

AMERICAN THORACIC SOCIETY DOCUMENTS

Treatment of Nicotine Use in Adolescents Under 18 Years of Age An Official American Thoracic Society Clinical Practice Guideline

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Abstract

Background: The rising popularity of electronic cigarettes (e-cigarettes), the nicotine product that is most used by adolescents since 2014, has reversed decades of progress in declining youth tobacco use. E-cigarette use in adolescents is associated with future smoking, and evidence is mounting of an increased association with nicotine dependence. Therapies used to treat nicotine dependence in adults include pharmacotherapy and behavioral interventions. Pediatric guidelines recommend routine screening for any tobacco product use beginning at age 10 years. The goal of this guideline was to develop an evidence-based clinical practice guideline for the treatment of nicotine use in adolescents.

Methods: We summarized evidence addressing five PICO (patients, intervention, comparator, and outcome) questions, which were formulated by a multidisciplinary panel of experts

and methodologists using the evidence-to-decision framework. The Grading of Recommendations, Assessment, Development, and Evaluation (or, GRADE) approach was used to evaluate the certainty in evidence and generate actionable recommendations, which were voted on by the panel.

Results: The panel members considered the strength of the evidence as well as the potential benefits of the treatment modality from a clinical standpoint. The overall quality of the evidence was weak. Recommendations for or against the treatment modality for nicotine use were developed.

Conclusions: This expert panel provides evidence-based recommendations for treating nicotine use in adolescents 10 to 18 years of age.

Keywords: tobacco; e-cigarette; cigarette; cessation; pediatric

Summary of Recommendations

Recommendation 1

For adolescents 10 to 18 years of age who use nicotine and/or tobacco products, we recommend a counseling-based nicotine use

intervention (*strong recommendation, very low–certainty evidence*).

(*conditional recommendation, very low–certainty evidence*).

Recommendation 2

For adolescents 10 to 18 years of age who use nicotine and/or tobacco products, we suggest a technology-based nicotine use intervention

Recommendation 3

For adolescents 10 to 18 years of age who use nicotine and/or tobacco products, no recommendation can be made for or against

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A data supplement for this article is available via the Supplements tab at the top of the online article.

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nicotine replacement therapy because of the lack of consensus.

Recommendation 4

For adolescents 10 to 18 years of age who use nicotine and/or tobacco products, we suggest a trial of varenicline (*conditional recommendation, very low-certainty quality evidence*).

Recommendation 5

For adolescents 10 to 18 years of age who use nicotine and/or tobacco products, we suggest a trial of bupropion (*conditional recommendation, very low-certainty quality evidence*).

Introduction

Tobacco use remains a leading preventable causes of morbidity and mortality worldwide (1). Youth tobacco and/or nicotine use is an urgent health concern. The majority of adults who use tobacco products started before 18 years of age (2–4). Without prompt recognition and treatment, adolescents are at risk for a lifetime of health problems associated with tobacco use, including, but not limited to, pulmonary disease, cardiovascular disease, cancer, stroke, diabetes, and premature death (3). Nicotine is highly addictive; is harmful to the developing brain; poses lifetime health risks with fetal exposure; and is a neurotoxin with adverse effects on brain function, cognition, and mood (2, 4–8).

The use of nicotine and other tobacco products by adolescents had been on the

decline for several decades (5). However, because of the emergence of electronic cigarettes (e-cigarettes), there has been a dramatic uptake in tobacco and nicotine use among adolescents and young adults (5, 9). Since 2014, e-cigarettes have been the most commonly used tobacco product among adolescents (10), and its use reached a peak in 2019, with 27.5% of U.S. high school students reporting current use (11). Although rates have since declined, use remains high. According to the 2024 school-based National Youth Tobacco Survey, 10.1% of U.S. high school and 5.4% of middle school students reported using a tobacco product within the past 30 days, the most common being e-cigarettes (12). These, as well as other new and novel nicotine products (e.g., nicotine pouches), are able to deliver high concentrations of nicotine, often in flavors that appeal to youth, such as candy, fruit, and mint (10). Highly addictive, these products are associated with nicotine dependence and future combustible cigarette use. As a result, a whole new generation of youth is at high risk to develop nicotine dependence, underscoring the need for clinical guidelines. Exclusive youth e-cigarette users exhibit symptoms of dependency, which may be higher for dual users of e-cigarettes and combustible cigarettes (13), and a harm reduction approach that is often taken with adult users of combustible cigarettes may not be suitable to adolescents, who are often naive to the use of any tobacco product at the time of e-cigarette initiation. Despite the Food and Drug Administration's (FDA's) 2020 ban on flavored cartridge-based products, novel

nicotine products—such as highly potent synthetic nicotine—continue to emerge in the U.S. market, evading regulations (14) and often escaping the attention of clinicians and parents. More recently, despite changes in FDA policy, including a ban on flavored, cartridge-based products in 2020, novel nicotine products continue to emerge onto the U.S. marketplace, such as potent synthetic nicotine products, which circumvent FDA regulations (14) and are often overlooked by clinicians and parents. In 2024, 5.28 million students (19.0%) of middle and high school students reported ever having used any tobacco product, and a novel product, nicotine pouches (12); however, limited evidence-based clinical guidelines exist to help clinicians manage tobacco/nicotine use and/or tobacco/nicotine dependence (12).

In 2020, the American Thoracic Society (ATS) published “Initiating Pharmacologic Treatment in Tobacco-Dependent Adults: An Official American Thoracic Society Clinical Practice Guideline,” which provided recommendations for initiating treatment in tobacco-dependent adults (15). There is no such guideline for patients under 18 years of age. This guideline seeks to fill this gap and expand similar guidance to the pediatric population.

Use of These Guidelines

These recommendations are intended to aid healthcare providers in the management of adolescents 10 to 18 years of age who use nicotine/tobacco products. The recommendations in this guideline should not be considered mandates, nor are they

intended to override clinical judgment. Application of the recommendations should be based on the clinical context of each individual patient at the discretion of the clinician.

Foundations of Screening for Nicotine and Tobacco Use in Adolescents

This guideline was created with the assumption that the accepted standards of care for screening adolescents are already in practice.

1. Adolescents ages 10 to 18 years should be routinely screened by clinicians for use of nicotine and tobacco (cigarettes, e-cigarettes, smokeless tobacco [tobacco that is chewed or snuffed], cigars, cigarillos, hookah/waterpipe, nicotine pouches, other novel nicotine products).
2. Adolescents ages 10 to 18 years should be routinely screened for comorbid mental health conditions and/or other substance use and should be provided treatment.

Terminology

The definitions, terms, and colloquial names used for nicotine and tobacco products vary widely across the world and are continually changing as new technology emerges and human language evolves. For the purpose of these guidelines, we use the term *nicotine product* to encompass all nonpharmacologic nicotine products containing the chemical compound nicotine from plant tobacco or synthetic nicotine with delivery to the user occurring by inhalation or oral absorption for recreational purposes.

We have divided behavioral (i.e., nonpharmacologic) interventions into two subtypes. *Counseling-based interventions* are defined as interventions that are synchronous discussions between a trained provider and the patient to provide social and behavioral support for nicotine and/or tobacco cessation. Counseling-based interventions may differ on a variety of factors, including intensity, frequency, who attends, modality, provider, and setting. Complementary and alternative medicine interventions are excluded from this definition. *Technology-based interventions* are defined as asynchronous interventions

delivered remotely to promote nicotine and/or tobacco cessation. Technology-based interventions can differ on a variety of factors, including proactive versus reactive interactions with content by patients, self-guided versus directed, and level of personalization.

Methods

This clinical practice guideline was developed in accordance with the ATS policies and procedures. The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) method was used to develop the questions, identify and summarize evidence, and create the final recommendations for use in clinical practice.

The project was proposed by the co-chairs (S.E.B. and D.R.R.) and was reviewed and approved by the Pediatrics ATS Assembly, Program Review Subcommittee, and ATS Board of Directors. A panel of international experts in nicotine, tobacco products, and the adolescent population was convened, consisting of pediatric pulmonologists; pediatricians; adult pulmonary, sleep, and critical care physicians; psychologists; a pharmacist; patient and parent representatives; and two methodologists with experience in evidence synthesis and guideline development using GRADE methodology.

Industry relationships and other potential conflicts of interest were disclosed and managed in accordance with the policies and procedures of the ATS (available at <https://www.thoracic.org/about/governance/ethics-and-coi/coi-principles.php>). No conflicts of interest were identified. The panel met regularly through virtual video meetings and in person at the 2024 ATS International Conference. The panel developed an initial list of questions that was discussed in detail considering the importance, availability of evidence, and patient perspectives before the final selection and wording of questions. A decision was made to focus on treatment of nicotine product use by adolescents rather than dependence, given that adolescents are at high risk for addiction (16), even with brief use (17), and given that cessation in the critical phase of adolescence, regardless of nicotine dependence, would potentially prevent both health complications (18) and future substance use in adulthood (7).

The panel prioritized five PICO (patients, intervention, comparator, and outcome) questions for the guideline to address and determined which key outcomes would take priority in decision making for all PICO questions per GRADE guidance. These key outcomes include abstaining from nicotine or tobacco use, adverse effects of the medication/therapy, and quality of life. Abstinence was defined by studies in terms of *point prevalence*, or the proportion of subjects abstaining from use at a defined point in time relative to the intervention (e.g., 7-d point prevalence 3 mo after study intervention indicates abstinence for 7 d at 3 mo postintervention); or *prolonged abstinence*, defined as a longer duration of abstinence, compared with point prevalence, at a specified time postintervention (19). The age range agreed on by the committee was based on the World Health Organization guideline of 10 to 19 years of age. As there are already ATS guidelines for individuals older than 18 years, the committee opted to truncate the range to include adolescents 10 to 18 years old.

Literature searches built on the Cochrane Tobacco Addiction Group search strategies for nicotine prevention and cessation were conducted for English-language observational studies and randomized controlled trials addressing the PICO questions of interest. Searches were limited to indexing terms and keywords for “child” and “adolescent” to capture ages 10 to 18 years. Studies that had cohorts up to age 21 were included as indirect evidence and downgraded accordingly. Medline, Cochrane CENTRAL (Central Register of Controlled Trials), Embase, and APA PsycINFO were searched on the Ovid platform. The search strategy for the nonpharmacological therapy PICO questions was to include research from 2007 to the present; the Agency for Healthcare Research and Quality’s “Treating Tobacco Use and Dependence: 2008 Update” included research up to 2007 (20). No date limits were applied for the pharmacotherapy PICO questions, including nicotine replacement therapy (NRT). Existing systematic reviews addressing the proposed PICO questions were reviewed for the latest evidence. When applicable, data from individual studies were pooled to create a meta-analysis. The direction and strength of recommendations was decided by panel consensus. (For detailed search strategies,

see the supplemental METHODS in the online supplement.)

Results

Question 1: Should Adolescents 10 to 18 Years of Age Who Use Nicotine and/or Tobacco Products Receive Counseling-based Nicotine Use Intervention?

Background. Counseling interventions are an important component of substance use treatment in adults and have been used in adolescents to modify a variety of health behaviors (21–25). Less is known about counseling interventions for nicotine product use in the adolescent population. Among published counseling interventions, there is significant heterogeneity in methodology, setting, and duration. With the advent of electronic platforms and virtual technology, the diversity of counseling intervention has increased. Counseling interventions with trained professionals include synchronous interactions conducted in person and/or virtually. These sessions often include motivational interviewing, a technique to enhance the patient's intrinsic motivation for cessation or similar motivational enhancing components to increase engagement in counseling (22). This question focuses on the use of counseling-based interventions for nicotine use in the adolescent population.

Summary of evidence. The systematic review identified 11 randomized controlled trials (RCTs) that enrolled adolescents with use of nicotine products and evaluated the effects of counseling-based interventions (see Table E1 in the online supplement). The outcomes of abstaining from nicotine use were self-reported or biochemically validated with salivary cotinine or exhaled carbon monoxide (CO).

A two-arm cluster trial in Malaysia randomized 422 adolescents ages 13–17 using cigarettes, e-cigarettes, or shisha to a cessation program in 10 visits from January to November 2018. The intervention consisted of school counseling, peer/buddy influence, community involvement, and implementation of school tobacco-free policies (School-Fit and Smart Adolescent Smoking Cessation Program) (26). Controls received no intervention. The quit rate at 4 weeks was 56.5% for the counseling group ($n = 168$; CO validated) versus 24.5% for the control group ($n = 98$); the 3-month quit rate

was 41.8% for the counseling group (salivary cotinine validated) and was not measured for controls.

An RCT randomized 2,151 student cigarette users aged 16–21 years to either motivational interviewing counseling sessions by means of telephone or no intervention (control group). At least three 15-minute calls were completed with those with no intention to quit, and up to six cessation calls were completed with students expressing quit readiness. The counseling was supplemented by cessation information both online (according to stage of quit readiness) and in print. The primary endpoint measured was 6-month prolonged abstinence 1-year postintervention eligibility. Among both daily and less than daily users of cigarettes, female users in the intervention group were found to have a higher rate of abstinence compared with female users in the control group (21.1% vs. 16.2%; $P = 0.03$). Male daily users of cigarettes in the intervention group had a higher rate of abstinence compared with male daily users in the control group (12.2% vs. 6.2%; $P = 0.06$). Combining genders, there was no significant difference (27). Cessation was not biochemically validated in this study.

Another trial randomized eight pediatric practices to either usual care or peer counseling per the 5As model (Ask, Advise, Assess, Assist, and Arrange) for 2,711 adolescents ages 13–17 years, of whom 362 were current cigarette users (28). Both users and nonusers of cigarettes received counseling. Adolescent users of cigarettes who received the intervention were more likely to report having abstained at 6 months postbaseline (odds ratio [OR] = 1.59; 95% confidence interval [CI] = 1.06–2.40).

Another study (29) randomized high schools to a 4-week, school-based counseling intervention in Massachusetts versus an information-only session for 1,039 students. The intervention was delivered to all students recruited by school nurses in four weekly visits over 1 month and was based on the 5As model and cognitive-behavioral therapy. Control high schools provided students with printed information by nurses. Male students in the intervention group were more likely to be abstinent per self-report at 3 months postbaseline compared with control participants (15.0% vs. 4.9% in controls; OR = 3.23; 95% CI = 1.63–6.43). There was no difference in the self-reported abstinence rates at 12 months postbaseline or for female students at 3 or 12 months.

Ismail and colleagues (30) assessed the effectiveness of a 4-month group counseling intervention over 10 sessions in Malaysia that was based on a “Stop Smoking Module,” compared with no intervention, among 346 secondary school students who reported smoking at least one day in the previous month, confirmed by CO, along with an intention to quit. The CO and cotinine validated abstinence rates were significantly higher in the intervention group 4 months postbaseline (45%), compared with no intervention (32%; $P = 0.013$). However, at 8 and 12 months postbaseline, the abstinence rates were not significantly different between groups.

A school-based RCT in rural California examined the effect of an intervention in 458 adolescents who use smokeless tobacco (i.e., tobacco that is chewed or snuffed) only and 271 adolescents who use both smokeless tobacco and cigarettes (31). The intervention consisted of a peer-led educational session, an oral exam (physical exam) with feedback, and three nurse-led group cessation counseling sessions. Control subjects received no intervention. Student who were sole users of smokeless tobacco, and not cigarettes (62% vs. 36%), were more likely to self-report abstaining from smokeless tobacco 3 months postintervention ($P = 0.03$).

In a pediatric office-based study, pediatric practices were (32) randomized to an intervention in which clinicians were trained on the 5As model or a control group in which clinicians were trained to use social media screening and counseling. There were no significant differences in self-report of successful quitting at 6 or 12 months postbaseline follow-up.

An RCT assigned 162 adolescents ages 14–18 who smoked from medical, school, and community settings to enhanced motivational interviewing (individual session, telephone booster, and brief telephone-based intervention) or brief advice (33). Cotinine and CO-validated 7-day point-prevalence abstinence rates at the 1-, 3-, and 6-month postbaseline follow-ups were not different between the groups.

Another study (34) tested the effectiveness of a single session of motivational enhancement therapy as compared with an education control group in 81 adjudicated adolescents. There were no differences in 7-day and 28-day point-prevalence self-reported and cotinine-validated abstinence between groups at the

1-month and 6-month follow-ups posttreatment.

A trial randomized 68 Alaska Native adolescents, ages 12–17 years, from eight western Alaska villages to one 8-hour, group-based counseling or a delayed-treatment condition (35). Adolescents reported use of cigarettes, tobacco chew, or Iqnik, a mixture of tobacco leaves and fungus ash commonly used in this region. Self-reported 7-day and 30-day point-prevalence self-reported tobacco abstinence rates were not significantly different at the end of the 6-week intervention or the 6-month postbaseline follow-up.

An RCT randomized participants ages 14–19 years who presented for treatment in a hospital emergency department to a theory-based motivational tobacco intervention or brief advice (36). The self-reported quit rates were not significantly different between the two groups 6 months postbaseline.

Pooled data of two studies that included psychoeducational counseling without a specific focus on increasing motivation showed significant differences in the 7-day point-prevalence, biochemically validated abstinence rates at 12–16 weeks postintervention (relative risk [RR] = 1.75; 95% CI = 1.03–2.95) (see Figure E3), favoring counseling (29, 30).

Pooled data of three studies that included psychoeducational counseling with a focus on increasing motivation showed significant differences in the 7-day (RR = 1.32; 95% CI = 1.19–1.47) (see Figure E1) and 30-day (RR = 1.37; 95% CI = 1.19–1.57) (see Figure E2) point-prevalence abstinence rates at 24 weeks postintervention, favoring counseling (27, 34, 35).

Quality of evidence. The panel's confidence in the accuracy of the estimated effects of counseling-based interventions for proposed outcomes was very low. Several studies had a high proportion of participants lost to follow-up (26, 27, 31, 32), and all but three studies included a cluster-randomization design (33, 34, 36), which contributed to an increased risk of bias. Additionally, differences in studied populations, such as inclusion of participants from certain geographical areas (35), adjudicated adolescents (34), people older than 18 years old (36), or adolescents using a wide range of nicotine products difficult to compare; this (35) further downgraded the quality of evidence because of indirectness. Most studies either did not report on or did

not meet the proposed sample size estimates for enrollment (imprecision).

Benefits. The two meta-analyses describing the effect of motivational-based counseling programs as well as psychoeducational counseling without a specific focus on motivation showed a benefit of counseling compared with control. Although some RCTs did not demonstrate benefit from counseling, many of those studies were underpowered or relied on self-report outcomes. The results of these studies do not support one modality of counseling (virtual, in-person, peer-based, etc.) over another, as this was not a specific outcome measure. On the basis of the meta-analyses, the results indicated an overall benefit from counseling for adolescents who use nicotine/tobacco products.

Harms. Studies included in this review did not show evidence of any harm with the counseling interventions. None of the studies reported any adverse events. However, previous research has demonstrated that nicotine use counseling could increase family conflict or feelings of stress or stigmatization (37).

Conclusions. Despite having low confidence because of very low-quality evidence, our panel concluded that the benefits of counseling-based interventions exceeded the harms of continued nicotine product use.

What others are saying. The American Academy of Pediatrics (AAP) recommends tobacco messaging (screening and behavioral interventions) to begin no later than age 11 or 12 (38). The American Academy of Family Physicians recommends screening for tobacco use in adolescents ages 12 and older and providing behavioral interventions for all tobacco users (39).

In 2008, the U.S. Public Health Service published recommendations on adolescent tobacco cessation, including a recommendation for counseling interventions to aid adolescents in quitting smoking (40). Updated guidelines from the U.S. Preventive Services Task Force (USPSTF) were released in 2020, which recommended behavioral interventions for prevention of tobacco use, but they concluded that there is insufficient evidence to recommend counseling interventions for cessation (41).

ATS recommendation. For adolescents 10 to 18 years of age who use nicotine and/or tobacco products, we recommend a counseling-based, nicotine use intervention

(strong recommendation, very low-certainty evidence).

Rationale for recommendation. This recommendation places high value on the potential for nicotine use cessation with an intervention that carries very little risk for harm. Despite the lower quality of evidence of included studies, a majority of committee members voted strongly in favor of counseling as an intervention because of the high degree of external validity, especially given that the studies were conducted recently and generalizable to current times. The current evidence, combined with the data before 2008 included in the previous U.S. Public Health Service report, suggests that the benefit of counseling outweighs any potential harm (40). The consensus decision was also based on decades of combined clinical experience noting the success rate and low risk for harm as well as low cost and low potential burden to families in addition to the substantial morbidity and premature mortality from continued nicotine product use. In conclusion, the panel made a strong recommendation, despite very low confidence in the estimated abstinence rates, because the panel was certain that the harms of smoking in adolescents far exceeded the burden and risk of counseling-based interventions.

Question 2: Should Adolescents 10 to 18 Years of Age Who Use Nicotine and/or Tobacco Products Receive Technology-based Nicotine Use Intervention?

Background. There are a myriad of new technology platforms that have emerged over the past decade to assist with nicotine cessation, including mobile-based and web-based applications. Some have been examined as tools to assist adults with smoking cessation (43). Less is known about technology-based interventions for nicotine use in the adolescent population, including the use of social media, texting, and other virtual communication technologies. For the purposes of this guideline, technology-based interventions were defined as asynchronous interventions delivered remotely to promote nicotine cessation. This question focuses on the use of technology-based interventions for nicotine use in the adolescent population.

Summary of evidence. The systematic review identified nine RCTs that enrolled adolescents who use nicotine products and evaluated the effects of technology-based interventions (see Table E2).

The types of technology-based interventions identified in the systemic review included Internet/computer-based, mobile applications, or text messaging platforms. The outcomes of abstaining from nicotine use were self-reported in all studies except two, which reported cotinine-validated abstinence rates (44, 45).

A two-armed RCT of 144 young people ages 16–26 years who smoked at least one day per week were randomized either to a cessation program on the basis of a social game played on a mobile phone, *HitnRun*, or to a control group who read a psychoeducational brochure (46). The *HitnRun* game was developed to connect participants who were interested in smoking cessation through cooperative, competitive, team-based gameplay. Participants in the *HitnRun* group also received tailored prompts. Abstinence rates at the 4-week (end of intervention) and 3-month follow-ups postintervention were not significant between the two groups ($P = 1.000$ and $P = 0.856$, respectively).

Another RCT (47) assessed the effectiveness of a 7-week, Internet-based, virtual reality world and motivational interviewing intervention conducted in real time by a smoking cessation counselor, compared with a nonintervention arm, among 136 high school students (ages 14–19 yr) who smoked cigarettes. Those who participated in the program were significantly more likely than control subjects to report themselves as “a former smoker” at the end of intervention ($P = 0.05$). However, at 3 and 12 months postintervention, the self-reported abstinence rates were no longer significantly different between the groups.

A three-arm RCT (44) randomized 146 high school students (average age, 16.9 yr) who smoked at least five cigarettes, on average, per day for the past 7 days to a 4-week mindfulness training delivered through a mobile smoking application (Craving to Quit), the NCI Quit Start smoking cessation application, or written cessation materials. The self-reported, 7-day point-prevalence abstinence rate at the 6-month follow-up confirmed by cotinine was similar between the three groups ($P = 0.88$). Each subject also met with a school nurse weekly over the 4 weeks, OR for abstinence 2.47 (95% CI = 1.10–5.50) for each additional 30 minutes spent with the school nurse.

Another trial randomized 179 students, ages 16–19, who smoked at least one cigarette per week for at least 12 weeks, to either a mobile-phone, text message–based smoking cessation intervention or a control group for 12 weeks (48). No significant difference was found between the groups in the self-reported 7-day ($P = 0.20$) or 30-day ($P = 0.49$) point-prevalence abstinence rates at the end of intervention; however, the intervention group had a significantly higher rate of smoking reduction compared with the control group (66% vs. 35%; OR = 1.9; 95% CI = 1.4–2.7).

A two-arm RCT (49) of 535 high school students (median age, 17 yr) who smoked cigarettes daily or weekly, compared a 12-week text-messaging smoking cessation intervention to a control group who received information on how to contact a smoking cessation helpline. There was no significant difference in self-reported prolonged abstinence at the 3-month follow-up between groups ($P = 0.46$). However, the self-reported 4-week point-prevalence of complete smoking cessation at the 3-month follow-up in the intervention group (24%) was significantly different compared with the control group (15.4%) ($P = 0.018$).

Another two-arm RCT (50) of 755 vocational school students (mean age, 18 yr) who reported daily or occasional cigarette smoking assessed the effectiveness of a 3-month, text message–based intervention for smoking cessation compared with an assessment-only control group. There were no differences in 7-day ($P = 0.92$) and 4-week ($P = 0.69$) point-prevalence self-reported abstinence rates between groups at 6 months postrandomization.

Another two-arm RCT (51) assigned 535 high school students (median age, 17 yr) who smoked daily or weekly either to a 12-week, automatic, unguided text messaging cessation program focused on the health risks of smoking and behavior change advice or to a control group that was told they could use the website for a quit line or contact their school’s health service. The 4-week point-prevalence abstinence rate at the 3-month follow-up was higher in the intervention group ($P = 0.02$). There was no difference between groups in the 8-week prolonged abstinence rate at the 3-month follow-up ($P = 0.46$) or the 5-month prolonged abstinence ($P = 0.39$) or 4-week point-prevalence abstinence ($P = 0.20$) rates at the 6-month follow-up.

Another study (52) randomized 1,160 high school students, of which 62 reported

smoking, to a CD-ROM–based smoking prevention and cessation curriculum intervention (A Smoking Prevention Interactive Experience, or ASPIRE) or to a standard of care control group that received a self-help booklet. There was no difference in smoking cessation rates between the intervention and comparison groups at 18 months postrandomization (OR = 1.0; 95% CI = 0.3–2.7).

Another RCT (45) of 261 participants, ages 14–18, who smoked or used smokeless tobacco in the past 7 days before enrollment compared a six-session, interactive, games-based, tobacco cessation program (ACTION) to a control group that completed six sessions consisting of videos and scripted discussion questions. Using intent-to-treat analyses, the treatment groups did not differ in cotinine-validated, 3-day point-prevalence abstinence rates or 7-day point-prevalence abstinence rates with 3-day cotinine verification at the end of intervention or at the 90-day follow-up.

Pooled data of two studies that included a mobile-phone, text-messaging–based smoking cessation intervention showed significant differences in the 4-week, self-reported point-prevalence abstinence rates at the end of the 12-week intervention (RR = 1.58; 95% CI = 1.08–2.30) (see Figure E4), favoring text messaging (48, 49).

Quality of evidence. The panel’s confidence in the accuracy of the estimated effects of technology-based intervention for proposed outcomes was very low. Studies had several limitations that contributed to an increased risk of bias, such as high attrition rates and cluster-randomization design. Differences in studied populations, such as the inclusion of participants up to 26 years old (46), and using self-reported measures of nicotine abstinence further downgraded the quality of evidence. Several studies either did not report on or did not meet the proposed sample size estimates for enrollment, which decreased confidence in the accuracy of estimated effects because of a lack of precision.

Benefits. Technology-based interventions—particularly text-messaging programs, given their applicability to modern adolescent habits—may offer short-term benefits to support nicotine cessation among adolescents, even in the absence of successful cessation. Although sustained long-term cessation may be challenging, given the evidence, the observed increases in quit attempts may reflect a meaningful shift

in adolescent attitudes toward cessation and represent an important first step in the cessation process. Although the included studies were affected by high attrition rates due to low adherence to intervention (44, 47) and loss to follow-up (48, 51, 52), technology-based interventions should be considered as a part of comprehensive tobacco control efforts targeting youth.

Harms. The authors did not specify harms attached to either the Internet-based or the mobile phone application-based interventions. In theory, there is a risk of increased aggregate screen time. There were no harms specific to the text-based smoking cessation programs. Text messages may interfere with important activities (e.g., school, work, driving) and may generate fees for the recipient.

Conclusions. Despite having very low confidence in the estimated effects, the panel felt that the benefits of technology-based intervention exceed the harms, burdens, and cost for adolescents ages 10 to 18 years of age who are using nicotine products. This was based on the large number of beneficial outcomes and absence of harmful outcomes; decades of clinical experience collectively managing thousands of such adolescents; and recognition that prolonged nicotine product use contributes to serious health consequences, such as heart and lung diseases and several cancers (2, 3). Technology-based interventions provide individualized support, deliver personalized messages, provide interactive tools, and leverage social networks as potentially effective platforms to engage adolescents in stopping the use of nicotine products.

What others are saying. In a recent systematic review in which a meta-analysis was performed in adults, smartphone-based interventions alone were less effective in achieving smoking abstinence but improved when combined with a pharmacotherapy-based cessation approach (53).

A relevant trial was published after the completion of our systematic review and final consensus recommendation decision. The trial randomly assigned 1,681 adolescent e-cigarette users either to an automated interactive text message program for vaping cessation designed for young people or to incentivized text message assessments. The trial found that the interactive text message program increased self-reported vaping cessation rates. Limitations of the study included the use of self-reported outcomes,

the possible influence of social desirability bias (the intervention group had more touch points), and the indirectness of the population (the trial enrolled adolescent e-cigarette users who wanted to quit, but the question asked about adolescent users of nicotine or tobacco products) (54). Although it was not considered during the initial committee discussions or finalization of the recommendations, the committee agreed *post hoc* that the trial provides additional support for our conditional recommendation in favor of a technology-based nicotine use intervention.

ATS recommendation. For adolescents 10 to 18 years of age who use nicotine and/or tobacco products, we suggest a technology-based, nicotine use intervention (*conditional recommendation, very low-certainty evidence*).

Rationale for recommendation. A majority of committee members voted in favor of the use of technology as an intervention as a conditional recommendation. The rationale for a conditional recommendation centered on the inclusion of older studies, some of which incorporated counseling alongside technology and lacked generalizability to the present day, given the rapid evolution of technology. However, recommendation in favor of technology as an intervention places high value on the potential for tobacco and/or nicotine use cessation with very little risk or harm. Although the interventions appeared to have little impact on long-term abstinence, the panel recognized that the abstinence rates at the end of Internet-based and text-messaging interventions favored the overarching group of technology-based interventions. Despite the very low certainty around these outcomes, the panel judged that the benefits of any of the three subgroups of technology-based intervention outweigh the risks and could provide a convenient pathway to initiate nicotine cessation interventions in a population well versed with technology.

The potential benefits of text-based interventions include that they are appealing, accessible, often free to most, and include content that is brief and tailored to an adolescent's interests. These interventions provide an opportunity for adolescents to request more help or information. Such functionality has been shown to be especially effective for adults who use text-based smoking cessation programs (55).

Question 3: Should Adolescents 10 to 18 Years of Age Who Use Nicotine and/or Tobacco Products be Treated with NRT?

Background. NRT, as approved by the FDA, uses specific products such as the transdermal patch, nicotine polacrilex gum, nicotine polacrilex lozenge, and nicotine nasal spray to provide nicotine in a slower release and, thus, a less addictive form to reduce withdrawal symptoms. NRT has been shown to be effective in the treatment of tobacco dependence in adults (15) but is not approved by the FDA for individuals younger than 18 years of age. Consideration of NRT has been suggested for adolescents with moderate to severe nicotine dependence (38). This question focuses on the use of NRT for nicotine use in the adolescent population.

Summary of evidence. The systematic review identified five randomized trials that enrolled adolescents who use nicotine products and evaluated the effects of NRT (see Table E3).

NRT was provided as either nicotine polacrilex gum or a nicotine transdermal patch. None of the studies evaluated combination NRT (i.e., both gum and patch) in the intervention group. The outcomes of abstaining from nicotine use were self-reported and biochemically validated by salivary cotinine or exhaled CO.

Hanson and colleagues (56) randomized 100 motivated adolescents, ages 13–19, who smoked 10 or more cigarettes per day for 6 months to a 10-week nicotine patch versus placebo patch intervention, with all participants receiving weekly 10- to 15-minute counseling visits. At 1 week post-quit day, the CO-validated, 7-day point-prevalence abstinence rates were higher in the active nicotine patch group than in the control group (50% vs. 26%; $P = 0.01$). Relapse after initial cessation was common. After 1 week, the abstinence rates for the nicotine patch and control groups were similar. Over 50% of the treatment group reported nonadherence with nicotine patch use.

A three-arm RCT (57) randomized 120 adolescents, ages 13–17, who smoked more than 10 cigarettes daily to a 12-week intervention of either nicotine patch, nicotine gum, or placebo. All participants received cognitive-behavioral therapy. There was a statistically significant difference in prolonged abstinence (abstinence maintained from 2 wk

post-quit date) at 3 months postquit in the nicotine patch group, compared with placebo (17.7% vs. 2.5%; $P = 0.04$). At study completion, 3 months after the quit date, the difference between the patch and placebo groups did not reach statistical significance (OR = 4.93; 95% CI = 0.95–25.6). Cessation was determined by self-report and exhaled CO. The nicotine patch was associated with a statistically significant increase in the nonsevere adverse effects of shoulder and arm pain, pruritus, and erythema. Nicotine gum was associated with sore throat, hiccups, and pruritus. There were no severe adverse effects. The study was limited by high attrition postrandomization.

A clinical trial of a city in the United Kingdom randomized 98 adolescents, ages 11–21, who smoked more than one cigarette a day to a 6-week nicotine patch intervention or a placebo group (58). All participants were offered regular behavior counseling. The CO-validated point-prevalence rate of abstinence at 4 weeks postrandomization was not different between the groups. The median patch use was 1 week, and only 5 subjects completed 6 weeks of NRT. No differences in adverse events were noted by group. The study was limited by a high rate of nonadherence to study medication.

Another study (59) compared a nicotine patch intervention to a placebo patch in 257 adolescents (mean age in years, 16.7 ± 1.13) attending secondary school in the Netherlands who smoked seven or more cigarettes per day. The duration of the intervention was either 6 weeks or 9 weeks, depending on the number of daily cigarettes. The difference in cessation rates after 2 weeks did not reach statistical significance (31.9% vs. 21.3%; $P = 0.057$). No serious adverse events were found. The same group of authors reported outcomes 6 and 12 months after intervention initiation in a separate analysis (60) of those same 257 adolescents. They found no differences between the groups in the 6-month (self-reported) and 12-month (cotinine-validated and self-reported) abstinence rates. The study was limited by a high rate of nonadherence to the prescribed study medication.

One meta-analysis showed that participants in the nicotine patch intervention group had a higher CO-validated, 7-day point-prevalence abstinence after 1 week of treatment, as compared with that of the control group (RR = 2.55; 95% CI = 1.02–6.33) (see Figure E5) (56, 57). This difference was

no longer evident at 4 weeks posttreatment (56, 58) (RR = 1.36; 95% CI = 0.79–2.33).

Quality of evidence. The panel's confidence in the accuracy of the estimated effects of nicotine patch intervention for proposed outcomes was very low. One of the studies included a monetary-based reward for treatment adherence (56). Three studies had a high proportion of participants lost to follow-up as well as nonadherence to prescribed treatment (56, 58, 59), which contributed to an increased risk of bias. Two studies relied on surrogate measures of nicotine abstinence, which downgraded the quality of evidence because of indirectness (59, 60). For two studies, abstinence was not a primary outcome (56, 57). Inclusion criteria varied among the studies (e.g., with one study including subjects who smoked only one cigarette per day), which may have biased results toward the null hypothesis (58). Only a limited number of studies contributed to the findings, further affecting the confidence in the estimate effects because of imprecision.

Benefits. Two studies demonstrated increased smoking abstinence at 1 week postintervention with NRT compared with the control group; one study demonstrated prolonged abstinence (defined as continuous abstinence as of 2 wk after randomization) with the NRT patch but not with NRT gum. However, this difference was not sustained at follow-up in either study (56, 57).

Harms. The following nonsevere adverse effects were higher in the nicotine patch group than in the placebo group at 12 weeks: shoulder/arm pain (incidence density ratio [IDR] = 4.63; $P = 0.0011$), pruritus (IDR = 1.63; $P = 0.033$), and erythema (IDR = 1.97; $P = 0.0045$) (57). Similarly, sore throat (IDR = 4.79; $P = 0.0007$), hiccups (IDR = 2.79; $P = 0.014$), and pruritus (IDR = 1.95; $P = 0.003$) were higher in the nicotine gum group than in the control group at 12 weeks (57). There were no severe adverse effects reported in either the treatment group or the control group.

Conclusions. In the included clinical trials, NRT provided to adolescents who use cigarettes, combined with cognitive-behavioral therapy, produced short-term abstinence. The interventions did not statistically result in improved abstinence at long-term follow-up compared with findings in control groups in the pooled data. There were nonsevere adverse effects associated with NRT use, which have the potential to be bothersome. No severe adverse events were

reported. Low treatment adherence rates and high dropout rates in most of the studies limited the quality of evidence and suggests that adolescents may struggle with NRT adherence more than adults. The committee did not reach consensus recommendation either for or against NRT use in adolescents who use nicotine products.

What others are saying. The USPSTF recommends, for nonpregnant adults who use tobacco, that clinicians provide behavioral interventions and FDA-approved pharmacotherapy (61). Additionally, the 2024 World Health Organization guidelines recommend pharmacologic treatments, including NRT for tobacco cessation in adults (62).

The AAP recommends considering the use of pharmacotherapy (including NRT) for the treatment of moderate to severe tobacco use disorder in adolescents who want to stop using tobacco products (38).

The USPSTF 2020 recommendations state that the current evidence is insufficient to assess the balance of benefits and harms of medications for the cessation of tobacco use among school-age children and adolescents (41).

ATS recommendation. For adolescents 10 to 18 years of age who use nicotine and/or tobacco products, no recommendation can be made for or against NRT because of lack of consensus.

Rationale for recommendation. The lack of a recommendation for use of NRT as an intervention was due to the lack of agreement in the committee; specifically, the required threshold needed to vote in favor of a recommendation (70%) was not reached. Those committee members who voted in favor of using NRT as an intervention felt that the favorable safety profile of NRT, potential short-term benefit for cessation, established efficacy of NRT in adults, and the need for a therapeutic modality in adolescents outweighed the low quality of evidence. In contrast, many committee members voted against NRT because of the poor quality of studies and lack of evidence of a long-term benefit of NRT on cessation.

Question 4: Should Adolescents 10 to 18 Years of Age Who Use Nicotine and/or Tobacco Products be Treated with Varenicline?

Background. Varenicline is a nonnicotine pharmacotherapy approved by the FDA for smoking cessation in adults. It is a partial agonist/antagonist of the nicotinic

acetylcholine receptors, which can block the effects of nicotine if further nicotine products are consumed and lessens withdrawal symptoms. Varenicline is a first-line pharmacotherapeutic treatment for tobacco dependence in adults (15). Although not approved for use in children younger than 18 years of age, varenicline has been suggested for treatment of moderate to severe nicotine dependence in adolescents (38). This question focuses on the use of varenicline for nicotine use in the adolescent population.

Summary of evidence. The systematic review identified three randomized trials that enrolled adolescents with use of nicotine products and evaluated the effects of varenicline therapy (see Table E4).

In the intervention groups, varenicline was provided as low dose (1 mg if >55 kg, 0.5 mg if ≤ 55 kg) or high dose (2 mg if >55 kg, 1 mg if ≤ 55 kg). The outcomes of abstaining from nicotine use were self-reported and biochemically validated by salivary cotinine or exhaled CO.

One study only reported the safety and tolerability of a 14-day varenicline therapy regimen in a total of 73 adolescents, ages 12–16 years (63). All participants used at least three cigarettes daily over the 4 weeks before study commencement. Of the 57 participants who received at least one dose of varenicline and the 15 who received at least one dose of placebo, there were no dose reductions or discontinuations due to adverse effects and no serious adverse effects. There were more adverse effects among participants who received varenicline versus placebo and among participants ≤ 55 kg versus those >55 kg.

Another RCT (64) compared a 12-week, high-dose varenicline intervention to placebo among 157 participants, ages 14–21, who smoked daily in the 6 months before enrollment and had at least one failed quit attempt. The high-dose varenicline and placebo groups did not differ in self-reported (RR = 1.17; 95% CI = 0.63–2.20), cotinine-validated (RR = 0.97; 95% CI = 0.29–3.18), or CO-validated (RR = 1.27; 95% CI = 0.64–2.50) 7-day point-prevalence abstinence rates at the end of the 12-week treatment. The self-reported 7-day point-prevalence abstinence rate was higher in the high-dose varenicline intervention group at Weeks 18 and 26 postbaseline (RR = 1.82; 95% CI = 1.01–3.28). No medication-related serious adverse events occurred in either group. No significant differences in any

and total adverse effects were noted in both groups at 12 weeks (RR = 0.95; 95% CI = 0.79–1.15; $P = 0.61$). Of note, a history of mood/psychiatric disorders, homicidality, aggression, and suicidality were part of the exclusion criteria.

A multicenter, multination RCT assigned 312 adolescents, ages 12–19, who smoke cigarettes to a 12-week high- or low-dose varenicline intervention or a placebo group (65). The participants were included if they smoked an average of five or more cigarettes per day during the 30 days before enrollment. The 4-week continuous abstinence rates at the end of treatment, as validated by cotinine, were not different between either low- or high-dose varenicline intervention groups and placebo (low-dose varenicline vs. placebo: OR = 1.73; 95% CI = 0.88–3.39; $P = 0.11$; high-dose varenicline vs. placebo: OR = 1.18; 95% CI = 0.59–2.37; $P = 0.63$). However, the continuous abstinence rates between 9 and 24 weeks ($P = 0.034$) and between 9 and 52 weeks ($P = 0.012$) postbaseline were higher in the low-dose varenicline group than in the control group. Most adverse effects were reported as mild, and no severe neuropsychiatric events were reported in either the low- or the high-dose varenicline group. Exclusion criteria were the same as those in the previous study by the authors (64).

Pooled data analyses were limited because of the heterogeneity in outcome assessments. Two meta-analyses showed that participants in the high-dose varenicline intervention group had a higher risk of developing gastrointestinal adverse events, particularly nausea, compared with the control group (total gastrointestinal events: RR = 1.93; 95% CI = 1.15–3.25; nausea: RR = 1.8; 95% CI = 1.18–2.74) (64, 65) (see Figures E6 and E7).

Quality of evidence. The panel's confidence in the accuracy of the estimated effects of varenicline for the proposed outcomes was very low. Of the two studies that were pharmaceutically sponsored (63, 65), one was a required postmarketing study (65), which contributed to an increased risk of bias. Additionally, differences in studied populations, such as inclusion of participants older than age 18 and reporting only self-reported abstinence, downgraded the quality of evidence because of indirectness (64, 65). Additionally, only a limited number of studies contributed to the findings, and there were high attrition rates due to loss to follow-up (64, 65). Therefore,

the quality of evidence was further downgraded because of imprecision.

Benefits. One study demonstrated improved CO-confirmed and self-reported smoking abstinence with high-dose varenicline compared with placebo at 18 and 24 weeks post-quit day (64), whereas another showed improved cessation success with low-dose varenicline compared with placebo for biochemically confirmed and self-reported continuous abstinence at Weeks 24 and 52 post-quit day (65). There were no differences in all other outcomes of smoking abstinence between varenicline and control in the two studies.

Harms. There were no differences in the self-reported adverse events between those receiving low- versus high-dose varenicline. With high-dose varenicline, there were no significant increases in neuropsychiatric adverse events compared with placebo. Gastrointestinal adverse events, including episodes of nausea, were greater with high-dose varenicline at 12 and 16 weeks of treatment compared with placebo, with RRs of 1.93 (95% CI = 1.15–3.25) and 1.80 (95% CI = 1.18–2.74), respectively. There were no differences in neuropsychiatric adverse events, dizziness, headaches, agitation, anxiety, and depressed mood/depression in the high- or low-dose varenicline groups compared with placebo.

Conclusions. The panel concluded that 1) the initiation of varenicline treatment in adolescents 10 to 18 years of age who use cigarettes showed an improved effect on abstinence, with low to moderate certainty in the estimated effects, and 2) the initiation of low-dose varenicline showed no increase in adverse events and that high-dose varenicline showed an increase in some gastrointestinal side effects with very low to low certainty in the estimated effects. The panel made a conditional recommendation for a trial of varenicline for adolescents 10 to 18 years of age who use nicotine products. This recommendation was based on the potential for benefit of varenicline, the relatively low risk of adverse events, and the recognized harm of ongoing use of nicotine products.

What others are saying. Clinical practice guidelines recommend varenicline as a first-line treatment for smoking cessation treatment in adults who smoke cigarettes because of its proven efficacy in increasing long-term abstinence rates (15). Additionally, the 2024 World Health Organization guidelines recommend pharmacologic therapies including

varenicline for tobacco cessation in adults (62).

The AAP recommends considering the use of pharmacotherapy, including varenicline, for the treatment of moderate to severe tobacco use disorder in adolescents who want to stop using tobacco products (38).

The USPSTF 2020 recommendations found the current evidence insufficient to assess the balance of benefits and harms of medications for the cessation of tobacco use among school-age children and adolescents (41).

A recent randomized controlled trial published after the completion of our systematic review provides evidence supporting the use of varenicline in adolescents with nicotine dependence. The study enrolled youth aged 16–25 who reported daily or near-daily nicotine vaping, evidence of nicotine dependence, and were not current users of combustible tobacco. Participants were randomized either to 12 weeks of varenicline versus placebo. Both groups received behavioral counseling plus referral to “This is Quitting”, a text messaging based vaping cessation program. Study medication adherence was facilitated by a \$1.00 incentive for each uploaded smartphone app video recording of medication self-administration. The varenicline group demonstrated higher rates of biochemically verified (saliva cotinine) continuous abstinence at weeks 9–12 (51%) compared to the placebo group (14%, aOR = 6.5, 95% CI = 2.1–16.9, $P < .001$). Sustained benefit was observed at 24 weeks, with 28% abstinence in the varenicline group versus 7% in the placebo group (aOR = 6.0, 95% CI = 2.1–16.9). Limitations of the study include lower adherence to behavioral counseling in the placebo group compared to the varenicline group, although per protocol analysis excluding participants with less than 80% adherence to study medication and behavioral counseling still demonstrated a large difference between varenicline and placebo arms. Additionally, findings may not extend to youth who both vape and smoke. Although it was not considered during the initial committee discussions or finalization of the recommendations, the committee agreed post hoc that the trial provides additional support for our conditional recommendation in favor of a trial of varenicline (42).

ATS recommendation. For adolescents 10 to 18 years of age who use nicotine and/or tobacco products, we suggest a trial of

varenicline (*conditional recommendation, very low-certainty quality evidence*).

Rationale for recommendation. This recommendation places high value on the importance of nicotine product cessation while balancing the reported adverse effects associated with varenicline. The consensus of the panel was that use of varenicline improved the likelihood of abstinence from nicotine in the adolescent population, with low risk for adverse effects. Despite the very low certainty around these outcomes, the panel judged that the benefits of varenicline would outweigh the risks. In addition to the aforementioned evidence, the consensus decision was based on decades of combined clinical experience, noting the success rate of varenicline, particularly in the adult population, and low risk for harm demonstrated in the pediatric population, as well as the low cost and low potential burden to families.

Question 5: Should Adolescents 10 to 18 Years of Age Who Use Nicotine and/or Tobacco Products be Treated with Bupropion?

Background. Bupropion hydrochloride, an aminoketone antidepressant, reduces nicotine withdrawal symptoms by inhibiting the uptake of dopamine and norepinephrine. Bupropion was the first nonnicotine pharmacotherapy approved by the FDA to aid in smoking cessation for adults (66–68). However, there is limited research in the adolescent population evaluating pharmaceutical interventions for smoking cessation (67). Use of bupropion in children as young as 6 years of age has been found to be safe in attention-deficit/hyperactivity disorder studies. Building on previously published smoking cessation studies, use of bupropion for smoking cessation in the adolescent population has been explored (66–68).

Although it is currently used in patients younger than 18 years of age for the treatment of attention-deficit/hyperactivity disorder and refractory depression, bupropion is not currently approved by the FDA for the treatment of tobacco dependence in patients younger than 18 years of age. It has been suggested that the use of bupropion should be considered in the treatment of adolescents with moderate to severe nicotine dependence (38). This question focuses on the use of bupropion for nicotine use in the adolescent population.

Summary of evidence. The systematic review identified four randomized trials that enrolled adolescents who use nicotine products and evaluated the effects of bupropion (*see Table E5*).

Bupropion was provided in a 150-mg or 300-mg daily dose. The outcomes of abstaining from nicotine use were self-reported and biochemically validated by salivary cotinine or exhaled CO.

One study (68) randomized 312 adolescents, ages 14–17, who smoked more than six cigarettes daily either to a 6-week intervention with sustained-release (SR) bupropion at 150 or 300 mg/d or to placebo. All participants received brief individual counseling. SR bupropion at 150 mg/d did not result in abstinence rates significantly higher than those with placebo at any time during follow-up. The 7-day self-reported point-prevalence abstinence rate was significantly higher for SR bupropion at 300 mg/d than for placebo at Weeks 1, 3, 5, and 6 after the target quit date. Similarly, the 7-day CO- or cotinine-validated point-prevalence abstinence rate was significantly higher for the SR bupropion intervention at 300 mg/d than for placebo at Weeks 1, 2, 5, and 6 after the target quit date. However, these differences between the intervention group receiving SR bupropion at 300 mg/d and the placebo group were no longer significant at 26 weeks after the target quit date. The treatment-emergent adverse events experienced at least once by more than 4% of the participants were not different between the 300-mg versus placebo and 150-mg versus placebo groups. The placebo group reported a statistically significant increase in cough, compared with the intervention group receiving 300 mg/d.

Another RCT (66) assigned 211 adolescents, ages 15–18, who smoked cigarettes either to a SR bupropion group receiving 150 mg/d or to a placebo group. All participants also received nicotine patch treatment and were offered weekly group skills training sessions. The participants were included if they smoked more than 10 cigarettes a day for at least 6 months. The CO-validated, 7-day point-prevalence abstinence rate 10 weeks after the first counseling session and the cotinine-validated, 7-day point-prevalence abstinence rate at 26 weeks after the first counseling session were similar between the groups. No differences by treatment group were found in experiencing moderate or severe adverse events.

Another RCT (67) randomized 134 participants, ages 12–21, who smoked more than five cigarettes daily to four different groups: bupropion SR+contingency management (CM), placebo+CM, bupropion SR+non-CM, and placebo+non-CM. CM is a therapeutic approach that uses positive reinforcement to encourage cessation. SR bupropion was dosed at 300 mg/d for 6 weeks. There were no differences in the 7-day point-prevalence abstinence rate at Weeks 3, 4, 5, 6, and 12 after treatment initiation between the bupropion SR+non-CM and placebo+non-CM groups. In comparison, the 7-day point-prevalence abstinence rate at Weeks 3 and 4 after treatment initiation was higher in the bupropion SR+CM group than in the placebo+CM group. There was no significant difference between treatment groups in the number of participants reporting at least one adverse event.

Another RCT (69) assigned 22 adolescents, ages 16–19, who smoked more than 15 cigarettes per day to an intervention group that received bupropion at 150 mg/d for 90 days or to placebo. All participants underwent inpatient nicotine withdrawal treatment before randomization. The cumulative prevalence rate of CO-validated abstinence at 90 days was higher in the group receiving bupropion at 150 mg/d than in the control group. There were no significant differences in adverse effects between the bupropion and placebo groups.

Three meta-analyses showed that CO- or cotinine-validated, 7-day point-prevalence abstinence rates were significantly higher in the group receiving SR bupropion at 300 mg/d than in the placebo group at 3 weeks (RR = 2.63; 95% CI = 1.48–4.66; see Figure E8), 5 weeks (RR = 1.88; 95% CI = 1.14–3.13; see Figure E9), and 6 weeks (RR = 1.71; 95% CI = 1.03–2.83; see Figure E10) after baseline (67, 68).

Quality of evidence. The panel's confidence in the accuracy of the estimated effects of bupropion for the proposed outcomes was very low. One of the studies included a monetary-based reward for study participation and modified the initial protocol to adjust for recruitment challenges, which contributed to an increased risk of bias (68). Two studies relied on self-reported nicotine abstinence, which downgraded the quality of evidence because of indirectness (66, 68). Only a limited number of studies contributed to the findings, some with a

very small number of participants (69). Additionally, few studies have either not estimated or not achieved the proposed sample size needed to detect significant differences in proposed outcomes (66, 67), further affecting the confidence in the estimated effects because of imprecision.

Benefits. Abstinence rates during treatment and at the end of treatment favored bupropion when combined with nonpharmacologic interventions for cessation; however, abstinence rates declined, and relapse to nicotine product use was common when the treatment period ended (67–69).

Harms. No significant differences in adverse effects were noted between the groups receiving 150 mg bupropion and placebo. Compared with that reported in the group receiving 300 mg bupropion, cough was more frequently reported in the control group at Follow-up Week 26 (RR = 0.54; 95% CI = 0.29–0.99) (68).

Two adverse effects were deemed serious in one study; both participants were assigned to the bupropion group. One participant was hospitalized after ingesting *Datura innoxia* while receiving bupropion, resulting in an anticholinergic crisis; and another, who had an undisclosed history of depression and a probable eating disorder, for a suicide attempt (68). In two studies, participants either decreased their dose or discontinued bupropion because of tolerability issues or adverse events such as feeling depressed, irritability, anxiety, anger, heart palpitations, sleep or dream disturbances, headache, urticaria, and pregnancy (67, 68).

Conclusions. This panel concluded that the benefits of bupropion, especially when combined with nonpharmacologic interventions, likely outweigh the risks for adolescent patients interested in smoking cessation, albeit with caution. SR bupropion, even at the higher dose of 300 mg/dl, appears to be well tolerated, although abstinence rates were lower compared with those observed in adult studies (68).

What others are saying. The 2024 World Health Organization guidelines recommend pharmacologic therapies including bupropion for tobacco cessation in adults (62).

The AAP recommends considering the use of pharmacotherapy for the treatment of moderate to severe tobacco use disorder in adolescents who want to quit tobacco products, with strength of recommendation as option and quality of evidence as low (38).

The USPSTF 2020 recommendations state that current evidence is insufficient to assess the balance of benefits and harms of medications for the cessation of tobacco use among school-age children and adolescents (41).

The FDA-approved product label states that bupropion is contraindicated in patients with a seizure disorder and is contraindicated in patients with a current or prior diagnosis of bulimia or anorexia nervosa because of a higher incidence of seizures noted in patients treated for bulimia with the immediate-release formulation of bupropion (70).

ATS recommendation. For adolescents 10 to 18 years of age with use of nicotine and/or tobacco products, we suggest a trial of bupropion (*conditional recommendation, very low-certainty quality evidence*).

Rationale for recommendation. This recommendation places high value on the potential for nicotine product cessation while balancing the reported adverse effects of bupropion. The consensus of the panel was that bupropion improved the likelihood of abstinence from nicotine in the adolescent population with low risk for adverse effects. Despite the very low certainty around these outcomes, the panel judged that the potential benefits of bupropion outweigh the risks in the adolescent population. In addition to the aforementioned evidence, the consensus decision was based on years of combined clinical experience using bupropion in the pediatric population as well as low cost and low potential burden to families.

Limitations and Future Research

The panel identified significant limitations. First, common to all recommendations in this guideline, many studies were performed with adolescents who used combustible cigarettes, which may limit generalizability to adolescents using other commercial and novel nicotine products. Second, the technology intervention studies may not be generalizable, given the rapid evolution of technologies in current use by adolescents, with some trials using older technology, such as CD-ROM (52). Third, in clinical practice, many providers treat nicotine dependence with a “controller” medication like NRT plus a “reliever” also in the form of NRT, and this method of cessation was not specifically covered in any of the studies we reviewed

(40, 41). Specifically, per the ATS Clinical Practice Guideline for “Initiating Pharmacologic Treatment in Tobacco-Dependent Adults,” the recommendation for tobacco-dependent adults in whom treatment is being initiated, it is suggested to start varenicline plus a nicotine patch over varenicline alone (15). This approach was not covered in any of the studies we reviewed. Fourth, and also common to all recommendations, we intended to report on the effect of an intervention on quality of life; however, none of the studies included quality of life as an outcome measure. Fifth, although our intention was to include studies with younger adolescents ages 10 and older, given the standard definition of “adolescent,” no 10- or 11-year-olds were included in any studies, and the mean age of all studies was 14 years and older. Sixth, no recommendations on the duration of counseling- or technology-based interventions or dosing of pharmacologic therapies can be made, as this is outside the scope of this guideline. Finally, as mentioned previously in each of the earlier sections, the overall quality of evidence of the studies included was very low, most commonly because of age ranges that included young adults, the use of self-report to assess abstinence, studies with short-term follow-up assessment of cessation, poor adherence to the intervention with high attrition rates, differences in randomization, and methods that incorporated different forms of counseling that were difficult to compare.

The low quality of the available research, the limited benefit of the studied interventions, and the emergence of novel nicotine products, particularly e-cigarettes, highlight the urgent need for further innovative research on treatment of nicotine use in adolescents. For text-based interventions, an improved approach regarding implementation and effectiveness is needed (71). Cessation intervention studies should examine the efficacy of multiple modalities, such as technology-based interventions tested in tandem with pharmacotherapy. Incorporation of patient input into study design is important to address the high levels of attrition and low adherence seen in the included studies. Implementation research is imperative to improve adherence to tobacco cessation interventions, including technology-based interventions, NRT, and nonnicotine pharmacotherapy. Comparative effectiveness research is also important to determine

the most effective and safest cessation options. Future studies should examine pharmacotherapy efficacy in adolescents compared with adults, as well as treatment mechanisms such as relevant neuropharmacological pathways and psychosocial factors such as social networks. These studies should include assessing cessation outcomes at 6 months or longer (72). Future research should elucidate factors to identify the adolescents who are most likely to benefit from pharmacotherapy and the optimal duration of medication use. As other psychiatric disorders and other substance use (including cannabis products) are common in adolescents with nicotine product use disorder (73–75), future research should examine relevant treatment strategies. Given some of the strengths noted in the studies analyzed, future researchers should continue school-based studies (PICO 1) and should incorporate community input into study design and implementation (26, 31) with the use of mixed methods (58).

It is important that diverse groups be included in clinical trials. Future studies should aim to include diverse populations to ensure health equity across ethnic, racial, gender, sexual orientation, and socioeconomic groups. Most of the trials reviewed included mostly White participants, with a few exceptions (35), and gender diversity of the samples was not extensively described. However, the prevalence of nicotine product use is variable among different racial and/or ethnic groups (12, 76–78). It is imperative that all peoples and genders, including the LGBTQ+ (lesbian, gay, bisexual, transgender, queer/questioning, plus others), African American, American Indian/Alaska Native, Native Hawaiian/Pacific Islander, and Hispanic communities, are appropriately represented in future research and prevention efforts. Funding for continued school-based interventions—as well as considering other settings, such as community centers and organizations—is necessary for a holistic community approach to nicotine use in adolescents.

We note that nicotine use disorder in adolescents is difficult to successfully treat (*see* PATIENT AND PARENTAL PERSPECTIVE in the following text). This places great importance on research as well as both public policy and clinical interventions to prevent the initiation of nicotine product use among young persons.

Implementation and Costs

In considering implementation of therapeutic interventions for nicotine product cessation, clinicians must be aware that adolescent behavior differs from that of adults in key ways, including increased risk-taking tendencies and powerful peer influence (79–81). Successfully implementing cessation treatment necessitates navigating issues of consent and assent in adolescents, often modulated by varying degrees of parental involvement. Adolescent behavior, which is influenced by social networks according to social cognitive theory, has been shown to influence the successful implementation of interventions in adolescents and is perhaps a more profound consideration in adolescents than adults, given peer network influence on nicotine product use (82). Other barriers to successful implementation of nicotine cessation interventions are access to healthcare, healthcare literacy, and cultural acceptance of cessation. Clinicians should consider other comorbidities that may reduce the likelihood of cessation success, including other substance use, mental health problems, and psychosocial stressors. Implementation of cessation interventions ideally should be coordinated with nursing professionals, pharmacists, social workers, mental health care providers, and other multidisciplinary team members. After initiation of a cessation intervention by a clinician, we recommend follow-up at regular intervals to examine effectiveness, barriers, adherence, and adverse effects and adapt treatment as needed.

Clinicians should be mindful that potential neuropsychiatric adverse effects of bupropion and varenicline may limit their successful implementation. Although meta-analyses of RCTs have found no increased risk of suicide, and the FDA has removed the black box warning for psychiatric side effects, these risks remain: A psychiatric adverse event was reported in a subject from one study reviewed in this guideline (68). Additionally, nicotine withdrawal itself can exacerbate anxiety and depression, potentially leading to psychiatric morbidity (83). Given the limited research on the use of these pharmacologic agents in adolescents—especially those with comorbid mental health conditions—clinicians must remain vigilant in monitoring for psychiatric effects. Both bupropion and varenicline also

carry a risk of seizures, with bupropion contraindicated in individuals with a seizure disorder (62). Therefore, careful evaluation of seizure risk and ongoing monitoring are essential for both medications before consideration of their use as an intervention. Before and during treatment, clinicians should review patient and family medical histories, current and new medications, and dietary supplement use to identify potential contraindications or necessary treatment modifications.

The costs of various therapies can be substantial for families and access can be limited. Mental health insurance benefits that cover the cost of counseling can be very limited, resulting in significant out-of-pocket costs. In addition, there is a shortage of counselors trained in nicotine and/or tobacco use that can result in long wait times or difficulty accessing services, particularly in lower resource states without Medicaid expansion, which also would cover prescription drug costs. Access to NRT, including through state-funded quit lines, varies from state to state. Availability of medications and counseling services may be limited in many countries outside of the United States, especially low- and middle-income countries.

Patient and Parental Perspective

We spoke with a young adult, 19 years old, and his mother regarding his nicotine dependence to provide context for our recommendations. The patient and his mother did not have any direct involvement with the committee in the formulation of PICO questions or voting on recommendations. They were given a summary of the clinical practice guideline, including the recommendations. Separate from the committee, an interview was held with one of the authors (D.R.R.) to discuss their experience with nicotine cessation, and their opinions were provided regarding the recommendation. The following is a summary of the interview.

The patient began vaping marijuana at age 16 and needed drug rehabilitation for this substance use. He was introduced

to vaping nicotine and cigarette use while in an outpatient rehab program when he was 18 years old. The patient has a younger foster brother in his teens who continues to vape and is actively trying to quit.

The patient tried NRT, counseling, and technology to quit smoking and vaping. Both the patient and his mother felt that counseling was the most important and effective approach but noted that better training for both counselors and providers is needed. They felt that there were too many untrained counselors making ineffective recommendations; for example, recommending cigarettes or nicotine-free vapes with melatonin to quit marijuana and nicotine, respectively. Online counseling was ineffective for the patient, as he would simply turn off his camera and lie that his computer was not working.

The patient and his mother found NRT dosing (initial dose, how to step down) to be confusing. The patient tried NRT for 2 months, and it was helpful to reduce withdrawal symptoms. He would use a patch and then additional nicotine lozenges as needed. However, if he felt any symptoms of nicotine withdrawal, he stated that “it’s much easier to hit a vape and feel better immediately” than experience the “long drawn-out” withdrawal symptoms associated with NRT.

Despite this, of the recommendations provided in this guideline, the only recommendation the mother disagreed with was that of NRT (PICO 3). She felt that NRT should be recommended but that primary care providers should be better trained on its use regarding dosing and weaning.

From a counseling perspective, the mother felt that parental advocacy for teens to begin cessation is most important to begin the process, and teenager buy-in is crucial for success. Initially, the patient was forced into counseling, which was ineffective. Eventually, a pulmonologist told him that his pulmonary function testing result was abnormal. The patient stated, “It was a blessing to do PFTs,” because the result inspired him at age 19 to quit “cold turkey” without NRT. Ultimately, he decided a shorter, more intense, withdrawal period was worth it. He experienced 1 week of withdrawal symptoms (e.g., insomnia, nausea,

irritability, jitteriness, and anxiety) and has not vaped or smoked since.

Regarding the other recommendations, he agreed. For example, a cell phone app to help track his “addictions” (previous and current) has helped him and his younger foster brother. The patient stated that because he also has mental health disorders, he never wanted to try medications because of the side effects of anxiety and depression, and he said that his friends who vape feel the same. He stated, “Kids want to stay away from medication. Trying to find a way to live without medication is important.” The mother highlighted that having the teen and parent on the same page with respect to cessation is the key to success.

Conclusions

Nicotine product use is common among adolescents, and there are limited clinical studies to guide cessation efforts. The purpose of this clinical practice guideline is to help providers navigate the complexity of treating nicotine use in adolescents, a high-risk and vulnerable patient population. There is a need for larger scale, multicenter trials assessing both single and multimodalities for nicotine-containing products, including cigarettes, e-cigarettes, cigars, cigarillos, and so forth, in a gender- and ethnic-diverse population.

Note from the ATS Documents Editor

All ATS clinical practice guidelines are reviewed by the ATS Quality Improvement and Implementation Committee for potential performance measures. The committee concluded, “None of the recommendations in this clinical practice guideline are considered suitable for performance measure development, given that the certainty of evidence threshold criteria was not met for the guideline’s lone strong recommendation. A lack of endorsement by the ATS Quality Improvement and Implementation Committee for performance measurement development does not diminish the strength of the clinical recommendation.” ■

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