Evaluating Alcohol, Tobacco, and Other Substance Use in Pregnant Women

Shumona Sharmin Salam and Caroline Mitchell

1 Background

Substance use disorder in pregnancy is a critical public health concern that is linked with several adverse maternal and newborn health outcomes including preterm birth (PTB), low birth weight (LBW), and small for gestational age (SGA) babies. The most widely used substances in pregnancy in high-, low-, and middle-income countries (LMICs) include tobacco, alcohol, cannabis, opiates, cocaine, and other illicit substances. This guidance has been developed to help health-care providers in identifying and managing smoking, alcohol, and substance use disorders in pregnant women and thereby reducing the risks of PTB and other adverse maternal and child health outcomes.

This guideline summarises information from the WHO, other guidance (where available), and recently conducted systematic reviews on the risks of and interventions for antenatal exposure to smoking, alcohol, and substance use for PTB.

2 Evidence Statement

Use of alcohol, tobacco, and other psychoactive substances during pregnancy leads to an increased risk of health problems for mother and child such as spontaneous abortion, stillbirth, low birth weight, birth defects, and prematurity (Table 1). Concurrent

S. S. Salam (✉)
Oncology and Metabolism, University of Sheffield, Sheffield, UK
e-mail: shumona.salam@sheffield.ac.uk

C. Mitchell
Academic Unit of Primary Medical Care, University of Sheffield, Sheffield, UK
e-mail: c.mitchell@sheffield.ac.uk

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Table 1 Summary of evidenced tobacco, alcohol, and other substance use-related risk factors and interventions for PTB

Evidenced risk factor for preterm birth	Evidence of risk	Recommended action for evidenced risk factor for preterm birth*	Evidence of effectiveness of action
Alcohol and substance use			
Generic measures	Screening and brief interventions for substance use: All pregnant women should be asked about their alcohol and illicit substance use at every antenatal visit and offered brief interventions.		Evidence related to PTB or birth outcomes unavailable. Reviews of brief interventions for alcohol use among pregnant women (low-quality evidence) indicate a reduction in use [24–26].
Alcohol	Moderate drinking (18 g or 1.5 drinks/day: No effect [4] 36 g or 3 drinks/day: RR 1.23 (95% CI 1.05–1.44) [4]	**Psychosocial interventions** (e.g. motivational interviewing, cognitive behavioural therapy and contingency management) [13]: Pregnant women with alcohol or other substance use disorders should be provided individualised care **Detoxification or quitting programmes** for substance dependence in pregnancy [13]: • All pregnant women should be advised to quit and offered/referred to detoxification services as applicable. • Opiates: Opioid substitution treatment as available and not detoxification. • Pregnant women with alcohol withdrawal symptoms should be managed with the short-term use of a long-acting benzodiazepine. • Psychopharmacological medications may be useful to assist with symptoms of psychiatric disorders in withdrawal management but are not routinely required. **Pharmacological treatment** (maintenance and relapse prevention) for substance dependence in pregnancy [13]: • Not recommended for dependence on amphetamine-type stimulants, cannabis, cocaine, or volatile agents in pregnant patients. • Due to lack of evidence on the safety and efficacy of alcohol dependency treatment medications in pregnancy, an individual risk-benefit analysis should be conducted for each woman. • Opioid maintenance therapy with methadone or buprenorphine recommended for opiate dependence.	**Psychosocial interventions:** • Conditionally recommend by WHO due to lack of evidence [13]. • Evidence related to birth outcomes is limited. Systematic review indicates no difference in PTB rates (RR 0.71, 95% CI 0.34–1.51: Three trials, 264 participants, moderate quality evidence [27]. No difference in abstinence in any intervention group compared to control [27]. **Detoxification or quitting programmes** • Recommendations based on narrative synthesis of evidence and highly recommended [13]. • Systematic reviews report no differences in rates of PTB between opioid detoxification and other treatment groups such as opioid substitution treatment. Due to increased risk of relapse with opioid detoxification, opioid substitution therapy is recommended [28–31]. **Pharmacological treatment:** • Due to lack of evidence, pharmacological treatment is not recommended (conditional) for alcohol, amphetamine-type stimulants, cannabis, cocaine, or volatile agents in pregnant women [13]. • Although opioid maintenance therapy is beneficial in pregnant women, systematic review provides inconclusive evidence of the superiority of one treatment over another (low-quality evidence, studies conducted in high-income settings) [13, 30]. • Pharmacological treatment should be combined with psychosocial interventions [13].
Crack cocaine	OR 2.22 (95% CI 1.59–3.10) [10]		
Cocaine	OR 3.38 (95% CI 2.72–4.21) [11]		
Opioid	OR 2.86 (95% cl 1.11–7.36) [7]		
Cannabis	Pooled OR 1.29 (95% CI 0.80–2.08) [6]		
Marijuana	Unadjusted pooled RR 1.32 (95% CI 1.14–1.54) [5] Adjusted pooled RR 1.08 (95% CI 0.82–1.43) [5]		
Amphetamine	Unadjusted OR 4.11 (95% CI 3.05–5.55) [12]		

Tobacco and exposure to second-hand smoke (SHS)			
Generic measures	Screening for tobacco use and exposure to SHS [14]: Pregnant women should be asked about their tobacco use and exposure to SHS at every antenatal care visit		
Smoking	Pooled OR 1.27 (95% CI 1.21–1.33) [1]	**Psychosocial interventions** (e.g. counselling, feedback, health education, incentives, peer/social support) should be regularly offered to pregnant women who are either current tobacco users or have recently quit [14] **Pharmacological interventions** for cessation of tobacco use [14]: • Inconclusive regarding the recommendation on related to use or non-use of NRT to support cessation of tobacco use in pregnancy. • Bupropion or varenicline to support tobacco-use cessation in pregnancy is not recommended. • Further research needed to assess safety, efficacy, and compliance to pharmacotherapeutic cessation agents. **Interventions for exposure to SHS in pregnancy** [14]**:** • Public places: All public places including health-care facilities, workplaces, and public transports should be smoke-free to protect everyone including pregnant women. Homes: Pregnant women, their partners and household members should be given advice and information on risks of SHS and strategies to reduce SHS including smoking cessation support.	**Psychosocial interventions:** • Although previous reviews indicated reductions in preterm birth [14, 32, 33], recent Cochrane review (high-quality evidence) indicates uncertainty in whether women who received psychosocial interventions had reductions in PTB or not compared to the control group (RR 0.93, 95% CI 0.77–1.11, 19 RCTs, $n = 9222$). None of the studies included in assessing PTB were from LMICs [34]. **Pharmacological interventions:** • Cochrane review indicated insufficient evidence to determine the impact of NRT on rates of PTB (RR 0.81, 95% CI 0.59–1.11, 7 studies, 2182 women, low-quality evidence) [35]. No studies explored the use of varenicline and electronic cigarettes and only two studies explored bupropion. All studies were conducted in HICs [35]. I**nterventions for exposure to SHS in pregnancy:** • Implementation of various smoke-free legislation was associated with reductions in rates of PTB (risk change −3.77%, 95% CI -6.37 to −1.16, ten studies, $n = 27{,}530{,}183$) [36]; (risk change −10.4% 95% CI -8.9 to −2.0, four studies, $n = 1366\,862$) [37]. The majority of the studies are from HICs. Systematic reviews explored several interventions targeted to either the women or partner (e.g. educational and behaviour change interventions, smoking cessation support) to reduce SHS in homes [38–41]. Results varied and studies were of low quality with moderate to high risk of bias and did not have a standardised way of assessing exposure or outcome. None explored the effect on birth outcomes. Some studies were from LMIC settings.
Passive smoking	At any place: OR 1.20 (95%CI 1.07–1.34) [2] Home: OR 1.16 (95%CI 1.04–1.30) [2]		
Smokeless tobacco (India)	Pooled OR 1.39, 95% CI 1.01–1.91) [3]		

PTB Preterm birth, *LMIC* Low- and middle-income countries, *RR* Relative risk, *CI* Confidence interval, *NRT* Nicotine replacement therapy, *SHS* Second-hand smoke

use of these substances (i.e. poly substance use) further increases the risk of adverse outcomes in all settings.

This guideline proposes interventions (Table 1) for the identification and management of the following:

(i) Tobacco smoking and exposure to second-hand smoke (SHS) (protection from SHS in homes and public places, screening, psychosocial, and pharmacological).
(ii) Alcohol and illicit substance use (screening and dependency management) in pregnant women during the antenatal period.

Despite gaps in research and knowledge, the potential benefits of the recommended actions may help improve PTB and other birth outcomes.

3 Synopsis of the best Evidenced Risk Factors for Preterm Birth

For a summary of the evidence of tobacco, alcohol, and substance use-related risk factors for preterm birth, please see Table 1, in Sect. 5.

3.1 Smoking and Exposure to Second-Hand Smoke

(i) A systematic review and meta-analysis (2000) of prospective studies for any *maternal tobacco smoking* versus no maternal smoking and preterm delivery found the pooled odds ratio to be 1.27 (95% CI 1.21–1.33, 20 studies, >100,000 participants) [1]. All the studies were conducted in high-income countries (HICs).
(ii) A meta-analysis (2016) reported the ORs of PTB for women who were ever exposed to *passive tobacco smoking* versus women who had never been exposed to passive smoking at *any place* and at *home* were 1.20 (95% CI 1.07–1.34, 24 studies, 88,200 participants) and 1.16 (95% CI 1.04–1.30, 11 studies, 73,211 participants), respectively [2]. The associations were statistically significant for studies conducted in Asia (OR 1.26, 95% CI 1.05–1.52) [2]. Several studies were from low- and middle-income countries (LMICs) including China, India, Korea, and Indonesia.
(iii) A systematic review and meta-analysis of observational studies in India also indicated that 0.19 million PTB (6% of all PTBs) could be attributed to the use *smokeless tobacco (SLT)* (pooled OR 1.39, 95% CI 1.01–1.91, 2 studies, 1800 participants) [3].

3.2 Alcohol Use

A dose-response relationship between *alcohol consumption* during pregnancy and the risks of PTB was observed in a meta-analysis (2011) of 14 observational studies (n = 280,443 pregnant women) primarily in HICs [4]. Compared with mothers who do not drink, the overall dose-response relationships for PTB showed (i) no effect up to 18 g pure alcohol or an average of 1.5 drinks/day and (ii) 23% increase in risk at an average of three drinks or 36 g/day (RR 1.23, 95% CI 1.05–1.44) [4].

3.3 Substance Use

(i) Two systematic reviews (2016) were identified that explored maternal *cannabis/marijuana* use and the risks of preterm birth [5, 6]. No association was demonstrated between in utero exposure to marijuana/cannabis and PTB (pooled OR 1.29, 95% CI 0.80–2.08, 9 studies) compared to non-users [6]. Three studies included in the review showed an increase in odds of PTB, while six showed no association. Only two studies included were from LMICs—Iran and Jamaica [6]. Although marijuana use during pregnancy was associated with an increased risk of PTB in the pooled unadjusted analysis, (15.3% compared with 9.6%, pooled RR 1.32, 95% CI 1.14–1.54), results were found to be insignificant after adjusting for tobacco use and other confounding factors (pooled RR 1.08, 95% CI 0.82–1.43) [5].

(ii) *Opiate use* (heroin, opium) is associated with an increased risk of premature birth and a number of other maternofoetal adverse outcomes. Findings from observational studies show that, compared to cocaine or opiate non-users, opiate users were 2.86 times as likely (95% Cl 1.11–7.36; p = 0.03) to deliver preterm [7]. Similar results were also seen in other observational studies conducted in Iran [8] and low-income, multi-ethnic US population [9].However research is heavily skewed to high-income country settings.

(iii) *Crack cocaine* use during pregnancy was associated with significantly higher odds of preterm delivery (OR 2.22, 95% CI 1.59–3.10) [10]. Eight observational studies were included (n = 5761) in the meta-analysis; only one was from a LMIC (Iran) [10]. Systematic review and meta-analysis of 24 observational studies in HICs (n = 39,860) shows that *cocaine* use during pregnancy was associated with significantly higher odds of PTB (OR 3.38, 95% CI 2.72–4.21) [11].

(iv) A significant increase in unadjusted risks of PTB (OR 4.11, 95% CI 3.05–5.55, 5 studies, n = 62,070) was identified among women exposed to *amphetamines* in pregnancy. All five studies included in the review were from HICs [12].

4 Practical Clinical Risk Assessment Instructions for PTB

4.1 Health-care providers should ask all pregnant women about their use of alcohol and other substances (past and present) early in pregnancy and at every antenatal visit. WHO recommends the use of validated screening instruments for this purpose [13, 14]. There may be cultural taboos which compound stigma and other difficulties in disclosure of substance use such as fear of judgement by health-care providers, breach of confidentiality, and fear of child removal after the birth.

4.2 All guidance encourages health-care practitioners to explore these issues sensitively, using a non-judgemental approach and in a confidential environment. There may, however, be child safeguarding issues which arise during this assessment which should be dealt with using in-country mechanisms, while optimising maternal physical and mental health. The presence of family members during maternal health checks may also act as a barrier to full disclosure.

4.3 Listed below are screening instruments that have been suggested to be used for prenatal assessment of pregnant women [13, 14]. There are variations in the tools regarding number of items, administration method (paper and pencil, computer), training needed, and location (prenatal clinic/outpatient/inpatient). Although some of the tools were validated, they will need to be further validated before use in an LMIC context.

- Tobacco, alcohol, and substances: Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST Version 3.0); Pregnancy Information Program (PIP).
- Alcohol and General Substance Use: 4P's Plus [15]; Substance Use Risk Profile—Pregnancy (SURP-P) [16].
- Alcohol: Alcohol Use Disorder Identification Test (AUDIT) [17]; Alcohol Use Disorder Identification Test—Consumption (AUDIT-C) [18]; CAGE [19]; Short Michigan Alcohol Screening Test (SMAST) [20]; Ten Question Drinking History (TQDH) [21]; T-ACE [22]; TWEAK [23].

5 Evidenced Effective Interventions for Risk Factors for Preterm Birth

These are summarised in Table 1.

6 Summary of Interventions for Smoking and Second-Hand Exposure to Smoke (Table 2)

7 Summary of Interventions for Alcohol and Substance Use (Table 3)

Table 2 Benefits statements of effectiveness of smoking cessation interventions to prevent preterm birth

Low (possible) benefit
• Identification of tobacco use and second-hand smoke (SHS) exposure in pregnancy [14].
• Psychosocial interventions (as per local in-country clinical guidelines and resources) [14].
• Pharmacological interventions (as per local in-country clinical guidelines and resources) [14].
• Protection from second-hand smoke in pregnancy (homes and public places) [14].

Table 3 Benefits statements of effective interventions to promote harm reduction to prevent preterm birth

Low (possible) benefit
• Screening and brief intervention [13].
• Psychosocial interventions (as per local in-country clinical guidelines and resources) [13].
• Detoxification or quitting programmes (as per local in-country clinical guidelines and resources) [13].
• Pharmacological treatment (as per local in-country clinical guidelines and resources) [13].

8 Research and Clinical Practice Recommendation

There is strong consensus within the literature about the negative effects of alcohol, tobacco, and substance use during pregnancy, and all women should receive necessary interventions to stop (preferably) or reduce use. The evidence is of low quality, and further primary research and controlled trials are needed on effective ways to assess exposure and the use of alcohol, tobacco (including second-hand exposure), and substances; measure the effect on maternal and child health outcomes and for determining the effectiveness and cost-effectiveness of recommended interventions in pregnancy. Additionally, there is also a dearth of studies conducted in LMICs. Assessment methods should include and integrate findings from policy, public health, behavioural and implementation science, and trials of interventions where PTB is the primary outcome measure. In addition, longitudinal cohort studies which include consideration of multi-factorial psychosocial factors are needed to assess the risks on women, children, and future generations.

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