

Effectiveness of brief alcohol interventions for pregnant women: A systematic literature review and meta-analysis

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Abstract

Background

Prenatal alcohol exposure (PAE) can result in a range of adverse neonatal outcomes, including Fetal Alcohol Spectrum Disorder (FASD). This systematic review and meta-analysis sought to investigate the effectiveness of brief interventions (BIs) in eliminating or reducing 1) alcohol consumption during pregnancy; and 2) PAE-related adverse neonatal outcomes.

Method

We conducted a systematic literature search for original controlled studies (randomized control trials (RCTs); quasi-experimental) in any setting, published from 1987 to 2021. The comparison group was no/minimal intervention, where a measure of alcohol consumption was reported. Studies were critically appraised using the Centre for Evidence-based Medicine Oxford critical appraisal tool for RCTs. Meta-analysis of continuous and binary estimates of effect-size for similar outcome measures for BIs versus control groups were pooled and reported as Cohens' d / Hedge's g and odds ratios (ORs), respectively.

Results

In total, 22 studies (4,865 participants), all from high income countries, met inclusion criteria. Abstinence outcomes available in 12 studies ($n = 2,620$) found modest effects in favor of BI conditions ($OR = 1.56$, $95\% CI = 1.15 - 2.13$, $I^2 = 46.75\%$). BI effects for mean drinks/week (Cohen's $d = -0.21$, $95\% CI = -0.78$ to 0.36) and AUDIT scores ($g = 0.10$, $95\% CI = -0.06$ to 0.26) were not significant. Among seven studies ($n = 740$) reporting neonatal outcomes, BI receipt was associated with a modest and significant reduction in preterm birth ($OR = 0.67$, $95\% CI = 0.46 - 0.98$, $I^2 = 0.00\%$). No statistically significant differences were observed for APGAR score, mean birthweight, or likelihood of low birth weight (LBW).

Conclusion

BIs are moderately effective in increasing abstinence during pregnancy and preventing preterm birth. More studies on the effectiveness of BIs are needed from low- and middle-income countries, as well as with younger mothers and with a broader range of ethnic groups. There is also an urgent need for systematic research seeking to enhance the efficacy of brief interventions.

Background

Alcohol use during pregnancy is a significant health concern globally. Decades of research have provided overwhelming evidence that alcohol is a teratogen that can significantly harm the developing fetus. Prenatal alcohol exposure (PAE) increases the risk for many adverse maternal and neonatal outcomes, including spontaneous abortion (1), stillbirth (2), low birthweight (LBW) (3, 4), intrauterine growth restriction (IUGR) (3, 5), and preterm birth (6, 7). PAE can also result in Fetal Alcohol Spectrum Disorder (FASD) in the child, a lifelong neurodevelopmental disorder that poses significant physical, mental and

social challenges to affected individuals. Even relatively low levels of maternal alcohol consumption can cause FASD (8). FASD affects approximately one in every 13 children who were prenatally-alcohol exposed (9), though this disorder is widely misdiagnosed and underdiagnosed (10). FASD can lead to many organ or system defects and is associated with more than 400 disease conditions (11). This poses an enormous cost to service systems related to increased use of health care services, involvement in child welfare, and correctional systems (12, 13).

Globally, approximately 10% of women consume alcohol during pregnancy and 3% of these women report having 4 or more drinks in one sitting (i.e., binge drinking) (14). These prevalences are expected to increase based on global trends such as increasing alcohol consumption among women of childbearing age, increasing social acceptability of women's alcohol use, as well as recent changes in alcohol use patterns due to the COVID-19 pandemic, all of which will increase the number of alcohol-exposed pregnancies and increase the risk of FASD. Alcohol use during pregnancy may be more common among women who have been exposed to intimate partner violence, have limited access to education or prenatal care, have substance use disorders, or use tobacco (15). In particular, negative attitudes toward the pregnancy or attitudes conducive of alcohol use during pregnancy are both predictive of maternal alcohol consumption (16, 17). Stigma experienced by pregnant women and by mothers of children with FASD can lead to these women avoiding contact with services that could help them (18). Notably, any decrease in alcohol use during pregnancy is beneficial in terms of fetal health outcomes (19), suggesting a potentially powerful role for obstetricians and midwives in preventing alcohol-related harms during pregnancy.

Prevention and treatment of substance use in pregnancy is central to the 2015 United Nations Sustainable Development Goals (20) and the WHO recommendations for FASD prevention are based on universal screening and early intervention for PAE (21). Brief interventions (BIs) are an evidence-based, healthcare-centric approach consisting of a short counselling session wherein a healthcare provider seeks to promote behavioral change, typically using motivational techniques. BIs are typically paired with universal proactive screening in approaches referred to as Screening and Brief Intervention (SBI) or Screening, Brief Intervention, and Referral to Treatment (SBIRT). In obstetric settings, BIs present the opportunity to educate and empower women to make their own choices to promote healthy outcomes for themselves and their children. BIs may be a low-cost option to prevent PAE that could simultaneously strengthen the provider-patient relationship and reduce the likelihood of FASD in the child. The efficacy of person- and technology-delivered BIs has been studied extensively in general populations (22), however, fewer studies have examined their utility during pregnancy. Although studies in this area have accumulated sufficiently to support early meta-analysis (23), this systematic review and meta-analysis sought to update those efforts with more recent studies and to add analysis of BI effects on neonatal outcomes.

Objectives

This study aimed to investigate the effectiveness of alcohol BIs (BIs) in eliminating or reducing 1) alcohol consumption during pregnancy and 2) PAE-related adverse neonatal outcomes; and to investigate the economic evaluation of BIs during pregnancy.

Method

Two methods were employed: a) A comprehensive systematic literature review; and b) Meta-analysis. A comprehensive systematic literature search was conducted for original quantitative studies (randomized control trials (RCTs); quasi-experimental) that reported on the effectiveness of alcohol BIs in pregnant women in any setting and /or PAE-related adverse neonatal outcomes. The search focused on studies published from 1987 to 2021, and the search was not restricted geographically or by language. Online databases: MedlineOvid (All), CINAHL, PsychInfo, and EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) were searched. Web of science (*social citation index expanded, social sciences citation index, science/ social science and humanities conference proceedings citation index, emerging sources citation index*), Google Scholar, International Committee on Harmonization of Good Clinical Practice (ICH-GCP) clinical trial registry, European Monitoring Centre for Drugs and Drug Addiction, Canadian Centre on Substance Use and Addiction were also searched. A detailed search strategy is available (Additional File 1).

Studies were included if they were experimental (individual or cluster-randomised control trials), or quasi-experimental (i.e., interrupted time series) studies, included a control group (no care, or any routine treatment as usual), where the intervention was a BI, which was mentioned as brief/ short, and this was regardless of the duration, frequency of sessions, components, provided by a personnel or computer; were conducted with pregnant women; and alcohol was reported separately from other substance use (tobacco, or drugs). We included studies regardless of maternal age, baseline alcohol use, parity, gestational age, or level of alcohol consumption during pregnancy. Studies were excluded if the BI was combined with pharmacological interventions on PAE or neonatal outcomes, or if the BI was conducted outside of the pregnancy period (e.g., preconception, post-partum, or breast-feeding).

Article screening and data extraction

Study selection was conducted in two phases: 1) title and abstract screening; and 2) full-text screening. Screening at both phases was conducted independently by two investigators (EP and DD). Studies deemed to be potentially relevant that were published in languages other than English were translated either by colleagues fluent in the respective language or using Google Translate, and subsequently cross-checked by a native speaker. Based on the articles agreed upon for inclusion, data were extracted and recorded in the Excel spreadsheet, designed based on Cochrane guideline by one investigator and then independently cross-checked by a second investigator (24). All discrepancies were reconciled by team discussion.

Outcomes

The primary outcome for this study was change in alcohol use, comparing the BI group to the control group. Any outcome measures which could quantify this effect were extracted and included in data synthesis (e.g., mean AUDIT scores or daily drinks per week or binge drinking days, percentage/ odds/ risk of abstainers, odds/ risk ratio of reduced risk drinking). The secondary measures of interest were neonatal outcomes related to PAE in the BI versus control group (e.g., percentage/ odds/ risk of pregnancies with FASD, low APGAR scores, small for gestation age, admitted in neonatal intensive care unit (NICU), mean birth weight, mean head circumference). The third outcome of the study was cost-effectiveness of BI versus controls.

Quality assurance

The quality of each study was appraised using a tool specifically for use in the systematic evaluation of RCTs, developed by the Centre for Evidence Based Medicine (CEBM) from Oxford University (25). This tool allowed to appraise each intervention study using specified criteria to assess the following domains: internal validity, randomization, measurement, reporting of results and external validity. Two investigators (EP and DD) independently conducted critical appraisal of the included studies.

Meta-analysis

Meta-analyses were conducted for those outcome measures that had at least two studies/ intervention arms and all the required statistical information to compute the pooled OR, or Cohen's *d* or Hedge's *g*. The effect-size for continuous outcome measure of reduced alcohol consumption or neonatal outcomes (e.g., mean drinking days/week, binge drinking days, mean head circumference, mean birth weight, mean AUDIT scores) were presented as standardized mean difference (Cohen's *d*) (26). Binary outcomes for alcohol reduction and neonatal outcomes (e.g., proportion or risk ratio of alcohol abstainers, risky drinkers, binge drinkers, pre-term births, small for gestational age) were reported as ORs. The standardized mean differences were then converted to Hedge's *g* to address the biased estimates of the population effect size, particularly for sample size < 20 (27). A separate analysis was conducted to deal with outliers or influences (small study effect) by excluding studies whose 95% confidence intervals (95% CI) does not overlap with the pooled 95% CI and conducting influence analysis (28, 29). A random-effect inverse-variance model was used under the assumptions that outcomes measures of studies are different yet related and follow normal distribution (30). The extent of heterogeneity between the studies was quantified by calculating I^2 statistic (0–40%: might not be important; 30–60%: moderate heterogeneity; 50–90%: substantial heterogeneity; 75–100%: considerable heterogeneity) (30). In cases where studies had more than one follow-up/ repeated measures of alcohol use during pregnancy, the time-point selection was based on the author's rationale for the importance of the time-point in the study (e.g., if there are three observation points in a study and 1 month, 2 month and 3 month and author suggests that alcohol use rate suddenly decreases in the second month and then stabilises after the third month post-intervention then the observation at 3 month should be considered).

Unit-of-analysis

For cluster-randomized control trials where design effect/ multilevel analysis was not considered (inappropriate analysis), the external intra-class correlation coefficients (ICC) were adopted for similar (clusters) C or outcomes to calculate effect size estimates and their standard errors/ deviations (6). These results were then combined with individual randomised control trials (where individuals are both unit of randomisation and analysis) in the same meta-analysis for a pooled effect size. Each intervention arm was considered a unit of analysis in studies where more than one intervention arm was compared to the control group.

Sensitivity analysis

For comparability, sub-groups of similar combinations of intervention and control were constructed. A sub-group analysis for each outcome of each interest was conducted, only if there were at least two studies in each sub-group. Meta-regression analysis was conducted to adjust for the influence of potential moderators on the effect size (study design, study setting, type of population, baseline group difference in alcohol use, alcohol use measurement scales, age, attrition (or retention rate), and delivery mode of intervention to provide more conservative estimates of effect size (31, 32).

Risk of bias/publication bias

The publication bias or small study effect assessment was conducted using the funnel plot of standard error plotted against the effect-size, and Egger's weighted regression test (33). At least 10 studies were required in the meta-analysis in order to have enough power to distinguish real asymmetry or skewed distribution in the funnel plots (34). The P-value of < 0.05 in Egger's weighted regression test suggests significant publication bias or small study effect (33).

Results

The systematic literature search generated 20,754 studies in total, identified from electronic sources and hand-searching. Only 26 articles met the inclusion criteria and were included in the review. Of these studies, 24 had BI and control groups and were eligible for inclusion in the meta-analysis: 17 studies reported only alcohol use, 6 studies reported both alcohol use and neonatal outcomes, and 1 study reported only neonatal outcomes. The remaining two studies reported alcohol use (one study each without control group, and control group having almost similar components as the BI group) and were synthesized narratively. No eligible studies were found on cost-effectiveness of BIs (Fig. 1).

Please insert Fig. 1 about here -

Most of the studies ($n = 15$; 57.7%) were conducted in the USA (35–49), followed by two studies (7.7%) in South Africa (50, 51), and one study (3.8%) each in Brazil (52), Ireland (53), Israel (54), Netherlands (55), Norway (56), Spain (57), Sweden (58), and UK (59).

Quality assessment

Only 25 studies had a control group and were assessed using the CEBM tool. Individuals were not randomized in 8 studies (40, 53, 58, 59), and 4 studies were cluster-randomized control trials (C-RCTs) (35, 44, 51, 55). Baseline characteristics were not comparable or were unclear for intervention versus control in 11 studies (35, 36, 38, 40, 45, 46, 51–55). In four studies, the intervention and control groups were treated equally, apart from the treatment itself (35, 36, 42, 43). Participants were not accounted for in nine studies (38.5%) (35, 42–44, 54–56, 58, 59). In all, 11 studies (44%) did not explicitly mention conducting intention to treat (ITT) analysis (36, 39, 42, 43, 47, 48, 52, 54, 56, 58, 59). In total, 18 studies (88.5%) did not mention blinding the assessor (data analyst) or the follow-up researcher to the intervention condition (37–41, 44–46, 48, 51–56, 58–60). Two studies did not report the effect-size (46, 56). In total, 6 studies did not report important statistics (e.g., range; 95% CI; p-value, etc.) to estimate the true effect (40, 42, 46, 47, 56, 59), (Additional File 2).

Study settings and designs

Half of the studies (n = 13; 50%) were conducted in obstetrics or prenatal clinics within hospitals (35, 36, 38, 42, 43, 45–49, 57, 59, 60), followed by 8 (30.8%) in clinics or health care centers in rural or urban areas (37, 39–41, 44, 50, 51, 53), and 2 (7.8%) in midwives' offices (55, 56), and maternity care or women health centers (52, 58). One (3.8%) study was conducted in an in-patient pre-delivery and emergency unit of the hospital (54) (Additional File 3).

Among the 25 studies that had a control group, 17 (65.4%) studies were RCTs (36–39, 41–43, 45–49, 52–54, 57, 60), and 4 were C-RCTs (35, 44, 51, 55). Among the remaining four studies, two studies selected non-equivalent controls from the same setting using different time points (56, 58), and two studies examined controls from a different setting (40, 59), (Appendix Table 2).

Characteristics of pregnant women included in the studies

In total, 11 (42.3%) studies had age criteria for inclusion of pregnant women in the study, with the majority (n = 9 studies, 34.6%) including only pregnant women aged 18 years and above (37, 41, 45–47, 49, 52, 53, 55). One (3.8%) study included pregnant women 16 years and over (38), and one (3.8%) study included participants 15 years and over (51).

In total, 14 studies recruited pregnant women based on their gestational age at baseline: majority of the studies recruited in third trimester (n = 9, 34.6%) (36–39, 41, 42, 45, 46, 54), three studies (11.5%) in second trimester (48, 49, 51), and one study each that included pregnant women in first trimester (55) and between 20–30 weeks of pregnancy, respectively (52).

The majority of studies (n = 15; 57.7%) recruited pregnant women who had indicated some alcohol use (any level) during their pregnancy (35, 37, 39, 42–44, 46, 47, 51, 53, 55–59), followed by 6 studies (23.1%) where women indicated alcohol or other substance use (any level of drinking, reported separately from other substances) (38, 40, 41, 48, 52, 54), four studies (15.4%) that specifically included women who were

deemed risky-level drinkers at baseline (36, 45, 49, 50), and one study (3.8%) that included moderate-level drinkers (60)

Screening tools used at baseline and post-intervention

More than one-third of the included studies ($n = 9$, 34.6%) used T-ACE (*positive/ scores ≥ 2*) (36, 39, 42, 45, 47, 48, 52, 55), followed by timeline follow back (TLFB) used in seven (26.9%) studies (36, 38, 45–47, 57, 60), and six (23.1%) studies that used the Alcohol Use Disorders Identification Test (AUDIT-10) (37, 46, 50, 51, 54, 57) for screening alcohol use among pregnant women (Additional File 4).

Components of intervention and control groups

The intervention group received alcohol use screening (T-ACE, AUDIT-10 or TLFB) in all studies. In addition to alcohol use screening, 15 (57.7%) studies also provided Motivational Interviewing (MI) (37–39, 42, 43, 45–48, 50, 51, 54, 55, 57, 58), 3 (11.5%) studies used Motivational Enhancement Therapy (MET) and Cognitive Behavioural Therapy (CBT) combined (MET-CBT) (36, 38, 52), and 2 studies used MET alone (41, 49). One (3.8%) study each used MI + CBT (44). In these studies, counseling focused on the importance of alcohol abstinence in pregnancy (35); harm reduction with drink-size assessment (34), or health communication for healthy lifestyle (40); brief advice to reduce alcohol intake (59); non-stigmatizing counseling advising a reduction in alcohol consumption for women not able to abstain completely (56); or a brief discussion with no specific recommendation on alcohol use (53). Counseling in most of the studies ($n = 10$ studies each, 38.5%) was provided by health professionals: in 4 (15.4%) studies by clinicians/ psychiatrists (36, 37, 41, 59), three studies by nurses (11.5%) (38, 46, 49), two studies by midwives (11.5%) (56, 58), one study (3.8%) by a nutritionist (44); and in 10 studies by trained field researchers (39, 40, 42, 43, 47, 50–54). In terms of the format of the intervention, three (11.5%) studies had self-administered computer-based counselling (45, 48, 57), and 3 (11.5%) studies had both intervention personnel and computer-based counseling (35, 55, 60). Most studies ($n = 14$) included one single session varying in length from 5–60 minutes (35, 36, 40, 42–47, 53, 54, 57, 59, 60), (Additional File 3).

Of the 25 studies that had a control group, two studies provided controls with no screening or other treatment component at baseline, who were only screened at follow-up to record their change in alcohol use (54, 56). While 23 studies provided their control group with alcohol use screening at both baseline and at follow-up (35–49, 51–53, 55, 57–60). Among these 23 studies, three provided only screening in their control groups with no other treatment component (35, 42, 46) while the remaining 20 (76.9%) studies had other treatment components in combination with the screening (36–41, 43–45, 47–49, 51–53, 55, 57–60). In these studies, the control group received advice or counseling to abstain from or reduce alcohol use or to minimize the impact of drinking during pregnancy on the fetus by: healthcare staff in seven (26.9%) studies (37, 39, 44, 49, 55, 57, 58), or in the form of educational material in the form of brochure/videotape/manual in eight (30.8%) studies (36, 38, 39, 43, 47, 48, 51, 59), or received information regarding local places to assist them with alcohol management in two (11.5%) studies (38,

60). Two studies mentioned providing usual care to the controls, but no detailed information was provided about the components (40, 53). In fact, two (7.7%) studies received more extensive treatment than control groups in other studies (41, 52), at a level of intensity comparable to that of the intervention condition. In one of these studies, for example, the control group received at least 3 sessions of MET from clinicians that were 60 minutes or more in duration (same as the intervention), with the only difference being the intentional removal of some MET principles (e.g., avoiding confrontation, asking open-ended questions, reflective listening) (41). In the other study, both the intervention and control groups were provided with the same CBT treatment (4 sessions, 7 minutes each), but the control group did not receive two post-intervention monitoring calls (52) (Additional File 3).

Changes in antenatal alcohol use

Of 25 studies reporting change in alcohol use pre-post intervention (Additional File 2), only 6 (24%) demonstrated significant reductions in alcohol use (36, 43, 44, 48, 51, 55). A total of 17 of the 25 studies (68%) found no significant changes in alcohol use between BI and control groups (37–39, 41, 42, 45–47, 49, 53–55, 57–60). One study involving adolescent pregnant women reported a substantial reduction in pre-post alcohol use in BI (22.3–13.1%) and controls (2.4–1.7%), without providing between group differences (40). Another study without a control group found that pregnant women with heavy drinking showed a significant drop in mean drinks/week in the second trimester (8.6, $P < 0.001$), and third trimester (8.1, $P < 0.001$) after receiving BI compared to baseline (16.0) (50). Finally, a study in Brazil found that both groups receiving BI with 2 weekly monitoring follow-up components (2 monitoring calls by the researcher in the first and second week post-intervention) versus those receiving BI without the monitoring component show higher reduction in mean-AUDIT, and mean T-ACE scores. No comparison for the change provided for between groups difference (52). However, the percentages of abstinent pregnant women observed post-intervention were (92.3%) in the BI alone group compared to (100%) in the BI with monitoring component group. Regardless of the monitoring component, the study highlighted the importance of early intervention (from the first antenatal visit) in pregnancy to achieve significant reduction in prenatal alcohol use.

Meta-analysis of alcohol abstinence post-intervention (BI v/s control)

Meta-analyses of 12 BI arms versus control groups (38, 39, 42, 43, 45, 55–58, 60) for a combined total of 2,620 pregnant women indicate that the BI group has 56% higher odds of being abstinent during pregnancy at any time-point (OR = 1.56, 95%CI = 1.15–2.13, moderate heterogeneity = 46.75%) (Fig. 2).

Please insert Fig. 2 about here -

Meta-analysis of mean AUDIT post-intervention (BI v/s control)

Only 3 studies reported mean AUDIT scores (46, 53, 54) during pregnancy. The pooled estimates of mean AUDIT scores for a total of 610 pregnant women show a small and statistically insignificant difference between the BI group versus the control group (hedge's $g = 0.10$, 95%CI = - 0.06 to 0.26, heterogeneity that can be ignored = 0.0%) (Fig. 3).

Please insert Fig. 3 about here -

Meta-analysis of mean drinks/week

The pooled estimates of 166 participants (55) (two intervention arms, one study) observed small and statistically insignificant difference in the mean drinks/week between BI versus control group (Cohen's $d = - 0.21$, 95%CI = - 0.78 to 0.36, substantial heterogeneity = 67.24%) (Fig. 4).

Please insert Fig. 4 about here -

Subgroup analysis

As this review found fewer than the required number of studies in meta-analysis for change in prenatal alcohol use and neonatal outcomes, sub-group/moderator analyses were not conducted.

Publication bias and small study effect

The funnel plot for the percentage of alcohol abstinence (Fig. 5) shows asymmetry indicating publication bias. However, the small study effect obtained from Peters test was not significant ($P = 0.255$), suggesting that smaller studies with larger effect size did not contribute to the publication bias.

Please insert Fig. 5 about here -

Neonatal outcomes (BI versus control)

In total, seven studies reported neonatal outcomes (39, 46, 47, 55, 58). The neonatal outcome measures reported in these studies were: preterm delivery (35); NICU admission (35); healthy pregnancy (live birth of $\geq 2,500$ grams with no admission to NICU) (45); mean difference in birth weight (47, 54); mean difference in head circumference (47, 49); body length; Appearance, Pulse, Grimace, Activity, and Respiration (APGAR 1- or 5-minute) (36, 40, 54); percentage of neonates born preterm (38), and LBW (35, 38).

Only 3 studies showed significant difference in the neonatal outcomes between intervention and control groups, two in favour of the intervention and one in favour of the control (35, 47, 49). Armstrong and colleagues observed that the intervention group had 72% lower odds of LBW compared to the control group (OR = 0.28 (0.10–0.80; 0.02) (35). Similarly, Tzilos and colleagues demonstrated a significant differences in birthweight (in favor of intervention) ($F(1, 44) = 0.13$), $P = 0.03$), mean birthweight of intervention group versus control was 3189.6 ± 328.0 and 2965.3 ± 387.7 , respectively; $d = 0.62$ (47). In

contrast, Rubio et al. reported significantly lower mean birth weight in the intervention group compared to the controls (3014 grams vs 3160 grams; $P = 0.04$) (49).

Meta-analysis of mean birth weight

The pooled estimate of difference in the standardized mean difference in birth weight (grams) (Cohen's d) (47, 49, 54) is small and statistically insignificant when comparing BI ($n = 406$) and control group (Cohen's $d = 0.16$, 95%CI= -0.36 to 0.68, with considerable – substantial heterogeneity = 81.40%), (Fig. 6).

Please insert Fig. 6 about here –

Meta-analysis of low birthweight

The pooled estimate of 2 studies (35, 38) for odds of LBW in the offspring of 1415 mothers studied does not show a significant difference between the BI (cases = 28) versus control group (cases = 33) (OR = 1.02, 95%CI = 0.44 to 2.40, moderate heterogeneity = 59.03%), (Fig. 7).

Please insert Fig. 7 about here –

Meta-analysis of preterm birth

The meta-analysis for 3 intervention arms (2 studies) versus control groups, in 740 participants (35, 38) observe 33% lower odds of preterm birth among pregnant women in the intervention groups (cases = 47) compared to the control groups (cases = 79) (OR = 0.67, 95%CI = 0.46 to 0.98, small heterogeneity that can be ignored = 0.00%), (Fig. 8).

Please insert Fig. 8 about here –

Discussion

This review found that BIs were overall effective in increasing abstinence from alcohol during pregnancy. Results show that the odds of abstinence were significantly (56%) higher in pregnant women who received BIs compared to controls. However, despite small effects in the expected direction, no statistically significant difference was observed for changes in frequency of drinking (i.e., mean drinks/week) and AUDIT scores. Abstinence from alcohol during pregnancy is the only manner in which to completely prevent FASD in the child; however, complete abstention may not be possible for women with alcohol use disorders (AUDs), for example. More research is needed on BIs for pregnant women with AUDs or who have concurrent substance use disorders. Furthermore, in women with high pre-pregnancy drinking levels, prenatal care providers can impart additional family planning counselling in order to prevent high levels of PAE that may occur in early pregnancy.

For neonatal outcomes, it was found that pregnant women who received a BI had significantly lower odds (33% lower) of preterm birth when compared to the control groups, but no statistically significant

differences were observed for APGAR score, mean birthweight, or LBW outcomes. It is important to understand that various chronic adverse effects of PAE, including changes in the brain structure and volume (61), immune system changes (62), and susceptibility to mental health disorders (63, 64), and of course FASD itself, cannot be assessed in neonates. Though there are many moderating factors such as nutrition and other substance use during pregnancy, it is worth noting that preventing PAE significantly reduces the risk of many adverse health and social outcomes that are typically associated with FASD.

No studies were found on cost-effectiveness of BIs for pregnant women and, therefore, the review did not analyze these outcomes. It is worth noting, however, that BIs can be as short as five minutes and formats such as computer-delivered are not resource-intensive. Ultimately, access to BIs begins with screening for alcohol use, which is underutilized in prenatal care settings globally (65). However, even a single question about alcohol use during pregnancy has immense potential to change a woman's alcohol use behaviours (47, 66). Women are generally accepting of alcohol use screening (67), and so it is important for care providers to use visits as an opportunity to screen women and offer non-judgmental support in this efficient and low-cost manner. Furthermore, women can be referred to more intensive, effective programs that reduce maternal substance use, such as the Parent-Child Assistance Program (PCAP), which has proven to be cost-effective (68).

These findings are in line with previous reviews on BIs for alcohol use in pregnant women. For example, Eng et al.'s systematic review of interventions seeking to prevent alcohol-related harm during pregnancy (69) also found some support, although inconsistent, for alcohol-focused BIs in pregnancy. The meta-analysis by Gomez and colleagues (23) found stronger support for psychosocial interventions for alcohol use during pregnancy than we report here, but included a broader range of intervention types.

Three key aspects of this literature merit highlighting. First, studies in this area are highly variable in inclusion criteria, intervention characteristics (including dose and duration), outcome measures, follow-up duration, and in the extent to which key details are reported. These factors certainly contribute to the inconsistency of results seen in the reviewed studies. Second, this area is marked by a lack of rigorous research seeking to identify subgroups that might respond best to BIs, or seeking to identify the key behavior change techniques, duration, or frequency needed to obtain stable effects on alcohol in pregnancy. Early work of this type has suggested that two sessions may be more effective than a single session (70), which if true would mirror the tobacco brief intervention literature (71). Third, the relatively small effects seen with BIs means that larger samples will be crucial for clearly identifying any positive BI effects.

Strengths and Limitations

This review has several notable strengths, including its inclusion of a wide range of studies with various outcome measures, its detailed meta-analyses, as well as its extension of previous literature by including neonatal outcomes from BIs. This study also has several limitations. Firstly, across all studies included, there was a high within-group variation among both BI groups and control groups, in terms of their

components, educational content, number of sessions, and duration of intervention. Studies utilized a variety of tools (n = 11) to screen alcohol use among pregnant women, with varying sensitivity, specificity and overall clinical utility, and even different approaches to scoring (65). Moreover, the baseline characteristics of pregnant women were also variable in terms of their biological age, gestational age, and levels of alcohol consumption. Due to a limited number of studies, it was not possible to conduct sub-group analysis to explore factors influencing the heterogeneity. For this reason, it is not possible to draw conclusions about which sub-populations of pregnant women may benefit most from specific formats or techniques used in BIs for alcohol use.

Conclusions

Based on the findings from this study, we can conclude that BIs are moderately effective in increasing abstinence during pregnancy and may also be modestly effective at preventing preterm births among infants at high risk for PAE. More studies on the effectiveness of BIs in alcohol use in pregnant women are needed from low- and middle-income countries, as well as among younger mothers, and some subpopulations who are at high risk for alcohol use during pregnancy. There is also a clear need for rigorous research seeking to optimize BI efficacy, in part by exploring subgroups that are most likely to benefit from these interventions.

Abbreviations

APGAR – Appearance, Pulse, Grimace, Activity, and Respiration

AUD – Alcohol use disorder

AUDIT - Alcohol Use Disorders Identification Test

BI – Brief intervention

CBT – Cognitive behavioural therapy

CEBM - Centre for Evidence Based Medicine

C-RCT – cluster randomized control trial

FASD – Fetal Alcohol Spectrum Disorder

IUGR – Intrauterine growth retardation

LBW – low birth weight

MET – Motivational enhancement Therapy

MI – Motivational interviewing

NICU – Neonatal intensive care unit

OR – odds ratio

PAE – prenatal alcohol exposure

RCT – Randomized control trials

SBI – Screening and Brief Intervention

SBIRT – Screening, Brief Intervention, and Referral to Treatment

TLFB – Timeline follow back

WHO – World Health Organization

Declarations

Ethics approval and consent to participate

Not applicable.

Consent to publish

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

All authors declare that they do not have any financial, personal, political, intellectual or religious competing interests relevant to this article to disclose.

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Availability of Data and Material (ADM)

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

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Authors' contributions

SP conceptualized the protocol for this study, supervised statistical data analysis and drafted, reviewed and revised the manuscript. EP conducted statistical analysis, quality appraisals and drafting the manuscript. DD assisted in the conception of the study and revised the manuscript. KB cross-checked the data and contributed in revising the manuscript critically for important intellectual content. LS contributed in revising the manuscript critically for important intellectual content. SJO contributed in drafting and revising the manuscript critically for important intellectual content.

All authors (SP, EP, DD, LS, KB, and SJO) have read and approved the final manuscript as it has been submitted and agree to be accountable for all aspects of the work.

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Figures

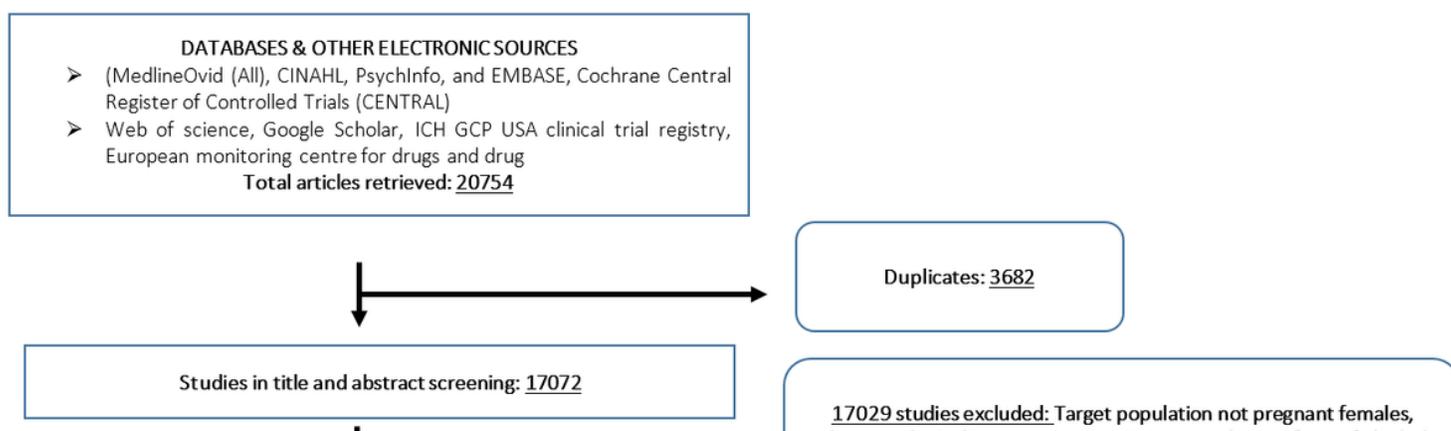


Figure 1

Study selection flow diagram

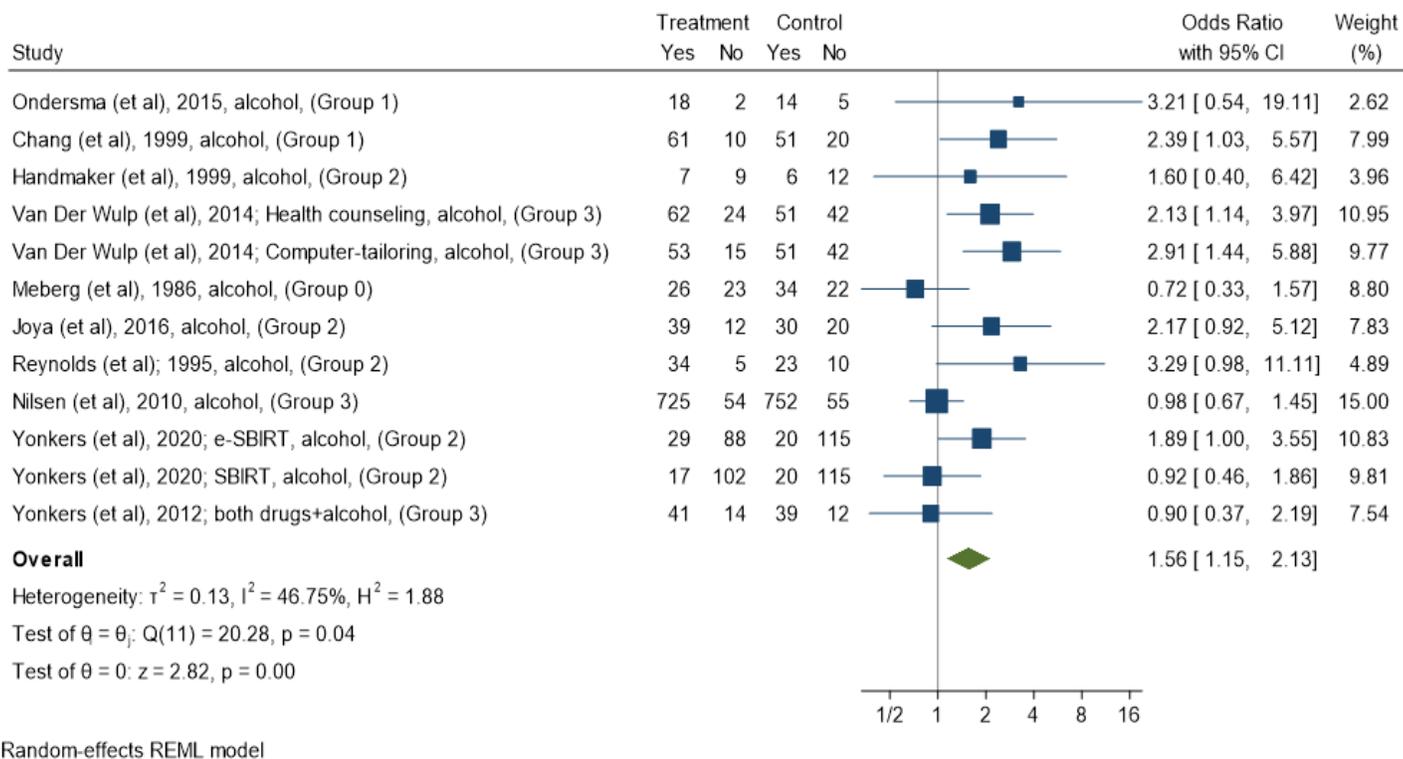


Figure 2

A meta-analysis of alcohol abstinence post intervention (BI vs Control)

Group 0: Screening + Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus No treatment/ Control condition not explained; **Group 1=** Screening + Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus screening; **Group 2:** Screening + Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus Screening + Information on AU during pregnancy provision (verbal or oral); **Group 3:** Screening + Extended-Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus Screening + Information on AU during pregnancy provision (verbal or written). **Extended interventions:** Session/s lasting for more than 60 mins. in total or have more than 5 sessions.

Figure 3

Meta-analysis of mean AUDIT scores post-intervention (BI v/s Control)

Group 0: Screening + Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus No treatment/ Control condition not explained; **Group 1=** Screening + Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus screening; **Group 2:** Screening +

Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus Screening + Information on AU during pregnancy provision (verbal or oral); **Group 3:** Screening + Extended-Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus Screening + Information on AU during pregnancy provision (verbal or written). **Extended interventions:** Session/s lasting for more than 60 mins. in total or have more than 5 sessions.

Figure 4

Meta-analysis mean drinks/ week post-intervention (BI v/s control)

Group 0: Screening + Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus No treatment/ Control condition not explained; **Group 1=** Screening + Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus screening; **Group 2:** Screening + Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus Screening + Information on AU during pregnancy provision (verbal or oral); **Group 3:** Screening + Extended-Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus Screening + Information on AU during pregnancy provision (verbal or written). **Extended interventions:** Session/s lasting for more than 60 mins. in total or have more than 5 sessions.

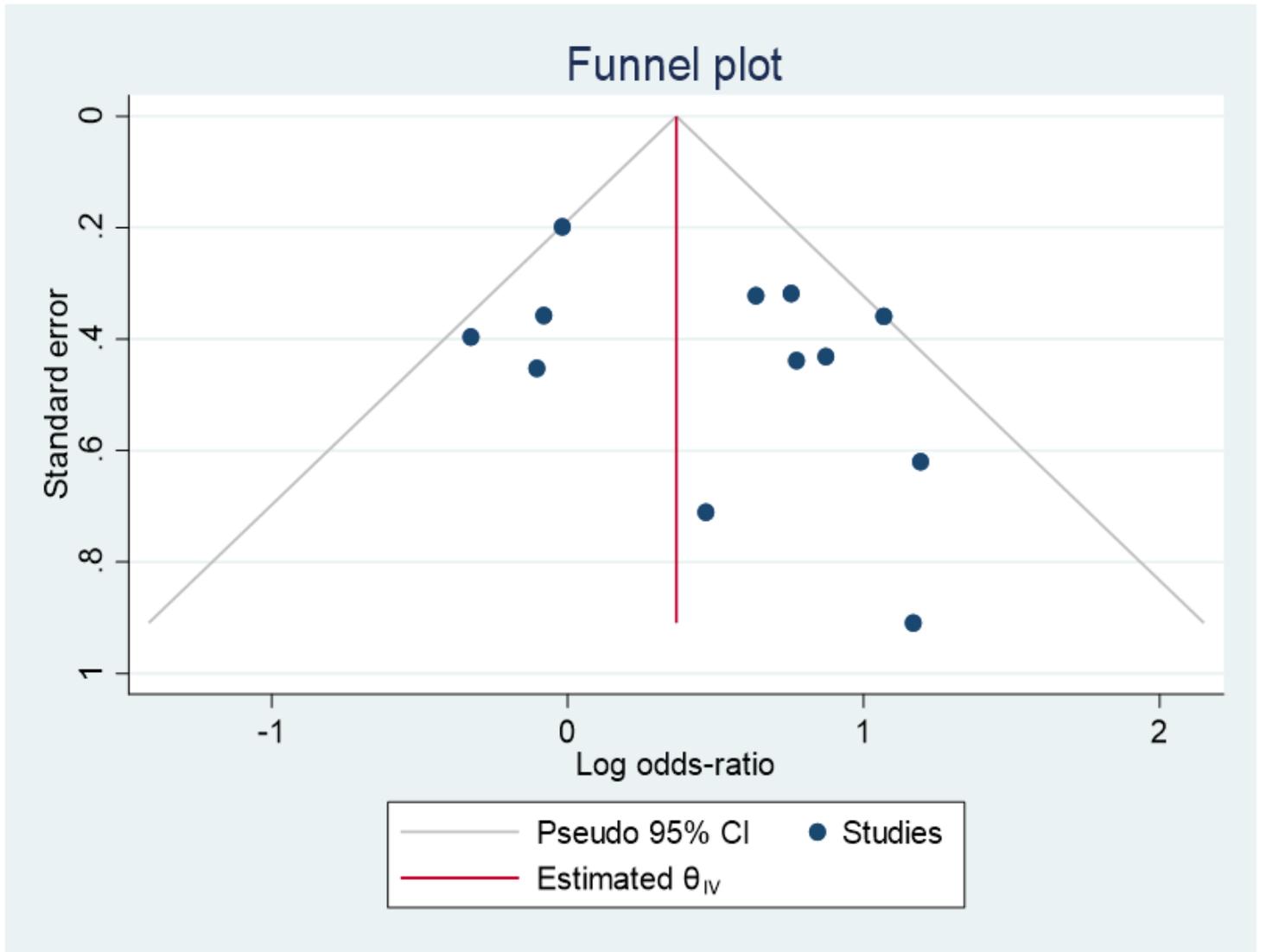
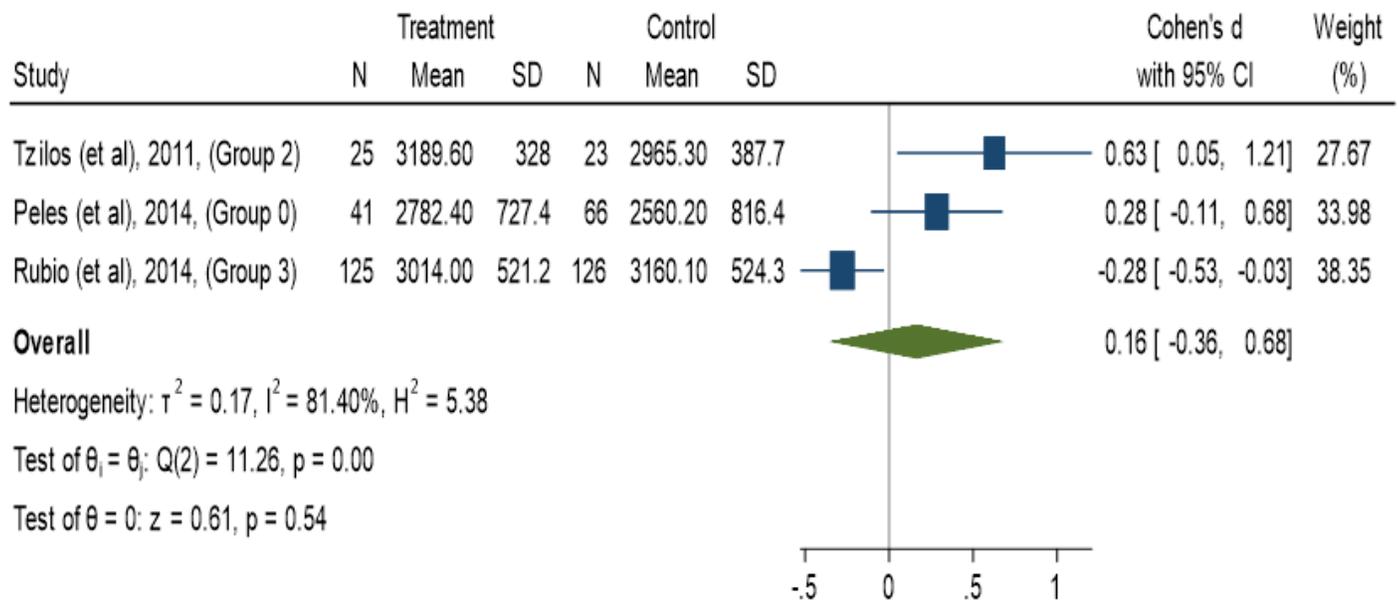


Figure 5

Funnel plot for publication bias for percentage of prenatal alcohol abstinence comparing BI v/s control



Random-effects REML model

Figure 6

Meta-analysis of mean birth weight (BI v/s control)

Group 0: Screening + Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus No treatment/ Control condition not explained; **Group 1=** Screening + Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus screening; **Group 2:** Screening + Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus Screening + Information on AU during pregnancy provision (verbal or oral); **Group 3:** Screening + Extended-Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus Screening + Information on AU during pregnancy provision (verbal or written). **Extended interventions:** Session/s lasting for more than 60 mins. in total or have more than 5 sessions

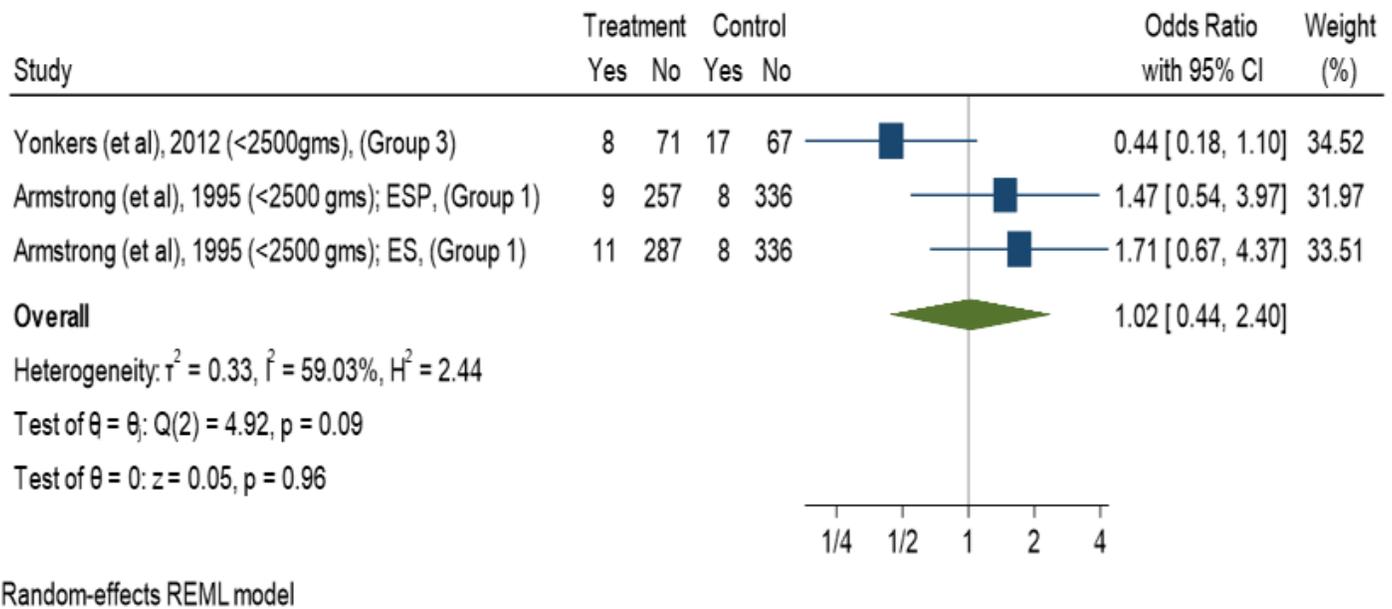


Figure 7

Meta-analysis mean low birth weight (BI v/s control)

Group 0: Screening + Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus No treatment/ Control condition not explained; **Group 1=** Screening + Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus screening; **Group 2:** Screening + Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus Screening + Information on AU during pregnancy provision (verbal or oral); **Group 3:** Screening + Extended-Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus Screening + Information on AU during pregnancy provision (verbal or written). **Extended interventions:** Session/s lasting for more than 60 mins. in total or have more than 5 sessions.

Figure 8

Meta-analysis preterm birth (BI v/s control)

Group 0: Screening + Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus No treatment/ Control condition not explained; **Group 1=** Screening + Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus screening; **Group 2:** Screening + Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus Screening + Information on AU during pregnancy provision (verbal or oral); **Group 3:** Screening + Extended-

Motivational Interview/ Cognitive Behavioural Therapy/ Comprehensive counseling versus Screening + Information on AU during pregnancy provision (verbal or written). **Extended interventions:** Session/s lasting for more than 60 mins. in total or have more than 5 sessions.

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