# Smoking Cessation Interventions in Pregnancy and Postpartum Care
## Executive Summary

## Background

Nearly 443,000 U.S. deaths are attributable annually to cigarette smoking, which makes tobacco, including secondhand smoke, the most preventable cause of disease, disability, and death in the United States.[1,2] An estimated 19.8 million women in the United States smoke.[3] Nationally, 23 percent of women report smoking in the 3 months before pregnancy, while 13 percent report smoking in the last 3 months of pregnancy. Rates vary significantly by State, with up to 30 percent of women in some States reporting continued tobacco use in the third trimester. Fewer than half of pregnant smokers report successfully quitting during pregnancy,[1] and self-report leads to an overestimation of cessation rates in pregnancy.[4] Nondisclosure of smoking status among pregnant smokers is common and ranges from 23[5] to 49 percent[6] in published reports.

Smoking during pregnancy can result in significant complications for the pregnant woman, her fetus, and members of the woman's household who are exposed to secondhand smoke. Smoking is associated with increased risk of placental abruption, anemia, preterm birth, chronic hypertension, and placenta previa.[7-10] Health risks to the fetus include low birth weight, restricted growth, and fetal death.[9,11-17]

Multiple interventions to promote smoking cessation exist. They include advice and counseling, self-help materials, nicotine replacement therapy (NRT), antidepressants including bupropion (Zyban®), and

## Evidence-based Practice Program

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

The full report and this summary are available at www.effectivehealthcare.ahrq.gov/reports/final.cfm.

pharmacologic cessation aids such as varenicline (Chantix®). While these pharmacologic aids may limit the exposure to tobacco smoke, little is known about their potential adverse effects on short- and long-term reproductive outcomes. The U.S. Food and Drug Administration places the transdermal nicotine patch in pregnancy category D, which indicates there are known risks to the fetus, but potential benefits may outweigh risks in some cases. The other nicotine replacement products, as well as varenicline and bupropion, are category C medications, meaning animal studies have shown adverse fetal effects and no adequate human studies are available, but potential benefits may outweigh risks.[18-22] The American College of Obstetricians and Gynecologists does not recommend pharmacologic interventions as first-line therapies in pregnant women due to lack of evidence on safety and efficacy.[23,24]

Overall, the findings from existing systematic reviews suggest that NRT, behavioral and educational cessation strategies, and multicomponent interventions may be beneficial to women who smoke in pregnancy or the postpartum period, but to date, evidence has been mixed.[25-29] Despite these previous systematic review efforts, however, the efficacy of specific components and the impact of these various strategies on smoking and infant outcomes in pregnant and postpartum women remain unclear.

## Scope and Key Questions

This review is focused on the evidence available to inform the provision of smoking cessation strategies for health care providers. The relevant population for this review consists of pregnant and postpartum woman who are current smokers or recent quitters. The literature reflects various strategies to promote smoking cessation and relapse prevention. Interventions include any behavioral, psychosocial, pharmacologic, or educational intervention intended to promote individual changes in cigarette consumption among pregnant smokers and recent quitters in the prenatal and postpartum period. Interventions targeting the behavior of smokers' partners or health care providers exclusively were not included. Interventions of interest are those that were conducted in or originated from a health care setting. The review does not include public health initiatives or system-level smoking cessation research.

Smoking outcomes are limited to biochemically validated reports of smoking cessation during pregnancy or in the postpartum period. Biochemical validation of smoking status includes measures of cotinine from saliva, urine, or serum; expired carbon monoxide; or serum thiocyanate. Although these measures do not verify continuous abstinence, they are accepted standards for evaluating point prevalence of smoking status. The review does not report smoking reduction.

We addressed the following Key Questions:

**Key Question 1**: What is the effectiveness of interventions intended to achieve or maintain smoking cessation in women who are pregnant or postpartum for promoting smoking cessation, relapse prevention, and continuous abstinence?

**Key Question 2**: What is the effectiveness of interventions intended to achieve or maintain smoking cessation in women who are pregnant or postpartum for improving infant and child outcomes?

**Key Question 3**: What are the harms of interventions intended to achieve or maintain smoking cessation in women who are pregnant or postpartum?

**Key Question 4**: What is the effect of components of the smoking cessation intervention, including who delivered the intervention (physician, nurse, midwife, etc.), the intervention itself, and where the intervention was delivered (clinic, hospital setting, etc.), on cessation of smoking or durability of cessation in women who are pregnant or postpartum?

**Key Question 5**: What is the effect of patient characteristics on outcomes of smoking cessation interventions (successful/unsuccessful cessation, relapse) in women who are pregnant or postpartum?
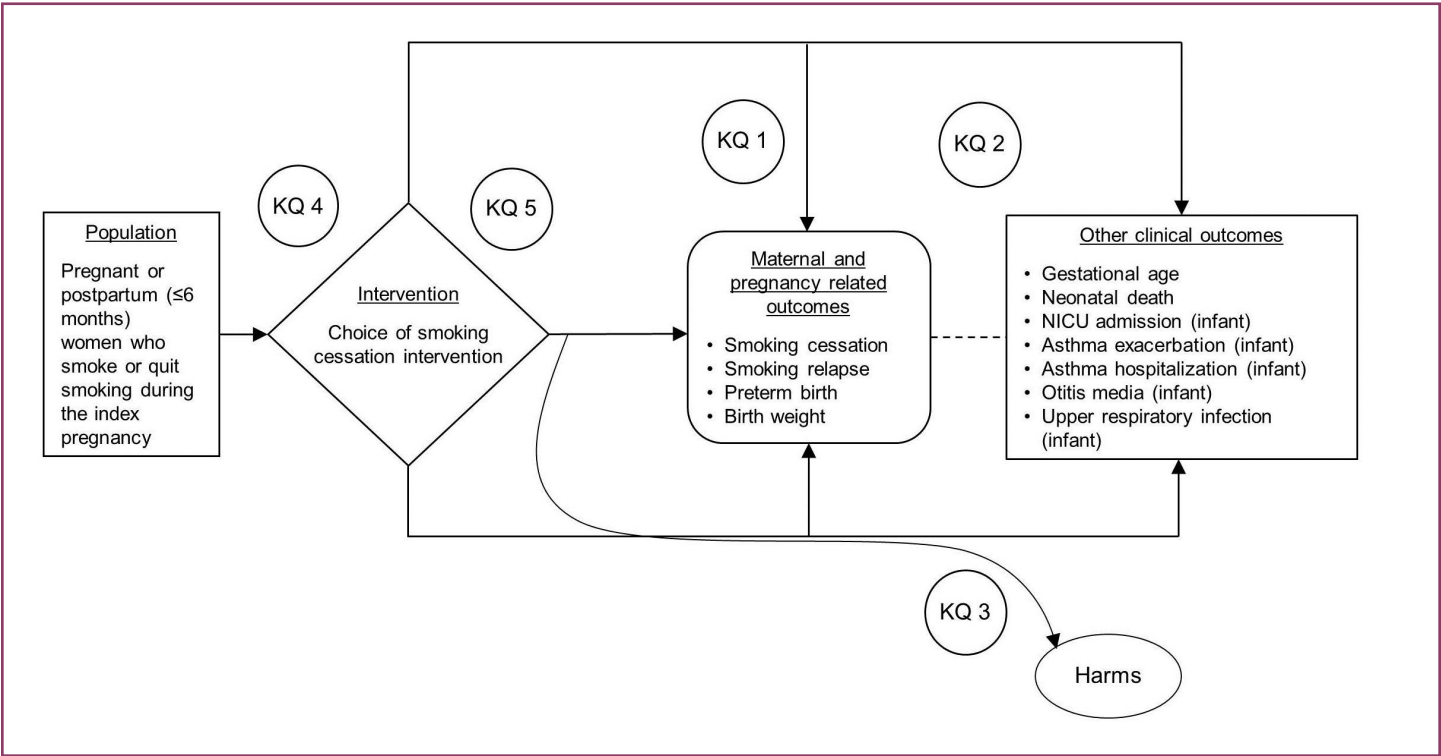
Because there is a high risk of relapse among individuals who attempt to quit smoking, we assessed relapse prevention outcomes in pregnancy and after parturition from studies of smoking cessation interventions for women defined as recent quitters. The review also reports infant and/or child outcomes (Key Question 2) from studies evaluating smoking cessation interventions, but does not include analysis of information about the effects of maternal smoking on child health. Data on harms or adverse effects of included interventions are captured in Key Question 3. The aim of Key Question 4 is to obtain information on components of the interventions that may have an impact on patient outcomes, while Key Question 5 is included to capture characteristics that potentially modify outcomes from eligible studies. We explicitly defined eligibility criteria using a PICOTS (population, intervention, comparator, outcome, timing, and setting) structure (Table A).

**Table A. PICOTS**

| PICOTS | Criteria |
|---|---|
| Population | • Pregnant or postpartum (≤6 months post-birth) women who smoke or quit smoking in the index pregnancy<br>• Infants and children of pregnant or postpartum (≤ 6 months post-birth) women receiving smoking cessation interventions<br>• Subgroups of pregnant and/or postpartum women by level of nicotine dependence, prior quit attempts, concomitant substance or alcohol abuse, partner smoking status, and/or employment |
| Intervention | Any smoking cessation intervention, including pharmacologic and nonpharmacologic interventions |
| Comparator | • Different intervention<br>• Usual care<br>• Placebo |
| Outcomes | **KQ1**<br>• Smoking cessation (biochemically validated)<br>• Continuous abstinence (biochemically validated)<br>• Relapse<br>**KQ2**<br>• Preterm birth<br>• Gestational age<br>• Birth weight<br>• Neonatal death<br>• NICU admission<br>• Asthma exacerbation<br>• Asthma hospitalization<br>• Otitis media<br>• Upper respiratory infection<br>**KQ3**<br>Harms (e.g., weight gain, emotional stress, adverse events associated with medication to the mother or fetus)<br>**KQs 4 and 5**<br>• Smoking cessation (biochemically validated)<br>• Continuous abstinence (biochemically validated)<br>• Relapse |
| Timing | Any length of followup |
| Setting | Clinician-initiated intervention or an intervention that intersects clinical care |

Abbreviations: KQ = Key Question; NICU = neonatal intensive care unit; PICOTS = population, intervention, comparator, outcome, timing, setting.

**Figure A. Analytic framework**



Abbreviations: KQ = Key Question; NICU = neonatal intensive care unit.

## Analytic Framework

We developed the analytic framework (Figure A) illustrating the population, interventions, and outcomes that guided the literature search, study eligibility, screening, and synthesis.

## Methods

### Literature Search Strategy

We searched MEDLINE®, CINAHL®, and PsycINFO®. Search results were limited to papers published in English. Search strategies used a combination of subject headings (i.e., controlled vocabulary) and keywords (Appendix A of full report). Searches were executed between October 2012 and January 2013. We also searched the reference lists of included publications and recent systematic reviews related to smoking cessation interventions for pregnant women.

### Inclusion and Exclusion Criteria

The inclusion and exclusion criteria for the review (Table B) were derived from our understanding of the literature and refinement of the review topic with the Task Order Officer and the topic nominators. We included studies of pregnant or postpartum (within 6 months of birth) women who currently smoked or who had quit during the index pregnancy.

We did not limit the search to studies conducted during any specific time period. We included studies published in English only. Two team members independently reviewed the titles and abstracts of the non–English-language literature published since 1990 located via the MEDLINE search (Appendix A of the full report) and determined that few studies would meet the inclusion criteria. Most non–English-language studies were cross-sectional or were not original research.

Studies were required to include a minimum of 20 participants with data in each study arm. The team established this minimum sample size to balance the need for smaller studies of specialized populations (e.g., studies in specific ethnic groups) with the need to preserve methodologic rigor.

**Table B. Inclusion and exclusion criteria**

| Category | Criteria |
|---|---|
| Study population | Pregnant or postpartum (up to 6 months post-birth at initiation of the intervention) women who smoke or quit smoking during the index pregnancy |
| Time period | Database inception to present |
| Publication languages | English only |
| Admissible evidence (study design and other criteria) | <u>Admissible designs</u><br>• KQs 1–5: RCT<br>• KQs 3–5: Prospective cohort stud<br><u>Other criteria</u><br>• Original research studies that provide sufficient detail regarding methods and results to enable use and adjustment of the data and results<br>• Studies targeting women who smoke and meet the population criteria described above<br>• Studies that address one or both of the following:<br>  ◆ Treatment modality aimed at smoking cessation in a relevant population<br>  ◆ Outcomes related to interventions; primary outcomes of interest include smoking cessation, continuous abstinence, smoking relapse, harms of intervention to the mother or fetus, gestational age, NICU admission, birth weight, and preterm birth<br>• Studies that include extractable data presented in text or tables (as opposed to solely in figures) on relevant outcomes |

Abbreviations: KQ = Key Question; NICU = neonatal intensive care unit; RCT = randomized controlled trial.

## Study Selection

We developed screening forms to assess eligibility for inclusion in the review (Appendix B of the full report). We revised the forms following testing by the team. We conducted screening in two phases: abstract and full-text screening. Publications were promoted to full-text review when one reviewer indicated that the publication met all inclusion criteria or when the title and abstract did not provide adequate information to make a determination. Two reviewers independently reviewed each publication at the full-text screening phase. Discordant classifications were resolved in team meetings including senior investigators.

## Data Extraction

Two reviewers independently extracted relevant data from all included publications using a predefined evidence table shell. A senior investigator reviewed the evidence tables for accuracy and completeness. The final evidence tables are provided in Appendix H of the full report.

## Risk-of-Bias Assessment

We assessed quality of randomized controlled trials (RCTs) using the Cochrane Collaboration Risk of Bias Tool,[30] which evaluates domains, including sequence generation,

allocation concealment, blinding, outcome data reporting, and reporting bias. Two reviewers independently assessed risk of bias as low, high, or unclear for each domain. Differences were resolved though discussion, review of the publications, and consensus with the team. We rated studies as good, fair, or poor quality and retained poor studies as part of the evidence base but did not include them in our assessment of strength of evidence.

## Data Synthesis

To synthesize the data, we first divided the studies into broad categories and described the studies qualitatively within this organization (Key Question 1). These categories were established a priori as accepted approaches to intervening during pregnancy to encourage women to stop smoking. The categories reflect broad approaches to cessation intervention, and the studies within a category are often very heterogeneous.

While studies may purport to examine effects of an individual intervention component, interventions are almost always multicomponent in practice. In addition, even usual care often includes an intervention, such as some level of counseling. Thus, we also conducted a meta-analysis, using a Bayesian approach to a logistic mixed-effects

model to quantify the relative influence of each component within the interventions across the body of literature. This served in part to answer Key Question 4. It also provided a quantitative basis for assessing strength of evidence (see below), in addition to providing a basis for users of the report to make intervention decisions.

Data for Key Questions 2, 3, and 5 were described qualitatively. Key Question 2 was organized by the infant outcomes being assessed, Key Question 3 was organized by the categories of interventions used in Key Question 1, and Key Question 5 was organized by factors that modify success of the intervention and factors related to probability of cessation.

## Strength of the Body of Evidence

Two senior investigators graded the body of evidence based on the "Methods Guide for Effectiveness and Comparative Effectiveness Reviews,"[31,32] and the final assignment was reviewed with the project team.

We assessed the strength of evidence for effectiveness, infant outcomes, and harms of interventions. Because of the heterogeneity of interventions within categories of approaches, we focused our strength-of-evidence assessment on the components that could be meta-analyzed and thus contributed quantitative data to our understanding of smoking cessation in pregnancy. We used the standard Evidence-based Practice Center approach to strength of evidence with this exception: if the posterior probabilities based on the Bayesian credible intervals (BCIs) suggested greater than 80-percent likelihood that the true effect was greater than the null, we considered the estimate of the effect to be positive and therefore assessed the strength of the evidence that there was benefit from the intervention.

Only studies of good quality were considered to be low risk of bias. For consistency, we required that the BCI of the estimate not cross the null. All outcomes were direct because they were biochemically validated. For precision, we considered a difference of less than 3 between the lower and upper BCI of the estimate to be precise. For effectiveness, we assessed strength of evidence based on the good and fair included RCTs because there were enough of these studies to form a "best evidence" set that would not be obscured by biased and poorly conducted studies.

To support this decision, we also assessed the likelihood that the poor studies would change our determination of strength of evidence. For infant outcomes and harms of interventions, we included poor-quality studies in the

strength-of-evidence assessment. These Key Questions warrant a more expansive assessment of the literature because they focus on outcomes that are rarely reported.

## Applicability

Assessments of applicability describe elements of the literature that would affect end-users' ability to apply our findings in a real-world setting. We assessed applicability by identifying potential factors from the PICOTS framework likely to affect the generalizability of the synthesized results. For this particular review, the most likely factors that could affect applicability are the patient population (e.g. whether or not results are available to assess the utility of given interventions in target populations) and the intervention (e.g., the difficulty of applying the intervention in a nonresearch setting given available resources). We noted where data were available for specific populations and made relative assessments of applicability for intervention components in the context of resource considerations.

# Results

We identified 2,454 titles and abstracts for screening; 417 publications were identified as potentially eligible for inclusion and were promoted for full-text review. We identified 72 publications from 59 unique studies that met criteria for inclusion. Of these, 56 were RCTs and 3 were prospective cohort studies. The complete list of excluded papers and exclusion reasons is provided in Appendix G of the full report. A summary of all component items and overall risk of bias/quality score for each included study is provided in Appendix I of the full report.

## Key Question 1. Intervention Outcomes for Pregnant and Postpartum Women

Fifty-six RCTs evaluated one or more interventions designed to reduce smoking or prevent relapse in pregnant or postpartum women. These RCTs had as their primary focus counseling (14 studies), educational materials (10 studies), multicomponent interventions (14 studies), NRT (5 studies), peer support (4 studies), and other interventions (9 studies). We assessed individual study quality as good for 13 studies, fair for 15 studies, and poor for 28 studies. Fifty-two studies enrolled women who were pregnant, and four RCTs enrolled women in the postpartum period (within 6 months of giving birth). Eight studies restricted enrollment to women who had recently quit smoking. Forty studies included current smokers only, and seven studies included both current smokers and women who had quit smoking immediately prior to or during pregnancy.

The duration of followup was generally short and usually limited to the prenatal period. Only 15 studies reported biochemically validated cessation after birth. Among studies evaluating an intervention delivered in the postpartum period, the longest period of followup was 6 months postpartum.

Eight of 24 studies of good or fair quality demonstrated effectiveness for cessation, with a difference in cessation between intervention and control groups ranging from 5.8 percent to 31.0 percent (Table C). Four of these studies used multicomponent interventions. Counseling,

educational materials, peer support, and voucher incentives were each the primary intervention in one study showing positive effects. This qualitative synthesis suggests that, generally speaking, multicomponent approaches were most effective, but does not provide evidence to drive selection of specific components to form those interventions. The most common interventions in successful multicomponent studies were also common in studies that failed to demonstrate effectiveness. For each study with a primary intervention that demonstrated effectiveness, there were other studies of this intervention that did not demonstrate effectiveness.

**Table C. Evidence map: smoking cessation**

| Intervention | Good Quality: Total Number of Studies (Number of Studies Showing Effectiveness) | Fair Quality: Total Number of Studies (Number of Studies Showing Effectiveness) | Poor Quality: Total Number of Studies (Number of Studies Showing Effectiveness) |
|---|---|---|---|
| Counseling | 1 (0) | 3 (1)[a] | 6 (0) |
| Education | 3 (1) | 2 (0) | 4 (2)[b] |
| NRT | 1 (0) | 1 (0) | 3 (2) |
| Peer Support | 2 (1) | 1 (0) | 1 (0) |
| Other | 1 (0) | 2 (1) | 5 (2) |
| Multicomponent | 3 (1) | 4 (3) | 5 (1) |

Abbreviations: NRT = nicotine replacement therapy.
[a]Demonstrated effectiveness at end of pregnancy but was no longer significant at 6 months postpartum.
[b]No demonstrated effectiveness at end of pregnancy. Smoking cessation was higher at 8 weeks postpartum for group who received quit guides.

One of five studies of good or fair quality demonstrated effectiveness for relapse prevention with a 35-percent higher cessation in the intervention group than in the control group (Table D). This study evaluated a unique intervention to promote mother-infant bonding. Additional studies are needed to confirm the effectiveness of this intervention, as the study included only 54 participants and cessation outcomes were not reported beyond 8 weeks postpartum.

**Table D. Evidence map: relapse prevention**

| Intervention | Good Quality: Total Number of Studies (Number of Studies Showing Effectiveness) | Fair Quality: Total Number of Studies (Number of Studies Showing Effectiveness) | Poor Quality: Total Number of Studies (Number of Studies Showing Effectiveness) |
|---|---|---|---|
| Counseling | 1 (0) | 0 (NA) | 5 (0) |
| Education | 0 (NA) | 1 (0) | 0 (NA) |
| NRT | 0 (NA) | 0 (NA) | 0 (NA) |
| Peer Support | 0 (NA) | 0 (NA) | 0 (NA) |
| Other | 1 (1) | 0 (NA) | 1 (0) |
| Multicomponent | 1 (0) | 1 (0) | 3 (0) |

Abbreviations: NA = not applicable; NRT = nicotine replacement therapy.

## Key Question 2. Intervention Effects on Infant Outcomes

We identified 13 studies that reported infant outcomes associated with smoking cessation and/or relapse prevention interventions among pregnant women. The interventions represented include counseling (3 studies), educational materials (2 studies), NRT (4 studies), incentives (3 studies), and one study each of a multicomponent intervention and point-of-care nicotine testing. One study is of good quality, three of fair quality, and nine of poor quality. All studies focused on infant outcomes during the immediate postpartum period; none of the studies included infant outcomes after hospital discharge or further followup of any child-related outcomes.

Findings regarding mean birth weight were inconsistent, and no clinically meaningful differences were identified. Only one of the seven studies that reported gestational age had statistically significant results, with women who received NRT in addition to cognitive behavioral therapy giving birth an average of 1 week later than women who received cognitive behavioral therapy only. No studies found statistically significant differences in the incidence of preterm birth, neonatal deaths, or neonatal intensive care unit (NICU) admissions between the intervention and control groups.

## Key Question 3. Intervention Harms for Pregnant and Postpartum Women

We identified four studies that reported harms or adverse events associated with smoking cessation interventions. The interventions included NRT (3 studies) and educational materials (1 study). None of the studies reported a higher incidence of adverse events in women receiving interventions than in the control groups; however, there were low numbers of participants and low adherence rates in NRT trials that assessed harms. None of the studies that evaluated relapse prevention interventions reported harms data.

## Key Question 4. Effectiveness of Intervention Components

Twenty-eight good- and fair-quality RCTs were available for this Key Question. Three studies targeted postpartum women, and the rest enrolled pregnant women. Twenty-two focused on current smokers, four focused on recent quitters, and two included both smokers and quitters. We did not find any cohort studies that had appropriate information for inclusion in the meta-analysis, which is the basis for this Key Question. We determined that inclusion of poor-quality studies in the analysis would not have modified our assessment.

We were able to combine 23 of these studies into a robust random-effects meta-analysis to quantify the relative impact of components of the interventions on smoking

cessation. One study was excluded because outcomes for smoking cessation and relapse prevention were reported together and could not be calculated separately. Nine components were evaluated individually: clinic reinforcement, feedback, incentives, information, NRT, peer support, personal followup, prescription to quit, and quit guides and "other." "Other" combined relatively rarer components, such as groups and quit contracts. Counseling was ubiquitous in both intervention and control arms of the studies; thus it could not be assessed as a driver of effect.

The use of incentives was most clearly associated with substantially increased smoking cessation. The odds of quitting with the use of incentives were three times the odds of quitting in the absence of incentives, holding all other interventions constant (odds ratio = 3.23; 95% BCI, 1.98 to 4.59). Additional intervention components that may have some positive effect, as demonstrated by 80-percent or greater probability that the odds are higher than the null for the intervention increasing smoking cessation, include feedback about biologic measures, information, personal followup, NRT, and quit guides. Data were not available to specifically address the impact of who delivered the intervention or where the intervention was delivered.

### Key Question 5. Effect of Patient Characteristics on Effectiveness

In total, studies from 18 populations provide information about how participant characteristics related to success in quitting smoking. This includes 14 randomized trials of which 4 are from studies with interventions proven effective, and 3 cohort studies. Across intervention types there were commonalities.

Predictors of achieving and maintaining cessation included lower levels of tobacco dependence at baseline, as measured by biomarkers and questions gauging dependence and cigarettes per day. Data were sparse to document the influence of maternal age, parity, other smokers in the home, a nonsmoking partner, and smoke-free policies in the home. Data were less consistent for the effects of education, prior experience with cessation, readiness to change, and self-reported motivation to quit.

Younger maternal age, which is correlated with fewer years of smoking, was reported to be associated with improved chance of cessation. No studies of interventions found to be effective addressed the influence of maternal education or of parity. Partner smoking status and household exposure to tobacco smoke are characteristics that are often considered predictors in the health behavior literature and in cohort analyses. We found three trials that commented on the influence of partner or household smoking status, and of these, only two addressed cessation during pregnancy.

Neither study showed that the intervention in the trial was effective.

Biomarkers and quantity of smoking were found to play a role in predicting cessation in a successful trial of a multicomponent intervention that centered on a pregnancy-specific quit guide. Five other trials, for which the intervention was not demonstrated to be more effective than the comparison group, reported similar findings: lower cigarette use at baseline improved chances of cessation. Self-reported readiness or motivation to quit, as well as confidence in one's own ability to do so, were evaluated in multiple studies as markers of being able to successfully quit. The only trial with an effective intervention reported that baseline self-efficacy did not predict who would be able to quit.

## Discussion

As clinicians and policymakers consider implementing smoking cessation interventions, their primary consideration is choosing those approaches that are most likely to be effective and feasible. Qualitatively, this review suggests that approaches that combine multiple components will have the best likelihood of success. Selecting which components to include is more complex and should be based on the particular considerations of the interventions and clinical setting. Efficacy is foremost in choosing the combination of interventions in a multicomponent strategy. The meta-analysis presented in this review allowed us to calculate the posterior probability that specific intervention components contributed to success in smoking cessation. Multiple components had a greater than 80-percent probability of having a positive effect, with incentives demonstrating the strongest effect. While incentives require a financial investment, they are not time intensive. In addition, prior research in other fields, such as weight loss, suggests that modest incentives can be adequate to change behavior.[33] The other components with high probability of success were feedback about biologic measures, information, personal followup, NRT, and quit guides. Our meta-analysis results suggested that clinic reinforcement, peer support, and prescriptions to quit contributed little in multicomponent interventions. With the exception of medications, for which limited data are available, the safety of smoking cessation interventions makes it reasonable to include a number of interventions in a multicomponent approach. Other important considerations in selecting which smoking cessation interventions to implement include the availability of financial and human resources. It may also be helpful to end-users to understand whether specific populations of patients are more amenable to behavior change. Although

few data are available to guide targeting of services, the research reviewed in this report suggests that women who are less tobacco dependent and younger may have a greater chance of successfully quitting. More intensive interventions are worth considering for women who are less likely to successfully quit smoking.

## Key Findings and Strength of Evidence

Overall the evidence to answer Key Questions about smoking cessation and relapse prevention interventions for pregnant and postpartum women did not reach standards for high strength of evidence. The strength-of-evidence tables (Table E and Tables 28–30 in the full report) summarize the total number of studies and, within those studies, the number of participants randomized. The tables also provide the assessment of the risk of bias, consistency of findings across trials, directness of the evidence, and precision of the estimate provided by the literature.

We assessed the strength of evidence for the effectiveness of intervention components using the meta-analysis (Table E) and using the approach described in our Methods section. Strength of evidence was moderate for the effectiveness of incentives and low for all other intervention components.

**Table E. Strength of evidence for effectiveness of intervention components for smoking cessation among current smokers in pregnancy**

| Intervention Component | Risk of Bias | Consistency | Directness | Precision | OR (BCI) Posterior Probability[a] Strength of Evidence[b] |
|---|---|---|---|---|---|
| Incentives | Medium | Consistent | Direct | Precise | 3.23 (1.98 to 4.59) 100% Moderate for effect |
| Feedback | Medium | Inconsistent | Direct | Precise | 1.43 (0.88 to 2.03) 95% Low for effect |
| Information | Medium | Inconsistent | Direct | Precise | 1.32 (0.88 to 1.79) 93% Low for effect |
| Personal followup | Medium | Inconsistent | Direct | Precise | 1.25 (0.94 to 1.57) 95% Low for effect |
| Nicotine replacement therapy | Medium | Inconsistent | Direct | Precise | 1.24 (0.84 to 1.68) 87% Low for effect |
| Quit guide | Medium | Inconsistent | Direct | Precise | 1.18 (0.82 to 1.56) 83% Low for effect |
| Prescription to quit | Medium | Inconsistent | Direct | Precise | 1.13 (0.46 to 1.95) 57% Low for no effect |
| Peer support | Medium | Inconsistent | Direct | Precise | 1.07 (0.70 to 1.46) 60% Low for no effect |
| Clinic reinforcement | Medium | Inconsistent | Direct | Precise | 1.05 (0.65 to 1.49) 55% Low for no effect |

Abbreviations: BCI = Bayesian credible interval; OR = odds ratio.

Note: Table shows data from 8, 086 participants randomized in 23 RCTs. BCI = Bayesian credible interval; OR = odds ratio.
[a]Probability that the OR is greater than the null.
[b]The effect is positive if the posterior probability is 80% or greater.

There is insufficient strength of evidence to determine the effect of smoking cessation interventions on birth weight, gestational age, and neonatal deaths. There is low strength of evidence for no significant effect on preterm birth and NICU admission. There is also insufficient strength of evidence to determine the harms of smoking cessation interventions.

## Applicability

Applicability for this literature is largely dependent on the target population and the feasibility of the interventions in the clinical setting. The target populations are defined by whether women were pregnant or postpartum, whether they were current smokers or recent quitters, and whether they were selected from at-risk populations. Interventions could be resource intensive across axes of time, money and personnel. Thus, to ascertain the applicability of any given intervention, potential end-users must consider whether research on the intervention has been conducted in their target population, and whether the intervention is appropriate and feasible in terms of resource allocation.

The majority of studies (55 studies) included in this review recruited pregnant women; 4 studies were conducted in the postpartum period. Most studies (42) were conducted in the United States and thus should be applicable to the U.S. health system. Studies enrolled women who were all current smokers (42 studies), all recent quitters (8 studies), or both types (9 studies). The duration of followup in the studies included in this review was generally short, and thus little is known about durability of effects.

It would be particularly helpful to end-users to know whether certain interventions were effective in high-risk populations. However, studies targeting high-risk populations were limited. One study enrolled adolescents only, six studies targeted income-specific groups, and one study specifically selected participants from the Medicaid population. Interventions were generally more effective among participants with lower levels of tobacco dependence, so even the more effective approaches may be less applicable in populations with extremely high levels of nicotine dependence. Younger maternal age, which is correlated with fewer years of smoking, was reported to be associated with improved chance of cessation.

Smoking cessation and relapse prevention interventions, both prenatal and postpartum, were overwhelmingly multifaceted. Studies deployed multiple components in the intervention being compared with usual care or an alternative level of standard cessation services. As described earlier, incentives had the highest independent effect, but given that the statistical model underlying the meta-analysis was additive and that the likelihood of positive effects was high for a number of intervention components, it would be reasonable for providers to select the set of components that might have greatest applicability in their setting and develop those into a multicomponent intervention. To that end, we have made relative assessments in the full report of the resources and considerations that end-users might have around implementation of the components assessed in this report.

## Limitations of the Evidence

Nearly half of the studies (n=28) were of poor quality, and the most common reason for high risk of bias was incomplete outcome data. Losses to followup varied by intervention, but the reasons for this variation and its impact on the results are unclear. Studies were most commonly rated fair quality (n=15) due to unclear risk of bias associated with allocation concealment and random sequence generation.

## Research Gaps

Future research needs around smoking cessation in pregnancy are both substantive and methodologic. Several interventions warrant additional research and replication, including better assessments. Priorities for future research about interventions include—

- Conducting additional studies of incentives, including the amount needed and under what circumstances they are effective.

- Replicating the evaluation of the mother-infant bonding intervention that was found to be effective in the relapse prevention study.

- Developing much more rigorous studies that isolate counseling and its components. Counseling was ubiquitous, and studies were heterogeneous in their approach.

- Studying intervention components, either in isolation or in multicomponent studies with very high rigor, identified in the meta-analysis as having a high probability of being effective so that the effect of individual components, or specific combinations of components, can be measured.

Methodologic and study design considerations for future research include—

- Clear characterization of the components of both the intervention and comparator.

- A plan for assessment and reporting of fidelity of intervention implementation and the potential for crossover of the intervention into the comparator group.

- Use of biochemically validated outcomes. Self-report is known to underestimate smoking prevalence. A sustained measure of smoking abstinence, as opposed to a point prevalence measure, would be ideal.

- Assessment of the degree to which timing matters in successfully achieving cessation. Intervention timing varies substantially across studies, including early and late in pregnancy. Some studies suggest that interventions may have potential for getting women to stop earlier in pregnancy even when overall differences are not significant.

- Adequate sample sizes with long-term followup. Current studies are short term and have no ability to assess effectiveness over time, including long-term health implications. This is in part due to the need for large numbers at study inception in order to maintain adequate power over time. Larger sample sizes are needed to assess comprehensively infant and longer term child outcomes as well as events and harms.

- Identification of the underlying study purpose. There is a lack of clarity overall in this body of research about whether encouraging women to stop smoking in pregnancy is for the purpose of optimizing fetal growth or creating a smoke-free home by the end of pregnancy. While both goals are important, identifying the specific underlying rationale for a study can help in intervention development in a way that is targeted and potentially more effective.

## Conclusions

Across interventions, data are sparse to evaluate sustained cessation among pregnant and postpartum women. This review suggests that approaches that combine multiple components will have the best likelihood of success. Selecting which components to include is more complex and should be based on the particular considerations of the clinical setting, including patient characteristics and resource allocation, but incentives demonstrated the greatest effect among components studied. Infant outcomes are limited to data collected at time of birth; no studies assessed longer term or child outcomes. Harms data were rarely reported.

## References

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## Full Report

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