

Use of e-cigarettes in pregnancy: A systematic review of evidence published from 2020-2022

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Abstract

Aim: This study synthesised evidence related to e-cigarette use in pregnancy published from 2020 to 2022.

Subject and Methods: Smoking cessation during pregnancy is a key public health focus given associations with adverse health and birth outcomes. E-cigarettes may facilitate quitting combustible cigarette use during pregnancy. A systematic search of online databases (MEDLINE, CINAHL, and PsycINFO) was conducted on 25 February 2022.

Results: Thirty-seven studies investigating e-cigarette use in pregnancy were included in the review the majority of which were of 'good' quality (n=33). Included studies reported on one or more of; prevalence of e-cigarette use during pregnancy (n=27), birth and health-related outcomes of e-cigarette use during pregnancy (n=13), the impact of e-cigarette use on smoking cessation behaviours (n=11) and attitudes and perceptions around e-cigarette use during pregnancy (n=9). Prevalence was found to range from 1.2% to 4.8%, whilst perceptions of e-cigarette use during pregnancy were found to be more positive than those towards combustible cigarette use. Findings regarding health and birth outcomes were notably mixed, and the efficacy of e-cigarettes as a smoking cessation tool remains unclear.

Conclusion: The majority of studies published in the last two years were on prevalence of e-cigarette use in pregnancy. More high-quality evidence focusing on the effectiveness of e-cigarettes for smoking cessation, and the health implications of e-cigarette use compared with combustible cigarette use during pregnancy is needed to support the implementation of e-cigarettes as a harm-reduction approach in practice.

Keywords: e-cigarettes, pregnancy, public health, systematic review, smoking cessation

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Background

Smoking tobacco during pregnancy is an established risk factor associated with multiple adverse health outcomes for both mother and baby (Shobeiri et al. 2017). Risks to mothers include increased risk of obstetric complications, compromised psychological health, micronutrient deficiencies, reduced placental blood flow, placental abruption, and placenta previa (Damron KR 2017; Shobeiri et al. 2017; Tuentner et al. 2019; Wantanabe and Fukuoka 2016), whilst risks to babies include miscarriage, premature delivery, perinatal morbidity and mortality, stillbirth, low birth weight, neonatal and sudden infant death (Abraham et al. 2017; Pineles et al. 2014; Turner-Warwick 1992). Around 11% of women in England self-reported smoking at the time of delivery in 2018, with the prevalence of women smoking during pregnancy closer to 2% on a global scale (Health & Social Care Information Centre 2018; Lange et al. 2018; McAndrew et al. 2012). Reducing smoking during pregnancy has been prioritised by the United Kingdom National Health Service Long-Term plan through establishing specialist stop smoking support services for pregnant women (Public Health England 2020). These services aim to achieve a national target of fewer than 6% of women smoking at the time of birth by 2022. Statistics from March 2022 indicate that the percentage of pregnant women smoking at the time of giving birth has so far only reduced from 11% to 9.1% (NHS Digital 2019). It has been difficult to produce effective interventions supporting pregnant women to quit smoking, with programmes often relying on Nicotine Replacement Therapies (NRTs) which have shown limited efficacy, as well as low adherence in smoking cessation trials (Claire et al. 2020). The reasons that NRT appears to be less effective in pregnancy remain unclear, however it has been suggested that variations in NRT adherence or nicotine metabolism in pregnant women compared to the general population may contribute to this (Claire et al. 2020).

One proposed means of harm reduction is offering e-cigarettes to women who are pregnant and smoke (National Institute of Health and Care Excellence 2021). E-cigarettes, commonly referred to as vapes, are battery powered, non-combustible tobacco products that deliver nicotine and other flavouring chemicals via inhaled aerosol (US Department of Health & Human Services 2016). E-cigarettes have been commercially available since the early 2010's (Hsu et al. 2013; Rose et al. 2014) and evidence from Public Health England commissioned reports (using systematic review, survey, and secondary data analysis methods), combined with toxicology analyses, suggests that they are less harmful than combustible tobacco cigarettes (Goniewicz et al. 2014; McNeill et al. 2018, 2020; Orr 2014). E-cigarette use in England in 2021 was approximately 6%, equating to around 2.7 million adults using e-cigarette products (Public Health England 2022). Since 2013, e-cigarettes are the most commonly reported smoking cessation aid in England, with more than half of people who formerly smoked in the general population now reported as using e-cigarettes on a daily basis (Public Health England 2022). In people who smoke and are not pregnant, e-cigarette use is more effective than traditional NRT for smoking cessation (Hajek et al. 2019; Tong et al. 2008). A Cochrane review reported that e-cigarette use significantly improves quit rates, with approximately three additional quitters per 100 when e-cigarettes were used instead of traditional NRTs, and approximately seven additional quitters per 100 when e-cigarettes were used instead of non-nicotine vaping products (Hartmann-Boyce et al. 2021).

E-cigarettes are being increasingly used as a smoking cessation tool in pregnancy (Bowker et al. 2018; Oncken et al. 2017), with the Smoking in Pregnancy Challenge Group (a coalition of organisations committed to

reducing rates of smoking in pregnancy in the UK), advocating for the use of e-cigarettes as part of smoking cessation in pregnancy services (Network 2020). The effectiveness and health-related safety of e-cigarette use to decrease smoking among pregnant women, however, remains relatively unknown (Siu 2015). As such, a growing number of studies are investigating the efficacy, health risks, and safety of e-cigarette use during pregnancy to inform evidence-based clinical practice. A systematic review of 23 studies examined e-cigarette use during pregnancy in terms of prevalence, patterns of use, reasons for use, efficacy as a smoking reduction/cessation tool, and health-related outcomes (Calder et al. 2021). Overall, this review suggested that prevalence of e-cigarette use during pregnancy is similar to that of combustible cigarette use, with most pregnant women who use e-cigarettes during pregnancy using them as a tool to help reduce (or stop) smoking combustible cigarettes. There was limited evidence suggesting that e-cigarette use may have less adverse health-related outcomes than combustible cigarette smoking during pregnancy, and insufficient data available to draw meaningful conclusions about the patterns of use, and efficacy of e-cigarette use as smoking cessation tool. Given the rapid emergence of evidence on e-cigarette use in pregnancy, a systematic review of the most recent evidence was conducted to inform stop smoking in pregnancy practice. Whilst some recent reviews have considered the impact of e-cigarette use in pregnancy, these have often focussed on health-related outcomes associated with foetal nicotine exposure in animal models, with included human studies limited to investigating one or two birth-related health outcomes, or focussing more on post-natal respiratory health (Bednarczuk et al. 2022; Mescolo et al. 2021; Zhang et al. 2022). This systematic review included only studies with human participants. We investigated a range of factors which must be considered when using e-cigarettes as a smoking cessation tool in pregnancy, including prevalence, perceptions, health-related outcomes, and efficacy as a stop smoking tool.

Methods

Design

A systematic review was carried out and written in accordance with the PRISMA 2020 guidelines (Page et al. 2021). Ethical approval was acquired from [blinded name] University (ref: P134385).

Eligibility Criteria

Eligible studies were randomised-controlled trials (RCTs), qualitative studies, or observational studies that investigated the use of e-cigarettes in human pregnancy and/or postpartum. Participants were people who were, had been, or planned to be pregnant, and their babies. Studies also had to report outcomes relating to (i) prevalence of smoking cessation or uptake of e-cigarettes during pregnancy, (ii) health-related outcomes, (iii) barriers and facilitators to using e-cigarettes whilst pregnant, or (iv) benefits or harms associated with e-cigarettes during pregnancy. Studies had to present primary evidence (e.g., not be an editorial or commentary article), be peer-reviewed, and be available in the English language. Literature review articles were also excluded; however, the reference lists of these articles were checked for any additional eligible articles to include. Dissertations, case studies, and conference abstracts were also excluded.

Search strategy and selection process

The Cumulative Index to Allied Health Literature (CINAHL), American Psychological Association (APA) PsycINFO, and Medline were searched for relevant studies on the 25th February 2022. Searches were filtered to search for available articles published from 2020 (which aligns with the final search date from Calder et al. 2021), the most recent published systematic review on this topic). The searches used for each database are included in the Supplementary Material.

Zotero referencing software was used to help manage articles identified from the search. Rayyan (Ouzzani et al. 2016), a free web and mobile application, was used to manage the screening and study selection process. Titles and abstracts were screened by two researchers (LB and EE) and ineligible articles were excluded. This process was repeated at the full-text stage by the same two researchers. Studies where eligibility remained unclear were screened by two new researchers (MW and RP). Reviewers worked independently in the screening process with conflicts resolved through discussion. A third researcher (LT) confirmed eligibility of the studies at the point of extraction and writing up, resulting in the removal of two studies previously included. Reference lists and forward citations of the included studies were checked for any additional eligible articles to include. During the time of the search, 14 studies were only available as pre-prints, but during the write up of the review they had been published and so the published article was cited in the report instead of the pre-print.

Data extraction

Data extraction for included studies was conducted by three reviewers (LB, EE, and LT) working independently and without any automation tools. Microsoft Excel was used to facilitate this process. Disagreements were resolved through revisiting the articles and, where needed, discussing articles with two further researchers (MW and RP). Original study authors were not approached regarding missing data. Data extracted from studies included author(s), year of publication, country of data collection, year(s) of data collection, topic of research, study method (e.g., qualitative, cross-sectional, longitudinal observational), sample characteristics (including sample size, age, and characteristics about the pregnancy e.g., trimester, singleton), outcomes, and study recommendations. Extracted data was summarised in a table and outcomes were synthesised narratively.

Study quality assessment

Two authors (LT and MW) independently assessed the quality of the included studies using the Joanna Briggs Institute (JBI) critical appraisal tools, designed for assessing cohort studies, prevalence studies, and qualitative studies (Lockwood et al. 2015; Moola et al. 2017; Munn et al. 2015). Any discrepancies in quality assessments were then discussed by both authors (LT and MW) and a final judgement agreed. Quality appraisal judgements did not determine inclusion/exclusion in the present review.

Results

Study selection

The search strategy identified 192 results in total, from the three databases plus reference and forward citation searches (Figure 1). 149 articles remained after 43 duplicates were removed. After title and abstract screening, 93 articles were screened at the full-text stage. The two main reasons for exclusion at full-text were articles not reporting primary evidence (n=35) and articles not reporting evidence related to e-cigarettes in pregnancy or postpartum (n=14). Finally, thirty-seven articles were included in this review (Figure 1).

Included study characteristics

Characteristics of the included studies are presented in Table 1 in the supplementary materials. The majority of studies were conducted in the United States (n=24) (Ashford et al. 2021; Beck et al. 2021, 2022; Cardenas et al. 2020; Coleman et al. 2021; Dobbs et al. 2021; Dobbs et al. 2021; Hawkins et al. 2020, 2021; Head et al. 2022; Kim 2020; Kim & Oancea 2020; Kurti et al. 2020; Liu et al. 2021; McCubbin et al. 2020; Obisesan et al. 2020; Regan et al. 2021; Regan & Pereira 2021; Rollins et al. 2020; Shittu et al. 2022; Testa et al. 2021b, 2021a; Wang et al. 2020) and the United Kingdom (n=13) (Bowker et al. 2020; Bowker, Lewis, Phillips, et al. 2021; Bowker, Lewis, Ussher, et al. 2021; Ford et al. 2021; Froggatt et al. 2020; Froggatt Reissland & Covey 2021; Froggatt Reissland Covey et al. 2021; Grant et al. 2020; Opondo et al. 2021; Phillips et al. 2021; Stacey et al. 2022), with one study conducted in Jordan (Hamadneh et al. 2021), one in Germany (Schilling et al. 2021), and one in the Republic of Ireland (McDonnell et al. 2020). Twenty-one studies were published in 2021, 13 were published in 2020, and three were published in 2022. Included studies reported data collected between 2013 and 2021.

Quality appraisal

Cohort studies were judged to be of moderate (Bowker Lewis Ussher et al. 2021) or good (Ashford et al. 2021; Beck et al. 2022; Froggatt et al. 2020; Froggatt Reissland Covey et al. 2021; McDonnell et al. 2020) quality.

The majority of prevalence studies were judged to be of good quality (Beck et al. 2021; Bowker, Lewis, Phillips, et al. 2021; Cardenas et al. 2020; Coleman et al. 2021; Hamadneh et al. 2021; Hawkins et al. 2020, 2021; Head et al. 2022; Kim 2020; Kim & Oancea 2020; Kurti et al. 2020; Liu et al. 2021; Obisesan et al. 2020; Opondo et al. 2021; Regan et al. 2021; Regan & Pereira 2021; Schilling et al. 2021; Shittu et al. 2022; Testa et al. 2021b, 2021a; Wang et al. 2020), whilst four were judged to be of moderate quality (Dobbs, Branscum, et al. et al. 2021; Dobbs, Lu, et al. et al. 2021; McCubbin et al. et al. 2020; Rollins et al. et al. 2020). Several of the studies analysed large population datasets, reflecting good external validity (Beck et al. et al. 2021; Bowker, Lewis, Phillips, et al. et al. 2021; Cardenas et al. 2020; Hawkins et al. 2020, 2021; Head et al. 2022; Kim & Oancea, 2020; Kurti et al. 2020; Liu et al. 2021; Obisesan et al. 2020; Opondo et al. 2021; Regan et al. 2021; Regan & Pereira 2021; Rollins et al. 2020; Shittu et al. 2022; Testa et al. 2021b, 2021a; Wang et al. 2020).

Twelve of the prevalence studies analysed the Pregnancy Risk Assessment Monitoring System (PRAMS) (Cardenas et al. 2020; Hawkins et al. 2020, 2021; Head et al. 2022; Kim & Oancea 2020; Liu et al. 2021; Regan et al. 2021; Regan & Pereira 2021; Shittu et al. 2022; Testa et al. 2021b, 2021a; Wang et al. 2020). However, this data only included recent live births so did not account for all birth outcomes. Five prevalence studies analysed data from the Population Assessment of Tobacco and Health study (PATH) (Beck et al. 2021, 2022; Coleman et al. 2021; Kim 2020; Kurti et al. 2020). Significant overlap of participants limits the power of

combined outcomes across these large population-based studies. Internal validity was rated weaker because of imprecise measures of smoking or dual use (such as retrospective recall), and not accounting for smoking behaviours throughout pregnancy. Most studies measured smoking and e-cigarette use through retrospective self-report, however some studies incorporated hair nicotine content (Cardenas et al. 2020) or other biological indicators, strengthening the validity of smoking behaviour reports (Ashford et al. 2021; Coleman et al. 2021; McCubbin et al. 2020). Qualitative studies were all categorised as being of good quality (Bowker et al. 2020; Ford et al. 2021; Froggatt, Reissland, & Covey 2021; Grant et al. 2020; Phillips et al. 2021; Stacey et al. 2022). However, there were some instances where increased transparency in data collection methods or analysis, or more detailed reporting of researcher reflexivity, would have improved rigour.

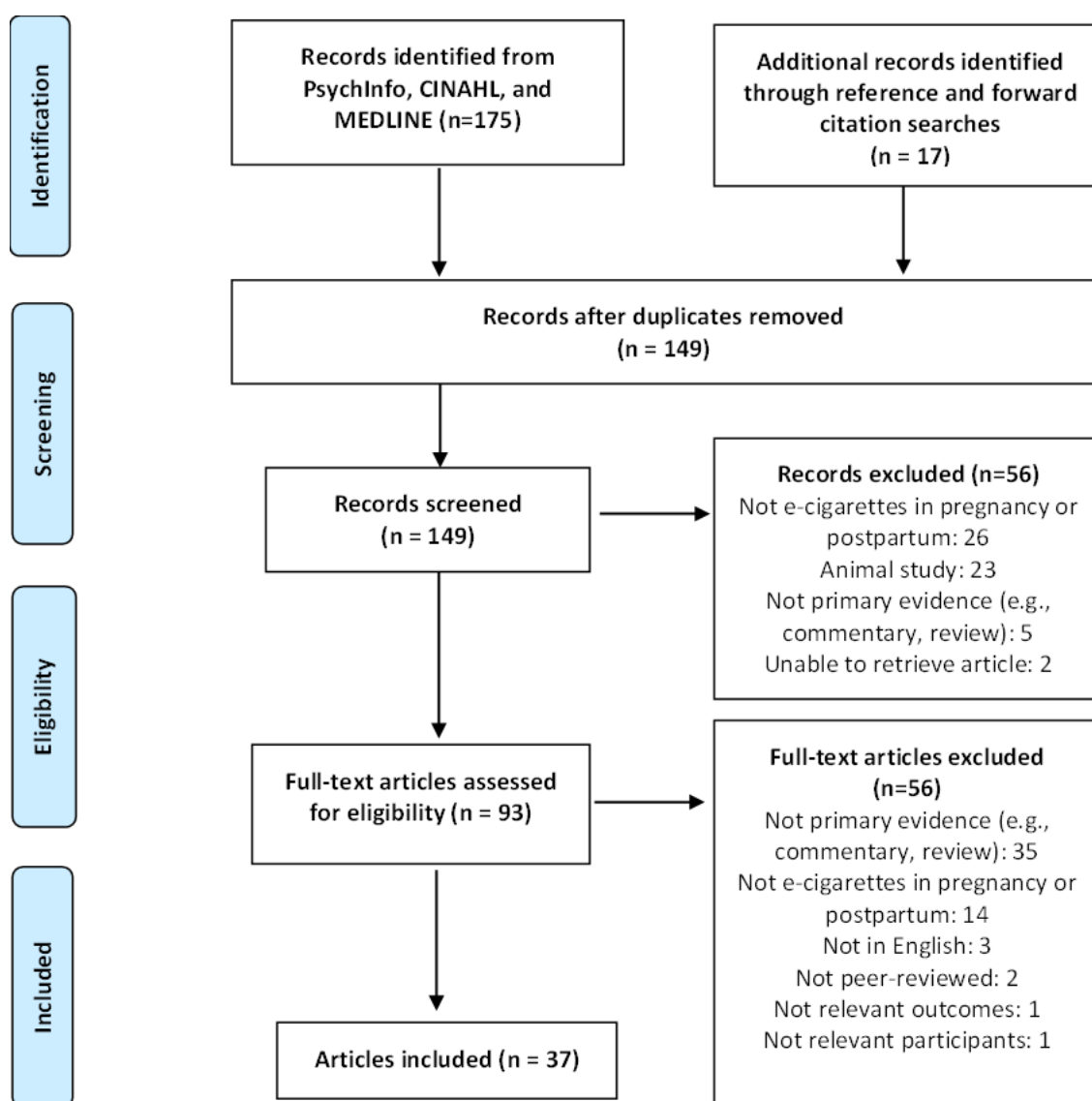


Fig. 1 PRISMA flowchart

Study design

Eighteen (48.6%) studies reported secondary analysis of nationally collected data or quantitative population studies (Beck et al. 2021, 2022; Cardenas et al. 2020; Coleman et al. 2021; Hawkins et al. 2020, 2021; Head et

al. 2022; Kim 2020; Kim & Oancea 2020; Kurti et al. 2020; Liu et al. 2021; Regan et al. 2021; Regan & Pereira 2021; Shittu et al. 2022; Testa et al. 2021b, 2021a; Wang et al. 2020). Nine further studies reported primary cross-sectional surveys (Bowker, Lewis, Phillips, et al. 2021; Dobbs, Branscum et al. 2021; Dobbs, Lu et al. 2021; Hamadneh et al. 2021; McCubbin et al. 2020; Obisesan et al. 2020; Opondo et al. 2021; Rollins et al. 2020; Schilling et al. 2021) and one study used a case-control design (Froggatt et al. 2020). Of the five studies that adopted a longitudinal design, one study examined e-cigarette behaviours during early/late pregnancy and postpartum (Bowker, Lewis, Ussher et al. 2021), one study collected initial surveys in the first or second trimester and again in subsequent trimesters (Ashford et al. 2021), one study examined data collected at ages 14-17 years and then 18-20 years (Beck et al. 2022), and two studies used a longitudinal observational design (Froggatt, Reissland, Covey, et al. 2021; McDonnell et al. 2020). Five studies reported qualitative interviews (Bowker et al. 2020; Ford et al. 2021; Froggatt, Reissland, & Covey 2021; Phillips et al. 2021; Stacey et al. 2022) (including one longitudinal qualitative study (Phillips et al. 2021)) and one further study adopted visual elicitation methods (Grant et al. 2020).

Participants

Twenty-five studies analysed data from women regardless of their smoking status (Beck et al. 2021, 2022; Bowker, Lewis, Phillips et al. 2021; Cardenas et al. 2020; Dobbs, Lu et al. 2021; Froggatt et al. 2020; Froggatt, Reissland, & Covey 2021; Froggatt, Reissland, Covey et al. 2021; Grant et al. 2020; Hamadneh et al. 2021; Hawkins et al. 2020, 2021; Head et al. 2022; Kim 2020; Kim & Oancea 2020; Liu et al. 2021; McDonnell et al. 2020; Obisesan et al. 2020; Opondo et al. 2021; Regan et al. 2021; Rollins et al. 2020; Schilling et al. 2021; Shittu et al. 2022; Testa et al. 2021b, 2021a; Wang et al. 2020). Three studies sought to recruit women who had smoked or used e-cigarettes before pregnancy (Bowker, Lewis, Ussher, et al. 2021; Ford et al. 2021; Kurti et al. 2020; Phillips et al. 2021; Regan & Pereira 2021), nine studies recruited women who smoked or used e-cigarettes during pregnancy (Ashford et al. 2021; Bowker et al. 2020; Bowker, Lewis, Ussher, et al. 2021; Coleman et al. 2021; Dobbs, Branscum et al. 2021; Ford et al. 2021; Froggatt et al. 2020; McCubbin et al. 2020; Stacey et al. 2022), and one study recruited postpartum women who had quit smoking during pregnancy (Phillips et al. 2021). Studies most commonly reported a mean participant age or modal age group between 25 and 34 years old (Ashford et al. 2021; Beck et al. 2021; Bowker et al. 2020; Bowker, Lewis, Phillips, et al. 2021; Dobbs, Branscum et al. 2021; Ford et al. 2021; Froggatt, Reissland, & Covey 2021; Grant et al. 2020; Hamadneh et al. 2021; Kim & Oancea 2020; Liu et al. 2021; McCubbin et al. 2020; Opondo et al. 2021; Regan et al. 2021; Rollins et al. 2020; Schilling et al. 2021; Testa et al. 2021b, 2021a).

Study outcomes

E-cigarette prevalence and patterns of use

Studies reported a prevalence of exclusive use of e-cigarettes among pregnant women between 0.4% and 1.6% (Ashford et al. 2021; Bowker, Lewis, Phillips, et al. 2021; Bowker, Lewis, Ussher, et al. 2021; Cardenas et al. 2020; Coleman et al. 2021; Hawkins et al. 2020, 2021; Head et al. 2022; Kim 2020; Kim & Oancea 2020; Liu et al. 2021; Obisesan et al. 2020; Regan et al. 2021; Regan & Pereira 2021; Rollins et al. 2020; Schilling et al. 2021; Shittu et al. 2022; Testa et al. 2021b, 2021a; Wang et al. 2020). When e-cigarette use during pregnancy

and postpartum was exclusively investigated among women who smoked or used e-cigarettes in the three months before pregnancy, prevalence increased from 15.9% to 23.1% (Bowker, Lewis, Ussher et al. 2021). One study in Jordan reported exclusive e-cigarette use in 2.9% of their sample of 269 women (Hamadneh et al. 2021), whilst a study in Germany revealed that exclusive e-cigarette use amongst participants reduced from 1.3% to 0% in later pregnancy (Schilling et al. 2021). Studies frequently reported that dual-use (both e-cigarettes and combustible cigarettes) was more prevalent than exclusive e-cigarette use (Ashford et al. 2021; Bowker, Lewis, Phillips, et al. 2021; Bowker, Lewis, Ussher, et al. 2021; Cardenas et al. 2020; Coleman et al. 2021; Hamadneh et al. 2021; Hawkins et al. 2020, 2021; Kim 2020; Liu et al. 2021; McCubbin et al. 2020; Regan et al. 2021; Regan & Pereira 2021; Rollins et al. 2020; Shittu et al. 2022; Wang et al. 2020). Accounting for dual use, population prevalence of e-cigarette use during pregnancy increased to between 2.2% and 4.8% (Beck et al. 2021, 2022; Bowker, Lewis, Phillips et al. 2021; Kim 2020; Obisesan et al. 2020; Opondo et al. 2021; Rollins et al. 2020), (increasing to 19% in one Jordanian study with 268 pregnant women (Hamadneh et al. 2021)), although several studies reported a prevalence of 0% to 2% when examining the last three months of pregnancy (Hawkins et al. 2021; Head et al. 2022; Kim & Oancea 2020; Liu et al. 2021; Regan et al. 2021; Schilling et al. 2021; Testa et al. 2021b; Wang et al. 2020). In two studies, almost half of women who were pregnant and smoked also used e-cigarettes in the past 30 days (Ashford et al. 2021; Dobbs, Branscum et al. 2021). Overall e-cigarette prevalence was reported to have increased from 1.9% in 2016 to 3.8% in 2019 (Head et al. 2022; Obisesan et al. 2020).

Exploration of sociodemographic variables such as ethnicity, education, and socioeconomic status in relation to e-cigarette prevalence showed women who used e-cigarettes were more likely to be non-Hispanic White (Cardenas et al. 2020; Head et al. 2022; Kim 2020; Liu et al. 2021; Regan et al. 2021; Wang et al. 2020), young adults (Cardenas et al. 2020; Head et al. 2022; Opondo et al. 2021; Regan et al. 2021; Shittu et al. 2022; Wang et al. 2020), and were less likely to be Black women (Hawkins et al. 2020; Testa et al. 2021b). Studies also reported that women who used e-cigarettes frequently had lower education (Cardenas et al. 2020; Hawkins et al. 2020; Head et al. 2022; Opondo et al. 2021; Regan et al. 2021; Testa et al. 2021b; Wang et al. 2020) and income levels than women who did not use e-cigarettes (Head et al. 2022; Testa et al. 2021b). Whereas, women who exclusively used e-cigarettes had higher education and income levels than both women who used both combustible and e-cigarettes (Coleman et al. 2021; Shittu et al. 2022) and women who smoked combustible cigarettes only (Coleman et al. 2021; Rollins et al. 2020; Shittu et al. 2022). One secondary cross-sectional analysis study found that lesbian women more often used e-cigarettes than heterosexual women in a sample of 1,842 women (0.5% (n=17) of whom identified as lesbian, 5.5% (n=177) as bisexual, and 2.5% (n=43) as something else). This study further reported that 5.1% of sexual minorities used e-cigarettes in the third trimester, however the relatively small number of sexual minorities included in this study's analyses must be acknowledged and interpreted with caution (Beck et al. 2021). Moreover, e-cigarette prevalence was higher among incarceration-exposed recent mothers (6.3%) compared with non-incarceration exposed recent mothers (1.0%) (Testa et al. 2021a). A further secondary cross-sectional analysis study reported that e-cigarette use was more prevalent among women with pre- or postnatal depression (Head et al. 2022), whilst another study found women who used e-cigarettes were more likely to report symptoms of depression (Rollins et al. 2020). Four studies reported e-cigarette use to be associated with increased alcohol consumption during (Cardenas et al.

2020; Liu et al. 2021; Obisesan et al. 2020) or in the three months prior to pregnancy (Head et al. 2022).

Another study reported that e-cigarette use in the third trimester was not associated with adolescent smoking in secondary analyses of longitudinal data (Beck et al. 2022).

Health and birth-related outcomes

Thirteen studies reported health or birth-related outcomes (Ashford et al. 2021; Cardenas et al. 2020; Coleman et al. 2021; Froggatt et al. 2020; Froggatt, Reissland, Covey, et al. 2021; Hawkins et al. 2021; Kim & Oancea, 2020; McDonnell et al. 2020; Opondo et al. 2021; Regan et al. 2021; Regan & Pereira, 2021; Shittu et al. 2022; Wang et al. 2020). Reported outcomes were pre-term birth, small-for-gestational-age, low birth weight, and other health-related outcomes.

Pre-term birth

Eight studies examined associations between e-cigarette use and pre-term birth or gestational age. Four studies reported no association (Ashford et al. 2021; Froggatt et al. 2020; Hawkins et al. 2021; Opondo et al. 2021) whilst two secondary cross-sectional analysis studies suggested that outcomes in this area did not differ between women who used e-cigarettes and women who smoked combustible cigarettes, with only abstinence from both smoking and e-cigarette use associated with lower prevalence of preterm birth (Kim & Oancea 2020; Regan & Pereira 2021). Elsewhere, secondary cross-sectional analysis indicated women who exclusively used e-cigarettes had a higher prevalence of pre-term birth when compared to women who did not use e-cigarettes, and did not differ from women who used both combustible and e-cigarettes (Regan et al. 2021). Another secondary cross-sectional analysis study reported that late pregnancy exclusive e-cigarette use had a similar risk of pre-term birth to non-use (Wang et al. 2020).

Small-for-gestational-age (SGA)

Seven studies examined associations between e-cigarette use and SGA. Most studies found that SGA was higher among children of women who used e-cigarettes compared to women who did not use e-cigarettes (Cardenas et al. 2020; Kim & Oancea 2020; Regan et al. 2021; Regan & Pereira 2021; Shittu et al. 2022; Wang et al. 2020). Secondary cross-sectional analyses reported this risk as equal to risk levels seen in women who exclusively smoked combustible cigarettes (Kim & Oancea 2020; Regan & Pereira 2021) and women who used both combustible and e-cigarettes (Regan et al. 2021). However, one secondary cross-sectional analysis study suggested that exclusive use of e-cigarettes was associated with a lower risk of SGA than dual use (Hawkins et al. 2021). Another secondary cross-sectional analysis study reported that women who used e-cigarettes pre-pregnancy who then quit during pregnancy had a lower risk of SGA than those who continued to use e-cigarettes throughout their pregnancy (Shittu et al. 2022). Fully switching from cigarettes to e-cigarettes during pregnancy was associated with a similar risk of SGA as in women who did not use e-cigarettes, with women who smoked combustible cigarettes who switched to dual-use during pregnancy demonstrating a lower risk of SGA than women who continued smoking combustible cigarettes only (Shittu et al. 2022). One observational

study reported no differences in head-circumference between e-cigarette exposed infants and non-exposed infants (Froggatt et al. 2020).

Low birth weight

Eight studies examined associations between e-cigarette use and low birth weight. Two studies reported no difference in birth weight between the children of women who used e-cigarettes and women who smoked combustible cigarettes, whilst abstinence from both was associated with a lower prevalence of low birth weight (Kim & Oancea 2020; Regan & Pereira 2021). Another secondary cross-sectional analysis found low birth weight was higher among children of women who used e-cigarettes than among women who did not use e-cigarettes, even when an adjustment for dual use was included (Regan et al. 2021). One longitudinal observational study described how children of mothers who switched from any product (combustible cigarette and/or e-cigarette) to no product weighed 304g more at birth than children of women who did not switch (Ashford et al. 2021). Women who used both combustible and e-cigarettes were found to have children who weighed 202.8g less than women who did not use either, whilst children of women who used e-cigarettes exclusively weighed 57.8g less than those of women who did not use e-cigarettes (although this difference was not statistically significant) in one secondary cross-sectional analysis study (Hawkins et al. 2021). Two studies reported no associations between e-cigarette use and birth weight in a cross-sectional population survey and an observational study (Froggatt et al. 2020; Opondo et al. 2021) whilst a further observational study found birthweight to be similar between women who did not smoke and women who exclusively smoked combustible cigarettes, and between women who exclusively smoked combustible cigarettes and those who used both combustible and e-cigarettes (McDonnell et al. 2020).

Other health-related outcomes

A longitudinal observational study reported that e-cigarette use was not associated with infant respiratory distress (Ashford et al. 2021), whilst secondary cross-sectional analysis from a cohort study indicated that infants of women who exclusive used e-cigarettes had lower levels of toxins (except metals) compared to children of women who used both combustible and e-cigarettes, where children of women who used both combustible and e-cigarettes did not differ from those of women who smoked only combustible cigarettes (Coleman et al. 2021). One observational study looked at foetal mouth movements and described how the degree of movement declined from 32 to 34 weeks for both fetuses of women who did not use cigarettes and e-cigarette-exposed fetuses (Froggatt et al. 2020). One case control study reported a significantly greater number of abnormal reflexes in both combustible cigarette- and e-cigarette-exposed infants compared to children of women who did not smoke (Froggatt et al. 2020).

Attitudes and perceptions towards e-cigarettes

In total, 13 studies reported attitudes or perceptions towards e-cigarettes in pregnancy. In one study, women perceived that e-cigarettes were less risky to health than cigarettes, irrespective of their own smoking status (Dobbs, Lu et al. 2021). In some studies, women had concerns about, or lacked awareness of, the safety and risks of e-cigarettes whilst pregnant or breastfeeding (Froggatt, Reissland, & Covey 2021; Phillips et al. 2021;

Stacey et al. 2022), although a longitudinal qualitative study reported that acceptability increased when e-cigarettes were recommended by a health professional (Phillips et al. 2021). Two qualitative interview studies recruited people who used cigarettes, some of whom reported perceptions that e-cigarette use could be as risky (Stacey et al. 2022) or riskier (Froggatt, Reissland, & Covey 2021) than conventional cigarettes. One cross-sectional survey study reported that people who used e-cigarettes were more likely than people who used combustible cigarettes to think e-cigarettes were safer than conventional cigarettes (Bowker, Lewis, Phillips et al. 2021). Another cross-sectional survey study found that 75% of women who were pregnant and smoked believed e-cigarettes were less harmful than cigarettes (Hamadneh et al. 2021). One qualitative study reported that women enrolled in a multi-centre randomised controlled trial investigating e-cigarettes and NRT as smoking cessation tools in pregnancy reported positive attitudes towards e-cigarette use, holding beliefs that e-cigarettes were necessary (e.g., for harm reduction) and this outweighed any concerns (Ford et al. 2021). Perceptions of the relative safety and economic benefits of e-cigarettes, alongside becoming confident with the use of e-cigarettes, and support from peers and health professionals, were also linked with positive attitudes towards e-cigarettes in a qualitative study (Bowker et al. 2020). Conversely, one cross-sectional survey study found that using e-cigarettes during pregnancy was perceived to be less acceptable than using e-cigarettes when not pregnant (McCubbin et al. 2020) whilst another study utilising visual elicitation interviews reported that pregnant women using e-cigarettes felt negatively judged by healthcare professionals and strangers (Grant et al. 2020).

A cross-sectional survey study reported that, among women who were pregnant and smoked, intentions to switch to e-cigarettes were associated with instrumental attitudes (e.g., believing e-cigarette use is good), descriptive norms (e.g., believing other pregnant people who smoke will switch during pregnancy), and autonomy (e.g., feeling in control of their decision to switch from cigarettes to e-cigarettes) (Dobbs, Branscum et al. 2021). A common reason for using e-cigarettes was to stop smoking (Bowker et al. 2020; Bowker, Lewis, Ussher et al. 2021; Coleman et al. 2021; McCubbin et al. 2020). Eight in ten women who smoked cigarettes and/or e-cigarettes expressed this in one cross-sectional study (McCubbin et al. 2020), whilst another secondary cross-sectional analysis study reported that women switched to e-cigarettes either to quit smoking or due to their appealing flavours (Coleman et al. 2021).

Effects of e-cigarette use on tobacco smoking cessation in pregnancy

Eleven studies reported the effects of e-cigarette use on smoking cessation behaviours during pregnancy (Ashford et al. 2021; Bowker, Lewis, Phillips et al. 2021; Bowker, Lewis, Ussher et al. 2021; Cardenas et al. 2020; Kim 2020; Kurti et al. 2020; McCubbin et al. 2020; Regan & Pereira 2021; Schilling et al. 2021; Shittu et al. 2022; Wang et al. 2020).

The proportion of women who quit all nicotine products during pregnancy ranged from 42.2% to 70.4% (Cardenas et al. 2020; Kim 2020; Regan & Pereira 2021; Schilling et al. 2021; Shittu et al. 2022; Wang et al. 2020) in women who exclusively smoked combustible cigarette, 24.1% to 57.1% (Cardenas et al. 2020; Regan & Pereira 2021; Schilling et al. 2021; Shittu et al. 2022; Wang et al. 2020) in women who used both

combustible and e-cigarettes, and 57.6 to 80.7% in women who only used e-cigarettes (Bowker, Lewis, Phillips et al. 2021; Shittu et al. 2022). The proportion of women who switched from dual-use to e-cigarettes only ranged from 5% to 11.4% (Ashford et al. 2021; Bowker, Lewis, Ussher et al. 2021; Cardenas et al. 2020; Shittu et al. 2022; Wang et al. 2020) whilst 26% to 30% of women dual-using switched in the opposite direction to combustible cigarettes only (Ashford et al. 2021; Shittu et al. 2022; Wang et al. 2020). One longitudinal observational study reported that 14% of women who only smoked combustible cigarette switched to dual use during their second trimester; however, one third of these participants then switched back to exclusively smoking combustible cigarettes during the third trimester (Ashford et al. 2021). In a longitudinal cohort study, 2.6% of participants exclusively used e-cigarettes at enrolment, 85.5% of whom still exclusively used e-cigarettes in later pregnancy, and 75% of whom continued this behaviour postpartum, with those who didn't continue exclusive e-cigarette use switching to dual use (Bowker, Lewis, Ussher et al. 2021). This study also reported that 60% of women who used both combustible and e-cigarettes at enrolment continued this behaviour in late pregnancy. By postpartum, however, one third of these participants had switched to combustible cigarettes only, with only 5% continuing with dual use. In this study, 11.4% of participants switched from dual use to e-cigarettes only during late pregnancy and continued this behaviour postpartum, whilst 9.9% of women who only smoked combustible cigarettes switched to dual use during late pregnancy, and 1.4% switched to e-cigarettes only. 78.6% of women who smoked combustible cigarettes and switched to dual use during pregnancy, however, returned to exclusively smoking combustible cigarettes postpartum (Bowker, Lewis, Ussher et al. 2021). A prospective observational study in the Republic of Ireland reported that 28.5% of pregnant women in their sample who exclusively used e-cigarettes, and 44.5% of women who formerly used e-cigarettes, formerly smoked combustible cigarettes (Kurti et al. 2020). When we consider smoking reduction as well as cessation, one secondary cross-sectional analysis study reported a similar proportion of women who only smoked combustible cigarettes and women who used both combustible and e-cigarettes stopped or reduced their cigarette use during pregnancy (76.8% and 73.9% respectively) (Cardenas et al. 2020) whilst a cross-sectional survey study found that more women who smoked combustible cigarettes only reported smoking daily than women who used both combustible and e-cigarettes (90% and 70% respectively) (McCubbin et al. 2020). This study also reported a higher proportion of women who used both combustible and e-cigarettes smoking more than one pack a day (11%) compared to women who only smoked combustible cigarettes (5%), although this difference was not statistically significant (McCubbin et al. 2020).

Discussion

Summary of findings

This systematic review aimed to synthesise evidence published since 2020 about the use of e-cigarettes in pregnancy. Thirty-seven eligible studies presented evidence on prevalence of e-cigarette use during pregnancy, attitudes and perceptions around e-cigarette use during pregnancy, associations of e-cigarette use with birth and health outcomes, and efficacy of e-cigarettes as a smoking cessation tool in pregnancy.

Our review indicated an overall prevalence of e-cigarette use during pregnancy of between 2.2% and 4.8%, although included studies suggested that this rate may be lower during the last three months of pregnancy. When

we excluded dual use of e-cigarettes and combustible cigarettes, such that only exclusive e-cigarette use was considered, population prevalence reduced to 0.5% to 1.6%, suggesting that e-cigarettes are more commonly used to supplement combustible cigarette use during pregnancy than to replace all combustible cigarette use. Our findings suggest women who used e-cigarettes during pregnancy were more likely to be non-Hispanic White young adults, with lower education and lower income levels than women who did not use e-cigarettes. Similarly, both women who smoked combustible cigarettes and women who used both combustible and e-cigarettes were found to generally have lower education and lower income levels than women who exclusively used e-cigarettes.

Studies included in this review reported frequent expressions of concern and/or lack of awareness about the safety of using e-cigarettes when pregnant or breastfeeding, whilst demonstrating the significant impact of health professionals' advice on people's attitudes towards this issue. With regards to health outcomes, our findings suggest that e-cigarettes do not pose greater risks to parent or infant health than combustible cigarettes, however it remains unclear to what extent e-cigarettes are advantageous over combustible cigarettes in terms of harm-reduction. Importantly, the majority of studies reporting health-related outcomes relied upon secondary analyses of retrospective data. The gold standard for research in this area is prospective longitudinal design; therefore, more studies using this study design are required to improve the quality of research evidence in this area. Finally, the efficacy of e-cigarettes as a tool for stopping smoking during pregnancy remains unclear, with quit rates for women who use both e-cigarettes and combustible cigarettes appearing similar. Return to combustible cigarette use during late pregnancy or post-partum was also reported in a number of studies, in particular in individuals who switched to dual use during pregnancy, rather than to e-cigarettes exclusively.

Consistency with other findings

The prevalence of e-cigarette use in our review is consistent with the findings from a previous review which reported a prevalence of e-cigarette use during pregnancy of around 1.2% to 7% in the USA, with a prevalence of below 1% in women who had not previously smoked (Calder et al. 2021). A similar prevalence of 5% of pregnant women using e-cigarettes has also previously been reported in the United Kingdom (Bowker et al. 2020). Some findings regarding patterns of use were consistent with wider evidence in non-pregnant populations, with e-cigarette use found to be most prevalent in socioeconomically disadvantaged, White, young adults, however a previous review of sociodemographic patterns in e-cigarette use found that they are more popular among those with higher educational attainment (Green et al. 2020; Hartwell et al. 2017).

Previous research has indicated that pregnant women generally perceive e-cigarettes as safer than combustible cigarettes, especially if they are being used as smoking cessation tools (Bowker et al. 2020; Kahr et al. 2015; Vickerman et al. 2017; Wagner et al. 2017). This was supported by our review, with a general reported perception that e-cigarettes are less harmful than combustible cigarettes, and are therefore a better option during pregnancy. This review also highlighted the significant influence that healthcare professionals can have on perceptions in this area. Previous qualitative research investigating healthcare professionals' beliefs and attitudes towards e-cigarettes during pregnancy and postpartum, however, has identified limited knowledge and a lack of training in this area (Hunter et al. 2021). Therefore the importance of adequate training, to allow professionals to

suitably advise pregnant women (as well as the general public) about the risks and/or benefits of e-cigarette use is key, and should be provided if e-cigarettes are to be offered as a harm reduction approach nationally and internationally.

Switching to e-cigarettes can significantly reduce pregnant women's exposure to carcinogens, however nicotine exposure is still an area of concern (Hickson et al. 2019). Previous studies with animals and humans have suggested that nicotine exposure alone during pregnancy may have adverse effects in terms of lung development/function and brain development, as well as impacting behavioural outcomes and reducing birthweight (Batstra et al. 2003; Dwyer et al. 2008; Holbrook 2016; Navarro et al. 1989; Nguyen et al. 2019), although similar birthweights for babies born to women who use e-cigarettes and women who do not smoke have also been reported (Dhalwani et al. 2019), as well as reduced risk of miscarriage, ectopic/tubal pregnancy, and stillbirth (Cohn et al. 2022). Our review revealed mixed findings relating to associations between e-cigarette use and birth-related outcomes. There were reports of the same apparent risk of pre-term birth in women who exclusively use e-cigarettes, women who use both combustible and e-cigarettes, and women who only smoke combustible cigarettes, as well as increased risk of SGA and low birthweight reported in women who use e-cigarettes compared to those who don't (although rates for both were lower in women who used e-cigarettes than for those who smoked combustible cigarettes). This has been supported by a recent investigation reporting a 62% increase in the risk of preterm birth and low birthweights among women who use e-cigarettes during pregnancy compared to those who don't (Galbo et al. 2022). It is notable, however, that this study also utilised the PRAMS dataset, therefore investigating the same participants as a large number of the studies included in this review. There were also instances of studies reporting no association between e-cigarette use and each of these outcomes as well as no association with infant respiratory distress or foetal mouth movements. Additionally, e-cigarette use was reported to result in reduced toxin exposure, however abnormal reflexes were reported in infants of both women who use e-cigarettes and women who smoke combustible cigarettes as compared to women who do not smoke. Hajek et al (2019) investigated the efficacy and safety of e-cigarettes in comparison to nicotine patches among pregnant women. The RCT concluded that the safety profile of e-cigarettes is similar to that of nicotine patches, however, low birthweight (<2,500g) was less frequent in the e-cigarette arm of this study (14.8% versus 9.6%; RR = 0.65, 95%CI: 0.47–0.90, $p = 0.01$) in comparison to nicotine patches. This data suggests e-cigarettes might be an optional treatment for pregnant women who are trying to quit smoking (Hajek et al. 2019) and supports the use of e-cigarettes in stop-smoking services for pregnant women.

Previous research has suggested that e-cigarettes are now the most commonly used smoking cessation aid in England (McNeill et al. 2018), with e-cigarette use self-reported as a key reason for quitting smoking in previous studies (England et al. 2016; Mark et al. 2015) as well as across the studies in the present review. E-cigarettes have also been reported to be notably more effective than traditional NRT methods (Hajek et al. 2019; Hartmann-Boyce et al. 2021; Tong et al. 2008), however a previous review of e-cigarette use during pregnancy suggested no difference in smoking cessation rates between pregnant women using e-cigarettes and those not using them (Calder et al. 2021). Additionally, one study included in this review reported that, whilst e-cigarettes are an effective means of reducing tobacco consumption through moving from combustible to non-combustible

products, moving to e-cigarettes appears to decrease the likelihood of quitting nicotine products entirely. Higher quit rates have previously been identified in women who exclusively use e-cigarettes than in women who use both combustible and e-cigarettes or women who smoke only combustible cigarettes (Calder et al. 2021). Notably, most women who switched from dual use to exclusive e-cigarette use during pregnancy reported returning to dual use postpartum, whilst some women who used both combustible and e-cigarettes also reported switching exclusively to combustible cigarettes either during late pregnancy or postpartum (Calder et al. 2021). This builds upon previous reports that the majority of transitions from dual-use to single use in reproductive-aged women involve dropping the non-cigarette product in favour of combustible cigarettes (Kurti et al. 2018). These results suggest that e-cigarettes may serve as a useful alternative to combustible cigarettes during pregnancy, but that their efficacy as a smoking cessation tool may decrease once the pregnancy has ended.

Strengths and limitations

All sections of the review were carried out and reported following international guidance set out by PRISMA. Evidence quality was assured by using multiple reviewers throughout key stages of the process, and high reliability between reviewers at all stages. The review included a large number of studies, all of which were judged to be of moderate or good quality. Included studies were also conducted across multiple countries, although the majority of research was carried out in the United Kingdom or United States. Limitations of this review include that we did not search grey literature or consider studies that were not available in English. Many studies also relied upon retrospective self-report measures, recruiting postpartum women who were asked to recall smoking behaviours during pregnancy, potentially limiting the accuracy of data collected (although four studies also incorporated biological indicators that could verify self-report findings). In addition, many of the prevalence studies included in this review used the same population of participants from the United States (44% used PRAMS, 18.5% used PATH), whilst national differences were indicated in smaller studies with different populations.

Implications and conclusions

Whilst there is increasing research examining the prevalence of e-cigarette use during pregnancy, the effectiveness of e-cigarettes as a stop-smoking tool remains unclear. The evidence presented throughout this review suggests that stop smoking in pregnancy interventions should support pregnant people to stop smoking both combustible cigarettes and e-cigarettes (though exclusive e-cigarette use may reduce harm compared to combustible cigarette use or dual use). E-cigarette use during pregnancy was reported to be more prevalent in women with symptoms of depression, in homosexual women, and in incarceration-exposed women, as well as being associated with increased alcohol consumption 3 months before or during pregnancy. Interventions using e-cigarettes as smoking cessation tool in pregnancy, therefore, should incorporate support for depression and alcohol consumption, as well as offering additional support for sexual minorities. It is also important for services to offer postpartum support if they wish to prevent a return to combustible cigarette smoking. Interventions must also ensure that health professionals are appropriately equipped with knowledge about the relative safety of e-cigarettes, to effectively advise and support service users.

More prospective longitudinal studies investigating the health and birth outcomes associated with e-cigarette use during pregnancy are required to improve the quality of research evidence in this area and to allow clearer conclusions about the safety of e-cigarettes in pregnancy to be drawn. Future studies must also aim to accurately measure, and account for, the role of dual use (i.e., use of both combustible cigarettes and e-cigarettes) as well as exclusive e-cigarette use when examining associations with health-related outcomes. More qualitative research is also needed to examine the views and experiences of people who begin e-cigarette use during pregnancy, to better identify barriers and facilitators affecting the use of e-cigarettes as a smoking cessation and harm reduction tool.

Supplementary Material

Search strategies used and the characteristics of included studies are included in the supplementary material.

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