



TITLE: Smoking Cessation Interventions for Pregnant Women and Mothers of Infants: A Review of the Clinical Effectiveness, Safety, and Guidelines

DATE: 1 March 2012

CONTEXT AND POLICY ISSUES

Smoking during pregnancy, despite being preventable, is among the leading causes of adverse effects on maternal and fetal health, such as infertility, complications during pregnancy, stillbirth, newborn death, preterm birth, infant low birth weight, infant small for gestational age, sudden infant death syndrome, and other child behavioral and cognitive function impairments.¹ A Canadian survey in 2006 on over 76,000 Canadian women ≥ 15 years old found 22.0% of Canadian women smoked before pregnancy, 10.5% smoked during pregnancy and 16.5% smoked after pregnancy.² Efforts to reduce the prevalence of pregnant mothers who smoke include the 5 A's approach (ask, advise, assess, assist, arrange), self-help materials (such as booklets, videos, and recorded telephone messages), cognitive behavioral counseling, financial incentives, and pharmacological therapies such as nicotine replacement therapy (NRT) (nicotine patch, gum, lozenge, inhaler, nasal spray), bupropion and varenicline.³⁻⁵

The effectiveness of smoking cessation interventions for pregnant women are not clear, as well as there are concerns about potential harm that NRT may cause to the fetus.¹ A review of the evidence on the clinical benefits, safety and guidelines of smoking cessation interventions for pregnant women and mothers of infants will be conducted.

RESEARCH QUESTIONS

1. What is the clinical effectiveness of smoking cessation interventions for pregnant women or mothers of infants?
2. What is the clinical evidence regarding the safety or risk associated with smoking cessation interventions for pregnant women, mothers of infants, and their babies?
3. What are the evidence-based guidelines regarding smoking cessation for pregnant women or mothers of infants?

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KEY MESSAGE

Smoking cessation interventions increased the quit rates among pregnant women, and decreased neonatal adverse outcomes as compared to no interventions. Nicotine replacement therapy was as effective as the cognitive behavioral therapy and did not seem to increase perinatal adverse outcomes. The Canadian Smoking Cessation Guideline Group recommends smoking cessation interventions for all pregnant, breastfeeding and post-partum women, and suggests counseling as first line therapy, and the use of NRT when counseling fails.

METHODS

Literature search

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2012, Issue 1), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials (RCTs), non-randomized studies, and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2007 and January 31, 2012.

Article selection

One reviewer screened the titles and abstracts of the retrieved publications and examined the full-text publications for the final article selection. Selection criteria are outlined in Table 1.

Table 1: Selection Criteria	
Population	Women who smoke and who are -pregnant -new mothers/mothers of infants -breastfeeding
Intervention	Smoking cessation interventions -pharmacologic -non-pharmacologic (e.g. behavioral)
Comparator	Any comparator (another intervention, or without intervention)
Outcomes	Effectiveness/success Risks/complications/safety Which methods work the best Guidelines
Study design	Health technology assessments, systematic reviews, meta-analyses, RCTs, non-randomized studies and evidence-based guidelines

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria in Table 1, if they were published prior to January 2007, if they were duplicate publications of the same study, or if they were referenced in at least one of the selected systematic reviews.

Critical Appraisal of Individual Studies

The quality of the included systematic reviews, randomized controlled trials and non-randomized studies, and guidelines was assessed using AMSTAR,⁶ Downs and Black,⁷ and AGREE⁸ checklists, respectively.

SUMMARY OF EVIDENCE

Quantity of Research Available

The literature search yielded 590 citations. Eight additional studies were identified by searching the grey literature. After screening of abstracts, 32 potentially relevant studies were selected for full-text review.

Two systematic reviews,^{9,10} nine studies, comprising of four RCTs,¹¹⁻¹⁴ and five non-randomized controlled studies¹⁵⁻¹⁹ and three guidelines²⁰⁻²² were included in the review. The PRISMA flowchart in Appendix 1 details the process of the study selection.

Summary of Study Characteristics

Study design

Included in the review are 14 studies, comprising of two systematic reviews,^{9,10} four RCTs,¹¹⁻¹⁴ three prospective cohort studies,¹⁵⁻¹⁷ two retrospective studies,^{18,19} and three guidelines.²⁰⁻²² Detailed characteristics of the included studies are summarized in Appendix 2.

Populations

Population was pregnant women who smoked on a regular basis

Interventions and comparators

Cognitive behavioral therapy, interventions based on stage of changes, feedback of fetal health status or measurements of byproducts of tobacco smoking to the mother, provision of rewards and incentives for smoking cessation, pharmacotherapies or other strategies, including hypnosis were the interventions in the trials included in the two systematic reviews.^{9,10} Nicotine replacement therapy was the intervention in three studies.^{12,17,19} Behavioral therapy was the intervention in four studies.¹³⁻¹⁶ Financial incentive was the intervention in two studies.^{11,18} Comparators were placebo gum¹², counseling only as opposed to counseling plus self-help material,¹⁵ or usual care.^{11,13,14,16-19}

Outcomes

Main study outcomes in the systematic reviews^{9,10} were smoking cessation rates (quit rates), rates of still birth, neonatal death, preterm birth, low birth weight, and neonatal intensive care unit admission. Main study outcomes in the trials included smoking cessation rates,¹¹⁻¹⁶ relapse rate,¹⁴ risk of still birth,¹⁷ duration of breastfeeding,¹⁸ adverse event rates.¹⁹

Summary of Critical Appraisal

The systematic reviews/meta-analyses^{9,10} were well conducted. A comprehensive literature search was performed following the establishment of a research question and inclusion criteria. The characteristics of included and excluded studies were provided in detail and the scientific

quality of included studies was assessed. It was unclear whether there was duplicate study selection and data extraction. There was no publication bias assessment in one review.⁹

The RCTs¹¹⁻¹⁴ were not always well conducted despite the objective, main outcomes and main findings were explicitly described. Methods of randomization were not adequately described. It was unclear whether baseline characteristics of patients were equally distributed between groups, and whether there was adequate adjustment for confounding in the analyses. The non-randomized studies¹⁵⁻¹⁹ were generally limited in strengths. Lack of randomization may have compromised the internal validity of the studies. The population may not represent the entire population of interest. It was unclear whether power calculation was performed to determine adequate sample size.

The guidelines' scope, purpose, and recommendations were clear.²⁰⁻²² Individuals from relevant professional groups were involved in developing two guidelines.^{21,22} It was unclear in the guidelines whether patients' views and preferences were sought and potential implications of applying the guidelines were not included. A detailed summary of the critical appraisal of the included studies and guidelines can be found in Appendix 3.

Summary of Findings

Main study findings and authors' conclusions can be found in Appendix 4.

What is the clinical effectiveness of smoking cessation interventions for pregnant women or mothers of infants?

Success rate:

One systematic review/meta-analysis examined the effects of smoking cessation interventions on promoting smoking cessation during pregnancy as compared to no interventions.⁹ The review included 72 RCTs, quasi-randomized controlled and controlled trials with a total of 25,000 women. Data showed that interventions significantly reduced the smoking rates among pregnant women as compared to no intervention. There was no significant difference in success rate between "high intensity" interventions (provision of strategies and continued support to quit) and "low intensity" interventions (provision of written and/or verbal advice to quit). Subgroup analyses based on intervention strategies showed that only the strategy that included an incentive component showed a significantly larger effect compared to the rest of the strategies. NRT was as effective as the cognitive behavioral therapy. Feedback strategy (feedback of fetal health status or measurements of byproducts of tobacco smoking to the mother) was not significantly effective as compared to no interventions. The interventions did not make a statistically significant difference in the prevention of smoking relapse among women who had stopped smoking. One systematic review/meta-analysis examined the effects of smoking cessation interventions on parental smoking cessation and its benefits to children as compared to no interventions.¹⁰ The review included 18 RCTs, quasi-randomized controlled trials and controlled trials with a total of 7053 participants. Data showed that intervention significantly increased the quit rate compared to no intervention. As compared to no interventions, the interventions were most beneficial in parents whose children were ≥ 4 years old, when interventions included use of medication, when the primary purpose of interventions were smoking cessation, or when the rate of participants follow up was high.

The effectiveness of smoking intervention programs in pregnant women was also examined in four RCTs.¹¹⁻¹⁴ Provision of financial incentives in addition to information was found to be more successful in terms of quit rate than provision of information alone. Participants in incentive-group had higher enrollment rates in a smoking-cessation program, and higher rates of completion of the program.¹¹ Nicotine gum did not give significantly higher quit rate than placebo.¹² Increased frequency and quality of support by a woman in the smoker's social network helped to increase the quit rate.¹³ Face-to-face counseling plus telephone counseling calls to post-partum women did not give any statistically significant differences in abstinence rates or relapse prevention rates up to 24 months follow up, as compared to the control group who received usual care plus self-help material.¹⁴

Three non-randomized studies evaluated the effectiveness of smoking cessation interventions in pregnant women.^{15,16,18} Smoking abstinence-contingent incentive vouchers were found to significantly increase the duration of breastfeeding as compared to vouchers which were delivered independent of smoking status.¹⁸ Pregnant women who received counseling and agreed to use self-help guide had statistically significant higher quit rate than those who received counseling alone.¹⁵ Counseling plus self-help material gave a significantly higher rate of smoking cessation as compared to intervention that comprised only of limited education about risk of smoking.¹⁶

Effect on perinatal outcomes:

One systematic review/meta-analysis⁹ showed a significant reduction in the rate of preterm birth, low birth weight, and a significant increase in mean birth weight in the intervention group. There were no significant differences in the rate of still birth, neonatal deaths and intensive care unit admission between the two groups. Nicotine gum significantly increased birth weight and gestational age as compared to placebo.¹²

What is the clinical evidence regarding the safety or risk associated with smoking cessation interventions for pregnant women, mothers of infants, and their babies?

Two non-randomized studies looked at the role of NRT with respect to perinatal adverse outcomes among pregnant mothers.^{17,19} There was no statistically significant difference in incidence of serious adverse events in pregnant women with NRT plus behavioral therapy group than in those with behavioral therapy only. The most common adverse events were preterm birth, followed by preeclampsia, low birth weight and placental abnormalities. Logistic regression modeling of serious adverse events, adjusting for covariates, found that the increased incidence was due to differences in predisposing baseline factors. History of adverse pregnancy, race, and use of analgesic medications during pregnancy were statistically significantly associated with perinatal adverse events. After adjusting for these covariates, it was found that NRT was not significantly associated with adverse outcomes.¹⁹ The risk of still birth does not seem to be affected by NRT.¹⁷

What are the evidence-based guidelines regarding smoking cessation for pregnant women or mothers of infants?

Three smoking cessation guidelines specifically on pregnant and breastfeeding women were found.²⁰⁻²²

The Canadian practice-informed and evidence-based smoking cessation guideline (2011)²⁰ stated (p.4):

“Smoking cessation should be encouraged for all pregnant, breastfeeding and postpartum women”

“During pregnancy and breastfeeding, counseling is recommended as first line treatment for smoking cessation”

“If counseling is found ineffective, intermittent dosing nicotine replacement therapies (such as lozenges, gum) are preferred over continuous dosing of the patch after a risk-benefit analysis”

“Partners, friends and family members should also be offered smoking cessation interventions”

“A smoke-free home environment should be encouraged for pregnant and breastfeeding women to avoid exposure to second-hand smoke”

The Royal Australian College of General Practitioners guideline (2011)²¹ stated: (p.47):

“Pregnant women should be encouraged to stop smoking completely”

“They should be offered intense support and proactive telephone counseling”

“Self-help material can supplement advice and support”

“If these interventions are not successful, health professionals should consider NRT, after clear explanation of the risks involved”

“Because of the uncertainty of the safety of NRT used during pregnancy, pregnant women wishing to quit using NRT should be monitored by a suitably qualified health professional”

“Those who do quit should be supported to stay non-smokers long term”

The National Institute for Health and Clinical Excellence (NICE) smoking cessation guideline for pregnant women (2010)²² recommended:

1. Identify pregnant women who smoke and refer them to National Health Services (NHS) Stop Smoking Services by health professionals and community organizations.
2. Contact pregnant women who have been referred for help by NHS Stop Smoking Services specialist advisers
3. Provide cognitive behavioral therapy, motivational interviewing and structured self-help and support
4. Use NRT and other pharmacological support if other interventions fail
5. Meet the needs of disadvantaged pregnant women who smoke
6. Recommend nonsmoking household

Limitations

It was not always feasible to blind the trials participants because of the nature of the interventions. In some cases, the population under study did not totally represent the whole population of interest. The self-reported system also may have affected the precision of the smoking interventions success rates.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

Smoking cessation interventions increased the quit rates among pregnant women, and decreased neonatal adverse outcomes. NRT was not more effective than the cognitive behavioral therapy and did not seem to increase perinatal adverse outcomes such as still birth or serious perinatal adverse events. Financial incentive-based treatments were associated with

the largest effect on smoking cessation. Guidelines recommended smoking cessation interventions to all pregnant women who smoke, and recommended the use of NRT only if behavioral therapy failed. There is need to maximize the efficacy of these tools, since over 67% of women who were smoking at the beginning of their pregnancy still continue to smoke through their pregnancy.²³

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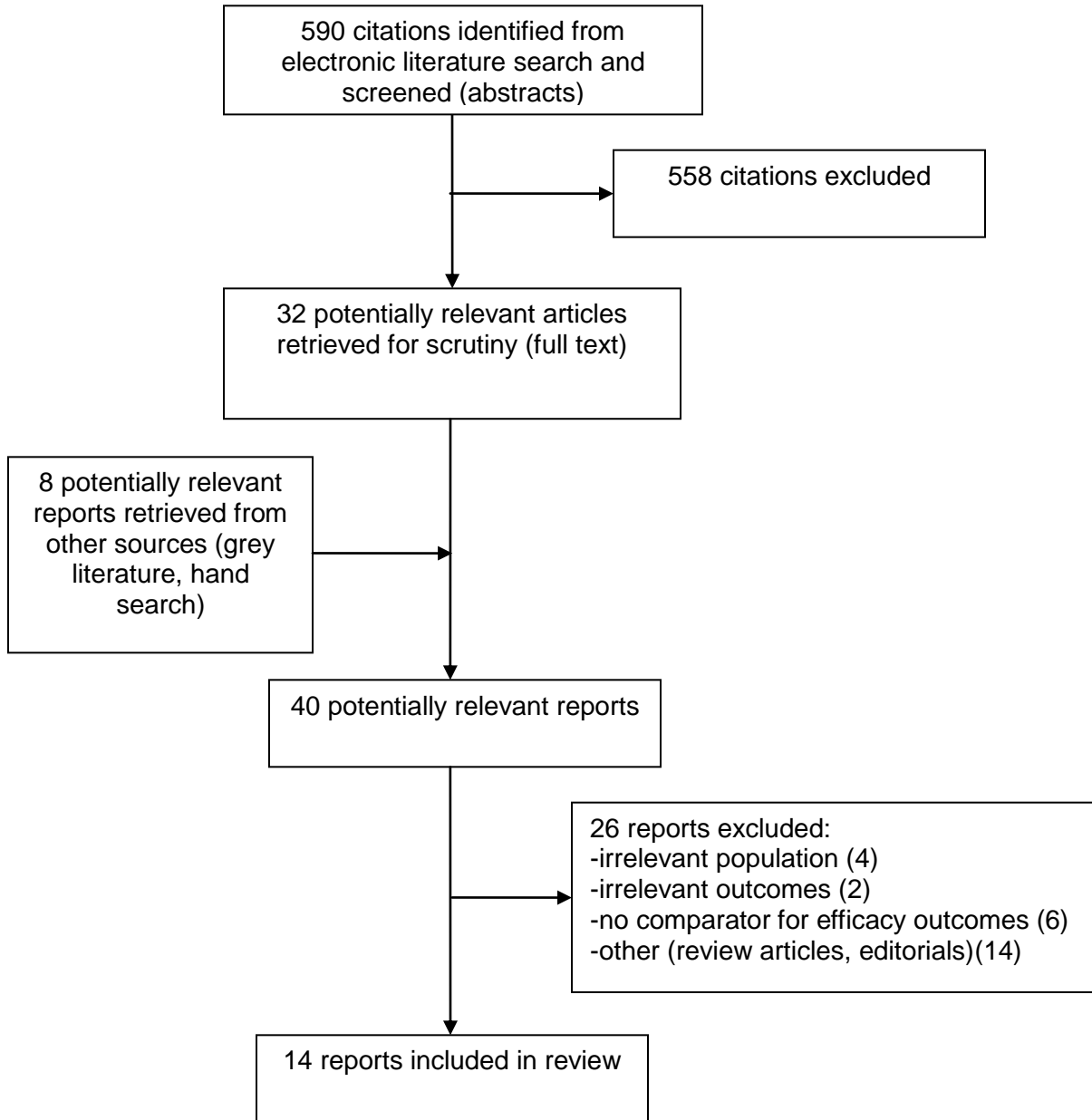
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Appendix 1: Selection of Publications



Appendix 2: Characteristics of Included Studies

Table A1: Characteristics of Included Systematic Reviews				
First Author, Publication Year, Country	Literature Search Strategy	Inclusion Criteria	Exclusion Criteria	Main outcomes
Rosen ¹⁰ 2012, US	"Medline, PsycINFO, Web of Science, and the Cochrane Library for articles published in English from any date through the end of March 2011" (p. 142)	"RCT using a cluster or individual-level randomization scheme, quasi-randomized RCT, CT" (p. 143)	Studies that did not meet the inclusion criteria	Smoking cessation rate
Lumley ⁹ 2009, Australia	"the Cochrane Pregnancy and Childbirth Group's Trials Register (June 2008), the Cochrane Tobacco Addiction Group's Trials Register (June 2008), EMBASE, PsycLIT, and CINAHL (from January 2003 to June 2008)" (p. 5)	"All randomized and quasi-randomized controlled trials where the primary aim of the study was smoking cessation in pregnancy were considered" (p. 4)	When: - outcome data were not reported in format or detail to enable inclusion in analysis; - design not adequately randomized - primary population was not pregnant women..." (p. 10)	Smoking cessation rate. Subgroup analyses such as rates of still birth, neonatal death, preterm birth, low birth weight and neonatal intensive care unit admission.

RCT: randomized controlled trial; CT: controlled trial

Table A2: Characteristics of Included Randomized and Non-randomized Studies					
First Author, Publication Year, Country	Study design; Length of follow-up	Patient Characteristics, Sample Size (n)	Intervention	Comparator(s)	Main study outcomes
Randomized Controlled Trials					
Henrikus ¹³ 2010, US	RCT, 3 months	82 pregnant women. Median number of cigarettes smoked /day: 5	One in-person visit and monthly telephone counseling sessions by a woman in the social network	No contact	Smoking cessation rate
Hannover ¹⁴ 2009, Germany	RCT, 18 months	871 pregnant women who smoked on a regular basis.	In-person and telephone counseling calls	Usual care* plus self-help material	Smoking cessation rate, relapse rate
Volpp ¹¹ 2009, US	RCT, 18 months	878 pregnant women (90% werewhite, 2/3 had income >500% of the poverty level) who smoked approximately one pack of cigarettes per day	Financial incentive (vouchers) plus information	Information only	Smoking cessation rate
Oncken ¹² 2008, US	RCT, 12 weeks	194 pregnant	Nicotine gum	Placebo gum	Smoking

Table A2: Characteristics of Included Randomized and Non-randomized Studies

First Author, Publication Year, Country	Study design; Length of follow-up	Patient Characteristics, Sample Size (n)	Intervention	Comparator(s)	Main study outcomes
		women. "Participants smoked an average of 18 cigarettes/day prior to pregnancy and approximately 10 cigarettes/day during the week prior to study enrollment" (p 5)	(nicotine 2mg). 6 weeks of treatment with the gum followed by a 6-week taper period.		cessation rate
Non-randomized Studies					
Higgins ¹⁸ 2010, US	Retrospective study, 24 weeks	158 pregnant women (over 90% were white, with the majority completing 12 or less years of education) who smoked approximately one pack of cigarettes per day	Abstinence-contingent financial incentive (vouchers)	Financial incentive independent of smoking status	Breastfeeding duration
Everett-Murphy ¹⁶ 2010, South Africa	Prospective study, 24 weeks	949 pregnant women of poor socio-economic status	Counseling plus self-help material	Usual care**	Smoking cessation rate
Edwards ¹⁵ 2009, US	Prospective study, 4 years	13,285 pregnant women	Counseling plus self-help material	Counseling only	Smoking cessation rate
Swamy ¹⁹ 2009, US	Retrospective, from 13-25 weeks gestation until birth	181 pregnant women	Nicotine replacement therapy plus cognitive behavioral therapy	Cognitive behavioral therapy only	Adverse event rate
Strandberg-Larsen ¹⁷ 2008, Denmark	Prospective, until birth	87,032 pregnant women	Nicotine replacement therapy	No nicotine replacement therapy	Risk of still birth

RCT: randomized controlled trial

*Interventions towards smoking and relapse prevention as usual within the health care system;

** Smoking status at booking visit, limited education about risks, prescriptive advice to quit or reduce smoking

Appendix 3: Summary of Critical Appraisal of Included Studies

First Author, Publication Year	Strengths	Limitations
Systematic Reviews		
Rosen ¹⁰ 2012	<ul style="list-style-type: none"> Comprehensive literature search performed based on pre-defined criteria Characteristics of included and excluded studies provided Meta-analyses were performed Scientific quality of the included studies was assessed and documented An assessment of publication bias was undertaken 	<ul style="list-style-type: none"> Conflict of interest was not stated
Lumley ⁹ 2009	<ul style="list-style-type: none"> Comprehensive literature search performed based on pre-defined criteria Characteristics of included and excluded studies provided Meta-analyses were performed Scientific quality of the included studies was assessed and documented Risk of bias of included studies were assessed and documented 	<ul style="list-style-type: none"> Unclear whether there was duplicate study selection and data extraction An assessment of publication bias was not undertaken
Randomized Controlled Trials		
Henrikus ¹³ 2010	<ul style="list-style-type: none"> Randomized controlled 	<ul style="list-style-type: none"> Method of randomization not adequately described Unclear whether baseline characteristics of patients were equally distributed between groups Unclear whether individuals measuring the outcomes were blinded Unclear whether there was adequate adjustment for confounding in the analysis Power calculation was not performed to determine adequate sample size Probability values were not provided
Hannover ¹⁴ 2009	<ul style="list-style-type: none"> Randomized controlled Power calculation performed to determine adequate sample size 	<ul style="list-style-type: none"> Method of randomization not adequately described Unclear whether baseline characteristics of patients were equally distributed between groups Unclear whether individuals measuring the outcomes were blinded Unclear whether there was adequate adjustment for confounding in the analysis Probability values were not provided
Volpp ¹¹ 2009	<ul style="list-style-type: none"> Randomized controlled Method of randomization adequately described Baseline characteristics of patients equally distributed between groups Power calculation performed to 	<ul style="list-style-type: none"> Unclear whether there was adequate adjustment for confounding in the analysis

First Author, Publication Year	Strengths	Limitations
	determine adequate sample size	
Oncken ¹² 2008,	<ul style="list-style-type: none"> • Randomized controlled • Baseline characteristics of patients equally distributed between groups • Adequate adjustment for confounding in the analysis • Power calculation performed to determine adequate sample size 	<ul style="list-style-type: none"> • Method of randomization not adequately described • Study subjects were not blinded to the intervention that they received • Unclear whether individuals measuring the outcomes were blinded • Unclear whether the randomized intervention assignment was concealed from both patients and health care staff
Non-randomized Studies		
Higgins ¹⁸ 2010	<ul style="list-style-type: none"> • Interventions of interest clearly described 	<ul style="list-style-type: none"> • Retrospective • The trial was not designed with a priori goal to measure the reported outcome • The population may not represent the entire population of interest • Baseline characteristics of patients were not equally distributed between groups • Unclear whether power calculation was performed to determine adequate sample size
Everett-Murphy ¹⁶ 2010	<ul style="list-style-type: none"> • Prospective • Baseline characteristics of patients equally distributed between groups • Interventions of interest clearly described • Power calculation performed to determine adequate sample size 	<ul style="list-style-type: none"> • The population may not represent the entire population of interest
Edwards ¹⁵ 2009,	<ul style="list-style-type: none"> • Prospective • Large population • Interventions of interest clearly described 	<ul style="list-style-type: none"> • Unclear whether baseline characteristics of patients were equally distributed between groups • The population may not represent the entire population of interest • Actual probability values not provided
Swamy ¹⁹ 2009	<ul style="list-style-type: none"> • Interventions of interest clearly described 	<ul style="list-style-type: none"> • Retrospective • Unclear whether baseline characteristics of patients were equally distributed between groups • Unclear whether power calculation was performed to determine adequate sample size
Strandberg-Larsen ¹⁷ 2008	<ul style="list-style-type: none"> • Prospective • Large population • Interventions of interest clearly described 	<ul style="list-style-type: none"> • Unclear whether baseline characteristics of patients were equally distributed between groups
Guidelines		
Canadian Smoking Cessation Guideline ²⁰ 2011	<ul style="list-style-type: none"> • Scope and purpose of the guidelines are clear • The recommendations are specific and unambiguous • Target users of the guideline are clearly defined 	<ul style="list-style-type: none"> • Guideline was built from the evidence and recommendations in existing guidelines • Unclear whether the guideline was piloted among target users • Unclear whether patients' views and preferences were sought • Procedure for updating the guidelines was not provided

First Author, Publication Year	Strengths	Limitations
		<ul style="list-style-type: none"> • Potential cost implications of applying the recommendation were not included in the recommendation • Unclear whether the guideline was reviewed externally prior to publishing
Royal Australian College of General Practitioners Guideline ²¹ 2011	<ul style="list-style-type: none"> • Scope and purpose of the guidelines are clear • The recommendations are specific and unambiguous • Target users of the guideline are clearly defined • References are provided for the recommendations • Guideline development group includes individuals from all the relevant professional groups 	<ul style="list-style-type: none"> • Unclear whether patients' views and preferences were sought • Unclear whether the guideline was piloted among target users • Unclear whether patients' views and preferences were sought • Unclear whether the guideline was reviewed externally prior to publishing • Potential cost implications of applying the recommendation were not included in the recommendation
NICE guideline ²² 2010	<ul style="list-style-type: none"> • Scope and purpose of the guidelines are clear • Methods used to develop the guideline are indicated • The recommendations are specific and unambiguous • Target users of the guideline are clearly defined • References are provided for the recommendations • Guideline development group includes individuals from all the relevant professional groups • The guideline was reviewed externally prior to publishing 	<ul style="list-style-type: none"> • Unclear whether patients' views and preferences were sought • Potential cost implications of applying the recommendation were not included in the recommendation

Appendix 4: Main study findings and authors' conclusions

First Author	Main study findings	Authors' conclusions
Systematic Reviews		
Rosen ¹⁰ 2012	<p>Interventions significantly increased the parental quit rates compared to no intervention (RR 1.34, 95% CI 1.05, 1.71)</p> <p>Quit rates averaged 23.1% in the intervention group and 18.4% in the control group.</p> <p>Subgroup analyses: Interventions were most beneficial in parents with children ≥ 4 years old (RR 1.57, 95% CI 1.14, 2.16, $p = 0.006$), when interventions included medication use (RR 3.13, 95% CI 1.19, 8.21, $p = 0.02$), when the primary purpose was cessation (RR 1.69, 95% CI 1.2, 2.4, $p = 0.003$); and when the follow up rate was $>81\%$ (RR 1.64, 95% CI 1.12, 2.42, $p = 0.01$)</p>	<p>"Interventions to achieve cessation among parents, for the sake of the children, provide a worthwhile addition to the arsenal of cessation approaches" (p. 141)</p>
Lumley ⁹ 2009	<p>Interventions were associated with a significant reduction in smoking among pregnant women compared to no interventions (RR 0.94, 95% CI 0.93, 0.96), low birth weight (RR 0.83, 95% CI 0.73, 0.95), preterm birth (RR 0.86, 95% CI 0.74, 0.98)</p> <p>Compared to no intervention both "high intensity" intervention and "low intensity" intervention appeared to show similar effect with respect to smoking cessation (RR 0.94, 95% CI 0.92, 0.96 and RR 0.95, 95% CI 0.93, 0.96, respectively).</p> <p>Compared to no interventions, strategies including an incentive component showed the largest effect on smoking cessation (RR 0.76, 95% CI 0.71, 0.81)</p> <p>Compared to no intervention the relative risks for both nicotine replacement therapy and behavioral therapy were similar.</p> <p>Compared to no interventions, feedback strategy was not associated with significant change in quit rate (RR 0.92, 95% CI 0.84, 1.02)</p> <p>Interventions did not demonstrate statistically significant prevention of smoking relapse compared with no intervention (RR 0.91, 95% CI 0.75, 1.10)</p>	<p>"Smoking cessation interventions in pregnancy need to be implemented in all maternity care settings" (p. 2)</p>
Randomized Controlled Trials		
Henrikus ¹³ 2010	<p>Quit rates were 13.0% for intervention group (social network support) and 3.6% for controls at the end of pregnancy. The authors reported that the difference was not</p>	<p>"Increasing the frequency and quality of support from a woman in the smoker's social network is a promising prenatal smoking cessation strategy"(p. 134)</p>

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	statistically significant , however no p value was reported	
Hannover ¹⁴ 2009	Abstinent rates were higher in the treatment group (face-to-face and telephone counseling) at 6, 12 , 18 and 24 months than the control group who received usual care plus self-help material (7% versus 1%, 7% versus 2%, 9% versus 1%, and 9% versus 4%, respectively).There was no statistically significant difference in relapse prevention up to 24 months follow up. P values were not reported	"Regarding aid to cessation we observed small effects, regarding relapse prevention no effect" (p. 1)
Volpp ¹¹ 2009	Higher rates of enrollment in the program (financial incentives), completion of the program and smoking cessation were achieved with the intervention as compared to the control group (14.7% versus 5.0%, 10.8% versus 2.5%, 20.9% versus 11.8%, respectively, all p values were < 0.001).	"Financial incentives for smoking cessation significantly increased the rates of smoking cessation" (p. 699)
Oncken ¹² 2008	Smoking cessation rates were not significantly higher with nicotine gum than placebo gum after 6 weeks of treatment (13% versus 9.6%, p = 0.45) Birth weights and gestational age were significantly greater with nicotine gum than placebo (3287g versus 2950g, p < 0.0001 and 38.9 weeks versus 38.0 weeks, p = 0.014)	"Despite not reducing smoking during pregnancy, use of nicotine gum increased birth weight and gestational age, two key parameters in predicting neonatal wellbeing" (p. 859)
Non-randomized Studies		
Higgins ¹⁸ 2010	Breastfeeding rates were higher in women with intervention (abstinence-contingent financial incentives) than in control group (financial incentives independent of smoking status) at 12 weeks post-partum (35% versus 17%, p = 0.002)	"These results provide evidence from controlled studies that smoking cessation increases breastfeeding duration" (p. 483)
Everett-Murphy ¹⁶ 2010	Smoking cessation rates as measured by urinary cotinine were higher in the intervention group (counseling plus self-help materials) than in group with only limited education about risk of smoking (5.8% versus 0.5%, p = 0.0001)	"A smoking cessation intervention based on best practice guidelines was effective among high risk, pregnant smokers in South Africa" (p. 478)
Edwards ¹⁵ 2009	Smoking cessation rates were higher in women who received counseling plus self-help guide than in those who received only counseling (24.2% versus 20.9%, p < 0.05)	"Counseling coupled with self-help materials can increase cessation rates in women during pregnancy" (p. 170)
Swamy ¹⁹ 2009	Higher rates of serious adverse events were observed in pregnant women with nicotine replacement plus behavioral therapy than in the group with only behavioral therapy. The difference was not statistically significant. (17% versus 31%, p =	"While race, poor pregnancy history, and use of analgesics were associated with serious adverse events, randomization to NRT during pregnancy was not a significant factor" (p. 354)

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Strandberg-Larsen ¹⁷ 2008	<p>0.06)</p> <p>Women who smoked and who used nicotine replacement therapy had adjusted HR of 0.57 (95% CI 0.28, 1.16) for stillbirth compared to women who did not use nicotine replacement therapy.</p> <p>Women who smoked and who used nicotine replacement therapy had adjusted HR of 0.83 (95% CI 0.34, 2.00) for stillbirth compared to women who did not smoke and who did not use nicotine replacement therapy.</p> <p>Women who smoked and did not use nicotine replacement therapy had adjusted HR of 1.46 (95% CI 1.17, 1.82) for still birth compared to non-smokers also not using nicotine replacement therapy</p>	<p>"Our study does not indicate that use of NRT during pregnancy increases the risk of stillbirth" (p. 1405)</p>

RR: relative risk; HR: hazard ratio; CI: confidence interval