

Prenatal Cannabis Use and Neonatal Outcomes

A Systematic Review and Meta-Analysis

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 Supplemental content

IMPORTANCE Prenatal cannabis use continues to increase, and cannabis remains the most commonly used illegal substance in pregnancy. Accumulating evidence suggests potential adverse effects on fetal and neonatal outcomes following cannabis use in pregnancy.

OBJECTIVE To update a living systematic review and meta-analysis to provide a timely understanding regarding cannabis use in pregnancy and fetal and neonatal outcomes.

DATA SOURCES The previous review was updated by searching bibliographic databases MEDLINE, CINAHL, PsycInfo, Global Health, and Evidence-Based Medicine Reviews Cochrane Database of Systematic Reviews from November 1, 2021, through April 4, 2024.

STUDY SELECTION Cohort or case-control studies comparing pregnancies with and without prenatal cannabis use on prespecified fetal or neonatal outcomes with adjustment for confounders, such as co-use of tobacco products, were included. Two independent reviewers screened studies, with disagreements resolved through discussion.

DATA EXTRACTION AND SYNTHESIS Included studies were extracted by 1 reviewer and confirmed by a second. Risk of bias was assessed with the Newcastle-Ottawa Scale. Random-effects meta-analyses of unadjusted and adjusted odds ratios (ORs) were performed for all primary outcomes. Results were synthesized using the Grading of Recommendations Assessment, Development, and Evaluation approach.

MAIN OUTCOMES AND MEASURES Primary outcomes were preterm birth (PTB; <37 weeks of gestation), small for gestational age (SGA), low birth weight (LBW; <2500 g), and perinatal mortality.

RESULTS For this update, 8 new studies with 1 709 998 participants were added, for a total of 51 studies synthesized (N = 21 146 938). From meta-analyses of adjusted effect sizes, moderate-certainty evidence indicated that cannabis use in pregnancy was associated with increased odds of LBW (20 studies; OR, 1.75; 95% CI, 1.41-2.18), PTB (20 studies; OR, 1.52; 95% CI, 1.26-1.83), and SGA (12 studies; OR, 1.57; 95% CI, 1.36-1.81), and low-certainty evidence indicated that it was associated with greater odds of perinatal mortality (6 studies; OR, 1.29; 95% CI, 1.07-1.55). Previously, the evidence was rated as very low or low certainty.

CONCLUSIONS AND RELEVANCE Cannabis use in pregnancy was associated with greater odds of PTB, SGA, and LBW even after adjusting for co-use of tobacco products, and confidence in these findings increased from low in the prior review to moderate in the current meta-analysis. The findings of this study may help inform patient counseling and future public health policies.

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During the past 2 decades, the prevalence of prenatal cannabis use has more than doubled.¹ Cannabis is now the most commonly used federally illegal drug in pregnancy.¹ Given that Δ^9 -tetrahydrocannabinol (THC, the main psychoactive component of cannabis) can cross the placenta and bind to endocannabinoid receptors on major fetal organs, there is cause for concern.² Nonetheless, clinicians are not consistently counseling patients regarding prenatal cannabis use, partly because of the limited and mixed available evidence.³ While the existing literature suggests that prenatal cannabis use is associated with a range of potential risks, including stillbirth and fetal growth restriction,^{4–6} studies are often limited by self-reported cannabis intake and polysubstance use. We aim to provide an updated understanding of the association, adjusted for tobacco use and other important confounding variables, between prenatal cannabis use and pregnancy, fetal, and neonatal outcomes.

Methods

We updated our previous systematic review and meta-analysis on prenatal cannabis exposure and fetal and neonatal outcomes,⁶ which we maintain as a living systematic review (LSR). Detailed methods can be found in the previous publication,⁶ with an updated protocol for the surveillance portion of the review registered a priori to PROSPERO (CRD42024578036). Briefly, we updated searches of MEDLINE, CINAHL, PsycInfo, Global Health, and Evidence-Based Medicine Reviews Cochrane Database of Systematic Reviews from November 1, 2021, to April 4, 2024 (see eMethods in Supplement 1 for search strategies). We included English-language cohort or case-control studies of in-pregnancy cannabis use vs less or no cannabis use that adjusted for confounding factors (tobacco use at minimum). We followed the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) reporting guidelines.⁷

Two researchers independently screened all citations, assessed eligibility, conducted risk-of-bias assessments, and independently assigned a certainty-of-evidence (CoE) rating using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach. Disagreements were resolved through discussion or a third reviewer. Primary outcomes were preterm birth (PTB; <37 weeks of gestation), small for gestational age (SGA; <10th percentile given sex), low birth weight (LBW; <2500 g), and perinatal mortality. For this update, we replaced 1 primary outcome, birth weight, with the more clinically relevant LBW—a secondary outcome in our previous review. No other secondary outcomes were updated.

Of note, it is not ethical to conduct randomized clinical trials of prenatal cannabis use; thus, we used comparative observational studies to derive conclusions on this topic. Therefore, we started our CoE ratings as high, then downgraded the evidence for internal validity concerns (risk of bias) given GRADE working group guidance regarding nonrandomized studies evaluating interventions.⁸

Key Points

Question Is cannabis use in pregnancy associated with neonatal outcomes?

Findings In this updated systematic review and meta-analysis of 51 studies, prenatal cannabis use was associated with increased odds of preterm birth, small for gestational age, low birth weight, and perinatal mortality.

Meaning Using cannabis in pregnancy was associated with increased risk of adverse neonatal outcomes; health care professionals should include this in their patient counseling, and increased public health measures are needed to raise awareness on safety of use.

Statistical Analysis

This article reports our quantitative data synthesis (ie, meta-analyses) of studies reporting unadjusted or adjusted effect size estimates. Where necessary, we calculated odds ratios (ORs) with 95% CIs, using count data from eligible studies. We calculated treatment estimates and standard errors within Excel (Microsoft Corp) using natural logarithms and constants, then used the DerSimonian-Laird random-effects model to conduct meta-analyses in R Studio version 2023.12.1 (R Foundation), expressing heterogeneity using the I^2 statistic.⁹ Prediction intervals were computed based on the random-effects model, taking into account both the heterogeneity between studies and the uncertainty in the pooled effect. To test whether the association of cannabis use was more pronounced among those known to be using cannabis heavily—a dose-response association—we performed post hoc sensitivity analyses of adjusted estimates removing studies with participants who had undefined or lower duration or frequency of cannabis use (for instance, if a study reported outcomes for people who used cannabis monthly or less, weekly, or daily, the daily-use group would be included in the analysis; eTable 1 in Supplement 1 lists definitions by study).

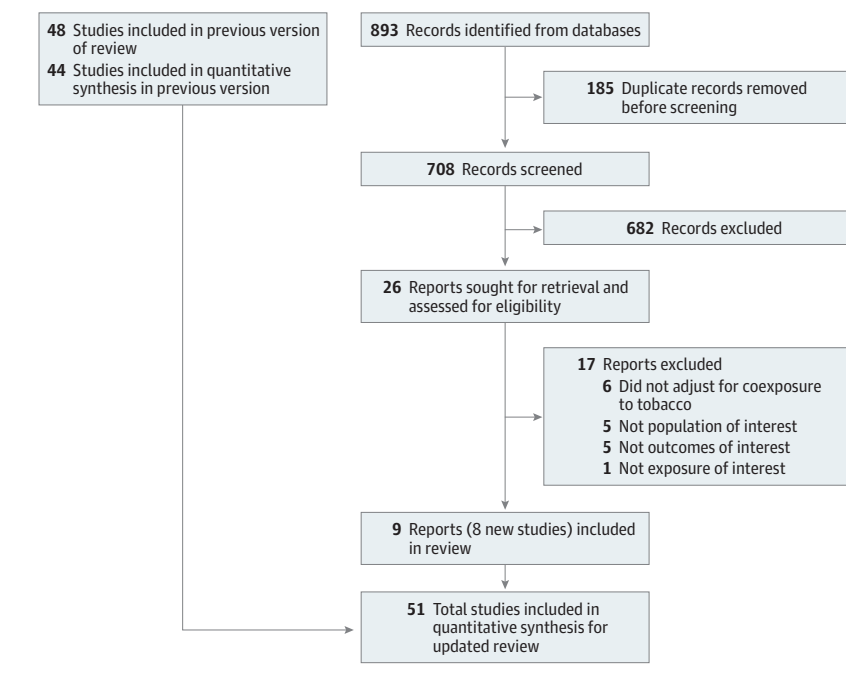
Results

From 2609 screened citations, we included 51 studies in 69 publications ($N = 21\,146\,938$) (Figure 1).^{10–60} Eight studies ($N = 1\,709\,998$) were added since the original publication (details of included studies are shown in Table 1).^{10–14,16,19,20} Few studies attempted to quantify the level of prenatal cannabis exposure; those that did classified individuals who used cannabis into categories of use based on either frequency (eg, heavy, moderate, irregular) or duration of use during pregnancy (eg, weeks of gestation, trimester), or they used diagnostic codes to identify individuals with cannabis use disorder.

Table 2 synthesizes our findings, including meta-analyses of unadjusted effect sizes. eFigures 1 through 4 in Supplement 1 show forest plots for unadjusted analyses; eFigures 5 through 8 in Supplement 1 show forest plots for adjusted sensitivity analyses.

We identified 24 studies analyzing the association between prenatal cannabis use and LBW ($N = 2\,412\,060$). In our meta-analysis of adjusted effect sizes in 20 studies controlling

Figure 1. Study Flow Diagram



for important confounding variables ($N = 1\,763\,753$), we found increased odds of LBW in those with prenatal cannabis use (OR, 1.75; 95% CI, 1.41-2.18) (Figure 2 and eTable 2 in Supplement 1). In our dose-response association sensitivity analysis of 5 studies with participants who specified heavy cannabis use, the odds of LBW increased (OR, 2.36; 95% CI, 1.50-3.72). Based on the consistency and stability of evidence across these analyses and acceptable levels of certainty across other GRADE domains, we rated the CoE as moderate for this finding.

We included 42 studies examining the association between prenatal cannabis use and PTB ($N = 21\,131\,345$). Based on 20 studies reporting adjusted effect sizes ($N = 20\,938\,125$), the odds of PTB increased for those using cannabis in pregnancy (OR, 1.52; 95% CI, 1.26-1.83). The sensitivity analysis including only individuals with heavy cannabis use revealed higher odds from those 7 studies combined (OR, 1.95; 95% CI, 1.40-2.73). Given this, we rated the CoE as moderate.

We identified 16 studies analyzing the association between prenatal cannabis use and perinatal mortality ($N = 16\,999\,369$). Our meta-analysis of 6 studies ($N = 16\,868\,920$) found increased odds of perinatal mortality with use (OR, 1.29; 95% CI, 1.07-1.55). In a sensitivity analysis of 3 studies of individuals with heavy cannabis use, the odds were no longer statistically significant (OR, 1.25; 95% CI, 0.92-1.69). Because of imprecision in the sensitivity analysis and clinical heterogeneity from varying outcome definitions (ie, stillbirth vs perinatal mortality), we rated the CoE as low.

We included 21 studies on the association of prenatal cannabis use and SGA ($N = 7\,816\,179$). From 12 studies reporting adjusted effects ($N = 4\,520\,474$), the odds of SGA increased with prenatal cannabis exposure (OR, 1.57; 95% CI, 1.36-1.81). A sensitivity analysis also showed increased odds among groups with

heavy use from 4 studies (OR, 1.63; 95% CI, 1.35-1.96). We rated the CoE as moderate for this finding.

Discussion

In this LSR, we synthesized 51 studies evaluating prenatal cannabis use and pregnancy, fetal, and neonatal outcomes. After adjusting for confounding factors, including tobacco use, we found moderate CoE that prenatal cannabis use is associated with increased odds of LBW, PTB, and SGA and low CoE that it is associated with greater odds of perinatal mortality. We reported similar findings in our prior review⁶ but had only very low to low CoE from studies available at the time. We were able to increase our certainty for these outcomes because of the increased number of studies and patients, consistency of findings, and the finding of a dose-response association. Our findings are also consistent with prior reviews of this topic, although some included studies that did not adjust for tobacco co-use or other important confounders,⁵ and multiple publications have added to the body of evidence since that time. Our review also analyzes more clinically relevant outcomes than previous reviews.^{4,61} As prenatal cannabis use is a modifiable risk factor, clinical and public health efforts to reduce it have the potential to mitigate pregnancy and offspring morbidity and mortality.

Strengths and Limitations

This study has several strengths. Clinicians can use our results to discuss the potential impact of prenatal cannabis use with pregnant individuals or those trying to conceive. Other strengths of this LSR include clinically relevant obstetric out-

Table 1. Characteristics of Studies Included in Quantitative Analysis

			Participants			Cannabis use ascertainment	Outcomes
Source (location)	Study design	RoB	Total No.	By group, %			
				Cannabis use	Unexposed		
Avalos et al, ¹⁰ 2024 (US) ^a	Retrospective cohort	Low	364 924	6.2	93.8	Self-report, toxicology screen	PTB, SGA, LBW
Dunn et al, ¹⁴ 2023 (Australia) ^a	Retrospective cohort	Moderate	3104	1.6	98.4	Self-report	PTB, SGA, perinatal death, LBW
Metz et al, ¹³ 2023; nuMoM2b (US) ^a	Prospective cohort	Low	9257	6.6	93.4	Toxicology screen	PTB, perinatal death
Umer et al, ¹¹ 2023; Project WATCH (US) ^a	Retrospective cohort	Low	34 412	6.5	87.8	Self-report, toxicology screen	PTB, SGA, LBW
Jones et al, ²⁰ 2022 (US)	Retrospective cohort	Low	1540	31.4	68.6	Meconium	PTB, LBW
Joseph-Lemon et al, ¹⁹ 2022; AABC PDR (US) ^a	Prospective cohort	Moderate	25 427	3.2	96.8	Self-report, toxicology screen	PTB, perinatal death, LBW
Koto et al, ¹⁸ 2022 (Canada)	Retrospective cohort	Low	106 282	2.9	97.1	Self-report	PTB, SGA
Luke et al, ¹⁶ 2022 (Canada) ^a	Retrospective cohort	Low	1 280 447	1.9	88.1	Self-report	PTB, SGA, perinatal death, LBW
Oni et al, ¹⁵ 2022 (Australia)	Retrospective cohort	Low	622 640	CUD, 0.3	99.7	Diagnostic code	PTB, perinatal death, LBW
Prewitt et al, ¹² 2023 (US) ^a	Retrospective cohort	Low	2 380 446	CUD, 0.38	99.62	Diagnostic code	PTB, SGA, perinatal death
Bandoli et al, ²⁴ 2021 (US)	Retrospective cohort	Low	3 067 069	Alone, 0.5; with tobacco, 0.2	99.1	Diagnostic code	PTB, SGA
Sasso et al, ²² 2021 (US)	Retrospective cohort	Low	362	44.0	56.0	Self-report, toxicology screen	PTB, SGA, perinatal death
Bailey et al, ²⁸ 2020 (US)	Retrospective cohort	Low	1062	50.0	50.0	Toxicology screen	PTB, LBW
Gabrhelik et al, ²³ 2021; MoBa (Norway)	Prospective cohort	Low	10 373	Short-term, 2.0; long-term, 0.6	97.4	Self-report	PTB, SGA
Klebanoff et al, ²⁶ 2020; LEAF (US)	Prospective cohort	Low	363	32.8	67.2	Self-report, toxicology screen	PTB, LBW
Lee et al, ¹⁷ 2022 (US)	Retrospective cohort	Low	466	9.7	9.0	Toxicology screen	PTB, SGA, perinatal mortality
Wong et al, ²⁵ 2020 (Canada)	Retrospective cohort	Low	25 263	2.2	97.8	Self-report	PTB, LBW
Corsi et al, ³² 2019 (Canada)	Retrospective cohort	Low	98 512	5.7	94.3	Self-report	PTB, SGA, perinatal mortality
Howard et al, ³¹ 2019 (US)	Retrospective cohort	Low	2173	Intake visit, 16.0; delivery, 1.2; intake + delivery, 5.3	77.5	Toxicology screen	Perinatal mortality
Kharbanda et al, ²⁷ 2020 (US)	Retrospective cohort	Low	3435	8.2	91.8	Toxicology screen	PTB, SGA, LBW
Petrangelo et al, ³⁰ 2019 (US)	Retrospective cohort	Low	12 578 557	CUD, 0.5	99.5	Diagnostic code	PTB, perinatal death
Rodriguez et al, ²⁹ 2019 (US)	Retrospective cohort	Low	1206	17.5	82.5	Self-report, toxicology screen	PTB, SGA, perinatal death
Straub et al, ²¹ 2021 (US)	Retrospective cohort	Low	5343	23.7	76.3	Toxicology screen	PTB, SGA, LBW
Coleman-Cowger et al, ³³ 2018 (US)	Prospective cohort	Low	414	14.5	85.5	Self-report, toxicology screen	PTB, perinatal death, LBW
Dotters-Katz et al, ³⁴ 2017; BEAM RCT (US)	Retrospective cohort	Low	1867	7.3	92.7	Self-report, toxicology screen	PTB, SGA, perinatal death
Leemaqz et al, ³⁶ 2016; SCOPE (Australia, New Zealand, UK, Ireland)	Prospective cohort	Low	5588	<15 wk GA, 2.6; 15 wk GA, 1.1; <20 wk GA, 0.4; 20 wk GA: 1.0; quit before pregnancy, 1.7	94.4	Self-report	PTB, SGA
Mark et al, ³⁵ 2016 (US)	Retrospective cohort	Low	396	29.3	70.7	Self-report, toxicology screen	PTB, LBW
Conner et al, ³⁸ 2015 (US)	Retrospective cohort	Low	8138	8.4	91.6	Self-report, toxicology screen	LBW

(continued)

Table 1. Characteristics of Studies Included in Quantitative Analysis (continued)

			Participants			Cannabis use ascertainment	Outcomes
Source (location)	Study design	RoB	Total No.	By group, % Cannabis use	Unexposed		
Warshak et al, ³⁷ 2015 (US)	Retrospective cohort	Low	6468	5.6	94.4	Self-report, toxicology screen	PTB, SGA, perinatal death
Bonello et al, ⁴⁰ 2014 (Australia)	Retrospective cohort	Low	13 480	CUD, 2.7	97.3	Diagnostic code	PTB, LBW
Varner et al, ³⁹ 2014; SCRN (US)	Case-control	Low	1610	3.0	97.0	Self-report, umbilical cord	PTB, SGA, perinatal death
Alhusen et al, ⁴¹ 2013 (US)	Prospective cohort	Low	166	38.5	61.4	Self-report	PTB, SGA, LBW
Hayatbakhsh et al, ⁴² 2012 (Australia)	Retrospective cohort	Low	24 874	2.6	97.4	Self-report	PTB, SGA, LBW
Gray et al, ⁴³ 2010; Growing Up Healthy (US)	Prospective cohort	Low	86	44.2	55.8	Self-report, toxicology screen, meconium	PTB
Schempf and Strobino, ⁴⁴ 2008 (US)	Retrospective cohort	Low	808	15.2	84.8	Self-report, toxicology screen	LBW
Lozano et al, ⁴⁵ 2007; Meconium Project (Spain)	Prospective cohort	Low	974	5.3	89.9	Meconium	PTB
Burns et al, ⁴⁶ 2006 (Australia)	Retrospective cohort	Low	416 834	CUD, 0.5	99.0	Diagnostic code	PTB, SGA
Bada et al, ⁴⁷ 2005; MLS (US)	Prospective cohort	Low	8637	9.4	90.6	Self-report, meconium	PTB, LBW
Fergusson et al, ⁴⁹ 2002; ALSPAC (England)	Prospective cohort	Low	12 129	NR	NR	Self-report	PTB, perinatal mortality
Quinlivan and Evans, ⁴⁸ 2002 (Australia)	Prospective cohort	Low	456	13.6	79.6	Self-report	PTB
Sherwood et al, ⁵⁰ 1999 (UK)	Retrospective cohort	Moderate	283	11.0	89.0	Toxicology screen	Perinatal mortality
Berenson et al, ⁵¹ 1996 (US)	Retrospective cohort	Low	238	38.2	61.8	Toxicology screen	LBW
Cornelius et al, ⁵³ 1995 (US)	Prospective cohort	Low	310	17.7	82.3	Self-report	SGA, LBW
Shiono et al, ⁵² 1995 (US)	Prospective cohort	Low	7470	11.0	89.0	Self-report, toxicology screen	PTB, LBW
Kliegman et al, ⁵⁴ 1994 (US)	Prospective cohort	Low	425	NR	NR	Self-report, toxicology screen	PTB, LBW
Hayes et al, ⁵⁵ 1988 (Jamaica)	Prospective cohort	Low	56	Irregular, 19.6; moderate, 19.6; heavy, 14.3	46.5	Self-report	PTB, perinatal mortality
Hatch and Bracken, ⁵⁶ 1986 (US)	Prospective cohort	Low	3857	≤1 Time/mo, 4.1; >1 time/mo, 5.4	90.5	Self-report	PTB, SGA, LBW
Tennes et al, ⁵⁷ 1985 (US)	Prospective cohort	Low	756	34.1	65.9	Self-report	PTB
Gibson et al, ⁵⁸ 1983 (Australia)	Prospective cohort	Low	7310	≤Weekly, 4.9; >weekly, 0.5	94.6	Self-report	PTB, perinatal mortality, LBW
Greenland et al, ⁵⁹ 1982 (US)	Prospective cohort	Low	71	49.3	50.7	Self-report, toxicology screen, umbilical cord	PTB, LBW
Fried, ⁶⁰ 1980; Ottawa Study (Canada)	Prospective cohort	Low	Initial cohort, 291; updated cohort, 583	Initial cohort: heavy, 3.8; moderate, 1.7; irregular, 14.1; updated cohort: heavy, 3.1; moderate, 3.1; irregular, 8.2	Initial cohort, 80.4; updated cohort, 85.6	Self-report	PTB

Abbreviations: AABC PDR, American Association of Birth Centers Perinatal Data Registry; ALSPAC, Avon Longitudinal Study of Pregnancy and Childhood; BEAM RCT, Beneficial Effects of Antenatal Magnesium Sulfate randomized clinical trial; CUD, cannabis use disorder; GA, gestational age; LBW, low birth weight; LEAF, Lifestyle and Early Achievement in Families; MLS, Maternal Lifestyle Study; MoBa, Norwegian Mother, Father, and Child Cohort Study; nuMoM2b, Nulliparous Pregnancy Outcomes Study Monitoring Mothers-to-Be;

NR, not reported; PTB, preterm birth; RoB, risk of bias; SCOPE, Screening for Pregnancy Endpoints; SCRN, Stillbirth Collaborative Research Network; SGA, small for gestational age; WATCH, Working in Appalachia to Identify At-Risk Infants, Critical Congenital Heart Disease, and Hearing Loss.

^a Indicates newly added study.

Table 2. Summary of Findings for Cannabis Use During Pregnancy and Perinatal Outcomes

Outcome ^a	Findings					CoE ^b	Meaning	Rationale
	Studies, No.	Participants, No.	Unadjusted OR (95% CI)	aOR (95% CI)	Sensitivity analysis aOR, (95% CI)			
LBW	24 ^{10, 11, 14-16, 19-21, 25-28, 33, 35, 38, 40, 41, 44, 47, 51, 52, 54, 56, 59}	2 412 060	2.06 (1.70-2.49) Based on 20 studies with 2 407 129 participants	1.75 (1.41-2.18) Based on 20 studies with 1 763 753 participants	2.36 (1.50-3.72) Based on 5 studies reporting groups with heavy use, with 1 028 011 participants	Moderate	After adjustment, increased odds of LBW with use of cannabis during pregnancy; results remained stable after sensitivity analysis removing studies with people who used low or undefined amounts of cannabis during pregnancy	Downgraded 1 level for RoB (if compared with a target RCT)
PTB	42 ^{10-30, 32, 33, 35-37, 40, 42, 43, 45-49, 52, 54-60}	21 131 345	1.60 (1.41-1.83) Based on 40 studies with 20 483 442 participants	1.52 (1.26-1.83) Based on 20 studies with 20 938 125 participants	1.95 (1.40-2.73) Based on 7 studies reporting groups with heavy use, with 16 382 469 participants	Moderate	After adjustment, increased odds of PTB with use of cannabis during pregnancy; results remained stable after sensitivity analysis removing studies with people who used low or undefined amounts of cannabis during pregnancy	Downgraded 1 level for RoB (if compared with a target RCT)
Perinatal mortality	16 ^{12-16, 22, 29-32, 34, 37, 39, 49, 50, 55}	16 999 369	1.92 (1.57-2.34) Based on 15 studies with 16 376 729 participants	1.29 (1.07-1.55) Based on 6 studies with 16 868 920 participants	1.25 (0.92-1.69) Based on 3 studies reporting groups with heavy use, with 15 581 643 participants	Low	After adjustment, increased odds of perinatal mortality with use of cannabis during pregnancy; after sensitivity analysis removing studies with people who used low or undefined amounts of cannabis during pregnancy, results were no longer statistically significant	Downgraded 1 level for RoB (if compared with a target RCT) and 1 level for indirectness (clinical heterogeneity due to varying outcome definitions)
SGA	21 ^{10-12, 14, 16-18, 21-24, 27, 29, 32, 34, 36, 37, 42, 46, 53, 56}	7 816 179	1.96 (1.65-2.33) Based on 20 studies with 7 815 869 participants	1.57 (1.36-1.81) Based on 12 studies with 4 520 474 participants	1.63 (1.35-1.96) Based on 4 studies reporting groups with heavy use, with 3 167 792 participants	Moderate	After adjustment, increased odds of SGA birth with cannabis use during pregnancy; results remained stable after sensitivity analysis removing studies with people who used low or undefined amounts of cannabis during pregnancy	Downgraded 1 level for RoB (if compared with a target RCT)

Abbreviations: aOR, adjusted odds ratio; CoE, certainty of evidence; LBW, low birth weight; OR, odds ratio;

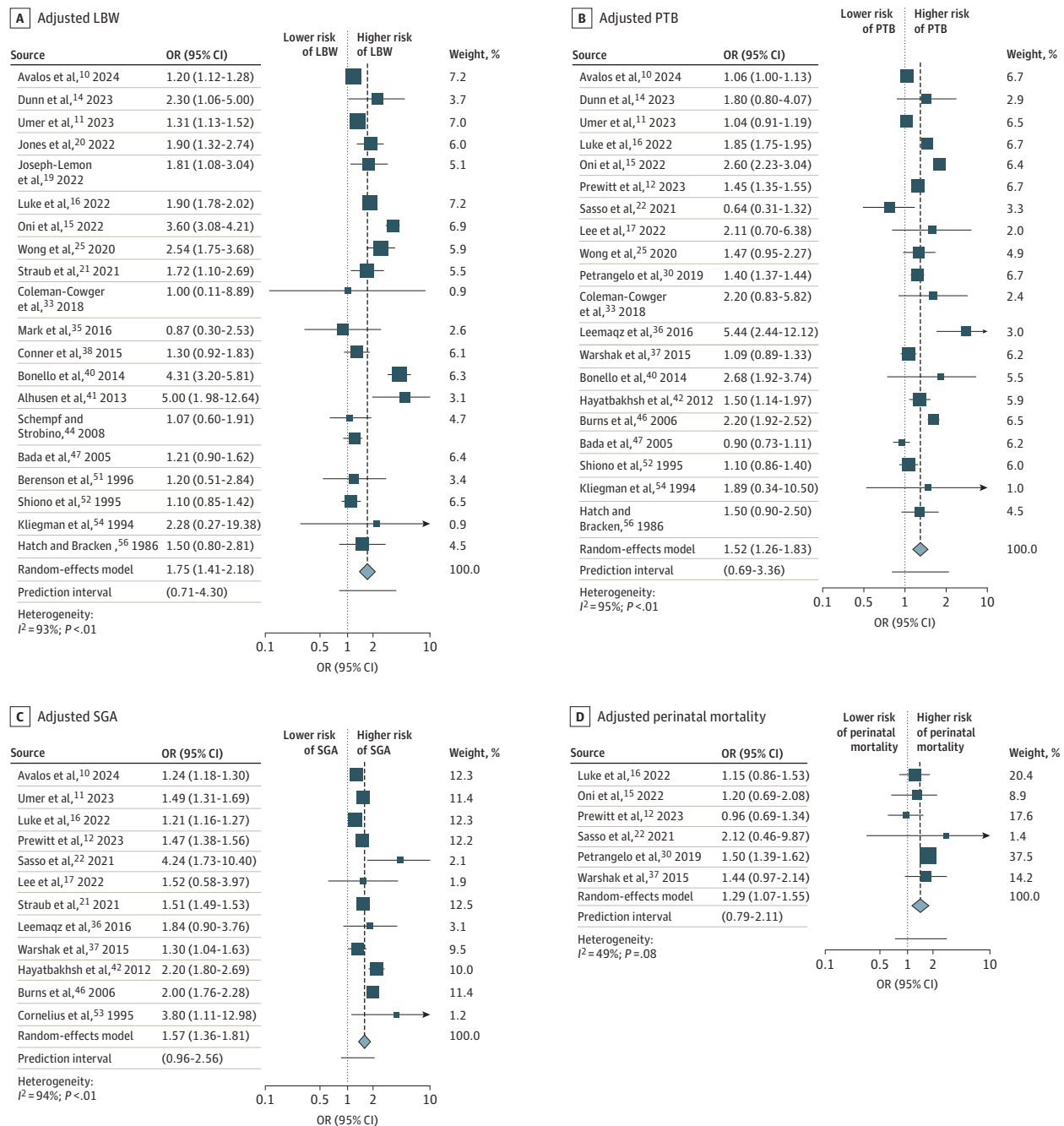
PTB, preterm birth; RCT, randomized clinical trial; RoB, risk of bias; SGA, small for gestational age.

^a Low birth weight indicates birth weight less than 2500 g; preterm birth, before 37 weeks' gestational age;

perinatal mortality, stillbirth or fetal demise; and small for gestational age, less than 10th percentile given sex.

^b The CoE was started as high, with downgrading, if compared with a target RCT per the Grading of Recommendations Assessment, Development, and Evaluation guidelines.⁸

Figure 2. Forest Plots for Adjusted Meta-Analyses of Primary Outcomes



LBW indicates low birth weight; OR, odds ratio; PTB, preterm birth; SGA, small for gestational age. The adjustments and stratification for each study are listed in eTable 2 in Supplement 1.

comes, strict exclusion criteria, and adjusted effect sizes in our meta-analyses to account for confounders not addressed in other prior large reviews.⁵ However, the study also has several limitations. Our study was limited by heterogeneity in the literature and lack of information on mode of delivery, timing, frequency, potency, or duration of prenatal cannabis use. In addition, we were unable to adjust for confounding from severe nausea and vomiting during pregnancy, which can also

increase the risk for adverse outcomes, including fetal growth restriction, low birth weight, and preterm birth.⁶²

Conclusions

The prevalence of prenatal cannabis use continues to increase. The results of our updated systematic review and meta-

analysis suggest that prenatal cannabis use is independently associated with increased odds of LBW, PTB, and SGA even after adjusting for co-use of tobacco products. Our confidence in these

findings is moderate. Our results may help guide patient counseling and harm reduction strategies and shape future public health policies focused on prenatal cannabis use.

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REFERENCES

- Volkow ND, Han B, Compton WM, McCance-Katz EF. Self-reported medical and nonmedical cannabis use among pregnant women in the United States. *JAMA*. 2019;322(2):167-169. doi:10.1001/jama.2019.7982
- Cristino L, Di Marzo V. Fetal cannabinoid receptors and the "dis-joint-ed" brain. *EMBO J*. 2014;33(7):665-667. doi:10.1002/emboj.201488086
- Lo JO, Hedges JC, Girardi G. Impact of cannabinoids on pregnancy, reproductive health, and offspring outcomes. *Am J Obstet Gynecol*. 2022;227(4):571-581. doi:10.1016/j.ajog.2022.05.056
- Conner SN, Bedell V, Lipsey K, Maccones GA, Cahill AG, Tuuli MG. Maternal marijuana use and adverse neonatal outcomes: a systematic review and meta-analysis. *Obstet Gynecol*. 2016;128(4):713-723. doi:10.1097/AOG.0000000000001649
- Marchand G, Masoud AT, Govindan M, et al. Birth outcomes of neonates exposed to marijuana in utero: a systematic review and meta-analysis. *JAMA*

Netw Open. 2022;5(1):e2145653. doi:10.1001/jamanetworkopen.2021.45653

- Lo JO, Shaw B, Robalino S, et al. Cannabis use in pregnancy and neonatal outcomes: a systematic review and meta-analysis. *Cannabis Cannabinoid Res*. 2024;9(2):470-485. doi:10.1089/can.2022.0262
- Stroup DF, Berlin JA, Morton SC, et al; Meta-Analysis of Observational Studies in Epidemiology (MOOSE) Group. Meta-analysis of observational studies in epidemiology: a proposal for reporting. *JAMA*. 2000;283(15):2008-2012. doi:10.1001/jama.283.15.2008
- Schünemann HJ, Cuello C, Akl EA, et al; GRADE Working Group. GRADE guidelines, 18: how ROBINS-I and other tools to assess risk of bias in nonrandomized studies should be used to rate the certainty of a body of evidence. *J Clin Epidemiol*. 2019;111:105-114. doi:10.1016/j.jclinepi.2018.01.012
- DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986;7(3):177-188. doi:10.1016/0197-2456(86)90046-2
- Avalos LA, Adams SR, Alexeeff SE, et al. Neonatal outcomes associated with in utero cannabis exposure: a population-based retrospective cohort study. *Am J Obstet Gynecol*. 2024;231(1):132.e1-132.e13. doi:10.1016/j.ajog.2023.11.1232
- Umer A, Watson E, Lilly C, et al. Substance exposure and adverse neonatal outcomes: a population-based cohort study. *J Pediatr*. 2023;256:70-76. doi:10.1016/j.jpeds.2022.11.040
- Prewitt KC, Hayer S, Garg B, et al. Impact of prenatal cannabis use disorder on perinatal outcomes. *J Addict Med*. 2023;17(3):e192-e198. doi:10.1097/ADM.0000000000001123
- Metz TD, Allshouse AA, McMillin GA, et al. Cannabis exposure and adverse pregnancy outcomes related to placental function. *JAMA*. 2023;330(22):2191-2199. doi:10.1001/jama.2023.21146
- Dunn ML, Bradley C, Ayonrinde OA, et al. The prevalence and significance of gestational cannabis use at an Australian tertiary hospital. *Aust N Z J Obstet Gynaecol*. 2023;63(1):6-12. doi:10.1111/ajo.13589
- Oni HT, Buultjens M, Mohamed AL, Islam MM. Neonatal outcomes of infants born to pregnant women with substance use disorders: a multilevel analysis of linked data. *Subst Use Misuse*. 2022;57(1):1-10. doi:10.1080/10826084.2021.1958851
- Luke S, Hobbs AJ, Smith M, et al; National Maternal Cannabis Working Group. Cannabis use in pregnancy and maternal and infant outcomes: a Canadian cross-jurisdictional population-based cohort study. *PLoS One*. 2022;17(11):e0276824. doi:10.1371/journal.pone.0276824
- Lee E, Pluym ID, Wong D, Kwan L, Varma V, Rao R. The impact of state legalization on rates of marijuana use in pregnancy in a universal drug screening population. *J Matern Fetal Neonatal Med*. 2022;35(9):1660-1667. doi:10.1080/14767058.2020.1765157

- Koto P, Allen VM, Fahey J, Kuhle S. Maternal cannabis use during pregnancy and maternal and neonatal outcomes: a retrospective cohort study. *BJOG*. 2022;129(10):1687-1694. doi:10.1111/1471-0528.17114

- Joseph-Lemon L, Thompson H, Verostick L, Shizuka Oura H, Jolles DR. Outcomes of cannabis use during pregnancy within the American Association of Birth Centers Perinatal Data Registry 2007-2020: opportunities within midwifery-led care. *J Perinat Neonatal Nurs*. 2022;36(3):264-273. doi:10.1097/JPN.0000000000000668

- Jones MJ, Lotfi A, Lin A, Gievers LL, Hendrickson R, Sheridan DC. Prenatal marijuana exposure and neonatal outcomes: a retrospective cohort study. *BMJ Open*. 2022;12(9):e061167. doi:10.1136/bmjopen-2022-061167

- Straub HL, Mou J, Drennan KJ, Pfluggeisen BM. Maternal marijuana exposure and birth weight: an observational study surrounding recreational marijuana legalization. *Am J Perinatol*. 2021;38(1):65-75. doi:10.1055/s-0039-1694793

- Sasso EB, Bolshakova M, Bogumil D, et al. Marijuana use and perinatal outcomes in obstetric patients at a safety net hospital. *Eur J Obstet Gynecol Reprod Biol*. 2021;266:36-41. doi:10.1016/j.ejogrb.2021.09.015

- Gabrielik R, Mahic M, Lund IO, et al. Cannabis use during pregnancy and risk of adverse birth outcomes: a longitudinal cohort study. *Eur Addict Res*. 2021;27(2):131-141. doi:10.1159/000510821

- Bandoli G, Jelliffe-Pawlowski L, Schumacher B, et al. Cannabis-related diagnosis in pregnancy and adverse maternal and infant outcomes. *Drug Alcohol Depend*. 2021;225:108757. doi:10.1016/j.drugalcdep.2021.108757

- Wong SPW, Twynstra J, Gilliland JA, Cook JL, Seabrook JA. Risk factors and birth outcomes associated with teenage pregnancy: a Canadian sample. *J Pediatr Adolesc Gynecol*. 2020;33(2):153-159. doi:10.1016/j.jpog.2019.10.006

- Klebanoff MA, Fried P, Yeates KO, et al. Lifestyle and Early Achievement in Families (LEAF) study: design of an ambidirectional cohort study of prenatal marijuana exposure and child development and behaviour. *Paediatr Perinat Epidemiol*. 2020;34(6):744-756. doi:10.1111/ppe.12693

- Kharbanda EO, Vazquez-Benitez G, Kunin-Batson A, Nordin JD, Olsen A, Romitti PA. Birth and early developmental screening outcomes associated with cannabis exposure during pregnancy. *J Perinatol*. 2020;40(3):473-480. doi:10.1038/s41372-019-0576-6

- Bailey BA, Wood DL, Shah D. Impact of pregnancy marijuana use on birth outcomes: results from two matched population-based cohorts. *J Perinatol*. 2020;40(10):1477-1482. doi:10.1038/s41372-020-0643-z

- Rodriguez CE, Sheeder J, Allshouse AA, et al. Marijuana use in young mothers and adverse pregnancy outcomes: a retrospective cohort study. *BJOG*. 2019;126(12):1491-1497. doi:10.1111/1471-0528.15885

30. Petrangelo A, Czuzoj-Shulman N, Balayla J, Abenheim HA. Cannabis abuse or dependence during pregnancy: a population-based cohort study on 12 million births. *J Obstet Gynaecol Can*. 2019;41(5):623-630. doi:10.1016/j.jogc.2018.09.009
31. Howard DS, Dhanraj DN, Devaiah CG, Lambers DS. Cannabis use based on urine drug screens in pregnancy and its association with infant birth weight. *J Addict Med*. 2019;13(6):436-441. doi:10.1097/ADM.0000000000000516
32. Corsi DJ, Walsh L, Weiss D, et al. Association between self-reported prenatal cannabis use and maternal, perinatal, and neonatal outcomes. *JAMA*. 2019;322(2):145-152. doi:10.1001/jama.2019.8734
33. Coleman-Cowger VH, Oga EA, Peters EN, Mark K. Prevalence and associated birth outcomes of co-use of cannabis and tobacco cigarettes during pregnancy. *Neurotoxicol Teratol*. 2018;68:84-90. doi:10.1016/j.ntt.2018.06.001
34. Dotters-Katz SK, Smid MC, Manuck TA, Metz TD. Risk of neonatal and childhood morbidity among preterm infants exposed to marijuana. *J Matern Fetal Neonatal Med*. 2017;30(24):2933-2939. doi:10.1080/14767058.2016.1269165
35. Mark K, Desai A, Terplan M. Marijuana use and pregnancy: prevalence, associated characteristics, and birth outcomes. *Arch Womens Ment Health*. 2016;19(1):105-111. doi:10.1007/s00737-015-0529-9
36. Leemaqz SY, Dekker GA, McCowan LM, et al; SCOPE Consortium. Maternal marijuana use has independent effects on risk for spontaneous preterm birth but not other common late pregnancy complications. *Reprod Toxicol*. 2016;62:77-86. doi:10.1016/j.reprotox.2016.04.021
37. Warshak CR, Regan J, Moore B, Magner K, Kritzer S, Van Hook J. Association between marijuana use and adverse obstetrical and neonatal outcomes. *J Perinatol*. 2015;35(12):991-995. doi:10.1038/jp.2015.120
38. Conner SN, Carter EB, Tuuli MG, Macones GA, Cahill AG. Maternal marijuana use and neonatal morbidity. *Am J Obstet Gynecol*. 2015;213(3):422.e1-422.e4. doi:10.1016/j.ajog.2015.05.050
39. Varner MW, Silver RM, Rowland Hogue CJ, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Stillbirth Collaborative Research Network. Association between stillbirth and illicit drug use and smoking during pregnancy. *Obstet Gynecol*. 2014;123(1):113-125. doi:10.1097/AOG.0000000000000052
40. Bonello MR, Xu F, Li Z, Burns L, Austin MP, Sullivan EA. Mental and behavioral disorders due to substance abuse and perinatal outcomes: a study based on linked population data in New South Wales, Australia. *Int J Environ Res Public Health*. 2014;11(5):4991-5005. doi:10.3390/ijerph110504991
41. Alhusen JL, Lucea MB, Bullock L, Sharps P. Intimate partner violence, substance use, and adverse neonatal outcomes among urban women. *J Pediatr*. 2013;163(2):471-476. doi:10.1016/j.jpeds.2013.01.036
42. Hayatbakhsh MR, Flenady VJ, Gibbons KS, et al. Birth outcomes associated with cannabis use before and during pregnancy. *Pediatr Res*. 2012;71(2):215-219. doi:10.1038/pr.2011.25
43. Gray TR, Eiden RD, Leonard KE, Connors GJ, Shisler S, Huestis MA. Identifying prenatal cannabis exposure and effects of concurrent tobacco exposure on neonatal growth. *Clin Chem*. 2010;56(9):1442-1450. doi:10.1373/clinchem.2010.147876
44. Schempf AH, Strobino DM. Illicit drug use and adverse birth outcomes: is it drugs or context? *J Urban Health*. 2008;85(6):858-873. doi:10.1007/s11524-008-9315-6
45. Lozano J, García-Algar O, Marchei E, et al. Prevalence of gestational exposure to cannabis in a Mediterranean city by meconium analysis. *Acta Paediatr*. 2007;96(12):1734-1737. doi:10.1111/j.1651-2227.2007.00535.x
46. Burns L, Mattick RP, Cooke M. The use of record linkage to examine illicit drug use in pregnancy. *Addiction*. 2006;101(6):873-882. doi:10.1111/j.1360-0443.2006.01444.x
47. Bada HS, Das A, Bauer CR, et al. Low birth weight and preterm births: etiologic fraction attributable to prenatal drug exposure. *J Perinatol*. 2005;25(10):631-637. doi:10.1038/sj.jp.7211378
48. Quinlivan JA, Evans SF. The impact of continuing illegal drug use on teenage pregnancy outcomes—a prospective cohort study. *BJOG*. 2002;109(10):1148-1153. doi:10.1111/j.1471-0528.2002.01536.x
49. Fergusson DM, Horwood LJ, Northstone K; ALSPAC Study Team. Avon Longitudinal Study of Pregnancy and Childhood. Maternal use of cannabis and pregnancy outcome. *BJOG*. 2002;109(1):21-27. doi:10.1111/j.1471-0528.2002.01020.x
50. Sherwood RA, Keating J, Kavvadia V, Greenough A, Peters TJ. Substance misuse in early pregnancy and relationship to fetal outcome. *Eur J Pediatr*. 1999;158(6):488-492. doi:10.1007/s004310051126
51. Berenson AB, Wilkinson GS, Lopez LA. Effects of prenatal care on neonates born to drug-using women. *Subst Use Misuse*. 1996;31(8):1063-1076. doi:10.3109/10826089609072288
52. Shiono PH, Klebanoff MA, Nugent RP, et al. The impact of cocaine and marijuana use on low birth weight and preterm birth: a multicenter study. *Am J Obstet Gynecol*. 1995;172(1, pt 1):19-27. doi:10.1016/0002-9378(95)90078-0
53. Cornelius MD, Taylor PM, Geva D, Day NL. Prenatal tobacco and marijuana use among adolescents: effects on offspring gestational age, growth, and morphology. *Pediatrics*. 1995;95(5):738-743. doi:10.1542/peds.95.5.738
54. Kliegman RM, Madura D, Kiwi R, Eisenberg I, Yamashita T. Relation of maternal cocaine use to the risks of prematurity and low birth weight. *J Pediatr*. 1994;124(5, pt 1):751-756. doi:10.1016/S0022-3476(05)81370-8
55. Hayes JS, Dreher MC, Nugent JK. Newborn outcomes with maternal marijuana use in Jamaican women. *Pediatr Nurs*. 1988;14(2):107-110.
56. Hatch EE, Bracken MB. Effect of marijuana use in pregnancy on fetal growth. *Am J Epidemiol*. 1986;124(6):986-993. doi:10.1093/oxfordjournals.aje.a114488
57. Tennes K, Avitable N, Blackard C, et al. Marijuana: prenatal and postnatal exposure in the human. *NIDA Res Monogr*. 1985;59:48-60.
58. Gibson GT, Baghurst PA, Colley DP. Maternal alcohol, tobacco and cannabis consumption and the outcome of pregnancy. *Aust N Z J Obstet Gynaecol*. 1983;23(1):15-19. doi:10.1111/j.1479-828X.1983.tb00151.x
59. Greenland S, Staisch KJ, Brown N, Gross SJ. The effects of marijuana use during pregnancy, I: a preliminary epidemiologic study. *Am J Obstet Gynecol*. 1982;143(4):408-413. doi:10.1016/0002-9378(82)90082-5
60. Fried PA. Marijuana use by pregnant women: neurobehavioral effects in neonates. *Drug Alcohol Depend*. 1980;6(6):415-424. doi:10.1016/0376-8716(80)90023-X
61. Baía I, Domingues RMSM. The effects of cannabis use during pregnancy on low birth weight and preterm birth: a systematic review and meta-analysis. *Am J Perinatol*. 2024;41(1):17-30. doi:10.1055/a-1911-3326
62. Lee NM, Saha S. Nausea and vomiting of pregnancy. *Gastroenterol Clin North Am*. 2011;40(2):309-334, vii. doi:10.1016/j.gtc.2011.03.009