

Primary Care—Relevant Interventions for Tobacco Use Prevention and Cessation in Children and Adolescents: A Systematic Evidence Review for the U.S. Preventive Services Task Force

Carrie D. Patnode, PhD, MPH; Elizabeth O'Connor, PhD; Evelyn P. Whitlock, MD, MPH; Leslie A. Perdue, MPH; Clara Soh, MPA; and Jack Hollis, PhD

Background: Interventions to prevent smoking uptake or encourage cessation among young persons might help prevent tobacco-related illness.

Purpose: To review the evidence for the efficacy and harms of primary care-relevant interventions that aim to reduce tobacco use among children and adolescents.

Data Sources: Three systematic reviews that collectively covered the relevant literature; MEDLINE, PsycINFO, the Cochrane Central Register of Controlled Trials, and the Database of Abstracts of Reviews of Effects through 14 September 2012; and manual searches of reference lists and gray literature.

Study Selection: Two investigators independently reviewed 2453 abstracts and 111 full-text articles. English-language trials of behavior-based or medication interventions that were relevant to primary care and reported tobacco use, health outcomes, or harms were included.

Data Extraction: One investigator abstracted data from good- and fair-quality trials into an evidence table, and a second checked these data.

Data Synthesis: 19 trials (4 good-quality and 15 fair-quality) that were designed to prevent tobacco use initiation or promote cessa-

tion (or both) and reported self-reported smoking status or harms were included. Pooled analyses from a random-effects meta-analysis suggested a 19% relative reduction (risk ratio, 0.81 [95% CI, 0.70 to 0.93]; absolute risk difference, -0.02 [CI, -0.03 to 0.00]) in smoking initiation among participants in behavior-based prevention interventions compared with control participants. Neither behavior-based nor bupropion cessation interventions improved cessation rates. Findings about the harms related to bupropion use were mixed.

Limitations: No studies reported health outcomes. Interventions and measures were heterogeneous. Most trials examined only cigarette smoking. The body of evidence was largely published 5 to 15 years ago.

Conclusion: Primary care-relevant interventions may prevent smoking initiation over 12 months in children and adolescents.

Primary Funding Source: Agency for Healthcare Research and Quality.

Ann Intern Med. 2013;158:253-260.

For author affiliations, see end of text.

This article was published at www.annals.org on 11 December 2012.

www.annals.org

Tobacco use is the leading cause of preventable death in the United States. An estimated 443 000 deaths occur annually that are attributable to smoking (1). Despite the fact that the legal age for purchasing tobacco products in the United States is 18 years (2), every day more than 3800 children and adolescents aged 12 to 17 years have their first cigarette, and an estimated 1000 young persons begin smoking on a daily basis (3). In 2011, 23.4% of high school students reported that they currently used a tobacco product (4, 5).

Reducing the prevalence of youth tobacco use can occur through 2 primary means: by decreasing the proportion of nonusing children who initiate tobacco use or by increasing the proportion of current users who quit. These strategies can occur within large community environments (mass media campaigns or state-level tobacco control programs), small social environments (families, health care settings, or schools), or through regulatory or legislative approaches (taxation and pricing or regulations on youth access). The 2012 Surgeon General's Report concluded that there is a "large, robust, and consistent" evidence base that documents known effective strategies for reducing tobacco use among youths and young adults (6). These strategies included coordinated, multicomponent interventions

that combine mass media campaigns, price increases, school-based policies and programs, and statewide or community-wide changes in policies and norms. The report found no clear evidence that prevention strategies delivered in health care settings effectively reduce adolescent smoking initiation. There was a warning to interpret these findings with caution, however, given limited data and the lack of replication of specific approaches (6). Similarly, youth cessation interventions in health care have not been well-studied. In addition, no smoking cessation medications are currently approved for use in young persons.

In 2003, the U.S. Preventive Services Task Force (USPSTF) issued an "I" statement, citing insufficient evidence to determine the net benefit of counseling interventions to prevent initiation and promote cessation of tobacco use in children and adolescents (7). We performed this systematic review to help update these recommendations.

METHODS

Using the methods of the USPSTF (8), we developed an analytic framework and 3 key questions to guide our

review (**Appendix Figure 1**, available at www.annals.org). Agency for Healthcare Research and Quality (AHRQ) staff and USPSTF liaisons helped refine the scope and reviewed the full draft report. Decisions about inclusion of individual studies, quality assessment, and data analysis were limited to authors with no conflicts of interest. The full report provides details of our methods, including search strategies and evidence tables (9).

Data Sources and Searches

We began by evaluating all trials included in the 2008 Public Health Service Clinical Practice Guideline on Treating Tobacco Use and Dependence report for possible inclusion (10). In addition, we evaluated all trials that were considered by 3 previous reviews that collectively covered the prevention literature through July 2002 (11, 12) and the cessation literature through August 2009 (13). We then searched MEDLINE, PsycINFO, the Cochrane Central Register of Controlled Trials, and the Database of Abstracts of Reviews of Effects through 14 September 2012.

Study Selection

Two investigators independently reviewed abstracts against prespecified inclusion and exclusion criteria; potentially included full-text articles were subsequently dually reviewed for inclusion. We included trials of interventions designed to prevent tobacco use or promote cessation (with or without the use of medication) that were published during or after 1980. We included interventions that targeted children, their parents, or both and were conducted in or potentially feasible for (or referable from) health care settings. We describe these collectively as “primary care–relevant.” Referable interventions are those that are not conducted within primary care itself but that patients could enroll in within the larger health care setting or community. Included trials had control groups that offered minimal or no treatment and had to report tobacco use prevalence or a similar outcome at least 6 months after baseline. We included studies that reported harms at any follow-up time point. We only considered controlled trials for questions related to benefits of treatment; observational studies were included for medication harms.

Data Extraction and Quality Assessment

Two independent investigators conducted quality assessments of all included trials, resulting in a rating of “good,” “fair,” or “poor” according to USPSTF methods (8). We assessed the validity of the randomization and measurement procedures, comparability of the groups at baseline, overall and group-specific attrition, intervention fidelity, and appropriateness of statistical methods. We excluded poor-quality trials. All trials meeting quality criteria for benefits of treatment were also examined for harms. One reviewer abstracted data from studies that were rated as “fair” or “good,” and all abstraction was checked for accuracy and completeness by another reviewer. Discrepancies were resolved by double-checking the article and through discussion.

Data Synthesis and Analysis

Using smoking status as our primary outcome, we critically examined results tables with important study characteristics to identify the range of results and potential associations with effect size. We relied on measures of self-reported smoking because biochemical verification was not reported or used consistently (14). We grouped studies according to the outcomes presented: prevalence of smoking among baseline nonsmokers and smokers (combined), smoking initiation among baseline nonsmokers (prevention), or continued smoking among baseline smokers (cessation). Behavior-based and medication trials were examined separately. Within each group, we qualitatively explored patterns of association between effect size and several intervention and study design characteristics, including the number and duration of intervention sessions, whether the intervention was tailored according to smoking status, whether there was a group component or motivational interviewing, the measure of tobacco use, and the average age of the participants. Our full report outlines the complete list of factors we examined (9).

We conducted random-effects meta-analyses to estimate the effect size of interventions for trials reporting sufficient data. We entered the raw number of smokers and the total number of participants in the analysis to calculate pooled risk ratio (RR) estimates by using Stata, version 11.2 (StataCorp, College Station, Texas). The meta-analysis was adjusted for the cluster randomization of 3 trials (15–17) by dividing the sample sizes in these studies by a design effect based on average cluster size and an estimated intraclass correlation (18). We did not conduct statistical analyses for small study effects (an indicator of publication bias) because we had fewer than 10 trials in all analyses (19). Statistical heterogeneity was assessed with the I^2 statistic (20).

Role of the Funding Source

Staff from the AHRQ provided oversight for the project. Liaisons from the USPSTF helped to resolve issues around the scope of the review but were not involved in the conduct of the review.

RESULTS

We reviewed 2453 abstracts and 111 full-text articles for inclusion (**Appendix Figure 2**, available at www.annals.org). No primary care–relevant trials were identified that assessed health outcomes or examined subsequent rates of adult smoking. We identified 18 trials (reported in 22 publications) that examined the efficacy of primary care–relevant interventions in preventing tobacco use initiation or promoting cessation among young persons (**Appendix Table 1**, available at www.annals.org) (15–17, 21–36). We examined all 18 trials for harms related to the intervention and 1 additional trial (37) that reported the harms of bupropion. Ultimately, 3 trials on the adjunctive use of bupropion reported on harms (32, 34, 37) and are discussed

Table. Summary of Evidence for Benefits and Harms of Tobacco Use Interventions

Outcome	Trials, <i>n</i>	Quality Ratings	Summary of Findings
Health*	0	NA	No trials assessed health outcomes
Behavior			
Behavior-based interventions			
Smoking prevalence: combined nonsmokers and smokers	7†	Good: 2 Fair: 5	12 mo of follow-up: Pooled absolute RD, -0.02 (95% CI, -0.05 to 0.01); $I^2 = 57.6\%$; $\kappa = 6$; $n = 8749$ Range of effects: smoking prevalence rates 7 percentage points lower to 4 percentage points higher in the intervention group Pooled relative RR, 0.91 (CI, 0.81 to 1.01); $I^2 = 29.4\%$
Smoking initiation: prevention among nonsmokers	10	Good: 2 Fair: 8	6 to 36 mo of follow-up: Pooled absolute RD, -0.02 (CI, -0.03 to 0.00); $I^2 = 57.1\%$; $\kappa = 9$; $n = 26\,624$ Range of effects: initiation rates 8 percentage points lower to 3 percentage points higher in the intervention group Pooled relative RR, 0.81 (CI, 0.70 to 0.93); $I^2 = 37.8\%$
Smoking cessation: cessation among smokers	7	Good: 2 Fair: 5	6 to 12 mo of follow-up: Pooled absolute RD, -0.04 (CI, -0.09 to 0.01); $I^2 = 46.1\%$; $\kappa = 7$; $n = 2328$ Range of effects: quit rates 21 percentage points higher to 5 percentage points lower in the intervention group Pooled relative RR, 0.96 (CI, 0.90 to 1.02); $I^2 = 48.7\%$ Lack of effect may reflect limited number of studies targeting regular, established smokers
Bupropion interventions: smoking cessation	2	Fair: 2	No statistically significant benefit of bupropion at 6 mo
Harms			
Behavior-based interventions	0	NA	No trials explicitly reported on harms of behavior-based interventions
Bupropion interventions	3	Fair: 3	Mixed results

NA = not applicable; RD = risk difference; RR = risk ratio.

* Health outcomes included child respiratory health, dental/oral health, and subsequent rates of adult smoking.

† Four of these trials were also included in the behavior-based smoking initiation and cessation categories (i.e., the categories are not mutually exclusive).

later in this article. A summary of evidence for benefits and harms of all interventions is presented in the **Table**.

Effects of Interventions on Smoking Prevalence, Initiation, and Cessation

The 18 studies that examined behavioral outcomes were generally of fair quality; 4 of the 18 trials were good-quality (16, 17, 29, 36). The fair-quality trials frequently did not report specific randomization procedures, potentially leading to selection bias. Although blinding of outcome assessors was not reported in several trials, this is unlikely to produce bias in studies that used standardized data collection tools, such as computer-assisted telephone interviewing. Three studies did not report baseline participant data by group (27, 30, 33), which makes ensuring that groups were comparable at baseline difficult. Both medication trials were rated as fair-quality, primarily because of attrition and compliance concerns.

Combined Smoking Prevention and Cessation Interventions

Seven trials reported the combined effect of interventions on overall smoking prevalence ($n = 12\,769$ randomly assigned) (15, 23, 29, 31, 33, 35, 36). Four of these trials also reported effects among baseline nonsmokers (initiation) and smokers (cessation) separately and are discussed in the “Prevention” and “Cessation” sections of this article (**Appendix Table 2**, available at www.annals.org) (15, 23, 29, 33).

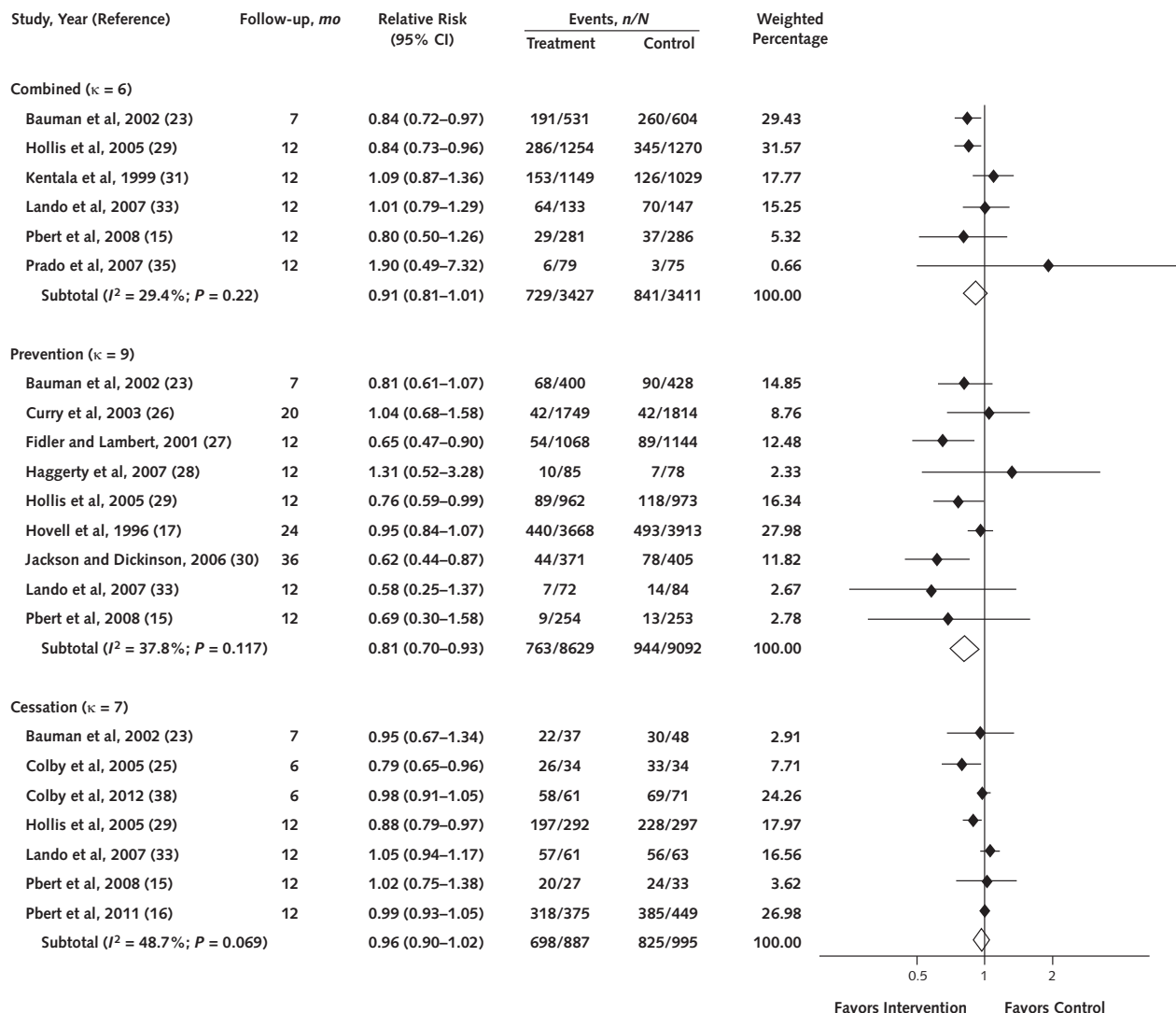
The average ages of participants in the combined trials ranged from 11 to 17 years, and most included an even

distribution of boys and girls. Intervention settings and components were very heterogeneous (**Appendix Table 1**). Four of the combined trials targeted intervention messages to the baseline smoking status of the young persons (15, 29, 31, 33), whereas the remaining 3 trials implemented the same intervention regardless of baseline smoking status (23, 35, 36). These 3 trials also included intervention components for parents and addressed additional behaviors beyond tobacco use, including alcohol and other substance use (23, 36) and unsafe sexual behaviors (35).

Most of the trials were conducted in the United States, with 1 trial conducted in Finland (31). Two of the 7 combined interventions were community- (35) or home-based (23, 36), whereas the other 5 trials were conducted in a primary care setting (15, 29, 36) or dental practice (31, 33) and included face-to-face interaction with a health care provider. These interactions included brief advice to quit smoking or to remain abstinent (29, 31, 33) or a single counseling session based on the 5A model (15). In 3 of the 5 trials conducted in health care settings, trained health counselors provided more in-depth counseling and follow-up telephone calls with participants after interaction with the primary provider (15, 29, 33).

Although all of the combined trials relied on self-reported smoking as the primary outcome, they used different measures (**Appendix Table 3**, available at www.annals.org). Three trials measured lifetime or “ever” use (23, 31, 36), 2 trials measured use in the past 30 days (29,

Figure. Smoking outcomes for intervention groups compared with control groups from all behavioral trials.



Combined prevention and cessation, prevention, and cessation are shown. Because of the clustering adjustment, the denominators for references 15 through 17 and the subtotal denominators do not match what is reported in the text and tables.

33), 1 trial evaluated the past 90 days (35), and 1 trial reported “regular or occasional” use (15). None of these trials used biochemical verification to confirm self-reports. One study, however, showed participants a carbon monoxide monitor and told them that they might use it to confirm their responses (a bogus pipeline approach) (15).

After pooling combined trials, we found a nonstatistically significant reduced RR for smoking prevalence in young persons assigned to the intervention at 7 to 12 months of follow-up (RR, 0.91 [95% CI, 0.81 to 1.01]; $I^2 = 29.4\%$; $\kappa = 6$; $n = 8749$) compared with the control group (Figure). The pooled absolute risk difference (RD) was -0.02 (CI, -0.05 to 0.01). Results were somewhat variable, with larger studies suggesting either a statistically significant benefit (23, 29) or no effect (15, 23, 31, 36) on

prevalence of smoking in intervention groups compared with control groups. Smaller studies, on the other hand, had no significant effects and relatively wide CIs (33, 35). Overall heterogeneity was low, suggesting no major inconsistency among studies. The single study that could not be pooled (36) found slightly more adolescents initiating smoking in the intervention group than in the control group, but this effect was not statistically significant (Appendix Table 3). Longer-term findings (after 2 to 3 years) generally mirrored the effects that were apparent at 7 or 12 months. In addition, a sensitivity analysis of 4 studies that had similar outcome measures (for example, smoking in the past 30 or 90 days) found an effect of similar magnitude across all studies (data not shown) (15, 29, 33, 35).

Prevention Interventions

We reviewed 10 trials that addressed prevention of smoking initiation among nonsmoking young persons: 6 trials that only included baseline nonsmokers (17, 21, 26–28, 30) and 4 of the combined trials already described (15, 24, 29, 33) ($\kappa = 10$; $n = 27\,603$ analyzed). Participants in the prevention trials were generally younger (average weighted age was 14 years). Again, intervention components were highly variable. Six of the 10 studies in this group targeted young persons directly (15, 17, 21, 27, 29, 33), 3 included intervention components for both young persons and parents (26, 28, 30), and 1 trial primarily targeted parents (24). Two of the 10 prevention trials were conducted outside of the United States (1 in the Netherlands [21] and 1 in the United Kingdom [27]). Four took place in a primary care (15, 29) or dental care setting (17, 33), and the remaining 6 studies primarily consisted of materials that were mailed to participants' homes. Most trials defined smoking initiation as "ever smoking" or "smoking within the past 30 days" among baseline nonsmokers or former smokers (**Appendix Table 4**, available at www.annals.org).

Results were consistent across trials, with all but 2 trials (26, 28) reporting reduced smoking initiation in the intervention groups compared with the control groups. We found a statistically significant reduced relative risk for smoking initiation among young persons receiving prevention interventions at 7 to 36 months of follow-up (RR, 0.81 [CI, 0.70 to 0.93]; $I^2 = 37.8\%$; $\kappa = 9$; $n = 26\,624$). The pooled absolute RD was 2 percentage points (CI, -0.03 to 0.00 percentage points), resulting in a number needed to treat of 50. The single study that could not be pooled found that fewer intervention group participants than control participants initiated smoking at 6 months, but this difference was not statistically significant (21). We conducted a sensitivity analysis in which we excluded 2 studies (24, 30) that both operationalized smoking initiation as "ever smoking," and the pooled RR remained statistically significant. Two trials (23, 28) showed consistent effects beyond 12 months. However, in the trials by Hollis and colleagues (29), the intervention significantly reduced smoking initiation among nonsmokers at 12 months, but the prevention effect was no longer statistically significant after 2 years.

As described in our methods, we qualitatively examined several specific intervention characteristics and study design issues to see if they were associated with effect size. No clear pattern emerged that explained any specific subgroup effects or why some trials had beneficial effects and others did not.

Behavior-Based Cessation Interventions

We included 3 behavior-based smoking cessation trials (16, 25, 38) in addition to the 4 combined studies (15, 22, 29, 33) that presented cessation outcomes separately (total

$\kappa = 7$; $n = 2328$ analyzed). Participants in the cessation trials were generally older than participants in the combined and prevention trials (average weighted age was 15.9 years). All but 1 trial targeted young persons directly and included face-to-face contact with an interventionist, such as a clinician, health counselor, or other study personnel (**Appendix Table 1**).

The definition of what constituted a smoker at baseline and the primary outcome measure differed among all of the cessation trials (**Appendix Table 5**, available at www.annals.org). For instance, 1 trial (25) required that the adolescent reported smoking daily (for the past 30 days), whereas another trial (16) enrolled adolescents who reported any smoking during the past 30 days and were interested in quitting. In terms of outcomes, 2 studies (25, 38) used 7-day abstinence, 4 studies (16, 22, 29, 33) used 30-day abstinence, and the remaining trial reported "occasional or regular" smoking at follow-up (15).

No group differences were found in cessation rates at 6 to 12 months (RR, 0.96 [CI, 0.90 to 1.02]; $I^2 = 48.7\%$; $\kappa = 7$; $n = 2338$) (**Figure**). The pooled absolute RD was -0.04 (CI, -0.09 to 0.01). A sensitivity analysis that included the 4 trials that involved tailored intervention components for baseline smokers, 12-month follow-up, and similar definitions of baseline smoking (15, 16, 29, 33) yielded a consistent result.

Bupropion Cessation Interventions

We included 2 cessation trials (32, 34) that evaluated the use of bupropion hydrochloride in addition to behavioral counseling to encourage adolescent smokers to quit ($n = 256$). We did not identify any trials meeting our eligibility criteria that estimated the independent effect of nicotine replacement therapy or varenicline. Both bupropion trials included relatively intense behavioral interventions for both the intervention and control groups.

Neither of the 2 trials showed a benefit. In the trial by Killen and colleagues (32), 12.5% of the young persons in the intervention group and 10% of the young persons in the control group reported 7-day abstinence at 6 months. Similarly, the trial by Muramoto and colleagues (34) reported that 6.3% of adolescents in the intervention group receiving bupropion, 150 mg/d, and 10.3% of adolescents receiving a placebo reported 7-day abstinence at 6 months (**Appendix Table 5**). Among those assigned the standard adult dose of bupropion (300 mg/d), 16.9% reported 7-day abstinence. Results were similar when rates of abstinence were examined via biological confirmation.

Harms of Interventions

None of the trials of behavior-based interventions explicitly reported on harms of treatment, such as demoralization due to failed quit attempts or depressive symptoms. Although some trials reported higher absolute prevalence of smoking in the intervention groups than the control groups after completing the interventions, none was statis-

tically significant. In the 3 trials reporting harms related to the use of bupropion (32, 34, 37), 1 trial found that a greater proportion of bupropion users (64%) reported an adverse effect than did those receiving the placebo (48%) (37). The other 2 studies, however, reported no increased risk for several specific adverse effects of bupropion, such as increased blood pressure or heart rate, nausea, sleep disturbance, headache, and cough (32, 34).

DISCUSSION

We found no primary care–relevant tobacco use trials that assessed health outcomes (beyond tobacco use behaviors) in children and adolescents or examined subsequent rates of adult smoking. Although we sought to include interventions that addressed all forms of tobacco use, this body of evidence primarily included studies focused on cigarette smoking. Sixteen trials examined the benefits of behavior-based interventions on cigarette smoking prevalence, initiation, or cessation. The total number of studies and participants varied considerably across smoking outcomes, with considerably more participants in the prevention studies. Three studies evaluated the effects or harms related to the adjunctive use of bupropion to aid adolescent smokers in quitting. Included studies were generally of fair quality, with various threats to internal validity. All of the studies differed widely in terms of sample size, types of interventions tested, and primary outcome measures.

Our review found that behavior-based interventions were effective only in reducing smoking initiation among nonsmoking young persons. Meta-analysis resulted in a 19% relative reduced risk for starting to smoke among intervention participants versus control participants at 7 to 36 months of follow-up. The pooled absolute RD was 2 percentage points, resulting in a number needed to treat of 50. Although no factors were clearly related to effect size in the included trials, high variability in the approaches of the interventions may have masked important relationships.

Combined behavioral interventions failed to show a statistically significant effect on overall smoking prevalence, as did cessation interventions conducted among current smokers. The absolute difference in the prevalence of smoking between intervention and control groups in the combined trials at follow-up was generally modest, ranging from 7 percentage points in favor of the intervention to 4 percentage points in favor of the control.

Quit rates among the included cessation studies were highly variable. The absolute difference in quit rates ranged from 21 percentage points higher among the intervention group to 5 percentage points higher in the control group (Appendix Table 5). The lack of effect seen across the cessation trials may reflect the limited number of studies that targeted established smokers or presented stratified data to examine the effects among these young persons. Smoking acquisition is a complex process, which may complicate the interpretation of cessation trials because youth

“smokers” can be quite heterogeneous in their use of tobacco. Although the overall results showed no benefit of cessation treatment, there were some promising approaches. A logical next step would be to replicate the few effective interventions (25, 29) and either limit the trial to established smokers or stratify the results according to the stage of acquisition of the young persons.

There are several limitations in the body of evidence and to our approach. First, there were inconsistent measures of baseline smoking status and outcome measures. Such variation makes it difficult to make concrete comparisons and generalize results. In addition, very few studies used biochemical verification to confirm self-reported smoking status. Second, very few studies evaluated other forms of tobacco use beyond cigarette smoking, even though other forms are readily available in the United States. Third, we did not perform formal analyses for publication bias due to small numbers of trials. Our analyses of abstracts and searches of trials registries did not suggest publication bias. We minimized the risk for selective reporting by requiring that reducing tobacco use was a primary aim of included studies. Fourth, all of the included studies were published in 2007 or earlier, with the exception of 3 trials (2 by the same author) (15, 16, 38). In recent years, substantial emphasis has been placed on tobacco-related legislation, environmental changes, and countermarketing. Although these public health efforts are imperative in reducing tobacco use (39), continuing to reach young persons on a more personal level through behavior-based interventions remains an important strategy (6). Another potential limitation to our approach is that we combined interventions that exclusively focused on cigarette smoking with those that targeted multiple behaviors (for example, alcohol and other substance use or sexual behaviors). These unrelated aims may have caused “noise” that masked the basic message to prevent smoking and may have led to null effects. Because of the variability in intervention approaches and populations, as well as inconsistencies in measurement, meta-analysis results should be interpreted with caution.

We did not include interventions that were designed to decrease tobacco use among parents as a secondary strategy for reducing smoking or secondhand tobacco smoke exposure. This could be a promising health care–based strategy for preventing youth smoking initiation, among other immediate health benefits. Similarly, we did not include interventions designed to restrict smoking in homes or cars as a strategy to reduce exposure to or use of tobacco among young persons. Research has shown, however, that having a strict smoke-free policy in the home is associated with fewer young persons smoking than in households with unrestricted or partial policies (that is, for only certain members of the household) (40, 41). More primary research that focuses on parental smoking and smoke-free family policies could add to the armamentarium of primary care clinicians.

The need to replicate promising interventions and specific intervention components in well-controlled trials is substantial. This research would include incorporating longer-term outcomes to examine the extent to which results hold over time, involving more diverse samples of young persons (including those at various stages of risk), estimating intervention effects in real-world settings, and determining the feasibility and sustainability of these interventions in a health care setting. Although 30- to 60-second advice messages or counseling using the 5A model may be feasible in primary care, it is not clear whether the additional components that many of the trials included (for example, in-person counseling after the provider encounter, tailored computer programming, and booster telephone calls) could be easily replicated in the real world unless other resources (for example, centralized telephone counselors) were employed.

Despite the substantial resources committed to reducing childhood and adolescent tobacco use over recent decades, approximately 10% of U.S. middle school students and nearly a quarter of high school students currently use tobacco. Consequently, youth tobacco users are a group at risk for the many negative health outcomes associated with tobacco use, including becoming regular users as adults. Our findings suggest that primary care–relevant interventions designed to reduce cigarette smoking among children and adolescents can have small, positive effects on smoking initiation among those who have not yet become regular smokers. The evidence on the effectiveness of cessation interventions for young persons who have experimented with cigarettes or are regular smokers is limited. Most studies included in this systematic review were published 5 to 15 years ago and were generally of fair quality. Primary care interventions are an essential component of a comprehensive tobacco control program that complements broader school-based, community-based, media, and policy interventions (6, 42).

From the Oregon Evidence-based Practice Center, Portland, Oregon.

Note: This review was conducted by the Oregon Evidence-based Practice Center under contract to the AHRQ. Staff from the AHRQ provided oversight for the project and assisted in external review of the companion draft evidence synthesis.

Disclaimer: Ms. Soh accepted a position at the Pharmaceutical Research and Manufacturers of America during the finalization of the full report and drafting and final submission of this manuscript; she contributed the majority of her intellectual content to this review while she was employed with the Oregon Evidence-based Practice Center at Kaiser Permanente Center for Health Research. The views and opinions expressed in this article are those of the authors and do not necessarily reflect the views of the Pharmaceutical Research and Manufacturers of America.

Acknowledgment: The authors thank the AHRQ staff; the USPSTF; Raymond S. Niaura, PhD, Steven Sussman, PhD, MA, Andrea C. Villanti, PhD, MPH, and Jonathan Winickoff, MD, MPH, for providing

expert review of the report; and Kevin Lutz, MFA, Daphne Plaut, MLS, and Heather Baird of the Kaiser Permanente Center for Health Research.

Financial Support: By contract HHS-290-2007-10057-I from the Agency for Healthcare Research and Quality.

Potential Conflicts of Interest: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M12-1962.

Requests for Single Reprints: Reprints are available from the AHRQ Web site (www.ahrq.gov).

Current author addresses and author contributions are available at www.annals.org.

References

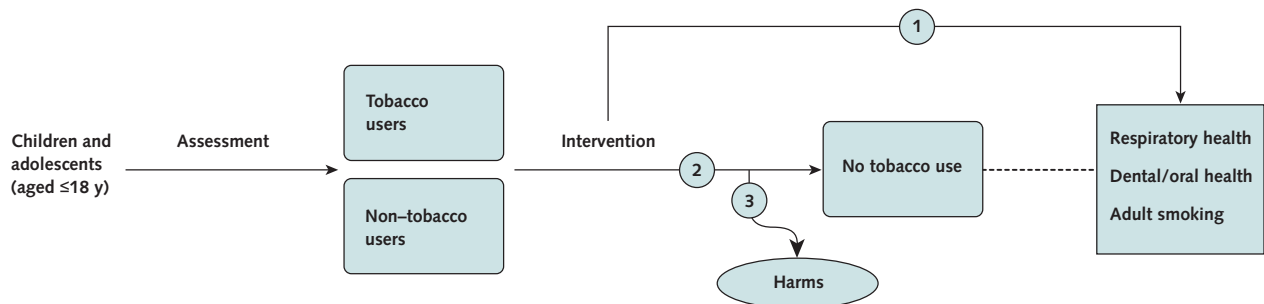
- Centers for Disease Control and Prevention (CDC). Smoking-attributable mortality, years of potential life lost, and productivity losses—United States, 2000–2004. *MMWR Morb Mortal Wkly Rep*. 2008;57:1226–8. [PMID: 19008791]
- U.S. Department of Health and Human Services. FDA Issues Final Rule Restricting Access and Marketing of Cigarettes and Smokeless Tobacco Products to Youth. Washington, DC: U.S. Department of Health and Human Services; 2011. Accessed at www.hhs.gov/news/press/2010pres/03/20100318a.html on 13 May 2011.
- Substance Abuse and Mental Health Services Administration. Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings. NSDUH Series H-41, HHS Publication no. SMA 11-4658. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2011.
- Centers for Disease Control and Prevention (CDC). Tobacco use among middle and high school students—United States, 2000–2009. *MMWR Morb Mortal Wkly Rep*. 2010;59:1063–8. [PMID: 20798668]
- Eaton DK, Kann L, Kinchen S, Shanklin S, Flint KH, Hawkins J, et al; Centers for Disease Control and Prevention (CDC). Youth risk behavior surveillance—United States, 2011. *MMWR Surveill Summ*. 2012;61:1–162. [PMID: 22673000]
- U.S. Department of Health and Human Services. Preventing Tobacco Use Among Youth and Young Adults: A Report of the Surgeon General, 2012. Washington, DC: U.S. Department of Health and Human Services; 2012.
- U.S. Preventive Services Task Force. Counseling to Prevent Tobacco Use and Tobacco-Caused Disease: Recommendation Statement. Rockville, MD: U.S. Preventive Services Task Force; 2003.
- U.S. Preventive Services Task Force. U.S. Preventive Services Task Force Procedure Manual. Rockville, MD: U.S. Preventive Services Task Force; 2008.
- Patnode CD, O'Connor E, Whitlock EP, Perdue LA, Soh C. Interventions for tobacco use prevention and cessation in children and adolescents: a systematic evidence review for the U.S. Preventive Services Task Force. Rockville, MD: Agency for Healthcare Research and Quality; 2012. [Forthcoming].
- U.S. Department of Health and Human Services. Treating Tobacco Use and Dependence: 2008 Update. Washington, DC: U.S. Department of Health and Human Services; 2008.
- Christakis DA, Garrison MM, Ebel BE, Wiehe SE, Rivara FP. Pediatric smoking prevention interventions delivered by care providers: a systematic review. *Am J Prev Med*. 2003;25:358–62. [PMID: 14580640]
- Thomas RE, Baker P, Lorenzetti D. Family-based programmes for preventing smoking by children and adolescents. *Cochrane Database Syst Rev*. 2007; CD004493. [PMID: 17253511]
- Grimshaw GM, Stanton A. Tobacco cessation interventions for young people. *Cochrane Database Syst Rev*. 2006;CD003289. [PMID: 17054164]
- Dolcini MM, Adler NE, Lee P, Bauman KE. An assessment of the validity of adolescent self-reported smoking using three biological indicators. *Nicotine Tob Res*. 2003;5:473–83. [PMID: 12959785]
- Pbert L, Flint AJ, Fletcher KE, Young MH, Druker S, DiFranza JR. Effect of a pediatric practice-based smoking prevention and cessation intervention for adolescents: a randomized, controlled trial. *Pediatrics*. 2008;121:e738–47. [PMID: 18381502]

16. Pbert L, Druker S, DiFranza JR, Gorak D, Reed G, Magner R, et al. Effectiveness of a school nurse-delivered smoking-cessation intervention for adolescents. *Pediatrics*. 2011;128:926-36. [PMID: 22007015]
17. Hovell MF, Slymen DJ, Jones JA, Hofstetter CR, Burkham-Kreitner S, Conway TL, et al. An adolescent tobacco-use prevention trial in orthodontic offices. *Am J Public Health*. 1996;86:1760-6. [PMID: 9003134]
18. Higgins JPT, Green S. *Cochrane Handbook for Systematic Reviews of Interventions*. Version 5.1.0. Cochrane Collaboration; 2011. Accessed at www.cochrane-handbook.org on 5 April 2012.
19. Sterne JAD, Egger M. Regression methods to detect publication and other bias in meta-analysis. In: Rothstein HR, Sutton AJ, Bornstein M, eds. *Publication Bias in Meta-Analysis: Prevention, Assessment and Adjustments*. Chichester, United Kingdom: J Wiley; 2006.
20. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327:557-60. [PMID: 12958120]
21. Aulsems M, Mesters I, van Breukelen G, De Vries H. Short-term effects of a randomized computer-based out-of-school smoking prevention trial aimed at elementary schoolchildren. *Prev Med*. 2002;34:581-9. [PMID: 12052017]
22. Bauman KE, Ennett ST, Foshee VA, Pemberton M, King TS, Koch GG. Influence of a family-directed program on adolescent cigarette and alcohol cessation. *Prev Sci*. 2000;1:227-37. [PMID: 11523750]
23. Bauman KE, Ennett ST, Foshee VA, Pemberton M, King TS, Koch GG. Influence of a family program on adolescent smoking and drinking prevalence. *Prev Sci*. 2002;3:35-42. [PMID: 12002557]
24. Bauman KE, Foshee VA, Ennett ST, Pemberton M, Hicks KA, King TS, et al. The influence of a family program on adolescent tobacco and alcohol use. *Am J Public Health*. 2001;91:604-10. [PMID: 11291373]
25. Colby SM, Monti PM, O'Leary Tevyaw T, Barnett NP, Spirito A, Rohsenow DJ, et al. Brief motivational intervention for adolescent smokers in medical settings. *Addict Behav*. 2005;30:865-74. [PMID: 15893085]
26. Curry SJ, Hollis J, Bush T, Polen M, Ludman EJ, Grothaus L, et al. A randomized trial of a family-based smoking prevention intervention in managed care. *Prev Med*. 2003;37:617-26. [PMID: 14636795]
27. Fidler W, Lambert TW. A prescription for health: a primary care based intervention to maintain the non-smoking status of young people. *Tob Control*. 2001;10:23-6. [PMID: 11226356]
28. Haggerty KP, Skinner ML, MacKenzie EP, Catalano RF. A randomized trial of Parents Who Care: effects on key outcomes at 24-month follow-up. *Prev Sci*. 2007;8:249-60. [PMID: 17987388]
29. Hollis JF, Polen MR, Whitlock EP, Lichtenstein E, Mullooly JP, Velicer WF, et al. Teen reach: outcomes from a randomized, controlled trial of a tobacco reduction program for teens seen in primary medical care. *Pediatrics*. 2005;115: 981-9. [PMID: 15805374]
30. Jackson C, Dickinson D. Enabling parents who smoke to prevent their children from initiating smoking: results from a 3-year intervention evaluation. *Arch Pediatr Adolesc Med*. 2006;160:56-62. [PMID: 16389212]
31. Kentala J, Utriainen P, Pahlkala K, Mattila K. Can brief intervention through community dental care have an effect on adolescent smoking? *Prev Med*. 1999;29:107-11. [PMID: 10446036]
32. Killen JD, Robinson TN, Ammerman S, Hayward C, Rogers J, Stone C, et al. Randomized clinical trial of the efficacy of bupropion combined with nicotine patch in the treatment of adolescent smokers. *J Consult Clin Psychol*. 2004;72: 729-35. [PMID: 15301658]
33. Lando HA, Hennrikus D, Boyle R, Lazovich D, Stafne E, Rindal B. Promoting tobacco abstinence among older adolescents in dental clinics. *J Smok Cessat*. 2007;2:23-30.
34. Muramoto ML, Leischow SJ, Sherrill D, Matthews E, Strayer LJ. Randomized, double-blind, placebo-controlled trial of 2 dosages of sustained-release bupropion for adolescent smoking cessation. *Arch Pediatr Adolesc Med*. 2007;161: 1068-74. [PMID: 17984409]
35. Prado G, Pantin H, Briones E, Schwartz SJ, Feaster D, Huang S, et al. A randomized controlled trial of a parent-centered intervention in preventing substance use and HIV risk behaviors in Hispanic adolescents. *J Consult Clin Psychol*. 2007;75:914-26. [PMID: 18085908]
36. Stevens MM, Olson AL, Gaffney CA, Tosteson TD, Mott LA, Starr P. A pediatric, practice-based, randomized trial of drinking and smoking prevention and bicycle helmet, gun, and seatbelt safety promotion. *Pediatrics*. 2002;109: 490-7. [PMID: 11875146]
37. Gray KM, Carpenter MJ, Baker NL, Hartwell KJ, Lewis AL, Hiott DW, et al. Bupropion SR and contingency management for adolescent smoking cessation. *J Subst Abuse Treat*. 2011;40:77-86. [PMID: 20934835]
38. Colby SM, Nargiso J, Tevyaw TO, Barnett NP, Metrik J, Lewander W, et al. Enhanced motivational interviewing versus brief advice for adolescent smoking cessation: results from a randomized clinical trial. *Addict Behav*. 2012;37:817-23. [PMID: 22472523]
39. Task Force on Community Preventive Services. Tobacco. In: Zaza S, Briss PA, Harris KW, eds. *The Guide to Community Preventive Services: What Works to Promote Health?* Atlanta, GA: Oxford Univ Pr; 2005:3-79.
40. Farkas AJ, Gilpin EA, White MM, Pierce JP. Association between household and workplace smoking restrictions and adolescent smoking. *JAMA*. 2000; 284:717-22. [PMID: 10927780]
41. Wakefield MA, Chaloupka FJ, Kaufman NJ, Orleans CT, Barker DC, Ruel EE. Effect of restrictions on smoking at home, at school, and in public places on teenage smoking: cross sectional study. *BMJ*. 2000;321:333-7. [PMID: 10926588]
42. Centers for Disease Control and Prevention. *Best Practices for Comprehensive Tobacco Control Programs—2007*. Atlanta, GA: Centers for Disease Control and Prevention; 2007.

Current Author Addresses: Drs. Patnode, O'Connor, Whitlock, and Hollis and Ms. Perdue: Kaiser Permanente Center for Health Research, 3800 North Interstate Avenue, Portland, OR 97227.
Ms. Soh: The Pharmaceutical Research and Manufacturers of America, 950 F Street, NW, Suite 300, Washington, DC 20004.

Author Contributions: Conception and design: C.D. Patnode, E. O'Connor, E.P. Whitlock, J. Hollis.
Analysis and interpretation of the data: C.D. Patnode, E. O'Connor, L.A. Perdue, C. Soh.
Drafting of the article: C.D. Patnode.
Critical revision of the article for important intellectual content: C.D. Patnode, E. O'Connor, L.A. Perdue, C. Soh.
Final approval of the article: C.D. Patnode, E. O'Connor, E.P. Whitlock, L.A. Perdue, C. Soh, J. Hollis.
Statistical expertise: C.D. Patnode, E. O'Connor.
Obtaining of funding: E.P. Whitlock.
Administrative, technical, or logistic support: C.D. Patnode, E. O'Connor, E.P. Whitlock, L.A. Perdue.
Collection and assembly of data: C.D. Patnode, L.A. Perdue, C. Soh.

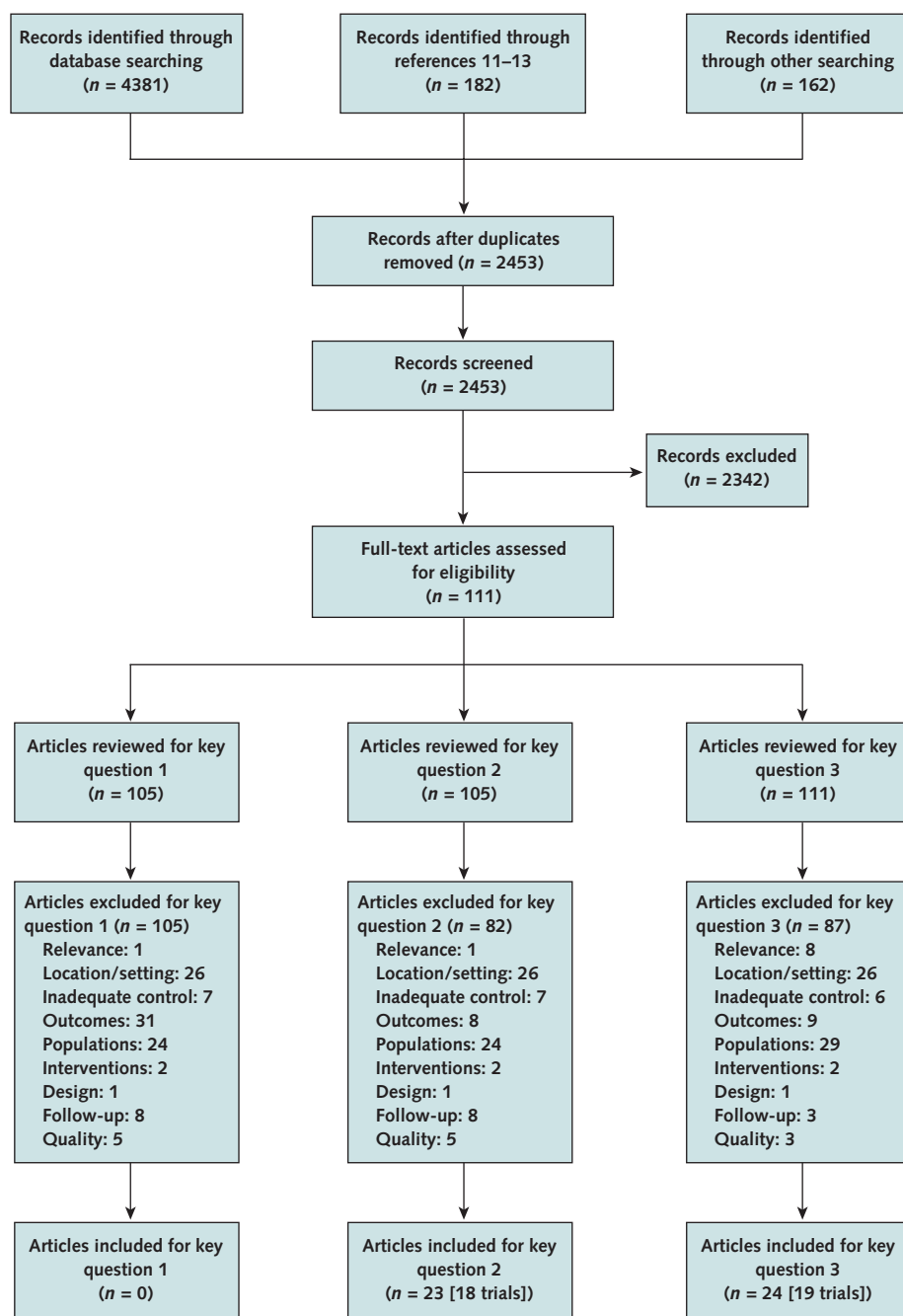
Appendix Figure 1. Analytic framework and key questions.



Key Questions:

1. Do primary care interventions designed to prevent tobacco use or improve tobacco cessation rates in children and adolescents improve health outcomes in children and adolescents (respiratory health and dental/oral health) and reduce the likelihood of adult smoking?
2. Do primary care interventions prevent tobacco use in children and adolescents or improve tobacco cessation rates in children and adolescents who use tobacco? What are elements of efficacious interventions? Are there differences in outcomes in different subgroups, as defined by age, sex, race, socioeconomic status, type or pattern of tobacco use, residential setting (urban vs. rural), or presence of depression?
3. What adverse effects are associated with interventions to improve tobacco cessation rates or prevent tobacco use in children and adolescents?

Appendix Figure 2. Summary of evidence search and selection.



Appendix Table 1. Characteristics of Included Trials

Study, Year (Reference)	Quality Rating	Focus	Age Range (Mean), y	Location	Intervention Setting	Method of Intervention	Duration of Intervention	Participants, n*		Time to Follow-up, mo	Follow- up, %
								Intervention Group	Control Group		
Bauman et al, 2002 (23)	Fair	Combined, prevention, cessation	12–14 (13.9)	United States	Home	Telephone, print	15 wk	658	658	7†, 16	81.2
Hollis et al, 2005 (29)	Good	Combined, prevention, cessation	14–17 (15.4)	United States	Medical office	Face-to-face, computer	1 visit plus 2 booster sessions within 12 mo	1254	1272	12†, 24	93.7
Kentala et al, 1999 (31)	Fair	Combined	NR (13.1)	Finland	Dental clinic	Face-to-face	1 visit	1348	1238	12†, 24	84.2
Lando et al, 2007 (33)	Fair	Combined, prevention, cessation	14–17 (15.4)	United States	Dental clinic	Face-to-face, telephone	1 visit plus 3 to 6 booster calls within 6 mo	175	169	12	65.4
Pbert et al, 2008 (15)	Fair	Combined, prevention, cessation	13–17 (16.9)	United States	Pediatric clinic	Face-to-face, telephone	1 visit plus 4 booster calls over 21 wk	1346	1365	6, 12†	99.2
Prado et al, 2007 (35)	Fair	Combined	NR (13.4)	United States	Home and community	Face-to-face	12 mo	91	84	12†, 24, 36	88.0
Stevens et al, 2002‡ (36)	Good	Combined	NR (11.0)	United States	Pediatric office	Face-to-face, telephone, print	36 mo	1780	1331	12†, 24, 36	95.5
Ausems et al, 2002‡ (21)	Fair	Prevention	NR (11.7)	The Netherlands	Home	Print	9 wk	871	793	6	91.5
Curry et al, 2003 (26)	Fair	Prevention	10–12 (11.0)	United States	Home	Print, telephone	6 wk plus 1 booster call within 14 mo	2020	2006	20	88.5
Fidler and Lambert, 2001 (27)	Fair	Prevention	10–15 (NR)	United Kingdom	Home	Print	12 mo	1456	1486	12	75.3
Haggerty et al, 2007 (28)	Fair	Prevention	NR (13.7)	United States	Home (IG1), after school (IG2)§	Face-to-face	7 wk	IG1: 107 IG2:118§	83	12†, 24	92.5
Hovell et al, 1996 (17)	Good	Prevention	11–19 (14.4)	United States	Orthodontic office	Face-to-face, print	2 y	7149	7626	24	92.5
Jackson and Dickinson, 2006 (30)	Fair	Prevention	7–8 (NR)	United States	Home	Print	10 wk plus 1 booster guide within 12 mo	426	447	36	87.5
Colby et al, 2005 (25)	Fair	Cessation	12–19 (16.3)	United States	NR	Face-to-face, telephone, print	1 visit plus 1 booster call within 1 wk	43	42	6	80.0
Colby et al, 2012 (38)	Fair	Cessation	14–18 (16.2)	United States	NR	Face-to-face, telephone, print	1 visit plus 1 booster call within 1 wk plus 1 parent discussion	79	83	6	81.5

Continued on following page

Appendix Table 1 —Continued

Study, Year (Reference)	Quality Rating	Focus	Age Range (Mean), y	Location	Intervention Setting	Method of Intervention	Duration of Intervention	Participants, n*		Time to Follow-up, mo	Follow- up, %
								Intervention Group	Control Group		
Pbert et al, 2011 (16)	Good	Cessation	NR (16.9)	United States	School health clinic	Face-to-face	4 wk	486	582	12	88.4
Killen et al, 2004 (32)	Fair	Cessation (bupropion)	15–18 (17.3)	United States	NR	Face-to-face	10 wk	103	108	6	63.5
Muramoto et al, 2007 (34)	Fair	Cessation (bupropion)	14–17 (16.0)	United States	Research clinic	Face-to-face	7 wk	IG1:105§ IG2:104	103	6	61.9

IG = intervention group; NR = not reported.

* Randomly assigned.

† Data from this follow-up point were used.

‡ Study not included in the meta-analysis.

§ Intervention group was used in the meta-analysis.

Appendix Table 2. Included Studies, by Group and Primary Outcome

Study, Year (Reference)	Combined (Prevalence)	Prevention (Initiation)	Cessation	
			Behavior-Based	Bupropion
Ausems et al, 2002 (21)		✓		
Bauman et al, 2002 (23)	✓	✓	✓	
Colby et al, 2005 (25)			✓	
Colby et al, 2012 (38)			✓	
Curry et al, 2003 (26)		✓		
Fidler and Lambert, 2001 (27)		✓		
Haggerty et al, 2007 (28)		✓		
Hollis et al, 2005 (29)	✓	✓	✓	
Hovell et al, 1996 (17)		✓		
Kentala et al, 1999 (31)	✓			
Killen et al, 2004 (32)				✓
Jackson and Dickinson, 2006 (30)		✓		
Lando et al, 2007 (33)	✓	✓	✓	
Muramoto et al, 2007 (34)				✓
Pbert et al, 2008 (15)	✓	✓	✓	
Pbert et al, 2011 (16)			✓	
Prado et al, 2007 (35)	✓			
Stevens et al, 2002 (36)	✓			
Total, <i>n</i>	7	10	7	2

Appendix Table 3. Results of Interventions: Combined Prevention and Cessation

Study, Year (Reference)	Analyzed, <i>n</i>	Time to Follow-up, <i>mo</i>	Primary Outcome Measure	Smoking at Baseline, %		Smoking at Follow-up, %		Relative Risk (95% CI)
				Intervention Group	Control Group	Intervention Group*	Control Group*	
Bauman et al, 2002 (23)	1135	7	Ever smoked even 1 puff of a cigarette	19.3†	24.8†	36.0	43.0	0.84 (0.72–0.97)
Hollis et al, 2005 (29)	2524	12	Smoked ≥1 cigarette in the past 30 d	23.3*	23.4*	22.8	27.2	0.84 (0.73–0.96)
Kentala et al, 1999 (31)	2178	12	NR	5.5	6.0	13.3	12.2	1.09 (0.87–1.36)
Lando et al, 2007 (33)	280	12	Smoked in past 30 d	34.9†	37.3†	48.1	47.6	1.01 (0.79–1.29)
Pbert et al, 2008 (15)	2478	12	Smoked occasionally or regularly	8.7	10.6	9.4	11.7	0.80 (0.50–1.26)
Prado et al, 2007 (35)	154	12	Smoked cigarettes in past 90 d	3.3	1.2	7.6	4.0	1.90 (0.49–7.32)
Stevens et al, 2002 (36)‡	3070	12	Ever smoked (specific measure NR)	5.3†	4.5†	NR	NR	NR§

NR = not reported.

* Calculated on the basis of data requested from the author.

† Calculated on the basis of presented data.

‡ Not included in the meta-analysis.

§ The adjusted odds ratio for having ever smoked for the intervention group compared with the control group was 1.05 (95% CI, 0.80 to 1.39).

Appendix Table 4. Results of Interventions: Prevention

Study, Year (Reference)	Analyzed, <i>n</i>	Time to Follow-up, <i>mo</i>	Primary Outcome Measure	Initiating Smoking at Follow-up, %		Relative Risk (95% CI)
				Intervention Group	Control Group	
Ausems et al, 2002 (21)	912	6	Ever smoked even 1 puff of a cigarette or smoked in past 30 d	10.4*	18.0*	NR*
Bauman et al, 2001 (24)	828	7	Ever smoked even 1 puff of a cigarette	17.0	21.0	0.81 (0.61–1.07)
Curry et al, 2003 (26)	3552	20	Smoked in past 30 d	2.4†	2.3†	1.04 (0.68–1.58)
Fidler and Lambert, 2001 (27)	2212	12	"Started to smoke" after baseline	5.1	7.8	0.65 (0.47–0.90)
Haggerty et al, 2007 (28)	241	12	"Started to smoke" after intervention	11.8‡	9.0‡	1.31 (0.52–3.28)
Hollis et al, 2005 (29)	1935	12	Smoked ≥1 cigarette in past 30 d	9.3	12.1	0.76 (0.59–0.99)
Hovell et al, 1996 (17)	14 775	24	Used tobacco in past 30 d§	12.0	12.6	0.95 (0.84–1.07)
Jackson and Dickinson, 2006 (30)	776	36	Ever smoked even 1 puff	11.9	19.3	0.62 (0.44–0.87)
Lando et al, 2007 (33)	156	12	Smoked in past 30 d	9.7	16.7	0.58 (0.25–1.37)
Pbert et al, 2008 (15)	2216	12	Smoked occasionally or regularly	3.2	4.5	0.69 (0.30–1.58)

NR = not reported.

* The number of baseline nonsmokers and the number of children initiating smoking at follow-up were not reported. The percentage of children initiating smoking at follow-up (as reported in the article) was 10.4% (95% CI, 6.9% to 14.0%) in the intervention group and 18.1% (CI, 12.5% to 23.7%) in the control group.

† Among the assessment cohort (*n* = 492), 2.5% of participants in the intervention group and 0% of participants in the control group reported smoking in the past 30 d at baseline. The authors do not report whether baseline smokers were included in the follow-up.

‡ At baseline, 22.0% of participants in the intervention group and 21.7% of participants in the control group reported smoking at baseline. These individuals were excluded from the analysis at follow-up.

§ Includes the use of cigarettes, pipes, cigars, or smokeless tobacco.

|| Baseline smokers were excluded from the analysis (specific numbers were not reported).

Appendix Table 5. Results of Interventions: Cessation

Study, Year (Reference)	Analyzed, <i>n</i>	Definition of Smoker at Baseline	Primary Outcome Measure	Smoking at Follow-up, %		Relative Risk (95% CI)
				Intervention Group	Control Group	
Behavior-based						
Bauman et al, 2000 (22)	85	Smoked ≥1 d in past 30 d	Smoked ≥1 d in past 30 d	59.5	62.5	0.95 (0.67–1.34)
Colby et al, 2005 (25)	68	Daily smoking for past 30 d	Smoked in past 7 d	76.5	97.1	0.79 (0.65–0.96)
Colby et al, 2012 (38)	132	Smoked at least once per week in past 30 d	Smoked in past 7 d and had biochemically confirmed expired CO level <9 ppm and saliva cotinine level <14 ng/mL	95.1	97.2	0.98 (0.91–1.05)
Hollis et al, 2005 (29)	589	Smoked ≥1 cigarette in past 30 d	Smoked ≥1 cigarette in past 30 d	67.5*	76.8*	0.88 (0.79–0.97)
Lando et al, 2007 (33)	124	Smoked in past 30 d	Smoked in past 30 d	93.4	88.9	1.05 (0.94–1.17)
Pbert et al, 2008 (15)	262	Smoked occasionally or regularly	Smoked occasionally or regularly	74.4	72.4	1.02 (0.75–1.38)
Pbert et al, 2011 (16)	1068	Smoked in past 30 d and interested in quitting in next 2 wk	Smoked in past 30 d	84.8	85.7	0.99 (0.93–1.05)
Bupropion						
Killen et al, 2004 (32)	134	Smoked ≥10 cigarettes per day, smoked ≥6 mo, had made 1 or more failed quit attempts, and scored ≥10 on the mFTQ	Smoked in past 7 d and had biochemically confirmed saliva cotinine level <20 ng/mL	87.5	90.0	0.97 (0.86–1.10)
Muramoto et al, 2007 (34)	122	Smoked ≥6 cigarettes per day, had an exhaled CO level ≥10 ppm, had at least 2 previous quit attempts, and motivated to quit; excluded those using other tobacco products	Smoked in past 7 d	93.8	89.7	1.05 (0.94–1.16)

CO = carbon monoxide; mFTQ = modified Fagerström Tolerance Questionnaire.

* Includes self-described experimenters and smokers.