on NRT that reported on harms¹³: 3 reviews compared harms of NRT

vs placebo^{62,81,82} and 1 compared harms from various types of NRT.⁶³ Twelve to 21 studies (n = 10 234 to 11 647) reported on cardiovascular harms. Statistically significantly more cardiovascular adverse events (in particular, heart palpitations and chest pain) were found for participants randomized to NRT vs placebo (RR, 1.81 [95% CI, 1.35-2.43]; 21 trials; n = 11 647).⁸² However, when analyses focused on major cardiovascular adverse events (combined outcome of cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke), findings were no longer statistically significant (RR, 1.38 [95% CI, 0.58-3.26]; 21 trials; n = 11 647).⁸² Other reported harms associated with NRT included nausea, vomiting, gastrointestinal symptoms, and insomnia. Localized increased skin irritation at the NRT patch site has also been reported. No statistically significant increase in headaches, dizziness, anxiety, or depression were found. Cardiac adverse events and other serious adverse events did not differ by type of NRT.⁶³

The USPSTF considered evidence on harms from bupropion SR for tobacco smoking cessation from 4 systematic reviews.¹³ No difference in serious adverse events (RR, 1.30 [95% CI, 1.00-1.69]; 33 trials; n = 9631),⁸³ cardiovascular adverse events (RR, 1.03 [95% CI, 0.71-1.50]; 27 trials; n = 10 402),⁸² or major cardiovascular events (RR, 0.57 [95% CI, 0.31-1.04]; 27 trials; n = 10 402)⁸² were found with bupropion SR (compared with placebo or no bupropion SR). No difference in moderate and severe neuropsychiatric events, including rates of suicidal behavior and ideation, were found with bupropion SR (compared with varenicline or NRT) in the recent Evaluating Adverse Events in a Global Smoking Cessation Study (EAGLES) trial.^{84,85}

Evidence on harms of varenicline for tobacco cessation are available from 3 systematic reviews on varenicline in unselected smokers, 4 systematic reviews of varenicline among persons with severe mental illness, and 1 review on varenicline for cessation of smokeless tobacco.¹³ Common adverse effects reported with varenicline include nausea, insomnia, abnormal dreams, headache, and fatigue.¹³ One review found an increase in serious adverse events with varenicline in unselected smokers (RR, 1.25 [95% CI, 1.04-1.49]; 29 trials; n = 15 370); however, many of these events included comorbidities that were mostly considered by the study authors to be unrelated to the treatments.⁶⁵ Across 3 systematic reviews (encompassing 18 to 38 studies; n = 8587 to 12 706), no statistically significant difference in cardiovascular adverse events or cardiovascular severe adverse events was found.¹³ Additionally, no statistically significant increase in neuropsychiatric adverse events (including depression, suicidal ideation, and suicide attempt) was found across several systematic reviews.¹³

Combinations of Behavioral Counseling Interventions and Pharmacotherapy

| The USPSTF did not identify any reports of adverse events related to combinations of behavioral counseling interventions and pharmacotherapy. Any harms of combined therapy are assumed to be similar to those of the pharmacotherapy being used.

Pregnant Persons

Behavioral Counseling Intervention | The primary review that informed the USPSTF on the benefits of behavioral counseling interventions for smoking cessation during pregnancy also summarized

evidence on harms of behavioral counseling interventions.⁶⁸ Based on analyses of 13 trials (n = 5831), no increase in adverse effects from psychosocial interventions was seen.

Pharmacotherapy | Nicotine in general has been shown in animal studies to cause fetal harms. However, NRT does not contain many harmful substances, such as hydrogen cyanide and carbon monoxide, that are present in cigarette smoke.⁸⁶ Evidence on harms of NRT during pregnancy is limited; the USPSTF identified 5 placebo-controlled trials (n = 3117), 2 non-placebo-controlled trials (n = 233), and 3 cohort studies (n = 306 721).¹³ Findings on potential harms of NRT on birth outcomes from trial evidence is mixed, although most studies reported findings in the direction of benefit rather than harm. Observational evidence from cohort studies generally did not indicate an increase in stillbirth or low birth weight with NRT. Based on observational evidence, there was no evidence of increased risk of premature delivery, small for gestational age, stillbirth, or congenital anomalies associated with the use of NRT, bupropion, and varenicline vs smoking. According to FDA labeling, some fetal harms with bupropion were noted in animal studies, but currently, no adequate, well-controlled studies of bupropion SR use during pregnancy (for any indication) in humans are available.⁸⁷ Labeling for varenicline states that available studies cannot definitively establish or exclude varenicline-associated risk during pregnancy.⁸⁸

e-Cigarettes in Nonpregnant Adults and Pregnant Persons

The USPSTF identified 9 RCTs (n = 3942) that reported on harms of e-cigarette interventions for tobacco smoking cessation in nonpregnant adults¹³ (the 5 trials previously described that reported cessation rates at 6 months or more, as well as an additional 4 trials that reported on cessation rates at less than 6 months). No trials on harms of e-cigarettes for smoking cessation in pregnant persons was identified. The most commonly reported adverse effects from e-cigarette use reported in trials include coughing, nausea, throat irritation, and sleep disruption.¹³ Generally, no significant difference in short-term serious adverse events associated with e-cigarette use was reported.¹³ Data on potential long-term harms of e-cigarette use are currently lacking.

Additional evidence on harms from e-cigarette use (whether used for tobacco cessation or not) considered by the USPSTF included data of the 2019 EVALI outbreak in the US⁵³ and the 2018 report Public Health Consequences of E-Cigarettes by the National Academies of Sciences, Engineering, and Medicine.⁵² In late 2019, an outbreak of EVALI occurred in the US. Symptoms of EVALI include cough, shortness of breath, chest pain, nausea, vomiting, stomach pain, diarrhea, fever, chills, and weight loss. As of February 2020, more than 2800 cases of EVALI were reported, with 68 deaths.⁵³ Based on testing of bronchoalveolar lavage fluid samples of patients with EVALI⁸⁹ and testing of products used by patients with EVALI,⁵³ vitamin E acetate (an additive in some THC-containing e-cigarettes) was found to be strongly linked to EVALI.⁵³ However, evidence is not sufficient to rule out the contribution of other chemicals of concern, including chemicals in either THC- or non-THC-containing products, in some reported EVALI cases.⁵³

The National Academies of Sciences, Engineering, and Medicine report found that in youth and young adults, there is substantial evidence that e-cigarette use increases risk of ever using combustible tobacco and moderate evidence that e-cigarette use

increases the frequency and intensity of subsequent cigarette smoking.⁵² The report also found conclusive evidence that e-cigarettes contain and emit potentially toxic substances, although substantial evidence shows that other than nicotine, there is significantly lower exposure to potentially toxic substances from e-cigarettes compared with combustible tobacco cigarettes.⁵²

Response to Public Discussion

A draft version of this recommendation statement was posted for public comment on the USPSTF website from June 2, 2020, to June 29, 2020. Several comments expressed concern about the insufficient evidence statement on e-cigarettes for cessation. Some respondents wanted the USPSTF to recommend against e-cigarettes for tobacco cessation, while others wanted the USPSTF to recommend in favor of e-cigarettes. Based on the evidence reviewed, the USPSTF could not determine whether e-cigarettes are effective in helping persons to quit smoking cigarettes, nor could it determine what the potential long-term harms of e-cigarette use are; thus, it cannot recommend for or against their use. Some comments were also received requesting that the USPSTF recommend NRT for smoking cessation during pregnancy. Too few trials were identified for the USPSTF to determine whether NRT during pregnancy provides overall more benefits or harms, and the USPSTF calls for more research on NRT and other pharmacotherapy to help pregnant persons quit using tobacco. Last, edits to clarify language, as well as additional information from the recent 2020 Surgeon General's Report on Smoking Cessation, have been provided in response to comments.

How Does Evidence Fit With Biological Understanding?

Because of the well-established health benefits of smoking cessation,^{1,12,47} most of the research on interventions for smoking cessation focuses on cessation (rather than health outcomes) as a primary outcome. The current review identified 1 study⁹⁰ of middle-aged men at high risk for cardiorespiratory disease that found lower (although not statistically significant) total mortality, fatal coronary disease, and lung cancer death at 20 years of follow-up in participants who received advice from medical practitioners.⁹¹ The study also found some reduction in all-cause mortality, coronary disease mortality, and lung cancer incidence and mortality at 20 years of follow-up, although these outcomes were not significant.⁹¹

Although not zero, less toxins have been found to be released by e-cigarettes than by cigarettes. It is hypothesized that health outcomes may be improved in adults who completely switch from cigarette smoking to e-cigarette use, although long-term data are not available yet to support this. Evidence on long-term harms of e-cigarette use in general is lacking and is needed. Additionally, emerging evidence suggests that toxicant levels in dual users of e-cigarettes and cigarettes may be higher than in conventional cigarette-only users.⁹²

Research Needs and Gaps

The greatest research needs are to gain a better understanding of the effectiveness of e-cigarettes for smoking cessation, as well as potential short- and long-term harms of e-cigarette use, and to understand whether there are effective pharmacotherapy options for pregnant persons.

- e-Cigarettes: Given the potential negative effect that increasing e-cigarette use in youth is having on overall tobacco control efforts, there is an urgent need for research that provides both a clearer understanding of whether e-cigarettes may increase adult tobacco smoking cessation, as well as the potential harms of e-cigarette use as a tobacco product. Future research on e-cigarettes for smoking cessation in adults should address the following:
 - Studies must be well-designed RCTs that compare e-cigarette interventions with placebo, as well as established, effective combinations of pharmacotherapy and behavioral support.
 - Studies should be adequately powered to detect differences in continued smoking abstinence rates at 6 months or more.
 - Given the high rate of continued e-cigarette use after smoking cessation, research on both the short- and long-term harms of e-cigarette use is needed, as well as the harms in dual users of e-cigarettes and conventional cigarettes. More research is needed on smoking relapse rates in adults who have used e-cigarettes for smoking cessation and how to help with cessation of e-cigarette use once smoking abstinence has been achieved.
 - Given the rapidly evolving landscape of e-cigarettes, trials should include current generations of e-cigarettes. Additionally, to successfully conduct these types of studies, standardization of how to quantify e-cigarette use and levels of nicotine exposure from e-cigarettes is needed.
 - More research is needed to understand the patterns of e-cigarette use in youth and the risk factors for their transition from e-cigarette use to conventional cigarette smoking.
 - More research is also needed to better understand patterns of e-cigarette use in pregnant persons and potential harms of e-cigarette use to both pregnant persons and their offspring.
 - More research is needed on understanding how to help adults quit e-cigarettes.
- Pharmacotherapy in pregnant persons: Although behavioral counseling interventions have been found to be effective in improving smoking cessation during pregnancy, additional research is needed on pharmacotherapy options, in particular NRT, for pregnant persons for whom behavioral counseling interventions alone are not effective.
- Larger studies adequately powered to detect an effect on both smoking cessation rates (during pregnancy and postpartum) and changes in perinatal and child health outcomes are needed.
- A better understanding of why adherence rates to NRT during pregnancy is so low would also be helpful.

Although the benefits of behavioral counseling interventions and pharmacotherapy in nonpregnant adults and the benefits of behavioral counseling interventions in pregnant adults are well established, additional research on effective components of behavioral counseling and who to target specific interventions to would be informative. More research on newer modalities and remotely delivered interventions (mobile phone apps, internet-based interventions) would also be helpful. Additionally, the effectiveness of interventions for cessation of other forms of tobacco and whether interventions need to be tailored to individual tobacco product types are also needed. Last, more research is needed on interventions to prevent relapse of tobacco use.

Recommendations of Others

Numerous professional societies and health organizations, including the American Academy of Family Physicians,⁹³ American College of Physicians,⁹⁴ and American College of Obstetricians and Gynecologists (ACOG),⁹⁵ recommend that clinicians screen for tobacco use and provide interventions to patients who smoke.

For pregnant persons, ACOG recommends brief behavioral counseling and the use of evidence-based smoking cessation aids as effective strategies for achieving smoking cessation, even for very heavy smokers.⁹⁶ ACOG also recommends that NRT should be considered only after a detailed discussion with the patient of the known risks of continued smoking, the possible risks of NRT, and need for close supervision.⁹⁵

The American Academy of Pediatrics also has a policy statement recommending that pediatricians screen for the tobacco exposure of children during pediatric care visits and recommend nicotine dependence treatment, including behavioral interventions and pharmacotherapy, to tobacco-dependent parents.⁹⁷

More recently some organizations have addressed e-cigarette use in their tobacco use guidelines. The American Academy of Family Physicians,⁹⁸ the American College of Preventive Medicine,⁹⁹ and the American Heart Association¹⁰⁰ recommend that clinicians screen for e-cigarette use. Organizations vary somewhat in terms of whether they recommend e-cigarettes for smoking cessation. ACOG recommends against use of e-cigarettes in pregnant and postpartum individuals.^{95,101} The American Cancer Society does not recommend e-cigarettes as a smoking cessation method,¹⁰² and the American Heart Association¹⁰⁰ states that there is not enough evidence for clinicians to counsel patients on using e-cigarettes as a primary smoking cessation aid.

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Additional Information: The US Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific preventive care services for patients without obvious related signs or symptoms. It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment. The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision-making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

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