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Smoking cessation and relapse-prevention interventions tailored for expectant and new fathers: protocol of a systematic review and network meta-analysis

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ABSTRACT

Introduction Exposure of pregnant women and newborns to secondhand smoke (SHS) can lead to adverse maternal and neonatal health outcomes. Among expectant and new fathers, who are the main source of SHS exposure for pregnant women, new mothers and babies, smoking rates remain high. A partner's pregnancy potentially constitutes a critical period where expectant and new fathers are motivated to quit smoking. However, there is no consensus on the optimal form and delivery of smoking cessation and relapse-prevention interventions. We present a systematic review and network meta-analysis protocol that aims to synthesise and evaluate the effectiveness of smoking cessation and relapse-prevention interventions tailored for this population.

Methods and analysis To identify relevant studies, we will conduct a comprehensive search, in English and Chinese, of 10 electronic databases. The review will include randomised and quasi-randomised controlled trials that compare behavioural interventions (tailored and non-tailored) with/without the addition of pharmacotherapy with usual care, a minimal or placebo control for assisting expectant and new fathers to quit smoking and prevent smoking relapse. The primary outcome of interest is the self-reported and/or biochemically verified smoking abstinence at ≥1-month follow-up. Two reviewers will independently screen, select and extract relevant studies, and perform a quality assessment. Disagreements will be resolved by a consensus or third-party adjudication. The Cochrane Risk of Bias tool V.2 will be used to assess the risk of bias in the included studies. We will obtain the results of the systematic review through pooled quantitative analyses using a network meta-analysis. Sensitivity and subgroup analyses will be performed.

Ethics and dissemination Ethical approval is not required for this systematic review of published data. The findings will be disseminated via peer-reviewed publication.

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STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This review, through a network meta-analysis, will compare diverse smoking cessation interventions for expectant and new fathers.
⇒ This review will offer knowledge that can be employed to support clinical practice and develop more effective interventions to maintain smoking abstinence.
⇒ Subgroup analyses will be performed to overcome the possible limitations of combining studies with diverse delivery modes and follow-up durations.

INTRODUCTION

Secondhand smoke (SHS) has adverse effects on the health of both adults and children.[1] SHS-associated pregnancy complications and undesirable birth outcomes include spontaneous abortion, preterm labour, low birth weight, fetal death, sudden infant death syndrome, otitis media, asthma and lower respiratory tract infections.[2–4] Although smoking cessation is crucial, home of non-smoking pregnant women and newborns remains the primary source of SHS exposure for most of this population.[5] In the USA, 36% of pregnant non-smokers had SHS exposure.[6] Moreover, indoor smoking resulted in three-quarters and two-thirds of infants being exposed to SHS in Japan and Indonesia, respectively.[7 8] In China, for 75.1% of 1181 non-smoking pregnant women, the primary source of regular SHS exposure was their spouse who smoked.[9] The high prevalence of SHS exposure-associated diseases indicates an urgent need to promote smoking abstinence among expectant and new fathers to ensure maternal and fetal health.

Although exposure to tobacco smoke harms both pregnant women and unborn children, few expectant fathers are prepared to quit smoking, and a large number of pregnant women are continually exposed to SHS. In a cohort study in the UK, 22.5% of pregnant women were living with a partner who

smoked.[10] In Japan and Canada, approximately 59% and 42% of non-smoking pregnant women, respectively, experience SHS exposure.[11 12] Data from 30 low-income and middle-income countries showed SHS exposure prevalence of 6–>70% among pregnant women, where a smoking partner was the main SHS source.[13] In China, SHS exposure prevalence in pregnant women varied from 39% to 75%.[14] Xu *et al* found that 40% of expectant fathers in five provinces of mainland China continued to smoke during their non-smoking partners' pregnancies.[15] In a study among Chinese expectant fathers, Xia *et al* found that 69.3% of the participants were current smokers and 47.1% did not attempt to quit smoking during their wife's pregnancies.[16] A major reason for expectant fathers to continue smoking may be misperceptions of the adverse effects of SHS and neglectful attitudes toward the impact of smoking, which decrease their motivation to quit.[17] Although some men are aware that they should not smoke near newborns, they are unconcerned about the hazards of gestational SHS,[18] especially as some expectant and new fathers have a misconception that the uterus can protect the fetus from SHS.[17]

Pregnancy and the postpartum period present expectant and new fathers with a golden opportunity to be motivated to quit smoking and accept smoking cessation interventions.[16 18–20] An expectant or new father feels daily life changes associated with fatherhood provide opportunities to establish new routines.[21] Adjusting to a new role may enhance an individual's openness to behavioural health knowledge and interventions.[22] Generally, expectant fathers focus on the health of their pregnant partner and unborn children. Therefore, intervention or information improving their awareness of the hazards of SHS for pregnant women and developing fetuses can potentially rectify pre-existing misconceptions and subsequently promote their attempt to quit smoking.[17] More than half of expectant fathers who smoke express willingness to quit smoking within 30 days after learning about the harmful consequences of SHS exposure for pregnant women, fetuses and newborns.[23] New fathers, to further their image of a 'good father', may be motivated to reduce or quit smoking.[24] Bottorff *et al* interviewed 29 new fathers about how they reduced or quit smoking and found that childbirth may play an essential role in motivating fathers to undertake behavioural change. Those who had quit smoking evinced that their responsibility as a 'good' father for enhancing the health of their children motivated their smoking cessation.[25] Despite the opportunity that a child's birth provides for new fathers to quit smoking,[26] it is hard to maintain smoking abstinence.[27] Numerous studies that have focused on postpartum smoking relapse have neglected the father's perspective in this regard.[27–29] Winickoff *et al* found that over half of expectant fathers who attempted to quit smoking subsequently relapsed.[26] Among new fathers, there is a need to determine relapse, because the smoking behaviour may change after a child's birth.[30] Changes in fatherhood identity and lifestyle often induce stress, which may lead to escape behaviours, including smoking.[31] One study reported a cumulative postpartum relapse rate of up to 78% among fathers.[27] In the English Midlands, less than 20% of new fathers attempted smoking cessation and, among them, 96% subsequently experienced postpartum relapse.[29] The results of previous studies indicate that the effects of smoking cessation during wives' pregnancies may not be sustained in the long run.[27] Therefore, to improve quitting attempts and maintain abstinence, it is important to assess current smoking cessation and relapse-preventive strategies that are targeted at expectant and new fathers.

Common smoking cessation interventions include, but are not limited to, behavioural therapy, which comprises behavioural support, and this is combined with pharmacotherapy. Behavioural support methods include counselling and advice to easily facilitate smoking cessation or a combination of these.[32] Behavioural support, as a method of smoking cessation, can improve quit rates at ≥6 months.[33] When pharmacotherapy was initiated first, behavioural support had less effect on smoking cessation.[32] The most crucial element of non-pharmacological interventions is counselling.[34] Self-help resources and practices, such as yoga, exercise and motivational videos, can increase the smoking abstinence rate.[33] However, neither counselling nor medication decreases the relapse rate.[34] A systematic review of supported abstainers indicated that behavioural therapies that enable the identification of circumstances that confer a high relapse risk and coping strategies are not markedly advantageous for preventing relapse.[34] Moderate evidence suggests that varenicline likely prevents relapse but requires more extended treatment than that of the standard regimen.[34] Thus, the effectiveness of extant interventions varies and the outcome remains uncertain, which may hinder improvements in cessation strategies during this golden period.

Both behavioural and pharmacological therapies increase quitting rates,[33 35 36] and although a few therapies have been tailored to expectant and new fathers, the effects have been limited.[20 37] Two trials have assisted expectant fathers and new fathers to stop smoking, in which couple-based counselling and tailored proactive telephone counselling induced no significant effect.[20 26] In contrast, Stanton *et al* evaluated the effect, among expectant fathers, of a minimal multicomponent smoking cessation intervention that consisted of tailored videos and print information together with restricted access to nicotine replacement therapy (NRT) and reminder devices to promote cessation rates in comparison with simply offering contact information of available smoking cessation services.[30] Nonetheless, there are limited data on smoking cessation among expectant and new fathers to enable the development of effective interventions.[21]

Smoking cessation interventions for expectant and new fathers were inconsistent, possibly because the motivation to quit differs for the general public and this population,

and thus may lead to insignificant intervention effectiveness. For the general public, concern about physical health is the most common reason for smoking cessation.[38 39] Analysis of individual interviews with 20 new fathers showed that young men were heavily influenced by the masculine concept of risk-taking together with physical control, power and endurance.[22] Among expectant and new fathers, smoking has usually not induced chronic diseases because the majority of this population is young, and this may lead to the adoption of neglectful or negative attitudes toward smoking cessation.[17] However, in their journey to fatherhood, expectant and new fathers should pay attention to the health of their partners and infants in addition to their own. A study also revealed that smoking cessation by expectant fathers is related to their awareness of the hazards of SHS to their partners during pregnancy, fetuses and newborns.[26] In becoming fathers, men may be driven to modify their smoking behaviours to fulfil their long-term responsibilities and parenting role as fathers.[24]

Compared with the general public, controlling smoking among expectant and new fathers is a markedly different issue; therefore, the available cessation measures may not be directly applicable to this specific population of expectant or new fathers. Diverse motivations for quitting and conflicting findings indicate that tailored interventions for expectant and new fathers may have different effects from that of general smoking cessation interventions. Two systematic reviews focused on interventions to reduce SHS exposure in pregnant women: the review published in 2014 identified five studies in total, and only one delivered smoking cessation interventions to partners of pregnant women,[40] and the other review published in 2020 identified nine studies, of which only two involved smoking partners.[41] Both systematic reviews focused on interventions to reduce SHS exposure among pregnant women rather than smoking cessation among expectant or new fathers. Additionally, these reviews missed the inclusion of studies of smoking cessation interventions for Chinese expectant fathers that have been developed in recent years. Despite several systematic reviews and meta-analyses of the impact of smoking cessation interventions and their implementation in the general population, the effectiveness of interventions for expectant and new fathers is unclear. Given the characteristics of smoking behaviour among expectant and new fathers as well as the need to seize the teachable moment, it is essential to implement validated, tailored, high-quality measures. Considering the inconsistent results of, and demand for, smoking cessation during the key above-mentioned period, assessment of the efficacy of targeted smoking cessation strategies among expectant and new fathers is essential to identify the most efficient intervention at different follow-up times. This strategy may provide insight that enables the development of optimal and sustainable smoking cessation measures for implementation during the teachable moment and help prevent relapse.[34]

This protocol for a systematic review and meta-analysis is aimed at compiling and comparing the evidence on the effect of smoking cessation and relapse-prevention interventions that aim to promote smoking quitting rates among fathers or to reduce home-based SHS exposure. The study objectives are: (1) to identify and compare the characteristics of the reviewed interventions, and (2) to compare the effectiveness of different interventions at different follow-up times.

METHODS AND ANALYSIS

This protocol will be implemented according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) extension for Network Meta-Analyses (NMAs).[42] The review and meta-analysis protocol was registered in the International Prospective Register of Systematic Reviews (ID number: CRD42022340617). The protocol followed the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols checklist protocol (online supplemental file 1).[43] The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach will be used to grade the quality of evidence under four categories (high, moderate, low and extremely low) to determine the accuracy of the estimated effect size.[44]

Eligibility criteria

The included studies will be fully peer-reviewed publications in English or Chinese (ie, reviews, reports and conference abstracts will be excluded). All other inclusion criteria will follow the Participants, Interventions, Comparators, Outcomes and Study design framework (table 1).[42]

Population

We will include studies with expectant fathers, defined as male partners of pregnant women, or new fathers, defined as male partners of women who have delivered within the preceding 18 months, who are adults and meet the definition of current smokers (having smoked, even a single puff, within the previous 30 days) or recent quitters (having smoked, even a single puff, 1 month before/during this pregnancy/childbirth and have quit smoking for more than 7 days).[45] In this review, smoking refers to smoking combustible tobacco products, smokeless tobacco products and/or alternative products (eg, e-cigarettes).

Interventions

Any intervention will be considered in this review. Given that there may be limited studies on preventing relapse among expectant and new fathers, and the similarity of some methods for smoking cessation and relapse prevention, smoking cessation, in this review, is generally referred to as smoking cessation intervention including or not including relapse-prevention components. We will include all studies that have addressed smoking

Table 1 Summary of PICOS eligibility criteria

	Inclusion criteria
Population	► Adults ► Expectant or new fathers Expectant fathers: male partners of pregnant women New fathers: male partners of women who had delivered within the preceding 18 months ► Current smoker or recent quitter 'Current smoker' is defined as someone who has smoked within the previous 30 days, even if only a single puff was taken 'Recent quitter' is defined as someone who has smoked, even a single puff, in the 1 month before/during this pregnancy/childbirth, and has quit smoking for more than 7 days
Interventions	► Behavioural smoking cessation interventions delivered directly to expectant or new father (eg, advice or counselling delivered to expectant or new fathers) ► Behavioural smoking cessation interventions delivered indirectly to expectant or new fathers (eg, health education of pregnant women targeted to reduce home-based SHS exposure) ► Behavioural smoking cessation interventions combined with pharmacotherapy (eg, nicotine replacement therapy or varenicline)
Comparators	Usual care (eg, brief advice on cessation, self-help resources and an offered brochure), a minimal (eg, enrolment on a waiting list or a self-help cessation) or placebo control (eg, none or attention-matched placebo)
Outcomes	Primary outcome: ► Smoking abstinence rate at 1, 3 and ≥6 months, from baseline, measured by self-report, biochemical validation or both Second outcomes: ► Smoking behaviour-related outcomes: self-reported 7-day point prevalence of abstinence, partner-reported smoking abstinence, smoking reduction, the number of smoking cessation attempts ► SHS-related outcomes: urine/salivary/hair cotinine level, SHS exposure reported by partners, birth outcomes, respiratory problems of children and children's hospitalisation
Study design	Randomised and quasi-randomised controlled trials

SHS, secondhand smoke

cessation or relapse-prevention intervention modules that include sufficient details, such as the timing of intervention, the length or frequency of the interventions, various modes of delivery (face-to-face intervention, online intervention, family-based intervention, etc) and measurement of smoking abstinence at follow-up. Interventions tailored or non-tailored for expectant and/or new fathers, behavioural therapy only or combined with pharmacotherapy (eg, NRT or varenicline) will be considered. Studies that used prescriptions (including varenicline, bupropion and NRT, such as patches or chew) for smoking cessation will be considered if they fulfil the eligibility requirements.

Comparators

To be eligible for inclusion in our study, trials had to compare a tailored smoking cessation intervention with an intervention for the general population or usual care, such as an offered brochure, self-help resources, brief advice on cessation or enrolment on a waiting list.

Outcomes

The smoking abstinence rate at 1, 3 and ≥6 months from baseline will be the primary outcome of this systematic review and NMA.[46] The carbon monoxide level in the expired air or cotinine concentrations (in the saliva, urine and plasma) will be used to verify the validated 7-day point prevalence of abstinence (PPA) at 6 months.[46] If biochemical validation was conducted, the study has to clarify the biomarker used (eg, the level of carbon monoxide to define abstinence or the level of salivary/urine/blood/hair cotinine to define SHS exposure). To determine the average uncontrolled effect size, baseline and post-treatment data for the primary outcome measures will have been gathered. Follow-up data (at 6 and/or 12 months, with or without intermediate measurements) will be used to evaluate the sustainability of the smoking cessation interventions and the relapse rate.[47] Self-reported 7-day PPA, smoking reduction, number of quitting attempts and additional outcomes related to SHS exposure will be also included as secondary outcomes. To evaluate the feasibility of the intervention, the retention and completion rates of the intervention will be evaluated for intervention adherence. To deal with missing data in the included studies, we will consider participants lost to follow-up as smokers.[46]

Study design

Randomised controlled trials (RCTs) and quasi-RCTs will be considered. Only studies with at least one control group or intervention will be included. Observational studies, reviews, opinions and case reports will be excluded from the analysis. Additionally, when there are more than two

arms to an intervention, we will select only those that match our eligibility requirements.

Data sources and search strategy

We will search for all relevant articles published before 1 July 2023, without restrictions on the start date. Relevant articles will be searched using PubMed, PsycINFO, ScienceDirect, Embase, the Cumulative Index to Nursing and Allied Health Literature (CINAHL Plus), the British Nursing Index, the China National Knowledge Infrastructure (CNKI) and Wanfang Database. Moreover, we will search ClinicalTrials.gov, ChiCTR, Cochrane Central Register of Controlled Trials, Google Scholar and OpenGrey for grey literature, and the references from the included papers will be manually reviewed.

To conduct an extensive literature search, keywords, such as smoking cessation, smoking relapse and expectant father, will be searched using a Boolean strategy (online supplemental file 2). Using the same strategies, the exact keywords in Chinese will be searched in the CNKI and Wanfang Databases. Since several online databases have unique search criteria and restrictions (eg, Medical Subject Heading terms used in PubMed are inappropriate in other databases such as PsycINFO), the fundamental search strategy will be adjusted according to each database's unique search parameters.

After the initial search round, a snowball manual search will be conducted by reviewing relevant articles, systematic reviews and research protocols for RCTs and ancestry.

Data collection

EndNote V.X9 bibliographical software[48] will be used to import the search results for screening, data extraction and removal of all duplicates. Two reviewers will independently screen titles and abstracts according to the eligibility criteria. Full texts of the relevant papers will be reviewed independently by two reviewers to determine conformance with the eligibility requirements. In case of incomplete information, authors will be contacted for clarifications and, if there is no response, the study will be excluded. Discussions between the two investigators or consultation with a more experienced researcher will be used to settle disagreements. Two reviewers will independently extract data on the characteristics of each eligible study and input these data in an Excel sheet. The characteristics will include articles' general data (country, sample size), population (expectant or new father, mean age of the children or gestational week), intervention and comparison (study design, type of intervention and comparison, tailored or not, use of any type of pharmacotherapy), outcomes (smoking cessation-related, SHS exposure-related or health-related outcomes) and follow-up time. A flow diagram is presented in figure 1.

Risk of bias assessment and study quality

Two reviewers will undertake quality appraisal and risk of bias separately using the Cochrane Risk of Bias (RoB) tool V.2.[49] Trial quality will be assessed based on selection, performance, detection, attrition, reporting and other biases. Studies that only used self-report abstinence to

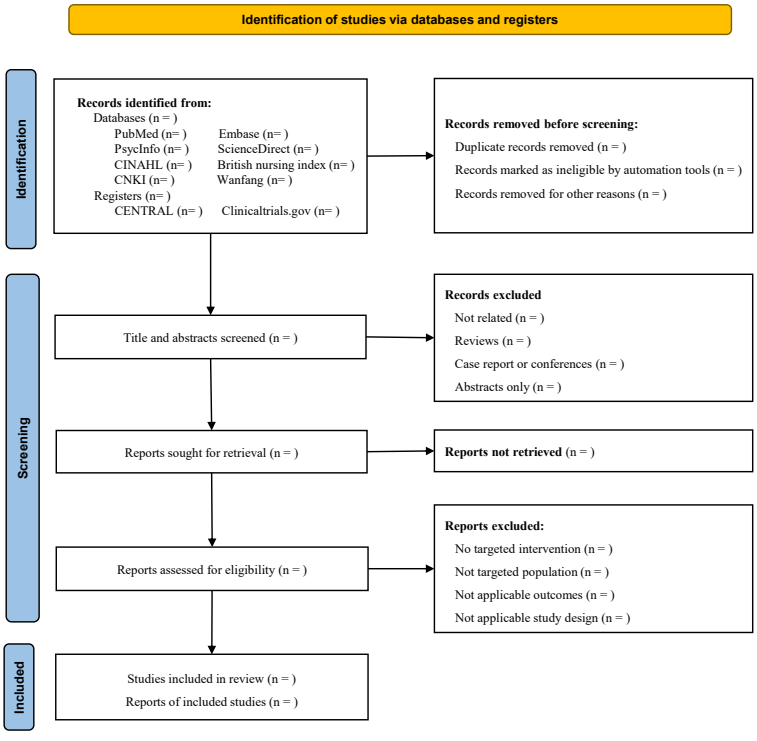

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 flow diagram for literature selection.

determine smoking status will be considered to have a high risk of detection bias. Two independent reviewers will conduct two separate assessments of the risk of bias, which will then be classified as high, low or unclear, if the data are ambiguous or insufficient. The paper's authors will be contacted for any incomplete information. A third reviewer will resolve disagreements.

The inter-rater reliability of the Cochrane RoB tool for RCTs will be examined.[50]

Statistical analysis

Data will be analysed using STATA (V.16.1) and R statistical computing and graphics programming language (V.4.2.1). Using a small sample of included papers, two reviewers will test the data extraction forms and make necessary revisions. The statistical results from every study will then be individually entered into an Excel spreadsheet and cross-checked.

Heterogeneity

Forest plots, Q statistics, p values, I^2 index values and their 95% CIs will be used to measure heterogeneity based on the percentages of the I^2 index values as follows: no heterogeneity (0–40%), modest heterogeneity (30–60%), considerable heterogeneity (50–90%) and significant heterogeneity (75–100%).[49] To address heterogeneity, after verification of data accuracy, we will consider using a random-effects model. For further exploration, subgroup and sensitivity analyses will be conducted.

Transitivity

An NMA can be conducted if the hypothesis of transitivity can be proven. Transitivity can be assessed by analysing the distribution of effect modifiers across various comparisons.[51] We will compile a table of the important characteristics of the intervention and population that could potentially modify the intervention effect. When all pairwise comparisons have balanced distributions of potential impact modifiers, such as study-level and individual-level variables, transitivity is maintained.[52 53]

Effect size

For categorical variables, the OR and 95% CI will be used to evaluate the magnitude of the effects, whereas for continuous variables (eg, number of quitting attempts), the standardised mean difference (SMD) and 95% CI will be used. An OR greater than 1 or an SMD greater than 0 will be interpreted as more effective when comparing the intervention group with the control group. Small, medium and high effect sizes will be represented by OR values of 1.68, 3.47 and 6.71, respectively.[54] Additionally, small, medium and large effect sizes will be defined by SMD values of 0.2–0.5, 0.5–0.8 and >0.8.[55]

Network meta-analysis

Unlike conventional pairwise meta-analysis, NMA enables simultaneous calculation of numerous comparisons. The Bayesian Markov chain Monte Carlo framework for NMA can combine direct and indirect treatment comparison results.[56] Smoking abstinence rates can be considered as time-related event outcome effect sizes. Analyses of dichotomous data will be available as long as outcome-related events are observed at fixed time points. Based on the type of data available, we will choose data-combining methods, including Peto's and the ordinary inverse variance methods.[49] For each intervention group in each trial, we will model the binary outcomes, and relationships between the ORs across studies will be described to facilitate various comparisons.[57] For each particular set of interventions, this strategy integrates both direct and indirect evidence. To determine significance, we will use $p<0.05$ and the 95% CI (depending on whether the CI contains the null value).[58] As in conventional pairwise meta-analysis, both the fixed-effects and random-effects approaches can be used in NMA. Effect size estimates in NMA are expected to differ not only between studies but also between comparisons (direct and indirect).[59] By calculating the OR for each intervention relative to a fictitious, widely used control group and subsequently measuring the percentage of rounds where each intervention had the largest OR, the second largest OR and so forth, we can determine the likelihood of each intervention being the most effective regimen, the second greatest regimen, the greatest best regimen and so forth. We will order interventions based on their efficacy.

We will examine the NMA consistency to ensure that direct and indirect evidence based on the same comparisons do not differ coincidentally. The ORs for indirect against direct proof to estimate consistency when it was possible to produce indirect estimates with a single universal comparison will be obtained. The disparity between direct and indirect evidence will be identified as inconsistency, with a 95% CI omitting 1. Whenever possible, the NMA results will be presented using a network diagram. On the other hand, qualitative analyses and quantitative meta-analysis will be conducted if the NMA is not applicable.

Subgroup analysis

Subgroup analyses will be conducted to investigate study heterogeneity and explore potential moderators that could offer guidance for future smoking cessation intervention designs. The following study characteristics may be used to conduct subgroup analysis: nation, features of participants (eg, expectant or new father, nicotine dependence level at baseline), features of interventions (eg, provider, setting, intensity, length, framework and delivery mode of the intervention), features of comparisons (eg, usual care or waiting list) and features of outcomes (self-reported abstinence only or combined with biomedical validation, time point of outcome at 1, 3 and ≥6 months).

Sensitivity analysis

To address the heterogeneity between the trials and test the robustness of the findings, we will perform a sensitivity analysis whenever possible by using the following methods: (1) change the inclusion criteria of study types,

interventions or outcomes; (2) include or exclude those studies with uncertain conformance with the inclusion criteria.[49] When different methods are used for sensitivity analysis, the heterogeneity and combined results do not change significantly, indicating that the sensitivity is low and the results are relatively stable and credible. Otherwise, the results and conclusions will be interpreted with caution.

Patient and public involvement

Patients or members of the public will not be involved directly in this protocol.

DISCUSSION

SHS exposure during pregnancy may cause serious complications for pregnant women and poor neonatal outcomes. Despite constituting a significant SHS source for pregnant women, most expectant fathers do not quit smoking during their partners' pregnancies, and the smoking rate increases even after childbirth.[5 60] The effectiveness of current interventions for expectant and new fathers in quitting smoking varies, and the quality of these trials has not yet been evaluated. Considering the differences in smoking characteristics between expectant fathers and the general population, it is essential to conduct a systematic review and NMA to assess the efficacy of tailored smoking cessation strategies and the intervention's effectiveness at different follow-up times. The results of this study will help identify more effective and optimal quitting strategies that are specialised for expectant and new fathers in order to protect pregnant women and newborns from SHS exposure.

Ethics and dissemination

Using already available trial data, this study is being performed by using NMA techniques. As data from primary sources will not be included, ethical problems are not considered. This study will compare the validity of smoking cessation interventions in expectant and new fathers, demonstrating data on the interventions that have the strongest correlation with results to promote quitting rates and lower relapse rates. Our findings will help formalise the most effective and regulated smoking cessation interventions targeting expectant and new fathers. Furthermore, the findings may support healthcare providers in considering the features of expectant and new fathers and their differences with regard to the general smoking population or possibly facilitate the modification of existing programmes to more efficiently enhance smoking cessation.

There will be extensive local, national and international dissemination of the review findings. The manuscript will be presented to a top peer-reviewed publication in this field, and the study's reporting will follow the PRISMA extension statement on reporting systematic reviews that combine NMAs of healthcare treatments.[42] In accordance with the guidelines in the GRADE handbook, the GRADE assessment for proof and recommendation quality will be performed when we report our study's findings.[44] If possible, the results will be shared at scholarly conferences.

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