Predictors of smoking cessation during pregnancy: a systematic review and meta-analysis

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Abstract

Aim: To conduct a comprehensive systematic review and meta-analysis for a wide range of characteristics associated with smoking cessation during pregnancy and to categorise these characteristics.

Methods: Electronic searches of the bibliographic databases of PubMed, EMBASE, PsycINFO, Elsevier, Scopus and ISI Web of Science were conducted to April 2017. All studies reporting factors associated with smoking cessation or continuing smoking during pregnancy were included and systematically reviewed, irrespective of study design. The Newcastle Ottawa Quality Assessment Scale was used to assess the study quality. The DerSimonian and Laird random effects model was used to conduct meta-analyses, and where effect estimates were reported for factors included in at least three studies.

Results: Fifty-four studies including 505,584 women globally who smoked before pregnancy, 15 clinical trials and 40 observational studies, were included in the review and 36 (65.5%) were considered to be of high quality. This review identified 11 socio-demographic, seven socially related, 19 smoking behaviour related, five pregnancy related, six health related and six psychological factors that were significantly associated with smoking cessation during pregnancy. The most frequently observed significant factors associated with cessation were: higher level of education, higher socio-economic status, overseas maternal birth, medicaid coverage or private insurance, living with partner or married, partner/other members of the household do not smoke, lower heaviness of smoking index score, lower baseline cotinine level, low exposure to second hand smoking, did not drink alcohol before and/or during pregnancy, primiparity, planned breastfeeding, perceived adequate pre-natal care, no depression, and low stress during pregnancy.

Conclusion: Many characteristics are associated with smoking cessation during pregnancy, falling into every category of socio-demographics, relationship and social factors, smoking behaviour, pregnancy related factors, health status and psychological factors.

Key words: Smoking, cessation, pregnancy, predictors, determinants, systematic review, meta-analysis, clinical trials, observational studies, interventions.

INTRODUCTION

Smoking in pregnancy is a serious public health problem and one of the main preventable causes of pregnancy-related morbidity and death. Smoking is associated with adverse pregnancy and birth outcomes, including miscarriage, stillbirth, prematurity, low birth weight, intrauterine growth restriction, congenital abnormalities, and neonatal or sudden infant death [1-5]. Smoking also presents immediate risks for the mother, including placental abruption [6], as well as the longer-term risks reported for smokers in general [7].

In high income countries, the prevalence of smoking in pregnancy is estimated to be between 10% and 26% and is decreasing rapidly in many of these countries [8-12]; whereas, in low and middle-income countries the prevalence is between 15% and 37% and is not declining in some of these countries [13-16]. Smoking cessation during pregnancy improves maternal and birth outcomes [17], yet only about 25% of pregnant smokers stop for at least part of their pregnancy and half to two thirds of them return to smoking after giving birth [18]. Regular sessions of face-to-face behavioural support is the main intervention demonstrated to be effective as an aid to smoking cessation during pregnancy [17], which can be enhanced when supplemented with financial incentives [19].

To promote successful maternal smoking cessation during pregnancy, clinicians and researchers need to identify factors that facilitate or inhibit the quitting process. These factors can then be targeted directly, by smoking cessation interventions, or indirectly by promoting cessation interventions to subgroups of women who are less likely to succeed at quitting [20, 21]. For example, this might include women from socially deprived groups, those with higher levels of cigarette dependence, and women living with a partner who smokes [22, 23].

The most recent systematic review of predictors of smoking cessation during pregnancy was conducted in 2010 [23] and it considered 19 studies which identified socio-demographic/economic, relationship, psychological, pregnancy and health related factors as predictors. However, this review was limited to studies in high-income countries published between 1997 and 2008, and excluded intervention studies. There have been a large number of studies published since this previous review was undertaken. Furthermore, additional factors have since been examined as predictors of cessation during pregnancy,

such as smoking dependence variables (e.g., Fagerström Test for Cigarette Dependence and urges to smoke), as well as variables related to pregnancy, such as adequate pre-natal care, planned breast feeding and planned pregnancy. Moreover, a meta-analysis has not been previously conducted on this topic.

This comprehensive systematic review was conducted to examine a wide range of factors that may be associated with smoking cessation during pregnancy. Further aims include conducting meta-analysis for the frequently reported factors and classifying factors associated with cessation into sub-categories, including socio-demographic/economic, relationship and social activity, smoking, psychological, pregnancy and health related factors, to help clinicians to target interventions towards different sub-groups of the pregnant population or to inform the development of interventions.

METHODS

This review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [24].

Strategies for searching the literature

We developed a search strategy and conducted the literature searches in the bibliographic databases of PubMed, EMBASE, PsycINFO, Elsevier, Scopus and ISI Web of Science. The search was designed to capture all studies reporting factors (predictors) associated with smoking cessation during pregnancy. The search terms were: “predictors”, “factors”, “determinants”, “characteristics”, “component”, “psychological”, “demographic” and “pregnancy or pregnant” combined with “smoking cessation” or “smoking or smoker”. Based on the combinations of these terms, several searches were conducted in the above-mentioned databases. For illustration, some of the search combinations were: “psychological predictors smoking cessation pregnancy”, “factors smoking cessation pregnancy”, “predictors smoking cessation pregnancy, “characteristics pregnant smokers”. We examined all the studies included in the previous review [23]. There was no restriction on language and the search was completed in April 2017.

Inclusion and exclusion criteria

Smoking cessation or continued smoking during pregnancy were considered as the analyses outcomes. This included bio-chemically validated and non-validated self-reported smoking cessation, and covered both planned and spontaneous quit attempts [25], at any time during pregnancy. Studies were included

which statistically examined the association of smoking cessation or continuing smoking during pregnancy with other factors, irrespective of study design. If a study was designed to evaluate an intervention, such as Nicotine Replacement Therapy, we did not report the intervention as a predictor. We excluded those studies which include non-smoking women before pregnancy, women who had stopped smoking prior to pregnancy, studies reporting predictors of postpartum smoking cessation, and qualitative studies (i.e., narrative and case reports). Studies identified by search strategies were screened for eligibility; initially on the basis of title and abstract, and then reading the full text of the remaining studies. One reviewer (M.R.) screened all studies for inclusion with one-third also screened independently by another reviewer (M.U.), with 100% agreement. A hand-search of the reference lists of included studies was also conducted. Corresponding authors were contacted for additional information where necessary.

Data extraction

The following data was extracted from each study by M.R. and was verified by M.U: first author name, year and location of publication, study aim and design, participant characteristics, including age and smoking behaviours, sample size and smoking cessation rate, main outcome measure, biochemical validation, whether all smokers made a quit attempt, variables examined as predictors, statistical methods used for the analysis, and statistically significant predictors reported, and effect estimates for the association (e.g., ORs and 95% confidence intervals CI).

To aid the description, those factors found to be significantly associated with smoking cessation were categorised by grouping thematically similar factors across the included papers. The categories were decided through reference to categories used in a review by Schneider and colleagues [23] and through discussion involving all authors. Potential predictors were grouped into the following domains: socio-demographic/economic, relationship, smoking/substance misuse, psychological, pregnancy and health related factors. They were also categorised according to the nature of association with smoking cessation (i.e., increasing or decreasing odds ratio).

Meta-analyses

A large number of factors significantly associated with smoking cessation during pregnancy are identified in this review. However, to pool the effect estimates in a way that will yield valuable information about

the direction and size of effects and to quantify heterogeneity among the included studies, we conducted meta-analyses for those factors whose effect estimates were available from at least three studies. We extracted the effect estimates (95% confidence intervals), reported as odds ratios (OR: majority), relative risk ratios (RR: one study [69]) or prevalence ratios (PR: one study [21]). If an effect estimate was not reported, an unadjusted OR and 95% confidence interval (95% CI) was estimated from the available data. To ensure consistency of the effect estimates for meta-analysis, for some of the studies, the effect estimates were transformed such that the appropriate reference category was used with smoking cessation as the outcome. For example, for the meta-analysis of older maternal age as a categorical predictor, we extracted effect estimate (ORs) for the oldest versus the youngest age category. If a study reported an effect estimate for the youngest age category versus oldest age category, we transformed the OR (95% CI) by taking the multiplicative inverse. Similarly, if a study reported OR (95% CI) for continuing smoking versus quitting, we used the multiplicative inverse to compute OR (95% CI) for quitting versus continuing smoking. Assuming heterogeneity of effects, we used DerSimonian and Laird [26] random effects model for the meta-analyses to compute pooled effect estimates and a heterogeneity index I^2. The meta-analyses results were reported as pooled OR (95% CI), along with I^2 and p-values.

Quality assessment

The included studies were randomised controlled trials (RCTs) and observational (cohort and cross-sectional). To assess study quality, we used the Newcastle Ottawa Quality Assessment Scale (NOQAS) developed for cohort studies [27] and the modified version of the (NOQAS) developed for cross-sectional studies [28]. In the modified version of the scale, criteria for the “ascertainment of exposure” was not applicable in this review, therefore we used the original criteria as given in the NOQAS for cohort studies. For predictors’ analyses, the overall sample of the RCT had been used as for observational cohorts; therefore, we assessed the quality of RCTs using the cohort studies scale of NOQAS. The maximum possible score of NOQAS was 9 and we used a standard cut-off of 7 to identify studies with high quality methodology. Studies were included in the review irrespective of their rating of quality. Quality assessment was conducted by two independent reviewers (M.R and S.L), who discussed any discrepancies until agreement was met.

RESULTS

The initial search returned more than ten thousand hits; on the basis of the title or abstracts this was reduced to 91 studies and, after reading the papers, 55 studies (40 observational and 15 RCTs) were included in this review (see Figure 1). The characteristics of these studies, including a summary of the results of the predictors' analysis, are presented in supplementary table S1.

Characteristics of the included studies

Design

Of the 40 observational studies, 19 were cross-sectional [21, 51-53, 55-57, 59, 61-63, 66, 73, 75, 77, 79-81, 82] and 21 were cohort studies [44-50, 54, 58, 60, 64, 65, 67-72, 74, 76, 78]. Fifteen studies used secondary data from RCTs [29-43].

Study location

Of the observational studies, 12 were from North America (USA=11, Canada=1), 19 were European (multinational=2, UK=2, France=1, Denmark=1, Italy=1, Netherland=2, Norway=4, Serbia=1 and Spain=5), five were from Asia (Japan=2, Lebanon=1, Taiwan=1 and Israel=1) and four were from Australasia (Australian=3, New Zealand=1). Twelve of the 15 RCTs were from the USA, two were from the UK and one from France.

Participants

Among the 55 included studies, the combined total number of women who smoked before pregnancy was 505,584. All the studies recruited participants who were at least 16 years of age and the mean age of the women ranged from 16 to 50 years. Of the seventeen studies (31.5%) that reported quit attempts, all or most of the participants made a quit attempt [21, 29, 30, 33, 34, 35, 36, 37, 39, 41, 42, 43, 49, 75, 81], whilst two other studies reported quit attempts for only 17% [32] and 30% [80] of the participants.

Outcome of biochemical validation

Sixteen studies, three observational [44, 52, 71] and thirteen RCTs [29, 31-37, 39-43], reported predictors of biochemically validated smoking abstinence in pregnancy, using salivary or urine cotinine and/or expired carbon monoxide (CO) or urine thiocyanate assays. Three of the observational studies [52, 62, 63]

and two of the RCTs [40, 43] reported predictors of spontaneous quitting during pregnancy without biochemical validation.

Sample size

Thirty of the observational studies and ten of the RCTs had large sample sizes (>300) to detect small-moderate effect sizes. These ranged from N=303 to N=231,143 for observational studies and N=316 to N=957 for the RCTs. Ten of the observational studies and five of the RCTs had small sample sizes (range N=35 to N=226) [44, 48, 52, 53, 55, 56, 58, 66, 70, 75] and (range N=81 to N=289) [30, 33, 35, 36, 40], respectively, which were likely to detect only large effect sizes. Of the 13 trials with biochemical validation, nine were sufficiently powered (range N= 316 to N=957) to detect small-moderate effect sizes for predictors of abstinence [29, 31, 32, 34, 37, 39, 41-43].

Quality Assessment

The median Newcastle-Ottawa Quality Assessment Scale [27, 28] score was 7.0 (range 5–9) for cohort studies (including RCTs) and 6.6 (range 4–8) for cross-sectional studies (see supplementary tables S2 and S3). Of the 55 included studies, 36 (65.5%) were considered to be of high quality (cohort: 29, 31, 32, 34, 36. 37, 39, 41, 42, 45-47, 49, 50, 54, 60, 64, 65, 67, 69, 72, 74, 76, 78; cross-sectional: 21, 51, 57, 61-63, 73, 77, 79-82). Nineteen (34.5%) were deemed to be of low quality. The main reasons for lower quality were non-representativeness of the underlying population, non-validation of self-reported outcome, low sample size or limited adjustment for potential confounders in the statistical analysis.

Smoking cessation rates

Smoking cessation rates reported in the 40 observational studies ranged from 4.0% to 76.2% and from 4.3% to 66.0% in the RCTs.

Analyses techniques

For the majority of the included studies, statistical analyses to assess the associations were performed using simple and multiple logistic regression, or mixed effect logistic models, with smoking status during pregnancy as the dependent variable and other factors as independent variables. However, it is worth mentioning that the outcome definition is very heterogeneous (see column 4 in supplementary Table S1). Moreover, four of the RCTs [29, 30, 33, 34] and five of the observational studies [53, 56, 59, 66, 75] did

not report adjusting for important potential confounders such as age, parity, cigarette dependence, or used analyses other than logistic or mixed effect logistic regression. In addition, seven of the RCTs did not report adjusting for the effect of intervention [30, 32-34, 38, 40, 43].

Predictors of smoking cessation

Fifty-four factors significantly associated with smoking cessation are presented in Table 1 and the forest plots are presented in supplementary Figure S1. When we repeated the synthesis for studies where most or all participants made a quit attempt, similar factors were identified, and in particular there were significantly reported factors of socio-demographics, relationship and social activity, smoking behaviour, pregnancy, health status, and psychological factors. No meaningful differences of predictors were identified in studies that used biochemical validation compared with those that did not.

In the following sections, the statistically significant factors are classified into sub-groups with a narrative description of the findings.

Socio-demographic factors

The socio-demographic factors that were significantly associated with higher likelihood of smoking cessation during pregnancy include older maternal age [21,37, 54, 64, 68, 67, 74], ethnicity - non-white [50] non-Puerto Rican Hispanic [61, 69] and non-aboriginal [74, 67], overseas maternal birth [61, 67, 74, 79], higher level of maternal education [21, 31, 32, 34, 40, 41, 43, 47, 49, 51, 54, 55, 60, 63, 64, 68, 69, 71, 76, 77, 80, 82] or paternal education [49], higher income level [21, 48, 67, 82], currently employed women [70], and private medicaid insurance [38, 40, 47, 51, 74]. In contrast, other studies found older age [38, 47, 50, 51, 66, 69, 76, 82] to be associated with a lower likelihood of smoking cessation during pregnancy.

Relationship and social activity factors

Women were more likely to quit during pregnancy if they were married or living with a partner [43, 51, 54, 64, 65, 69, 71, 77], were housewives [77], and had support from partner and/or others [46]. Women were less likely to quit if they had a partner or household member who smoked [21, 38, 44, 46, 59, 62, 70, 71, 72, 73,75, 76, 78, 79, 82] or had exposure to second-hand/environmental smoking [32, 42, 44, 63, 71], had a poor maternal childhood, defined as brought up without father being around or father’s employment

status was unknown to her, or had a poor current circumstances, which is defined as becoming a mother at a younger age and currently not cohabiting [60].

Smoking or substance use related factors

Smoking related variables that significantly predicted lower odds of cessation in pregnancy included: higher cigarette consumption before pregnancy as a categorical variable [32, 34, 36, 39, 40, 44, 45, 47,48, 51, 54, 55, 56, 58, 61, 62, 63, 65, 66, 68, 69, 72, 73, 80, 82] and as a continuous variable [37, 43, 76], higher baseline cotinine level [31, 41, 42] or expired CO level [39], higher Fagerstrom Test of Cigarette Dependence score [39], higher scores for Heaviness of Smoking Index [36, 39, 59] or non-Heaviness of Smoking Index [39], higher ratings of urges to smoke [39, 59] or withdrawal symptoms [59], if women reported shorter time to smoke their first cigarette on awaking [37,36, 38], younger age at the onset of smoking [43, 78] and consumption of more coffee during pregnancy [72]. Women were more likely to quit if they: had smoked for a shorter duration [42, 48], did not smoke their first cigarette within 30 minutes of awaking [37,36, 38], maintaining complete abstinence during the initial two weeks of quit attempt in early pregnancy [35], had a pre-pregnancy/prior quit attempt [34, 36], interaction of age and duration of smoking (i.e., younger (18-24 years) women who smoked for shorter duration (< 10 years)) [81], used marijuana before pregnancy [61], did not drink alcohol before and/or during pregnancy [47, 49, 58, 82], and interaction of delayed discounting and smoking rate at baseline (i.e., those who had delayed discounting of spontaneous quit and lower smoking rate at baseline) [43].

Pregnancy related factors

Pregnancy related factors found to be significantly associated with a higher rate of smoking cessation during pregnancy were: primiparity (i.e., women with no previous pregnancy) [33, 44, 45, 47, 48, 49, 51, 52, 60, 61, 63, 65, 67, 70, 71, 73, 74, 75, 77, 78, 79, 82], perceiving to have received adequate prenatal care [48, 67, 69, 73, 74, 80], having planned breast feeding [50,58, 69, 82], having had a prior pre-term birth [69], and having had planned pregnancy [77, 79].

Health related factors

The health related factors that were significantly associated with higher rates of smoking cessation were: severe nausea [44, 70], family history of diabetes [61], use of folic acid [77], and had a known higher risk

of foetal harm [59]. Women were less likely to quit who had short sleep duration [63], and were holders of a community services card (a healthcare subsidy for low-income earners) [70].

Psychological factors

Finally, the psychological predictors that were reported to be significantly associated with lower likelihood of smoking cessation were: higher levels of anxiety [57] or stress [34, 43, 57, 59, 61], and domestic violence [57]. Women were more likely to quit during pregnancy if they had no depression [30, 31, 40, 52], had higher self-efficacy for quitting [32, 37, 42, 53] or readiness to quit [52], or held a stronger belief that smoking will harm their baby [43].

Meta-analyses results

For eighteen of the factors, which have been reported by at least three studies and have effect estimates available, meta-analysis were conducted. For all except age, the pooled effect estimates were significant statistically. The number of studies included in the meta-analysis, direction and sizes of effects (ORs , 95% CI) were as follow: older maternal age (categorical, 11 studies: 0.96 (0.72-1.28) and (continuous, 4: 0.98 (0.95-1.02)), overseas maternal birth (4: 2.00 (1.40-2.84)), higher level of maternal education (20: 2.16 (1.80-2.59)), higher income level (3: 1.97 (1.20-3.24)), private medicaid insurance (5: 1.54 (1.28-1.85), living with partner/married (7: 1.49 (1.38-1.61)), partner or household member smokes (14: 0.42 (0.35-0.50)), higher exposure to second-hand smoking (3: 0.45 (0.20-1.02)), higher level of Heaviness of Smoking Index (3: 0.45 (0.27-0.77)), higher pre-pregnancy cigarette consumption (categorical, 20: 0.28 (0.22-0.35) and continuous, 3: 0.57 (0.38-0.85)), higher baseline cotinine level (3: 0.78 (0.64-0.94)), pre-pregnancy lower time to first cigarette on waking (3: 0.37 (0.23-0.59)), did not drink alcohol before and/or during pregnancy (4: 2.03 (1.47-2.80)), primiparity (18: 1.85 (1.68-2.05)), women who were perceived to have adequate prenatal care (5: 1.74 (1.38-2.19)), planned breastfeeding (4: 1.99 (1.94-2.05)), women not having depression (3: 2.65 (1.62-4.30)) or having stresses (3: 0.58 (0.44-0.77)) during pregnancy, (Table 1 and Figure 1S).

Sources of heterogeneity

In the meta-analyses, the heterogeneity index I^2 ranged from 0% to 98.6%; it was very high (≥75%) for ten of the factors (e.g., I^2 for categorical age is 96.0% and for continuous age is 88.9%, $p<0.001$), and

moderate (50%≤ I^2 <75%) for four factors [97]. For no alcohol use before and/or during pregnancy, planned breastfeeding, not having depression or having stress during pregnancy, there was no heterogeneity (I^2=0%); however, meta-analyses for the latter two factors exclude effect estimates from some of the studies (Table 1 and Figure S1). Heterogeneity among the studies may be due to the design (i.e., RCT, observational cohort and cross-sectional), the use of different analytical techniques, outcome definition, differences in how the predictors (exposure) were measured or analysed in different studies, rates of smoking cessation, time of outcome assessment during pregnancy, study follow-up period and gestational age at baseline.

DISCUSSION

We extracted a wide range of factors that are associated with smoking cessation during pregnancy from 55 studies including over a half a million women who smoked before pregnancy. The observed significant predictors of cessation were: higher socio-economic status (i.e., higher level of maternal education, higher income level or private medicaid insurance), overseas maternal birth, living with partner or married, lower exposure to passive smoking (i.e., partner/other members of the household do not smoke or low exposure to second hand smoking), low cigarette dependence(i.e., pre-pregnancy cigarettes consumption, lower time to first cigarette on waking, low baseline cotinine or heaviness of smoking index), low exposure to second hand smoking, not drinking alcohol before and/or during pregnancy, primiparity, perceived adequate pre-natal care, planned breast feeding, good mental health during pregnancy(i.e., no depression or stress), and higher levels of self-efficacy for quitting.

The findings have implications for the design of smoking cessation interventions and for public health policy. First, our findings, especially regarding socio-demographic and pregnancy related factors, can help identify and prioritise women who are at increased risk of failing to quit or relapsing. This might include women who are of lower education, lower socio-economic status, multiparous and single. Secondly, some characteristics are likely to have a more direct impact on smoking cessation and might be most appropriate for including as intervention components. For example, high cigarette dependence, having a partner who smokes and low levels of self-efficacy for quitting, can be targeted, respectively, by pharmaceutical

interventions [84], behavioural support that attempts to boost self-efficacy [90], and couple-focused interventions to help partners to quit [85-87] where probably the most work is needed.

There are also characteristics that are likely to have a less direct impact on cessation, but that can still inform interventions. For example, more work is needed on depression focussed interventions [83] and interventions providing encouragement and incentives for breastfeeding [88, 89].

There are some similarities and some difference between the factors associated with smoking cessation observed in this review, and those reported for the general population of smokers. Factors which are also associated with cessation in the general population include higher socio-economic status, low cigarette dependence, and higher levels of self-efficacy [92]. Whereas factors reported here, but not found for smokers in general, include marital status, no use of alcohol, good mental health, and low exposure to second-hand smoke. Thus, while targeting and developing interventions for pregnant smokers there are several additional factors, including pregnancy related factors, that needed to be considered.

Compared with a previous review of the predictors of smoking cessation during pregnancy [23], we identified a broader set of predictors and included a larger number of studies based on up to date searches using robust review procedures. Also, we included studies from high-income countries globally and sought to include studies from low-middle income countries (LMICs), but identified only two studies from LMICs. Furthermore, a major limitation in previous reviews is the lack of included studies using biochemical confirmation of self-reported smoking cessation and without such validation it is unclear what proportion of participants have falsified their smoking status. In our review, we included 15 studies that used data from RCTs, 13 of which used biochemical validation, and three of the observational studies also used biochemical validation. A further strength of our review compared with previous reviews is that we included a thorough study quality assessment using established scales [27, 28].

A limitation with the literature reviewed is that the majority of studies are observational, used varied definitions for smoking cessation and had varying sample sizes. Some of the studies did not specifically seek to identify the predictors of smoking cessation but reported them while evaluating the effect of an intervention. A further limitation with the findings is that the majority of the studies either did not report whether all participants made a quit attempt or reported that only some made an attempt. These studies

combined those who actively attempted to quit with those who did not. This may have distorted the findings, as a review of predictors of smoking behaviour in the general population of smokers identified that while many factors predict making a quit attempt, very few factors predict abstinence when only including those who actually made a quit attempt [92]. A further limitation was the quality of the studies included. On the basis of our quality assessment, 19 (35%) of the studies were considered to be of low quality due to low representativeness, low statistical power, design, analyses and no adequate follow ups; however, we have highlighted the findings separately for the high quality studies. It is worth acknowledging that NOQAS itself has known limitations, such as it often does not inform the evidence synthesis process, particularly for systematic reviews of non-randomised studies, including sensitivity analysis, narrative assessment and restricting the synthesis to studies at a lower risk of bias, which have been discussed elsewhere in some detail [94, 95, 96]. However, NOQAS is a widely used tool for quality assessment in systematic reviews and we assessed the quality using NOQAS only and did not exclude any studies based on it.

This is the first study to conduct meta-analysis for a range of predictors of cessation in pregnancy. Meta-analysis was conducted only for factors with effect estimates reported by at least three studies, and we could not include all estimates as the appropriate data was not always available. These analyses yielded important information about the strength of association and the amount of heterogeneity between studies. For example, when the effect estimates for maternal older age were pooled, no significant effect was observed statistically, and there was high heterogeneity in effect estimates among the studies. There was a high degree of heterogeneity for many of the factors investigated, and we used a random effects model to allow for between study heterogeneity. We have described potential sources of heterogeneity including study design, study population, measuring and assessing factors, outcome measure, and timing of outcome measure during pregnancy and when there are sufficient studies, this could be explored in the future through meta-regression. The pooled analysis was weighted by the inverse of variance but we did not use meta-regression, to further explore heterogeneity. As such, the aim of this review was to report the findings narratively and for the majority of the factors meta-analysis was not conducted due to being

reported by less than three studies, hence, the meta-analyses results must be viewed and interpreted cautiously.

This review identified only two studies from LMICs (Serbia and the Lebanon); interestingly, the factors associated with smoking cessation in these countries were similar to those identified in women from the high-income nations (i.e., higher socio-economic status, other members of the household do not smoke, low cigarette dependence, perceived adequate pre-natal care). Further work is needed to explore whether the predictors are the same for LMICs versus high income nations, particularly in relation to factors which are likely to be distinct in poorer nations, such as provision of health services and education. This issue is particularly important due to concerns that smoking among pregnant women in LMICs is declining more slowly compared with high income countries.

Further research is also needed focusing on predictors for which there were not consistent findings (e.g., maternal age) or where there were few high quality studies showing significant effects (e.g., ethnicity, nicotine dependence, urges to smoke, and psychological variables such as readiness to quit). It is not clear why the findings were inconsistent for maternal age, although this is likely to be partly due to variation in how the age variable was defined (e.g., categorical versus continuous) in the different studies. However, our thorough meta-analysis for age concluded that it is not a significant predictor. Research is also required to investigate predictors of quit attempts, which are likely to be distinct from the predictors of success of those attempts [92]. Finally, as has been done with predictors of post-partum return to smoking [93], studies are needed to explore direct and indirect pathways linking predictors with smoking cessation during pregnancy, thereby further focussing the priorities for intervention development.

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Figure 1: Flow diagram of eligible studies

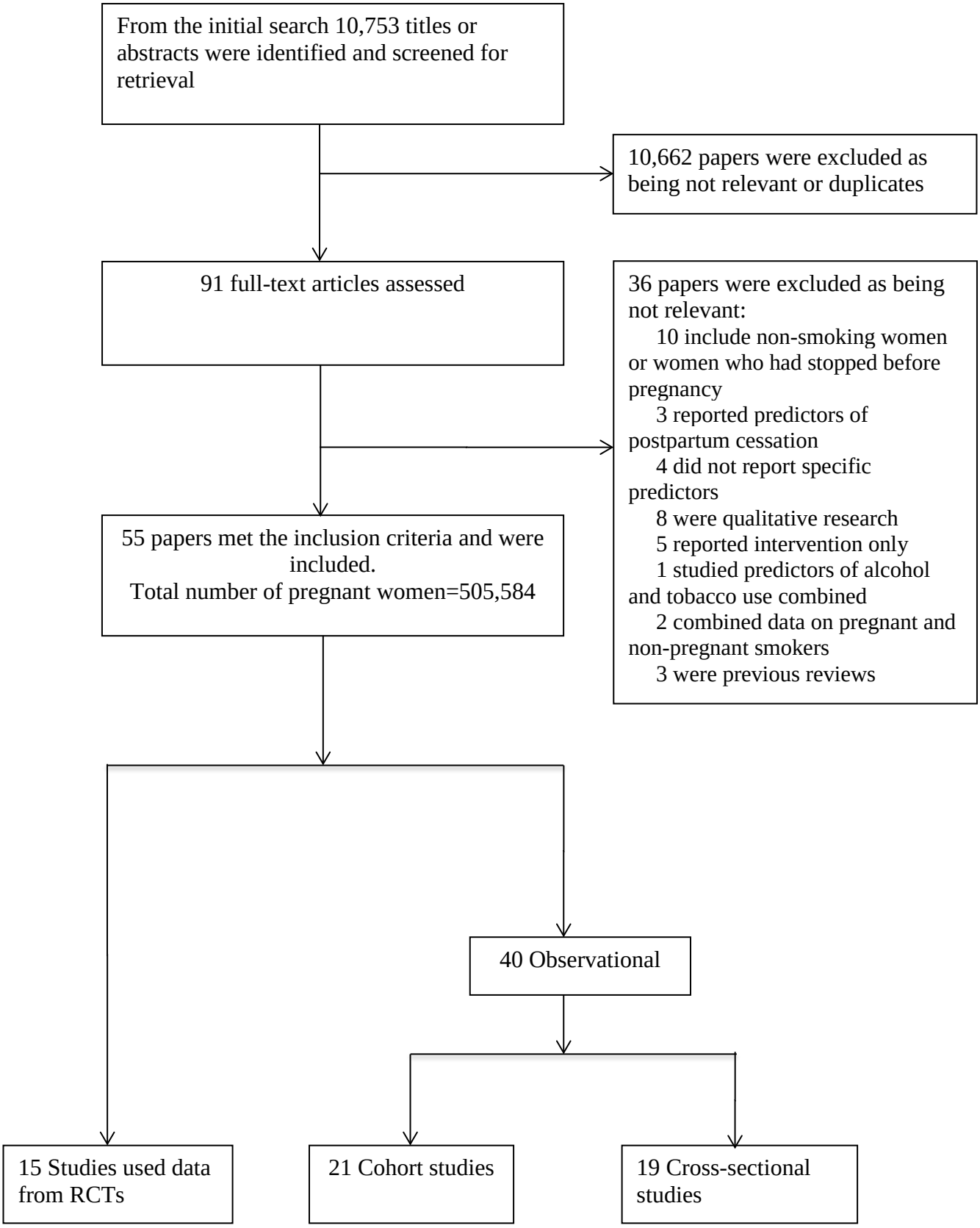

Table 1: Factors significantly associated with smoking cessation during pregnancy

Factors associated with cessation	**Study no: extracted effect estimates[a] and pooled[c] odds ratios**	
	ORs/RRs (95% CI)[b]	**MA: Pooled OR[c] (95% CI), (I^2, p)**
Socio-demographic and economic factors		
Older age	38: 0.98 (0.97-0.99), [21: 1.55 (1.17-2.05), 54: 2.09 (1.00-4.30), 64: 1.42 (1.28-1.57), 68: 2.10 (1.10-4.20), 69: 0.75 (0.70-0.79), 74: 1.89 (1.56-2.27), 47: 0.30 (0.16-0.56), 50: 0.92 (0.88-0.97), 51: 0.71 (0.62-0.83), 66: 0.22 (0.07-0.76), 67: 1.19 (1.01-1.41), 76: 0.96 (0.94-0.98), 82: 0.31 (0.19-0.53)]*, [37: 1.11 (1.04-1.17)]*ǂ	[d]: 0.96 (0.72-1.28), (96.0%, <0.001) [e]: 0.98 (0.95-1.02), (88.9%, <0.001)
Ethnicity-non-White women	[50: 2.70 (1.31-5.58)]*	
Ethnicity-non-Puerto Rican Hispanic	[61: 1.54 (1.11-1.88), 69: 2.12 (1.95-2.31)]*	
Ethnicity (Australian-aboriginal)	[74: 0.60 (0.50-0.70), 67: 0.54 (0.43-0.66]*	
Overseas maternal birth (immigrant)	[61: 1.73 (1.02-2.94), 67: 2.71 (2.15-3.43), 79: 2.17 (1.03-4.54), 74: 1.60 (1.44-1.78)]*	2.00 (1.40-2.84), (81.9%, 0.001)
Non-Urban resident	[74: 0.70 (0.60-0.90)]*	
Higher level of maternal education	[21: 2.69 (1.60-4.53), 34: 4.40 (1.5-12.8), 41: 1.82 (1.24-2.67), 49: 1.24 (1.07-1.43)]*ǂ 31: 2.43 (1.30-4.54), 40: 1.37 (1.05-1.75), 43: 4.62 (1.70-12.54), 47: 1.90 (1.40-2.70), 51: 1.74 (1.44-2.10), 54: 2.73 (1.90-4.00), 55: 2.50 (1.20-5.50), 60: 1.72 (1.04-2.86), 63: 1.83 (1.28-2.62), 64: 1.31 (1.23-1.38), 68: 2.60 (1.30-5.20), 69: 2.29 (2.18-2.40), 71: 3.20 (1.60-6.50), 76: 1.91 (1.55-2.35), 77: 3.64 (2.58-5.14), 80: 2.03 (0.99-4.15), 82: 3.33 (1.67-5.00)]*	[f]: 2.16 (1.80-2.59) (93.2%, <0.001)
Higher socioeconomic status	[21: 1.45 (0.96-2.20)]*ǂ, 48: 2.79 (2.51-3.10), [67: 1.8 (NR), 82: 1.67 (1.00-3.33)]*	1.97 (1.20-3.24), (82.3%, 0.004)
Higher level of partner's education	[49: 1.10 (1.00-1.20)]*ǂ	
Employed (currently)	70: 2.37 (1.16-4.85)	
Medicaid coverage or private insurance	38: 2.17 (1.15-4.17), 40: 3.57 (1.16-11.11), [51: 1.33 (1.18-1.52), 74: 1.61 (1.29-2.01), 47: 1.60 (1.10-2.30)]*	1.54 (1.29-1.85), (41.5%, 0.145)
Relationship and social activities		
Living with partner/married	[43: 2.45 (1.17-5.09)]ǂ, [51: 1.32 (1.17-1.48), 54: 1.84 (1.20-2.80), 64: 1.42 (1.34-1.51)], 65: 2.63 (1.41-4.76), 69: 1.52 (1.47-1.57), 77: 1.75 (1.30-2.35)]*	1.49 (1.38-1.61), (60.5%, 0.019)

House wife	[77: 0.70 (0.51-0.96)]*	
Support from partner and others	[46: #]*	
Partner or household member smokes	[21:0.5 (0.44-0.57)]*ǂ, 38: 0.49 (0.26-0.93), 44: (NR), 59: 0.20 (0.12-0.32), 70: 0.35 (0.17-0.70), 71: 0.20 (0.10-0.20), [46: 0.37 (0.20-0.69), 62: 0.56 (0.36-0.87), 72: 0.40 (0.30-0.50), 73: 0.57 (0.38-0.87), 76: 0.44 (0.37-0.52), 78: 0.55 (0.37-0.83), 79: 0.46 (0.30-0.70), 82: 0.60 (0.50-0.80)]*, [75: 0.17 (0.03-0.68)]ǂ	0.42 (0.35-0.50), (71.9%, <0.001)
Exposure to second-hand /environmental/passive smoking	[42: 0.66 (0.42-1.03)]*ǂ, [63: 0.70 (0.60-0.81), 32: (NR)]*, 44: (NR), 71: 0.20 (0.10-0.20)	0.45 (0.20-1.02), (95.3%, <0.001)
Poorer childhood circumstances	[60: 0.70 (0.54-0.91)]*	
Poorer current circumstances	[60: 0.35 (0.23-0.54)]*	
Smoking and related factors		
Higher Fagerstrom test of Higher cigarette dependence	[39: 0.60 (0.45-0.81)]*ǂ	
Higher Heaviness of Smoking Index	[36: 0.59 (0.47-0.74), 39: 0.65 (0.48-0.87)]*ǂ, 59: 0.21 (0.13-0.35)	0.45 (0.27-0.77), (87.5%,<0.001)
Higher Non-Heaviness of Smoking Index	[39: 0.65 (0.48-0.88)]*ǂ	
Higher pre-pregnancy cigarette consumption	[34: 0.50 (0.40-0.60), 36: (NR), 37: 0.85 (0.83-0.87), 39: (NR)]*ǂ, [43: 0.37 (0.30-0.47)]ǂ, 40: 0.15 (0.06-0.32), 44: (NR), 48: (NR), 55: 0.83 (0.77-0.91), 56: 0.38 (0.16-0.88), 58: 0.36 (0.18-0.69), 66: 0.13 (0.05-0.37), 68: 0.08 (0.04-0.16), [32: (NR), 45: 0.02 (0.01-0.04), 47: 0.23 (0.16-0.34), 51: 0.27 (0.24-0.30), 54: 0.40 (0.29-0.59), 61: 0.36 (0.19-0.68), 62: 0.21 (0.13-0.35), 63: 0.41 (0.33- 0.51), 65: 0.45 (0.31-0.64), 69: 0.35 (0.34-0.36), 72: 0.30 (0.20-0.30), 73: 0.12 (0.05-0.31), 76: 0.57 (0.52-0.63), 80: 0.43 (0.24-0.74), 82: 0.30 (0.30-0.40)]*	[d]: 0.28 (0.22-0.35), (96.5%, <0.001) [e]: 0.57 (0.38-0.85), (98.2%, <0.001)
Higher baseline cotinine level	[31: 0.92 (0.88-0.95)]*, [41: 0.96 (0.92-0.99), 42: 0.09 (0.05-0.17)]*ǂ	0.78 (0.64-0.94), (96.6%, <0.001)
Higher baseline carbon monoxide level	[39: 0.55 (0.37-0.80)]*ǂ	
Higher Urges/craving to smoke	[39: 0.69 (0.51-0.93)]*ǂ, 59: 0.27 (0.15-0.49)	
Higher sensation of withdrawal	59: 0.27 (0.17-0.44)	
Shorter duration (years) of smoking	[42: 2.79 (1.61-4.82)]*ǂ, 48: (NR)	
Pre-pregnancy, lower time	[37:0.51 (0.34-0.76), 36: 0.26 (0.11-0.65)]*ǂ,	0.37 (0.23-0.59),

to first cigarette on waking	38: 0.28 (0.15-0.55)	(42.2%, 0.177)
Smoking status in the first two weeks following the quit attempt.	[35: 30.4 (6.0-154.6)]†	
Pre-pregnancy/prior attempt to quit	[34: 2.30 (1.10-4.50), 36: 3.55 (1.65-7.63)]*†	
Attempts to quit during pregnancy	[36: 1.18 (1.00-1.38)]*†	
Interaction of age and number of years smoked	[81: 2.83 (1.44-5.58)]*†	
Age at onset of smoking	[43: 1.15 (1.04-1.28)]†, [78: 1.16 (1.08-1.25)]*	
Daily use of pre-pregnancy marijuana	[61: 0.54 (0.31-0.87)]*	
No alcohol use before and/or during pregnancy	[47: 2.10 (1.00-4.10), 58: 2.58 (1.00-6.66), 82: 2.00 (1.11-3.33)]*, [49: 1.86 (1.07-3.24)]*†	2.03 (1.47-2.80), (0.0%, 0.950)
Interaction of delayed discounting of spontaneous quit and smoking rate	[43: 0.74 (0.61-0.90)]†	
Coffee consumption during pregnancy	[72: 0.20 (0.20-0.30)]*	
Pregnancy related factors		
Primiparity	[33:(NR), 75: 3.92 (1.78-8.99)]†, 44: (NR), 48: 2.19 (NR), 52: 1.48 (1.09-2.01), 70: 5.05 (1.90-13.27), 71: 1.67 (1.11-2.00), [49: 2.00 (1.15-3.45)]*†, [45: 2.04 (1.16-3.57), 47: 1.90 (1.40-2.50), 51: 1.88 (1.69-2.10), 60: 2.29 (1.92-2.72), 61: 2.78 (1.54-5.00), 63: 2.17 (1.85-2.50), 65: 1.64 (1.04-2.57), 67: 1.68 (1.62-1.73), 73: 1.49 (1.03-2.17), 74: 2.22 (2.04-2.44), 77: 1.24 (1.03-1.49), 78: 1.59 (1.06-2.38), 79: 1.54 (1.17-2.03), 82: 1.67 (1.25-2.00)]*	[g]: 1.85 (1.68-2.05), (78.4%, <0.001)
Women who were perceived to have adequate prenatal care	48: (NR), [67: 2.33 (1.91-2.85), 69: 1.67 (1.56-1.75), 73: 2.72 (1.3-5.68), 74: 1.27 (1.18-1.37), 80: 1.72 (1.02-2.91)]*	1.74 (1.38-2.19), (92.3%, <0.001)
Planned breastfeeding	58: 3.70 (1.60-8.80), [50: 1.73 (1.01-2.98), 69: 1.99 (1.94-2.05), 82: 2.00 (1.67-2.50)]*	1.99 (1.94-2.05), (0.0%, 0.514)
Prior preterm birth	[69: 0.82 (0.76-0.88)]*	
Planned pregnancy	[77: 1.31 (1.00-1.72), 79: (NR)]*	
Health Related factors		
Severe nausea	44: (NR), 70: 2.59 (1.11-6.04)	
Community services card holders	70: 0.41 (0.19-0.86)	
Known higher risk of foetal harm	59: 3.67 (1.73-7.78)	
Short sleep duration	[63: 0.62 (0.51-0.75)]*	
Use of folic acid	[77: 1.59 (1.22-2.06)]*	
Psychological factors		
No depression	[30: 6.28 (0.76-52.17)]†, [31: 2.69 (1.27-5.68)]*, 40: 2.39 (1.22-4.70),	[h]: 2.65 (1.62-4.30),

	52: 1.09 (1.01-1.17)	(0.0%, 0.694)
Per unit increase in anxiety score	[57: 0.99 (0.98-1.00)]*	
Stress during pregnancy	[34:0.80 (0.70-0.90)]*ǂ, [43: 0.86 (0.76-0.97)]ǂ, [57: 0.57 (0.35-0.94), 61: 0.64 (0.38-1.06)]*, 59: 0.54 (0.34-0.85),	[i]: 0.58 (0.44-0.77), (0.0%, 0.887)
Perception of harm to baby due to smoking	[43: 14.42 (1.77-117.25)]ǂ,	
Higher self-efficacy/confidence for quitting	[42: 3.59 (2.29-5.65), 37: 0.84 (0.76-0.93)]*ǂ, [32:(NR)]* 53: (NR),	
Higher readiness for quitting	[52: 1.05 (1.02-1.08)]	
Domestic violence,	[57: 0.31 (0.12-0.84)]*	

[a]: Effect estimates extracted are odds ratios (OR: adjusted majority), relative risk ratios (RR: one study [69]) or prevalence ratio (PR: one study [21]). If an effect estimate was not reported, an unadjusted OR and 95% confidence interval (95% CI) was estimated from the available data.

[b]: The effect estimate (e.g., OR) shows the direction of association; a factor is said to be associated with an increase likelihood of smoking cessation if OR>1 and decrease likelihood if OR<1. To ensure consistency of the effect estimates for meta-analysis, for some of the studies, the effect estimates are transformed to represent smoking cessation outcome and/or (appropriate category versus reference) of the predictor.

[c]: Using DerSimonian and Laird random effects model for meta-analysis, the effect estimates were combined to compute a pooled OR for the association.

p: Represents the p-values for testing the hypothesis that the studies are homogeneous.

[d]: The predictor (factor) is assessed as a categorical variable.

[e]: The predictor is assessed as a continuous variable.

[f]: Excluded [40] from meta-analysis as it reported OR (95% CI) for continuous age (years) of education.

[g]: Excluded [52] from meta-analysis as it reported OR (95% CI) for continuous number of children.

[h]: Excluded [52] from meta-analysis as it reported OR (95% CI) for continuous score of the depression scale.

[i]: Excluded two studies [34 and 43], as they reported OR (95% CI) for continuous score of the stress scale.

*: Studies methodology is classed as of high quality by the NOQAS (i.e., score of 7 and above).

ǂ: Study(ies) with all or most of the participants made a quit attempt.

ǂ: Studies enclosed are fulfilling both of the above two criteria (and ǂ.

#: The OR (95% CI) interpretation is wrong in the original study, therefore it was not reported.

(NR): Effect estimate and/or 95% CI are not reported and can not be estimated from the available results published in the study.

I^2: I-square is the measure (index) of heterogeneity among the studies included in the meta-analysis. More than 75% can be considered as high heterogeneity, more than 50% moderate, and 25% as low heterogeneity [97].

p: Represents the p-values for testing the hypothesis that the studies are homogeneous.