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SUMMARY WITH CRITICAL APPRAISAL

Smoking Reduction and Cessation Interventions for Pregnant Women and Mothers of Infants: A Review of the Clinical Effectiveness

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Context and Policy Issues

Cigarette smoking during pregnancy can result in serious health risks for pregnant women and their infants.[1] Nicotine, carbon monoxide, and other chemicals in the tobacco smoke can cause cancer, still births, preterm births, low birthweight, miscarriages, prenatal deaths, and sudden infant death syndrome.[1] In Canada, the prevalence of smoking among pregnant women dropped from 17% in 2000/2001 to 10.5% in 2005/2006,[2] and pregnant mothers consumed an average of seven cigarettes per day.[2] Smoking rates during pregnancy were most prevalent in the Northern Territories (39.4%) and Prince Edward Island (20.8%) compared to the rest of Canada.[2] The prevalence of smoking during pregnancy was higher in women, who were younger than 25 years old, unmarried, limited education, low income, non-immigrants, and poor in overall health.[3]

Many different pharmacological (e.g., nicotine replacement therapy [NRT], bupropion and varenicline) and non-pharmacological interventions (e.g., behavioral therapy), given alone or in combination, were effective in helping the adult population to stop smoking.[4] Despite an effective smoking cessation profile in the general population, evidence regarding the use of these interventions in pregnant women is less clear. Furthermore, it is uncertain whether there exists a program that is effective in helping pregnant women, who have difficulty to stop smoking, to change their smoking behaviour (i.e., reduce the number of cigarettes smoked per day).

The aim of this report is to review the clinical effectiveness of smoking reduction programs and smoking cessation interventions for pregnant women and mothers of infants.

Research Questions

1. What is the clinical effectiveness of smoking reduction programs for pregnant women or mothers of infants?
2. What is the clinical effectiveness of smoking cessation interventions for pregnant women or mothers of infants?

Key Findings

Evidence on the effectiveness of smoking reduction interventions was limited. Psychosocial interventions for smoking cessation appeared to be effective, while the effect of health education and social support was less certain. The results suggested that psychosocial interventions reduced the risk of infants born with low birthweight, increased the mean birthweight, and decreased the risk of neonatal intensive care unit admission. Pharmacological interventions appeared to be effective during treatment or at the end of pregnancy. Nicotine replacement therapy did not seem to have any positive or negative effects on infant outcomes, while the safety of bupropion was inconclusive.

Methods

Literature Search Methods

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Filters were applied to limit the retrieval to health technology assessments, systematic reviews, meta-analyses, non-randomized studies, and randomized controlled trials. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2012 and June 6, 2017.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Women who smoke and who are pregnant, new mothers or mothers of infants, breastfeeding
Intervention	Q1: Smoking reduction interventions Q2: Smoking cessation interventions - pharmacologic (e.g., nicotine replacement therapy) or non-pharmacologic (e.g. behavioural)
Comparator	Any comparator (another intervention or without intervention)
Outcomes	Effectiveness, success, risks, complications, safety (e.g., preventing low/very low birth weight, premature birth, infant mortality, fetal growth retardation, respiratory complications, behavioural disorders, apgar scores, maternal anemia, placental abruption)
Study Designs	Health technology assessments (HTAs), systematic reviews (SRs), meta-analyses (MAs), randomized controlled trials (RCTs) or non-randomized studies

Exclusion Criteria

Studies were excluded if they did not satisfy the selection criteria in Table 1, and if they were published prior to 2012. Conference abstracts, duplicates of publication of the same study, or systematic reviews (SRs), in which their included studies were overlapped with another SR published at a later date, were excluded. Non-randomized studies were excluded if SRs of randomized controlled trials (RCTs) or recently published RCTs were found.

Critical Appraisal of Individual Studies

The SIGN checklists were used to assess the quality of SRs and MAs,[5] and RCTs.[6]

Summary of Evidence

Quantity of Research Available

A total of 492 citations were identified in the literature search. Following screening of titles and abstracts, 443 citations were excluded and 49 potentially relevant reports from the electronic search were retrieved for full-text review. Two potentially relevant publications were retrieved from the grey literature search. Of these potentially relevant articles, 44 publications were excluded for various reasons, while seven publications, including two SRs and five RCTs, met the inclusion criteria and were included in this report. Appendix 1 describes the PRISMA flowchart of the study selection.

Summary of Study Characteristics

The characteristics of the SRs and MAs[7,8] and RCTs[9-13] are summarized below and are presented in Appendix 2.

SRs and MAs

Study Design

One SR[7] included 88 RCTs with 106 study arms involving over 26,000 pregnant smokers and provided data on psychosocial interventions to support pregnant women to stop smoking. Another SR[8] included nine RCTs (eight trials with NRT and one trial with bupropion) on pharmacological interventions for promoting smoking cessation during pregnancy of 2,210 pregnant smokers.

Country of Origin

Both SRs were conducted by authors from the United Kingdom (UK)[7,8] and were published in 2017[7] and 2015.[8]

Population

The overall populations of the included trials in both SRs[7,8] were in the first or second trimester of pregnancy. Most were healthy women of 16 years or older, with different ethnic backgrounds, education, and socioeconomic status.[7,8] The gestational age ranged from 9 to less than 30 weeks.[8]

Interventions and Comparators

The psychosocial interventions were categorized as counselling (54 trials), health education (12 trials), feedback (6 trials), incentives (13 trials), social support (7 trials) and exercise (1 trial).[7] These interventions were compared with usual care, a less intensive intervention, or an alternative intervention.[7] The pharmacological interventions included NRT (8 trials) and bupropion (1 trial) as an adjunct to behavioral support.[8] Transdermal nicotine patches were mostly used as an intervention in NRT compared to gum and lozenge. The comparators were either placebo or behavioral support alone.

Outcomes

The primary outcomes in both SRs[7,8] were smoking abstinence rates that were biochemically validated. The secondary outcomes included continued abstinence after childbirth,[7] smoking reduction in late pregnancy,[7] infant outcomes[7,8] and adverse effects.[7,8] The infant outcomes included low birthweight (under 2,500 g),[7,8] very low birthweight (under 1,500 g),[7] preterm birth (under 37 weeks),[7,8] mean birthweight,[7,8] stillbirth,[7,8] perinatal

death,[7,8] neonatal death,[7] neonatal intensive care unit admissions,[7] and congenital abnormalities.[8]

Follow-up Period

The follow-up periods in the trials included in both SRs[7,8] were conducted during pregnancy and up to two years after childbirth.

Data Analysis and Synthesis

Meta-analyses were conducted to synthesize data in the both SRs.[7,8] Both clinical and statistical heterogeneity were considered by performing subgroup analyses, meta-regressions, or sensitivity analyses.[7,8]

Quality Appraisal

The Cochrane risk of bias tool was used to assess the methodological quality of included studies in both SRs.[7,8] The strength of evidence for each body of evidence was assessed using GRADE (the Grading of Recommendations Assessment, Development and Evaluation) approach in one SR.[7]

RCTs

Study Design

Of the five included RCTs, one was active-controlled,[9] one was double-blind placebo controlled,[10] two were single-blinded,[11,13] and one was of a cluster design.[12] Three RCTs recruited patients from multiple centres,[11-13] and two RCTs enrolled patients from a single centre.[9,10]

Country of Origin

The RCTs were conducted in the UK,[11] United States,[9,10] Argentina[12] and the Netherlands,[13] and were published in 2017,[9-11] 2016[12] and 2014.[13]

Population

All RCTs included pregnant smokers with a mean age ranging from 19[13] to 26.5 years.[10] One RCT included negative affect pregnant smokers who had emotional issues, such as anxiety, dysthymia, anger, and stress.[9] One RCT included young pregnant women with low education levels.[13] The mean gestational age ranged from 15[9,11] to 20 weeks,[13] the average smoking at enrolment ranged from 8[9,13] to 12[10] cigarettes per day.

Interventions and Comparators

The comparisons were emotional regulation treatment (ERT) versus health and lifestyle intervention (HLS),[9] self-help smoking cessation text message (MiQuit) versus usual care,[11] counselling (based on the 5As [Ask, Advise, Assess, Assist, and Arrange]) versus control,[12] nurse home visitations versus usual care,[13] and bupropion sustained release versus placebo.[10] The purpose of the nurse home visitations was to help reduce cigarette smoking and promote breastfeeding among young pregnant smokers.[13]

Outcomes

The outcomes included biochemically validated smoking abstinence rates,[9-11] the number of cigarettes smoked per day,[9,13] continuous and quit smoking during pregnancy,[12] infant outcomes,[10,13] and maternal outcomes.[10]

Follow-up Period

The follow-up periods in the included RCTs were done both during pregnancy and up to four months after childbirth.

Analysis

The evaluations of study endpoints in three RCTs[10-12] were performed on an intention-to-treat (ITT) basis, while the analysis in two RCTs[9,13] was performed on a per-protocol (PP) basis. Three RCTs[10-12] presented a sample size calculation to obtain sufficient power for the primary outcome, and two RCTs[9,13] did not reported a sample size calculation.

Summary of Critical Appraisal

The summary of the quality assessment for the SRs and RCTs were briefly described below and are presented in Appendix 3.

SRs and MAs

The SRs[7,8] were of high quality as most of the criteria were fulfilled, including an explicit research question, a comprehensive literature search, and at least two people were independently involved in the study selection and data extraction. Also, the publication status was not used as an inclusion criterion, and relevant study characteristics, quality assessment of included studies and a declaration of the conflicts of interest were completed. Appropriate methods of meta-analysis were used to combine the individual study findings. Publication bias was assessed in one SR,[7] and was not applicable in the other SR[8] as there were eight individual studies included. Both SRs provided a list of excluded studies.

RCTs

One RCT[10] was of high quality as all criteria were fulfilled, including an explicit question, a detailed description of methodology on randomization, adequate method of concealment, blinding. As well, there was similarity between treatment groups, relevant outcome measures, an ITT analysis was conducted, and the trial was multi-centric. Four RCTs[9,11-13] were of moderate quality as some criteria were partially reported or not fulfilled, such as the method of concealment,[9,11-13] blinding[9,11-13] and ITT analysis.[9,13] The percentages of dropouts before study completion in both arms were 44% and 53%[9] and 49% and 43%[10] in two RCTs.[9,10]

Summary of Findings

The main findings and conclusions of the included SRs and RCTs are presented in Appendix 4.

Question 1: What is the clinical effectiveness of smoking reduction programs for pregnant women or mothers of infants?

One trial[13] was identified that assessed a home visitation program by trained nurses to help young pregnant women with a low education level in reducing cigarette smoking and promoting breastfeeding.

Percentage of smokers

The percentages of smokers in both intervention and control groups were not significantly different at either 32 weeks of pregnancy (33% vs 35%) or at two months after childbirth (48% vs 65%). After conducting the last observation carried forward approach to correct for missing data, the percentages of smokers in the intervention group were significantly lower than those in the control group; 40% versus 48% at 32 weeks of pregnancy, and 49% versus 62% at two months after childbirth.

Number of cigarettes smoked per day

There was no difference in the number of cigarettes smoked per day between the intervention and control groups (2 versus 3 cigarettes) at 32 weeks of pregnancy, although the numbers of cigarettes smoked in both groups reduced compared to those at enrolment (7 versus 8 cigarettes). At two months after birth, women in the control group increased their daily cigarettes smoked as of at baseline (8 cigarettes), while women in the intervention group smoked an average of 4 cigarettes per day.

Pregnancy outcomes

Birth weight, gestational age, the prevalence of low birth weight (i.e., <2,500 g), and the prevalence of premature babies (i.e., <37 weeks) were similar in both groups.

Breastfeeding

Breastfeeding initiation was similar in both groups (82% versus 78%). The percentage of women, who continued to breastfeed at 6 months after childbirth, was higher than in the intervention group than in the control group (13% versus 6%).

Question 2: What is the clinical effectiveness of smoking cessation interventions for pregnant women or mothers of infants?

One SR[7] and three RCTs[9,11,12] were identified that reported relevant outcomes for the psychosocial interventions, and one SR[8] and one RCT[10] were identified that reported relevant outcomes for pharmacological interventions.

<u>Psychosocial Interventions</u>

Smoking abstinence in late pregnancy

There was evidence from the SR[7] that counselling was more effective than usual care or less intensive intervention. It was uncertain about the effectiveness of counselling (i.e., cognitive behavioral therapy) compared with alternative intervention (i.e., health education or motivational interview).[7]

There was uncertainty about the effectiveness of health education compared with usual care, less intensive intervention, or alternative interventions.[7]

There was evidence that feedback significantly increased the rate of smoking cessation compared to usual care.[7] There was uncertainty if the feedback was more effective when compared to less intensive interventions.[7]

There was evidence that incentives significantly increased the rate of smoking cessation compared to alternative interventions.[7] However, it was uncertain about the effectiveness of incentives compared to usual care or less intensive interventions.[7]

There was uncertainty on whether social support (i.e., peer or partner) increased the chance of smoking cessation when compared to less intensive interventions.[7] There was also uncertainty whether exercise increased the chance of smoking cessation when compared to usual care.[7]

One RCT[12] showed that smoking cessation counselling based on the 5As had no difference in the frequency of women who smoked until the end of pregnancy compared to the control group. One RCT[9] showed that the emotional regulation treatment had a higher chance to stop smoking in negative affect pregnant smokers compared to health and lifestyle intervention, but the difference was not statistically significant. One RCT[11] showed that a test message intervention program may increase the abstinence rates of smoking compared to usual care, although the difference was not statistically significant.

Continued abstinence (relapse prevention) in late pregnancy

There was no evidence to suggest that counselling could prevent smoking relapse compared to usual care or less intensive interventions.[7] There was also uncertainty about the effectiveness of health education compared to usual care, or social support compared to less intensive interventions in smoking relapse prevention.[7]

Continued abstinence in the postnatal period

There was evidence that counselling increased the rate of smoking abstinence during post-partum periods (i.e., 0 to 5 months, 6 to 11 months and 12 to 17 months), compared to usual care.[7] However, there was uncertainty on whether counselling increased postpartum smoking abstinence compared to less intensive interventions or alternative interventions.[7]

There was evidence that health education increased the rate smoking cessation in the early postpartum period (i.e., 0 to 5 months) compared to usual care or less intensive interventions.[7]

There was evidence that incentives increased smoking abstinence during 6 to 11 months postpartum compared to usual care.[7] There was also evidence that incentives increased smoking abstinence at 0 to 5 months compared to less intensive interventions.[7] However, there was uncertainty if there was an increase in smoking cessation when incentives were compared to usual care at 0 to 5 months, or when incentives were compared to alternative interventions at 0 to 5 months or 6 to 11 months postpartum.[14]

There was no evidence to suggest that social support was more effective than less intensive interventions, or exercise was more effective than usual care in promoting continued smoking abstinence during postnatal period.[7]

Smoking reduction in late pregnancy

It was uncertain on whether there were differences in smoking reduction that was biochemically validated in different comparisons including counselling versus usual care, counselling versus less intensive interventions, feedback versus usual care, incentives versus usual care, incentives versus alternative interventions, and social support versus less intensive interventions.[7]

Mean cigarettes smoked per day in late pregnancy

There was evidence that health education, feedback and incentives significantly reduced the mean number of cigarettes smoked per day compared to usual care.[7] There was uncertainty that counselling and health education could decrease the number of cigarettes smoked per day compared to less intensive interventions.[7]

Results from the included RCT[9] showed that emotion regulation treatment intervention given to a difficult-to-treat population did not significantly reduce the number of cigarettes smoked per day compared to a healthy lifestyle intervention.

Infant outcomes

Data from each of the infant outcomes were pooled from "all interventions" to increase the detection of rare events.[7]

There was evidence that smoking cessation interventions reduced the risk of infants born with low birthweight (i.e., <2,500 g) by 17%, increased the mean birthweight by 55.6 g, and decreased the risk of neonatal intensive care unit (NICU) admission by 22%.[7]

There was uncertainty whether there was any difference between smoking cessation interventions and controls with respect to the rates of very low birthweight (i.e., <1,500 g), preterm births (i.e., <37 weeks), stillbirths, perinatal deaths, and neonatal deaths.[7]

Pharmacological Interventions

Smoking abstinence in late pregnancy

There was evidence that NRT increased the rates of biochemically validated smoking cessation by about 40% compared to the control group.[8] However, there was no difference in the self-reported smoking abstinence rates between NRT and the control group at 3, 6 or 12 months postpartum.

Bupropion sustained release increased abstinence rates during treatment compared to placebo, but there was no significant difference in the abstinence rates between groups at the end of treatment, at the end of pregnancy, and during the postpartum period.[10]

Mean cigarettes smoked per day in late pregnancy

There was no significant difference in percent reduction in the number of cigarettes smoked per day between bupropion and placebo at the end of treatment, at the end of pregnancy, and during the postpartum period.[10]

Infant outcomes

There were no significant differences in all infant outcomes between NRT and control[8] or between bupropion and placebo.[10]

Maternal outcomes

There were no significant differences in body mass index, blood pressure, and pulse rate between bupropion and placebo.[10] Treatment side effects, such as headaches, difficulty sleeping, running nose, dry mouth, and anxiety, were similar in both groups.[10]

Limitations

There was limited evidence on the clinical effectiveness of the smoking reduction programs for pregnant women or mothers of infants. One trial on smoking reduction program was identified that used self-reported questionnaires instead of biochemically assessments to measure cigarette smoking behavior of participants. The evidence on pharmacological interventions was derived from a SR published in 2015, has not been updated yet, and was limited to NRT only, with limited or no information on other medications. Given the difficulty in recruitment (i.e., 11[8] and 63[10] participants) and the rate of early withdrawal (i.e., near 50%[10]) from the bupropion trials, the effectiveness and safety of the medication were questionable.

Conclusions and Implications for Decision or Policy Making

There was limited evidence on the effectiveness of smoking reduction interventions, and it was unclear if a nurse home visitation program was effective in helping pregnant women to reduce smoking. There was strong to moderate evidence that suggested that psychosocial interventions for promoting smoking cessation during pregnancy can increase the proportion of women who stopped smoking in late pregnancy. Among the psychosocial interventions, counselling, feedback, and incentives appeared to be effective, while the effect of health education and social support was less certain. Counselling and incentives appeared to be effective for continued abstinence during the postpartum period. It was unclear if smoking cessation interventions can help pregnant women to reduce smoking. Pooled results suggested that psychosocial interventions reduced the risk of infants born with low birthweight, increased the mean birthweight, and decreased the risk of NICU admission. Pharmacological interventions, such as NRT and bupropion, appeared to be effective only during treatment or in late pregnancy, but not after pregnancy or during postpartum period. There was no evidence that NRT had any positive or negative effect on infant outcomes and the safety of bupropion was less clear. More evidence is needed, particularly, on the programs promoting smoking reduction for pregnant women, and on the effectiveness and safety of smoking cessation drugs, such as bupropion, varenicline, or other medications for pregnant smokers.

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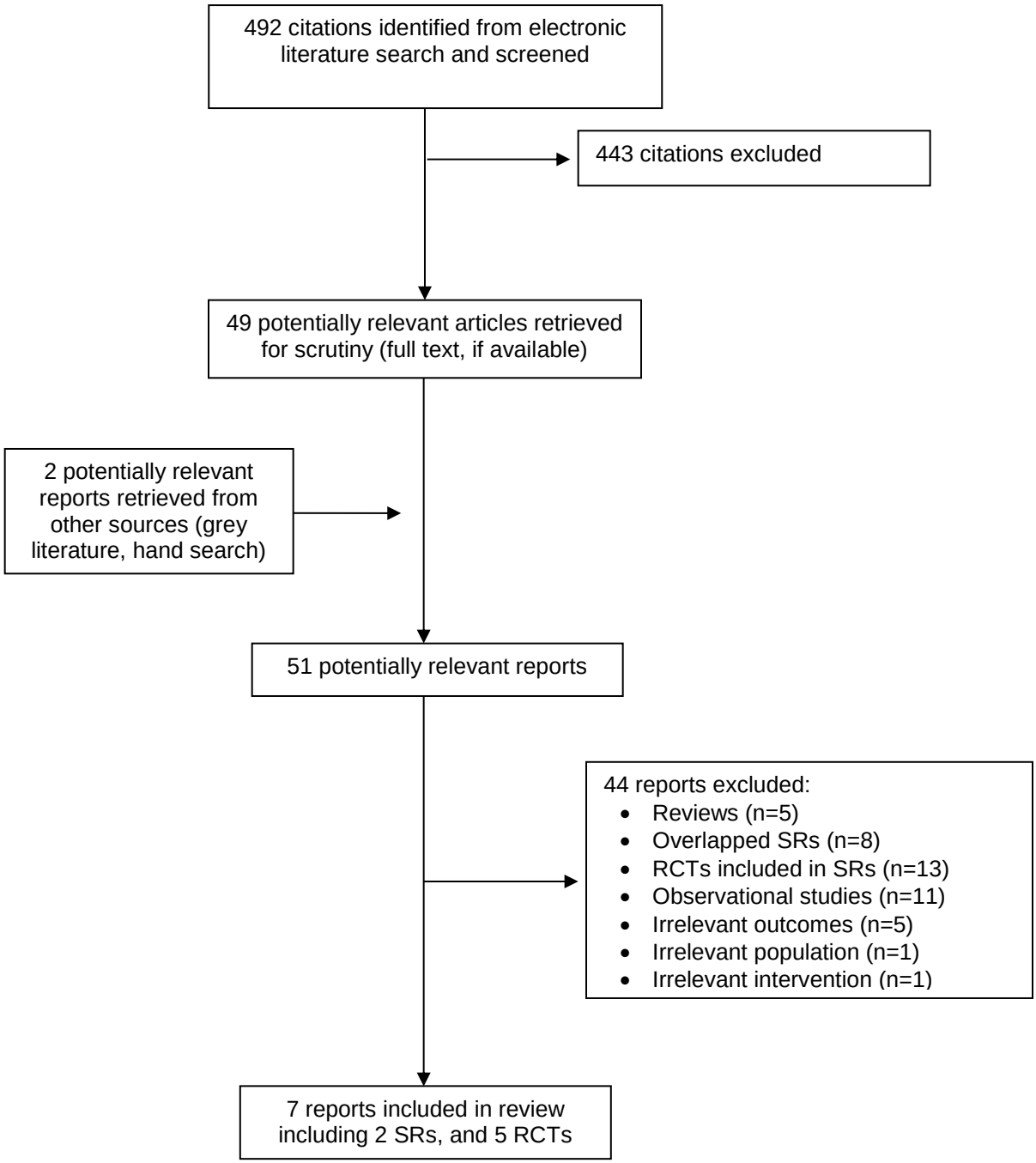
Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Studies

Table A1: Characteristics of Included Systematic Reviews

First Author, Publication Year, Country, Funding	Types and Numbers of Primary Studies Included	Population Characteristics	Interventions	Comparators	Clinical Outcomes, Length of Follow-up
Chamberlain et al., 2017[7] Australia, UK Public Funding	SR of 88 RCTs (n=106 study arms) related to smoking cessation in late pregnancy. This was the sixth update review of the previous versions published in 1995, 1999, 2004, 2009 and 2013 Quality assessment using Cochrane risk of bias	Over 26,000 pregnant smokers, most were at first antenatal clinic visit and during the second trimester of pregnancy. Four trials had women who continued to smoke in late pregnancy • Healthy pregnant women (≥16 years old, 23 trials) • Low socioeconomic status (≥16 years old, 52 trials) • Young women under 20 years (2 trials) • Women with psychosocial risk factors (8 trials) • Women required for methadone treatment for opioid addition (2 trials) • Ethnic minority population (10 trials); indigenous communities (5 trials)	• Counselling (n=54) • Health education (n=12) • Feedback (n=6) • Incentives (n=13) • Social support (n=7) • Exercise (n=1) Many interventions during pregnancy continued support into the postpartum period and measured postpartum outcomes. Interventions differed in intensity, duration and people involved in implementation • Single intervention (n=57) • Multiple intervention (n=36) • Tailored intervention (n=12) • Face-to-face counselling with different strategies (n=56) • Counselling	• Usual care (n=56) • Less intensive intervention (n=44) • Alternative intervention (n=6)	Primary outcomes • Smoking abstinence (biochemically validated) Secondary outcomes • Continued abstinence in the postnatal period 0 to 5 months Six to 11 months 2 to 17 months 14+ months • Smoking reduction • Infant outcomes Low birthweight Preterm births Mean birthweight Other perinatal outcomes Non pre-specified infant outcomes • Breastfeeding • Psychological effects • Adverse effects Follow-up: during pregnancy and more than 14 months postnatal

First Author, Publication Year, Country, Funding	Types and Numbers of Primary Studies Included	Population Characteristics	Interventions	Comparators	Clinical Outcomes, Length of Follow-up
			including lottery (n=4) • Support from peers and/or partners (n=9) • Duration and frequency generally increased overtime		
Coleman et al., 2015[8] Australia, UK Public Funding	SR and MA of 9 RCTs (8 trials with NRT and 1 trial with bupropion) published between 2000 and 2015 Quality assessment using Cochrane risk of bias	2,210 pregnant smokers Age: ≥16 years old Gestational age: 9 to <30 weeks Smoking: ≥1 cigarette per day	NRT (8 trials) and bupropion (1 trial) as adjuncts to behavioral support NRT: • Nicotine gum (n=1) • Nicotine patch (n=6) • Choice of NRT formulations (n=1)	• Behavioral support • Placebo	Primary outcomes • Smoking abstinence rates (biochemically validated) Secondary outcomes • Abstinence from smoking after childbirth • Safety Miscarriage or spontaneous abortion Stillbirth Mean unadjusted birthweight Low birthweight (<2,500 g) Preterm birth (<37 weeks) NICU admissions Neonatal death Caesarian section Maternal hypertension Infant respiratory symptom Infant development • Adherence • Compliance • Side effects

First Author, Publication Year, Country, Funding	Types and Numbers of Primary Studies Included	Population Characteristics	Interventions	Comparators	Clinical Outcomes, Length of Follow-up
					Follow-up: during pregnancy and up to two years after childbirth

MA = meta-analysis; NICU = neonatal intensive care unit; NR = not reported; NRT = nicotine replacement therapy; RCT = randomized controlled trial; SR = systematic review; UK = United Kingdom

Table A2: Characteristics of Included Primary Studies

First Author, Publication Year, Country, Study Name (if reported), Funding	Study Design and Analysis	Patient Characteristics	Interventions	Comparators	Clinical Outcomes, Length of Follow-up
Bradizza et al., 2017[9] USA Funding: National Institute on Drug Abuse and the Office of Research on Women's Health at the National Institute of Health	Active-controlled RCT, single center, parallel, 1:1 ratio Analysis: per protocol Sample size calculation: NR	70 pregnant smokers with negative affect (i.e., emotional factors including greater anxiety, dysthymia, anger, and stress) Mean age: 25 years Mean gestational age: 15 weeks Average smoking • At enrolment: 8 cigarettes per day	Emotional regulation treatment (ERT)* + CBT for smoking cessation (n=36) *8 sessions: (1) ERT program rationale, introduction to emotions; (2) Dedicated mindfulness practice and mindfulness in daily activities; (3) Preparing for guided imagery/exposure to negative affect smoking situations, mindfulness; (4) Emotions and urges, physiologically-focused guided	Health and lifestyle intervention (HLS)* + CBT for smoking cessation (n=34) *8 sessions: (1) Benefits of healthy lifestyle; (2) Personal value and priority; (3) Nutrition 1; (4) Nutrition 2; (5) Avoid carbon monoxide poisoning; (6) Reducing HIV risk; (7) Balancing life role; (8) Review of health and lifestyle changes	• Smoking abstinence rates (biochemically validated) • Number of cigarettes smoked per day Follow-up: pre-treatment, 2 months and 4 months post-quit

First Author, Publication Year, Country, Study Name (if reported), Funding	Study Design and Analysis	Patient Characteristics	Interventions	Comparators	Clinical Outcomes, Length of Follow-up
			imagery/ exposure to negative affect smoking situations; (5), (6), (7) Mindfulness review; (8) Review of progress		
Nanovskaya et al., 2017[10] USA Funding: National Institute on Drug Abuse	DB, placebo-controlled RCT, single center, parallel, 1:1 ratio Analysis: ITT Sample size calculation: Yes	65 pregnant smokers Mean age: 26.5 years Mean gestational age: 19 weeks Average smoking: • Before pregnancy: 18 cigarettes per day • At enrolment: 12 cigarettes per day Attempt to quit during pregnancy: 57%	Sustained release bupropion (150 mg BID) + behavioral support* (n=30) *35 minute counseling sessions at each of the first 2 visits and 10 minutes of smoking cessation counselling at subsequent visits, delivered by a research nurse using a motivational interview approach	Placebo + behavioral support (n=35)	• Smoking abstinence rates (biochemically validated) • Birth and delivery outcomes (birthweight, infant length, head circumference, Apgar score at 5 minutes, pH value of arterial and venous cord blood) • Maternal outcomes (BMI at end pf pregnancy, blood pressure, bupropion side effects) • Compliance with study medication and retention Follow-up: during pregnancy and 6 months postpartum
Naughton et al., 2017[11] UK Funding: NIHR	Single blinded RCT, multicenter, parallel, 1:1 ratio Analysis: ITT Sample size calculation: Yes	407 pregnant smokers Mean age: 26 years Mean gestational age: 15 weeks Average smoking: • Before pregnancy: 16 cigarettes per	MiQuit* (n=203) *an automated 12-week advice and support program for quitting smoking in pregnancy delivered by short message service (SMS) text message	Usual care (n=204)	Smoking abstinence rates (biochemically validated) Follow-up: Abstinence data collected at 4-week follow up and at 36 weeks gestation

First Author, Publication Year, Country, Study Name (if reported), Funding	Study Design and Analysis	Patient Characteristics	Interventions	Comparators	Clinical Outcomes, Length of Follow-up
		day • At enrolment: 9 cigarettes per day			
Althabe et al., 2016[12] Argentina Funding: Centers for Disease Control and Prevention	Cluster RCT, 1:1 ratio Analysis: ITT Sample size calculation: Yes	3333 pregnant smokers Mean age: 21 years Mean gestational age: NR Percent smoking during pregnancy: 22%	Counseling* (10 clusters, n=1562) *based on the 5As (Ask, Advise, Assess, Assist, and Arrange)	Control (10 clusters; n=1771)	Primary outcome • Recall receiving 5As Secondary outcomes • Continuous smoking • Quit smoking during pregnancy Follow-up: Baseline, first 48 hours after delivery and during postpartum hospital stay
Mejdoubi et al., 2014[13] The Netherlands Funding: Netherlands Organization for health Research and Development	Single blinded RCT, multicenter, parallel, 1:1 ratio Analysis: per protocol Sample size calculation: NR	460 pregnant smokers with low education level Mean age: 19 years Mean gestational age: 20 weeks Average smoking: • At enrolment: 8 cigarettes per day Attempt to quit during pregnancy: 81%	Nurse home visitation* (n=237) *10 home visits during pregnancy, 20 during first year and 20 during the second life year of the child by trained nurses advising how to reduce smoking and how to promote breastfeeding	Usual care (n=223)	Primary outcome • Prevalence of cigarette smoking Percentage of smokers Average number of cigarettes smoked per day Secondary outcomes • Birthweight • Week of gestation • Adverse pregnancy outcomes (low birthweight, prematurity, small gestational age) • Breastfeeding initiation Follow-up: Baseline, 32 weeks of pregnancy and two months postpartum

BID = twice daily; BMI = body mass index; DB = double blind; ITT = intention-to-treat; NIHR = National Institute for Health Research; NR = not reported; RCT = randomized controlled trial

Appendix 3: Quality Assessment of Included Studies

Table A3: Quality Assessment of Systematic Reviews

SIGN Checklist: Internal Validity[5]	Chamberlain et al., 2017[7]	Coleman et al., 2015[8]
1. The research question is clearly defined and the inclusion/exclusion criteria must be listed in the paper	Yes	Yes
2. A comprehensive literature search is carried out	Yes	Yes
3. At least two people should have selected studies	Yes	Yes
4. At least two people should have extracted data	Yes	Yes
5. The status of publication was not used as an inclusion criteria	Yes	Yes
6. The excluded studies are listed	Yes	Yes
7. The relevant characteristics of the included studies are provided	Yes	Yes
8. The scientific quality of the included studies was assessed and reported	Yes	Yes
9. Was the scientific quality of the included studies used appropriately?	Yes	Yes
10. Appropriate methods are used to combine the individual study findings	Yes	Yes
11. The likelihood of publication bias was assessed appropriately	Yes	NA
12. Conflicts of interest are declared	Yes	Yes
Overall Assessment of the Study		
High, Moderate, Low	High	High

For overall assessment of the study: *High* indicated that all or most criteria have been fulfilled; where they have not been fulfilled, the conclusions of the study or review are thought very unlikely to alter. *Moderate* indicates that some of the criteria have been fulfilled; those criteria that have not been fulfilled or not adequately described are thought unlikely to alter the conclusions. *Low* indicates that few or no criteria fulfilled; the conclusions of the study are thought likely or very likely to alter.

Table A4: Quality Assessment of Primary Studies

SIGN Checklist: Internal Validity[6]	Bradizza et al., 2017[9]	Nanovskaya et al., 2017[10]	Naughton et al., 2017[11]	Althabe et al., 2016[12]	Mejdoubi et al., 2014[13]
1. The study addresses an appropriate and clearly focused question.	Yes	Yes	Yes	Yes	Yes
2. The assignment of subjects to treatment groups is randomized.	Yes	Yes	Yes	Yes	Yes
3. An adequate concealment method is used.	Can't tell	Yes	Can't tell	No	Can't tell
4. Subjects and investigators are kept 'blind' about treatment allocation.	No	Yes	No	No	No
5. The treatment and control groups are similar at the start of trial.	Yes	Yes	Yes	Yes	Yes
6. The only difference between groups is the treatment under investigation.	Yes	Yes	Yes	Yes	Yes

SIGN Checklist: Internal Validity[6]	Bradizza et al., 2017[9]	Nanovskaya et al., 2017[10]	Naughton et al., 2017[11]	Althabe et al., 2016[12]	Mejdoubi et al., 2014[13]
7. All relevant outcomes are measured in a standard, valid and reliable way.	Yes	Yes	Yes	Yes	Yes
8. What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	Active control (HLS): 44% Intervention (ERT): 53%	Placebo: 49% Bupropion SR: 43%	Usual care: 19% MiQuit: 13%	NR	Usual care: 14% Nurse home visit: 4%
9. All the subjects are analyzed in the groups to which they were randomly allocated (often referred to as intention to treat analysis).	No	Yes	No	Yes	Yes
10. Where the study is carried out more than one site, results are comparable for all sites.	No	Yes	Yes	Yes	No
Overall Assessment of the Study					
High, Moderate, Low	Moderate	High	Moderate	Moderate	Moderate

For overall assessment of the study: *High* indicated that all or most criteria have been fulfilled; where they have not been fulfilled, the conclusions of the study or review are thought very unlikely to alter. *Moderate* indicates that some of the criteria have been fulfilled; those criteria that have not been fulfilled or not adequately described are thought unlikely to alter the conclusions. *Low* indicates that few or no criteria fulfilled; the conclusions of the study are thought likely or very likely to alter.

Appendix 4: Main Study Findings and Author's Conclusions

Table A5: Summary of Findings of Included Systematic Reviews

Main Study Findings	Author's Conclusions
Chamberlain et al., 2017[7]	

Primary outcome:

Smoking abstinence in late pregnancy

Comparison	No. of study	RR (95% CI)	I^2, %
1) Counselling vs usual care			
All	30	1.44 (1.19 to 1.73)	49
Validated only	21	1.23 (1.04 to 1.45)	22
2) Counselling vs less intensive interventions			
All	18	1.25 (1.07 to 1.47)	28
Validated only	15	1.31 (1.10 to 1.56)	23
3) Counselling vs alternative interventions	1	1.15 (0.86 to 1.53)	--
4) Health education vs usual care			
All	5	1.59 (0.99 to 2.55)	0
Validated only	3	1.45 (0.82 to 2.58)	20
5) Health education vs less intensive interventions			
All	4	1.20 (0.85 to 1.70)	33
Validated only	3	1.15 (0.70 to 1.91)	52
6) Health education vs alternative interventions	1	1.88 (0.19 to 18.60)	
7) Feedback vs usual care			
All	2	4.39 (1.89 to 10.21)	0
Validated only	1	3.88 (1.38 to 10.93)	--
8) Feedback vs less intensive interventions			
All	3	1.29 (0.75 to 2.20)	0
Validated only	3	1.29 (0.75 to 2.20)	0
9) Incentives vs usual care	1	Not estimable	
10) Incentives vs less intensive interventions	4	Not pooled	93
11) Incentives vs alternative interventions			
All	4	2.36 (1.36 to 4.09)	0
Validated only	4	2.36 (1.36 to 4.09)	0
12) Social (peer or partner) support vs less intensive interventions			
All	7	1.21 (0.93 to 1.58)	0
Validated only	6	1.42 (0.98 to 2.07)	0
13) Exercise vs usual care	1	1.20 (0.72 to 2.01)	--

Secondary outcomes:

Continued abstinence (Relapse prevention) in late pregnancy

Comparison	No. of study	RR (95% CI)	I^2, %
1) Counselling vs usual care	8	1.06 (0.93 to 1.21)	45
2) Counselling vs less intensive interventions	5	1.06 (0.99 to 1.13)	0

"Psychosocial interventions to support women to stop smoking in pregnancy can increase the proportion of women who stop smoking in late pregnancy and the proportion of infants born low birthweight. Counselling, feedback and incentives appear to be effective, however the characteristics and context of the interventions should be carefully considered. The effect of health education and social support is less clear."[7] p.2-3

Main Study Findings	Author's Conclusions

3) Health education vs usual care	1	1.02 (0.86 to 1.23)	--
4) Social (peer or partner) support vs less intensive interventions	1	1.02 (0.89 to 1.16)	--

Continued abstinence in the postnatal period

Comparison	No. of study	RR (95% CI)	I^2, %
1) Counselling vs usual care			
0 to 5 months	11	1.59 (1.26 to 2.01)	0
6 to 11 months	6	1.33 (1.00 to 1.77)	0
12 to 17 months	2	2.20 (1.23 to 3.96)	0
18+ months	3	0.98 (0.50 to 1.92)	0
2) Counselling vs less intensive interventions			
0 to 5 months	8	1.15 (0.93 to 1.43)	23
6 to 11 months	4	1.09 (0.91 to 1.31)	0
12 to 17 months	3	1.11 (0.87 to 1.41)	26
3) Counselling vs alternative interventions			
0 to 5 months	1	1.05 (0.63 to 1.76)	--
6 to 11 months	1	0.76 (0.33 to 1.73)	--
4) Health education vs usual care			
0 to 5 months	2	3.56 (1.31 to 9.67)	0
5) Health education vs less intensive interventions			
0 to 5 months	2	1.55 (1.01 to 2.36)	0
6) Incentives vs usual care			
0 to 5 months	2	1.09 (0.56 to 2.13)	0
6 to 11 months	1	3.88 (2.10 to 7.16)	--
7) Incentives vs less intensive interventions			
0 to 5 months	1	3.63 (1.54 to 8.58)	--
8) Incentives vs alternative interventions			
0 to 5 months	3	1.79 (0.57 to 5.61)	52
6 to 11 months	3	0.93 (0.85 to 1.01)	0
9) Social (peer or partner) support vs less intensive interventions			
0 to 5 months	2	1.34 (0.35 to 5.14)	34
6 to 11 months	3	1.08 (0.81 to 1.44)	0
12 to 17 months	1	1.07 (0.76 to 1.51)	--
10) Exercise vs usual care			
6 to 11 months	1	1.50 (0.81 to 2.79)	--

Smoking reduction in late pregnancy

Comparison	No. of study	RR or MD* (95% CI)	I^2, %
1) Counselling vs usual care			
Validated	2	0.79 (0.49 to 1.28)	4
Self-reported (various definition)	5	1.66* (1.27 to 2.17)	0
Decrease in mean cotinine	6	-0.44 (-0.76 to -0.12)	87
2) Counselling vs less intensive interventions			
Validated	2	1.35 (0.98 to 1.87)	0
Self-reported >50% reduction	2	1.35 (1.07 to 1.71)	0

Main Study Findings	Author's Conclusions

3) Feedback vs usual care			
Validated	1	1.48 (0.93 to 2.37)	--
Self-reported (various definition)	1	1.88 (1.24 to 2.84)	--
4) Incentives vs usual care			
Validated	2	Totals not selected	--
Decrease in mean cotinine	2	-2.00 (-6.61 to 2.60)	85
5) Incentives vs alternative interventions			
Validated	1	0.71 (0.18 to 2.88)	--
6) Social (peer or partner) support vs less intensive interventions			
Self-reported >50% reduction	1	0.96 (0.64 to 1.44)	--

Mean cigarettes per day in late pregnancy

Comparison	No. of study	MD (95% CI)	I^2, %
1) Counselling vs usual care	11	Totals not selected	--
2) Counselling vs less intensive interventions	2	-0.11 (-0.30 to 0.09)	0
3) Health education vs usual care	2	-0.55 (-0.94 to -0.15)	77
4) Health education vs less intensive interventions	1	-0.70 (-3.37 to 1.97)	--
5) Feedback vs usual care	1	-3.0 (-4.68 to -1.32)	--
6) Incentives vs usual care	1	-8.2 (-10.83 to -5.57)	--

Low birthweight (<2,500 g)

Comparison	No. of study	RR (95% CI)	I^2, %
All interventions	18	0.83 (0.72 to 0.94)	0
Counselling	8	0.83 (0.68 to 1.01)	0
Health education	2	0.87 (0.49 to 1.55)	40
Feedback	1	0.82 (0.63 to 1.06)	--
Incentives	5	0.63 (0.37 to 1.08)	0
Social support	1	1.00 (0.33 to 2.99)	--
Exercise	1	0.88 (0.58 to 1.32)	--

Very low birthweight (<1,500 g)

Comparison	No. of study	RR (95% CI)	I^2, %
All interventions	3	1.11 (0.62 to 2.01)	0
Counselling	2	1.27 (0.60 to 2.71)	0
Feedback	1	0.90 (0.35 to 2.32)	--

Preterm birth (<37 weeks)

Comparison	No. of study	RR (95% CI)	I^2, %
All interventions	19	0.93 (0.77 to 1.11)	18
Counselling	8	0.93 (0.71 to 1.20)	0
Health education	2	0.92 (0.55 to 1.56)	0
Feedback	2	0.60 (0.28 to 1.29)	63
Incentives	6	0.91 (0.52 to 1.59)	33
Exercise	1	1.32 (0.81 to 2.14)	--

Main Study Findings	Author's Conclusions

Mean birthweight

Comparison	No. of study	MD (95% CI)	I^2, %
All interventions	26	55.6 (29.8 to 81.4)	31
Counselling	14	42.2 (11.8 to 72.6)	0
Health education	2	27.4 (-53.9 to 109)	33
Feedback	2	79.43 (-53.1 to 212)	58
Incentives	6	114 (63.9 to 164)	23
Social support	1	28.0 (-152.5 to 208)	--
Exercise	1	-14.4 (-104 to 75.4)	--

Stillbirth

Comparison	No. of study	RR (95% CI)	I^2, %
All interventions	8	1.20 (0.76 to 1.90)	0
Counselling	5	1.14 (0.55 to 2.33)	0
Feedback	2	1.28 (0.69 to 2.39)	0
Exercise	1	1.01 (0.14 to 7.10)	--

Perinatal death

Comparison	No. of study	RR (95% CI)	I^2, %
All interventions	4	1.13 (0.72 to 1.77)	0
Counselling	2	1.10 (0.52 to 2.31)	NA
Health education	1	4.40 (0.49 to 39.08)	--
Feedback	1	1.05 (0.59 to 1.87)	--

Neonatal death

Comparison	No. of study	RR (95% CI)	I^2, %
All interventions	5	1.04 (0.41 to 2.64)	0
Counselling	3	2.06 (0.61 to 6.92)	0
Feedback	1	0.40 (0.08 to 2.07)	--
Exercise	1	0.34 (0.01 to 8.31)	--

NICU admission

Comparison	No. of study	RR (95% CI)	I^2, %
All interventions	8	0.78 (0.61 to 0.98)	0
Counselling	2	0.82 (0.52 to 1.29)	25
Incentives	5	0.77 (0.51 to 1.15)	0
Exercise	1	0.76 (0.47 to 1.22)	--

Coleman et al., 2015[8]

Primary outcomes (efficacy):

Smoking abstinence (NRT vs control)

Outcome	No. of study	RR (95% CI)	I^2, %
Validated in later pregnancy	8	1.41 (1.03 to 1.93)	18
Self-reported at 3 or 6 months postnatal	3	1.22 (0.84 to 1.77)	0
Self-reported at 12months postnatal	1	1.04 (0.57 to 1.88)	--

"NRT used in pregnancy for smoking cessation increases smoking cessation rates measured in late pregnancy by approximately 40%. There is evidence, suggesting that when potentially-biased, non-placebo RCTs are excluded from the analyses, NRT is more effective than

Main Study Findings	Author's Conclusions
Secondary outcomes (safety): **NRT vs control** **Outcomes** / **No. of study** / **RR or MD* (95% CI)** / **I^2, %** 1) Miscarriage and spontaneous abortion — 4 — 1.47 (0.45 to 4.77) — 0 2) Stillbirth — 4 — 1.24 (0.54 to 2.84) — 0 3) Mean birthweight (g) — 6 — 100.5* (-20.8 to 222) — 75 4) Low birthweight (<2500 g) — 6 — 0.74 (0.41 to 1.34) — 71 5) Preterm birth (<37 weeks) — 6 — 0.87 (0.67 to 1.14) — 0 6) NICU admission — 4 — 0.90 (0.64 to 1.27) — 0 7) Neonatal death — 4 — 0.66 (0.17 to 2.62) — 0 8) Congenital abnormalities — 2 — 0.73 (0.36 to 1.48) — 0	*placebo. There is no evidence that NRT used for smoking cessation in pregnancy has either positive or negative impacts on birth outcomes. However, evidence from the only trial to have followed up infants after birth, suggests use of NRT promotes healthy development outcomes in infants. Further research evidence on NRT efficacy and safety is needed, ideally from placebo-controlled RCTs which achieve higher adherence rates and which monitor infants' outcomes into childhood. Accruing data suggests that it would be ethical for future RCTs to investigate higher doses of NRT than those tested in the included studies"*[8] p.2

CI = confidence interval; MD = mean difference; NICU = neonatal intensive care unit; No. = number; NRT = nicotine replacement therapy; RCT = randomized controlled trial; RR = relative risk

Table A6: Summary of Findings of Included Primary Studies

Main Study Findings	Author's Conclusions
Bradizza et al., 2017[9]	
Treatment attendance, credibility and satisfaction No significant differences between groups **7-Day point prevalence abstinence rates*** - at pre-treatment: 0% ERT + CBT vs 3% HLS + CBT; OR 0.31 (95% CI 0.01 to 7.77) - at 2-month post-quit date: 23% ERT + CBT vs 0% HLS + CBT; OR 13.51 (95% CI 0.70 to 261.59) - at 4-month post-quit date: 18% ERT + CBT vs 5% HLS + CBT; OR 2.98 (95% CI 0.39 to 22.72) *cotinine-verified **Number of cigarettes smoked per day** - at pre-treatment: 7.5 ERT + CBT vs 7.5 HLS + CBT; OR 0.003 (95% CI -4.68 to 4.69); *p*=1.00 - at 2-month post-quit date: 2.7 ERT + CBT vs 5.8 HLS + CBT; OR 3.11 (95% CI 0.03 to 6.25); *p*=0.05 - at 4-month post-quit date: 2.2 ERT + CBT vs 5.2 HLS + CBT; OR 3.03 (95% CI -0.31 to 6.37); *p*=0.07	*"The development and initial test of the ERT + CBT intervention supports its feasibility and acceptability in this difficult-to-treat population."*[9] p.578
Nanovskaya et al., 2017[10]	
7-Day point prevalence abstinence rates* during treatment: 19% bupropion SR vs 2% placebo (*p*=0.003) *no smoking in the last 7 days, levels of CO in exhaled air <4 ppm, and concentrations of cotinine in	*"Individual smoking cessation counseling along with the twice-daily use of 50 mg bupropion sustained release increased smoking cessation*

Main Study Findings	Author's Conclusions

urine <50 ng/ml

Abstinence rates

at end of treatment: 17% bupropion SR vs 3% placebo (p=0.087)
at end of pregnancy: 10% bupropion SR vs 3% placebo (p=0.328)
during postpartum period: bupropion SR vs placebo (NS)

Percent reduction in number of cigarette consumption per day

at end of treatment: 65% bupropion SR vs 53% placebo (p=0.068)
at end of pregnancy: 66% bupropion SR vs 85% placebo (p=0.665)
during postpartum period: 69% bupropion SR vs 60% placebo (p=0.550)

Birth and delivery outcomes

Outcomes	Bupropion Mean (SD)	Placebo Mean (SD)	*P* value
Birthweight, g	3223 (501)	3111 (543)	0.299
Infant length at birth, cm	50 (2.3)	49 (2.5)	0.250
Head circumference, cm	34.1 (1.22)	33.5 (1.8)	0.265
Apgar score at 1 min	8.3 (1.0)	7.8 (1.6)	0.064
Apgar score at 5 min	9.0 (0.3)	8.8 (0.6)	0.201
Cord blood arterial pH	7.3 (0.06)	7.3 (0.04)	0.541
Cord blood venous pH	7.3 (0.12)	7.3 (0.05)	0.898
Infant length at hospital stay, day	2.4 (2.8)	2.8 (3.1)	0.612
NICU admission, n, %	1 (4%)	3 (11%)	0.611
Gestational age, weeks	38.7 (1.6)	38.2 (1.4)	0.058
Preterm birth <34 weeks, n, %	1 (4%)	1 (3%)	1.0

Maternal outcomes

Outcomes	Bupropion Mean (SD)	Placebo Mean (SD)	*P* value
BMI, kg/m^2	32.9 (9.4)	39.8 (9.6)	0.520
SBP, mmHg	116 (8)	122 (14)	0.464
DBP, mmHg	70 (9)	75 (11)	0.396
Pulse rate, bpm	81 (12)	82 (12)	0.721
Side effects of bupropion, %			
Headache	29	11	0.157
Difficulty sleeping	25	7	0.123
Running nose	17	7	0.397
Dry mouth	38	14	0.308
Anxiety	33	18	0.220

Compliance and retention

Adherence to treatment: 87% bupropion SR vs 82% placebo, p=0.31
Completion of trial: 30% bupropion SR vs 11% placebo, p=0.31

rates and reduced cravings and total nicotine withdrawal symptoms during treatment period. However, there was no significant difference in abstinence rates between groups at the end of medication treatment and at the end of pregnancy, likely because of small sample size."[10] p. 420.e1

Naughton et al., 2017[11]

Abstinence rates (validated)

- From 4 weeks post-randomization until late pregnancy:
  5.42% MiQuit vs 1.96% usual care; OR 2.70 (95% CI 0.93 to 9.35); p=0.064
- 7-day point prevalence abstinence at both 4 weeks post-randomization and late pregnancy:
  3.94% MiQuit vs 0.98% usual care; OR 3.28 (95% CI 0.90 to 17.36); p=0.062

"There was some evidence, although not conclusive, that a text-messaging programme may increase cessation rates in pregnant smokers when provided alongside routine NHS cessation care."[11] p.1238

<table>
<tr><th>Main Study Findings</th><th>Author's Conclusions</th></tr>
<tr><td colspan="2">Althabe et al., 2016[12]</td></tr>
<tr><td>Recall 5As during antenatal care
34% counseling vs 17% control; p=0.001

Continuous smoking during pregnancy
24% counseling vs 22% control; OR 1.16 (95% CI 0.98 to 1.37); p=0.082

Quit smoking during pregnancy
11% counseling vs 8% control; OR 1.29 (95% CI 0.84 to 1.97); p=0.239</td><td>"The intervention showed a moderate effect in increasing the proportion of women who recalled receiving the 5As, with a third of women receiving counselling in more than one visit. However, the frequency of women who smoked until the end of the pregnancy was not significantly reduced by the intervention"[12] p.1083</td></tr>
<tr><td colspan="2">Mejdoubi et al., 2014[13]</td></tr>
<tr><td>Cigarette smoking
<table>
<tr><th></th><th>Control (n=223)</th><th>Intervention (n=237)</th><th>OR (95% CI) or MD* (95% CI)</th><th>P value</th></tr>
<tr><td>Smoking at baseline (16-28 weeks of pregnancy)</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Current smoker, %</td><td>47</td><td>43</td><td>0.7 (0.5 to 1.2)</td><td>NS</td></tr>
<tr><td>Average no. cigarettes smoked per day, n</td><td>8</td><td>7</td><td>1.4* (-3.3 to 0.5)</td><td>NS</td></tr>
<tr><td>Smoking at 32 weeks of pregnancy</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Current smoker, %</td><td>35</td><td>33</td><td>0.9 (0.5 to 1.5)</td><td>NS</td></tr>
<tr><td>Current smoker (LOCF), %</td><td>48</td><td>40</td><td>0.5 (0.3 to 0.9)</td><td>0.03</td></tr>
<tr><td>Average no. cigarettes smoked per day, n</td><td>3</td><td>2</td><td>0.5* (-0.6 to 1.7)</td><td>ns</td></tr>
<tr><td>Smoking at 2 months after birth</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Current smoker, %</td><td>65</td><td>48</td><td>0.5 (0.3 to 1.1)</td><td>0.08</td></tr>
<tr><td>Current smoker (LOCF), %</td><td>62</td><td>49</td><td>0.5 (0.3 to 0.9)</td><td>0.02</td></tr>
<tr><td>Average no. cigarettes smoked per day, n</td><td>8</td><td>4</td><td>4.4* (1.0 to 7.9)</td><td>0.01</td></tr>
<tr><td>Average no. of cigarettes smoked per day in the presence of baby, n</td><td>2</td><td>0</td><td>1.6* (0.2 to 2.1)</td><td>0.03</td></tr>
</table>
Pregnancy outcomes
No significant differences between groups in mean birthweight, mean gestational age, the prevalence of baby with low birth weight, the prevalence of premature babies, and the prevalence of being small for gestational age.

Breastfeeding
Breastfeeding initiation was similar in both groups (OR 1.3; 95% CI 0.7 to 2.4)
Breastfeeding at 6 months post-birth was higher in the intervention group (OR 2.6; 95% CI 1.0 to 6.8)</td><td>"VoorZog (a nurse home visitation intervention) seemed to be effective in reducing cigarette smoking and in increasing breastfeeding duration. No effect was found on pregnancy outcomes."[13] p.688</td></tr>
</table>

bpm = beats per minute; CBT = cognitive behavioral therapy for smoking cessation; CI = confidence interval; DBP = diastolic blood pressure; ERT = emotional regulation treatment; HLS = health and lifestyle intervention; LOCF = last observation carried forward; MD = mean difference; NICU = neonatal intensive care unit; NS = no significant difference; OR = odds ratio; RCT = randomized controlled trial; SBP = systolic blood pressure; SD = standard deviation; SR = sustained release; vs = versus