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Short communication

Characteristics of pregnant illicit drug users and associations between cannabis use and perinatal outcome in a population-based study☆

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ABSTRACT

Background: According to the 2004 National Survey on Drug Use and Health, 4.6% of American women reported use of an illicit drug during pregnancy. Previous studies on illicit drug use during pregnancy and perinatal outcomes showed inconsistent results.
Methods: This population-based study included mothers who delivered live-born infants without birth defects between 1997 and 2004 and completed interviews for the National Birth Defects Prevention Study (response rate 69%; $n = 5871$). Prevalence of self-reported illicit drug use (specifically cannabis, cocaine, and stimulants) during pregnancy and its associations with demographic and social factors were assessed. We used multivariable linear and logistic regression analyses to study the associations of cannabis use with birth weight and gestational age.
Results: The prevalence of reported illicit drug use during pregnancy was 3.6% (standard error 0.24). Pregnant users of cannabis, cocaine, and stimulants were younger, had a lower level of education and lower household income, and were less likely to have used folic acid in the periconceptional period than nonusers. Illicit drug users were also more likely to have used alcohol and tobacco. After adjustment for confounding, cannabis use was not associated with mean birth weight or gestational age or with low birth weight or preterm delivery.
Conclusion: Women who report use of illicit drugs during pregnancy differ in demographic and socioeconomic background from nonusers. Reported cannabis use does not seem to be associated with low birth weight or preterm birth.

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1. Introduction

In 2004, the National Survey on Drug Use and Health indicated that 4.6% of American women of 15–44 years of age reported use of an illicit substance during pregnancy (Substance Abuse and Mental Health Services Administration, 2005). Studies recently conducted in the U.S. report even higher prevalences of perinatal illicit drug use up to 12.4% (El-Mohandes et al., 2003). A few studies have shown that pregnant cannabis and cocaine users differ in background characteristics from non-using pregnant women (Shiono et al., 1995; Hutchins and DiPietro, 1997; El Marroun et al., 2008), but studies using a population-based random sample of U.S. live births are scarce.

Infants of women who used cannabis during pregnancy have been reported to have lower birth weights (Fergusson et al., 2002; El-Mohandes et al., 2003) and a decreased gestational age (Cornelius et al., 1995) compared to infants of nonusers. However, most studies did not find an association between cannabis use and low birth weight (LBW) (Shiono et al., 1995; English et al., 1997), gestational age, or preterm birth (Shiono et al., 1995; Fergusson et al., 2002). Nevertheless, several biological mechanisms by which cannabis could influence perinatal outcome have been proposed (Frank et al., 1990; Khare et al., 2006). Since children born preterm or with LBW have an increased risk of infant mortality and long-term morbidity (Phillips et al., 2006; Saigal and Doyle, 2008), identifying risk factors for these adverse outcomes is of importance.

☆ The findings and conclusions of this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention or the National Center on Birth Defects and Developmental Disabilities.

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2. Methods

2.1. The National Birth Defects Prevention Study (NBDPS)

The NBDPS is an ongoing population-based case–control study that includes case infants with major structural congenital malformations identified via 10 birth defects surveillance systems in Arkansas, California, Georgia, Iowa, Massachusetts, New Jersey, New York, North Carolina, Texas, and Utah. Control infants are live-born infants without major birth defects from the same geographical areas, randomly selected from birth hospital records or birth certificates. Mothers are interviewed by trained interviewers via telephone in either English or Spanish between 6 weeks and 24 months after the estimated date of delivery. Questions are asked about demographic characteristics, maternal health, lifestyle factors, and occupation. The methods and enrollment of the infants have been described in detail elsewhere (Yoon et al., 2001; Cogswell et al., 2009). For this study, we selected all control infants born between October 1, 1997, and December 31, 2004 whose mothers completed the interview ($n = 5871$). The response rate was 69%.

2.2. Exposure and outcome assessment

Detailed information on the type, timing, and frequency of maternal illicit drug use during the period from 3 months before pregnancy until birth of the index child was available from the interview. We grouped the illicit substances reported by the mothers into five drug categories (cannabis, cocaine, stimulants, hallucinogens, and opioids) as described elsewhere (van Gelder et al., 2009). Nonusers were defined as women who did not report use of any illicit drug from 3 months before pregnancy through birth of the index child.

Data on birth weight and gestational age were obtained through abstraction of birth hospital records or birth certificates depending on how the infants were selected. During the examination of these data, some reporting inconsistencies were observed (e.g., an infant of 3104 g at 21 weeks of gestation). To address these implausible birth weight–gestational age combinations, we used the cut-points of birth weight values within the range for their specific gestational age as proposed by Alexander et al. (1996). For the perinatal outcome analyses, infants with implausible birth weight–gestational age combinations ($n = 16$), infants with missing birth weight or gestational age data ($n = 20$), and mothers with multiple gestations ($n = 174$) were excluded.

2.3. Statistical analyses

We used basic descriptive statistics to describe the characteristics of women who used or did not use illicit drugs during pregnancy. The characteristics of interest were maternal age at delivery, race or ethnicity, level of education, household income, employment status, prepregnancy body mass index (BMI), gestational weight gain (women with a weight gain of >40 kg or a weight loss of >20 kg were excluded), parity, previous induced abortions, use of contraception before or during pregnancy, any periconceptional folic acid use (from 1 month before through the first month of pregnancy), and any use of alcohol and cigarette smoking during pregnancy as well as paternal drug use, since most of these factors are known to affect pregnancy outcome.

A priori power analyses ($\alpha = 0.05$, study power 80%) showed that the prevalence of use of cocaine, stimulants, hallucinogens, and opioids was insufficient to study their effects on perinatal outcome with satisfactory statistical power. We used multivariable linear regression techniques to study the associations between cannabis use and birth weight and gestational age, in which we included the potential confounders maternal race/ethnicity (non-Hispanic white or other), level of education (0–12 years or >12 years), cigarette smoking, binge drinking (≥4 drinks per sitting), and maternal age, prepregnancy BMI, and gestational weight gain as linear covariates. For the birth weight analyses, we also included gestational age as a linear term. These potential confounders were selected based on a priori knowledge and exploratory data analyses, including the findings of the descriptive analyses. Potential confounders were dropped from the model when their removal did not change the effect estimate for cannabis use by more than 10%. Similarly, we used multivariable logistic regression to study the associations between prenatal cannabis exposure and LBW (birth weight < 2500 g) and preterm birth (gestational age < 37 weeks), in which maternal age (<25 years or ≥25 years) and prepregnancy BMI (<18.5 kg/m^2 or ≥18.5 kg/m^2) were categorized, because they did not show linear relationships with the outcomes. In subanalyses, we conducted stratified analyses by trimesters of use, which were not mutually exclusive since the numbers of women who only used cannabis in the second or third trimester were very small. Statistical analyses were performed using SPSS Version 16.0 for Windows (SPSS Inc., Chicago, IL).

3. Results

Of the 5871 women, 277 [4.7%, standard error (S.E.) 0.27] reported use of an illicit drug in the 3 months before pregnancy. Illicit drug use during pregnancy was reported by 210 women (3.6%, S.E. 0.24). Cannabis was the most commonly used illicit drug ($n = 189$), followed by cocaine and stimulants ($n = 27$). Of the cocaine users, 22 women used powder cocaine, 1 woman used crack, and 4 women used a combination of both. Opioids and hallucinogens were reported by only 4 and 2 women, respectively. Most illicit drug users (84.3%) took one illicit substance, while 15.7% used two or more illicit drugs.

Women who reported use of cannabis, cocaine, or stimulants during pregnancy were on average younger than nonusers (Table 1). Cannabis users were more often non-Hispanic black and less often Hispanic than nonusers, whereas pregnant cocaine users were more often of Hispanic origin. Women who reported illicit drug use were more likely to have a low level of education, to have a household income below $20,000, or to be unemployed. They were also more often underweight (BMI < 18.5 kg/m^2) than women who did not report use of illicit drugs during pregnancy. Cannabis users were more likely than nonusers to have excessive weight gain during pregnancy. Women who reported use of any illicit drug were less likely to have used folic acid in the periconceptional period. In addition, cannabis users were less likely to have had children before, but more likely to have had an induced abortion in the past. A similar pattern was seen for women who reported use of stimulants, but not for women who reported use of cocaine. Illicit drug users more often reported any use of alcohol or cigarette smoking during pregnancy and far more often reported that their partners used illicit drugs.

We included 5661 infants in the analyses of the associations between cannabis use and perinatal outcomes. After adjustment for confounding factors, there was no difference in mean birth weight (−17 g, $P = .65$) or gestational age (−0.1 weeks, $P = .75$) between cannabis-exposed and non-exposed infants (Table 2). No associations between cannabis use and LBW [adjusted odds ratio (OR) 0.7, 95% confidence interval (CI): 0.3–1.6] or preterm birth (OR 1.0, 95% CI: 0.6–1.9) were found either. Stratification by trimester of use did not alter these results greatly, although cannabis use during the second trimester, especially among cigarette smokers, seemed to have a detrimental effect on birth weight. In addition, the risks of preterm birth seemed slightly increased among women who used cannabis in the second (OR 1.6, 95% CI: 0.8–3.3) or third trimester (OR 1.8, 95% CI: 0.9–4.0). We did not detect a dose–response effect of prenatal cannabis exposure on perinatal outcome (data not shown).

4. Discussion

In our study, women who reported using cannabis, cocaine, or stimulants during pregnancy were similar to one another, but different from other pregnant women in a number of demographic and lifestyle characteristics. In general, prenatal cannabis use did not seem to be associated with infant birth weight or gestational age. Although we adjusted for a broad range of confounders, residual confounding by factors that we were unable to measure remains possible.

The use of illicit substances during pregnancy is likely underestimated because respondents often falsely deny use for fear of judgment or prosecution or because of feelings of shame and guilt. Previous studies have shown that 18–34% of participants who test positive through toxicological screening were missed when a questionnaire was used (Lester et al., 2001; Bauer et al., 2005; Eyler et al., 2005). Therefore, misclassification of the exposure status of study infants has occurred, but this is most likely non-differential, especially since birth weight and gestational age were not the primary outcomes of interest in the NBDPS and evidence for recall bias among case–control studies of pregnancy outcome is scarce. Non-differential misclassification may have resulted in underestimation

Table 1
Odds ratios with 95% confidence intervals for the characteristics of cannabis, cocaine, and stimulants users during pregnancy compared with pregnant nonusers. Data from the National Birth Defects Prevention Study, 1997–2004.

Maternal characteristics	Nonusers ($n=5547$)[a]		Cannabis users ($n=189$)[a]			Cocaine users ($n=27$)[a]			Stimulants users ($n=27$)[a]		
	N	%	*N*	%	OR (95% CI)[b]	*N*	%	OR (95% CI)[b]	*N*	%	OR (95% CI)[b]
Age at delivery											
<20 years	560	10.1	52	27.5	4.6 (2.9–7.3)	12	44.4	8.0 (2.6–24.9)	11	40.7	7.3 (2.3–23.1)
20–24 years	1196	21.6	86	45.5	3.6 (2.3–5.5)	7	25.9	2.2 (0.6–7.5)	10	37.0	3.1 (1.0–10.0)
25–29 years	1493	26.9	30	15.9	Reference	4	14.8	Reference	4	14.8	Reference
≥30 years	2298	41.4	21	11.1	0.5 (0.3–0.8)	4	14.8	0.6 (0.2–2.6)	2	7.4	0.3 (0.1–1.8)
Race or ethnicity											
Non-Hispanic white	3320	59.9	122	64.6	Reference	10	37.0	Reference	17	63.0	Reference
Non-Hispanic black	623	11.2	33	17.5	1.4 (1.0–2.1)	3	11.1	1.6 (0.4–5.8)	1	3.7	–
Hispanic	1263	22.8	29	15.3	0.6 (0.4–0.9)	14	51.9	3.7 (1.6–8.3)	6	22.2	0.9 (0.4–2.4)
Other	320	5.8	5	2.6	0.4 (0.2–1.0)	0	0	–	3	11.1	1.8 (0.5–6.3)
Education ≤12 years	2249	40.6	130	68.8	3.2 (2.4–4.4)	21	77.8	5.1 (2.1–12.7)	22	81.5	6.4 (2.4–17.0)
Household income <$20,000	1515	27.3	105	55.6	3.6 (2.6–4.9)	17	63.0	4.8 (2.1–11.2)	16	59.3	3.6 (1.6–8.0)
Employment status											
Employed	3980	71.8	141	74.6	Reference	17	63.0	Reference	15	55.6	Reference
Unemployed	47	0.8	6	3.2	3.6 (1.5–8.6)	2	7.4	10.0 (2.2–44.3)	2	7.4	11.3 (2.5–50.8)
Other[c]	1502	27.1	41	21.7	0.8 (0.5–1.1)	8	29.6	1.2 (0.5–2.9)	10	37.0	1.8 (0.8–3.9)
Prepregnancy BMI											
Underweight (<18.5 kg/m^2)	284	5.1	21	11.1	1.9 (1.2–2.9)	7	25.9	5.3 (2.1–13.2)	5	18.5	3.5 (1.3–9.7)
Normal weight (18.5–24.9 kg/m^2)	2991	53.9	115	60.8	Reference	14	51.9	Reference	15	55.6	Reference
Overweight (25.0–29.9 kg/m^2)	1194	21.5	23	12.2	0.5 (0.3–0.8)	5	18.5	0.9 (0.3–2.5)	5	18.5	0.8 (0.3–2.3)
Obese (≥30.0 kg/m^2)	850	15.3	28	14.8	0.9 (0.6–1.3)	1	3.7	–	2	7.4	0.5 (0.1–2.0)
Gestational weight gain[d]											
Weight loss or limited weight gain (≤11.5 kg)	1910	34.4	51	27.0	1.0 (0.7–1.6)	7	25.9	0.8 (0.3–2.4)	6	22.2	0.8 (0.3–2.6)
Appropriate weight gain (11.6–16.0 kg)	1595	28.8	41	21.7	Reference	7	25.9	Reference	6	22.2	Reference
Excessive weight gain (16.1–40.0 kg)	1911	34.5	93	49.2	1.9 (1.3–2.8)	12	44.4	1.4 (0.6–3.6)	13	48.1	1.8 (0.7–4.8)
Parity ≥1	3378	60.9	78	41.3	0.5 (0.3–0.6)	14	51.9	0.7 (0.3–1.5)	9	33.3	0.3 (0.1–0.7)
Induced abortions ≥1	696	12.5	41	21.8	1.9 (1.4–2.8)	5	18.5	1.6 (0.6–4.2)	6	22.2	2.0 (0.8–5.0)
Use of contraception	1561	28.1	60	31.7	1.2 (0.9–1.6)	7	25.9	0.9 (0.4–2.1)	7	25.9	0.9 (0.4–2.1)
Periconceptional use of folic acid	2882	52.0	58	30.7	0.4 (0.3–0.6)	5	18.5	0.2 (0.1–0.6)	7	25.9	0.3 (0.1–0.8)
Any alcohol use or cigarette smoking during pregnancy											
No alcohol used, no cigarette smoking	3615	65.2	22	11.6	Reference	2	7.4	Reference	2	7.4	Reference
Alcohol used, no cigarette smoking	1110	20.0	31	16.4	4.6 (2.6–8.0)	9	33.3	14.7 (3.2–67.9)	2	7.4	3.3 (0.5–23.1)
No alcohol used, smoked cigarettes	450	8.1	45	23.8	16.4 (9.8–27.6)	4	14.8	16.1 (2.9–88.0)	5	18.5	20.1 (3.9–104)
Alcohol used and smoked cigarettes	351	6.3	91	48.1	42.6 (26.4–68.7)	12	44.4	61.8 (13.8–277)	18	66.7	92.7 (21.4–401)
Paternal use of											
Cannabis	274	4.9	141	74.6	69.9 (47.9–102)	12	44.4	25.1 (10.5–60.1)	17	63.0	45.7 (18.8–111)
Cocaine	42	0.8	20	10.6	16.2 (9.3–28.2)	10	37.0	99.5 (41.3–239)	4	14.8	27.2 (8.9–83.4)
Stimulants	17	0.3	18	9.5	35.4 (17.9–70.0)	3	11.1	50.7 (13.7–187)	17	63.0	909 (320–2,587)

[a] Numbers do not add up to total group size due to missing values.
[b] Odds ratio with 95% confidence intervals.
[c] Other: homemaker/parent, student, or disabled.
[d] Classification is the recommendation for a woman with a normal prepregnancy BMI (Institute of Medicine, 1990).

of exposure frequencies and less precise estimates. However, the possibility of differential misclassification of prenatal illicit drug exposure status cannot completely be excluded.

In our study, women who reported cannabis and cocaine use during pregnancy had similar characteristics as those previously reported in the literature. However, there were some discrepancies, such as the lower level of education for cannabis users, the younger maternal age of cocaine users, and the fact that the majority of cocaine users were Hispanic as opposed to African American (Hutchins and DiPietro, 1997; Finch et al., 2001; Fergusson et al., 2002). Differences in selection and participation of the various study populations may explain these differences and our lower prevalence rates. The fact that pregnant stimulant users are very similar to pregnant cannabis users has not been reported before.

In the U.S. in 2001, the prevalences of LBW and preterm birth were 7.7% and 11.9%, respectively (Martin et al., 2002), which is higher than those for LBW (4.7%) and preterm birth (7.9%) in our study population. This difference could be due to the fact that vital statistics data, in contrast with our study population, include children with birth defects who are often born preterm (Honein et al., 2009), but it could also be due to some selection in our population. A recent study showed that the NBDPS control participants, who constitute our study population, are generally representative of their base populations (Cogswell et al., 2009). Our findings suggest that prenatal cannabis use overall is not associated with birth weight or gestational age, which is consistent with previous studies (Shiono et al., 1995; English et al., 1997; Fergusson et al., 2002). However, cannabis use in later stages of pregnancy might have some detrimental effect on perinatal outcome.

Further research is needed to determine the true association between illicit drug use and perinatal outcome, in which other approaches, such as blood, urine, or meconium analyses, might be used to assess exposure status. Furthermore, it remains uncertain whether prenatal cannabis exposure as well as exposure to other illicit drugs affects the occurrence of birth defects and developmental problems later in life.

Table 2
Effects of prenatal cannabis exposure on birth weight and gestational age and on the occurrence of low birth weight and preterm birth stratified by cigarette smoking status. Data from the National Birth Defects Prevention Study, 1997–2004.

Drug group	Cannabis		Birth weight	Low birth weight			Gestational age	Preterm birth		
	Users	Nonusers	β (95% CI)[a]	Number (%) of cases		Odds ratio (95% CI)	β (95% CI)[a]	Number (%) of cases		Odds ratio (95% CI)
				Exposed	Non-exposed			Exposed	Non-exposed	
Any cannabis use during pregnancy	185	5343	−17 (−90 to 56)[b]	9 (4.9)	243 (4.5)	0.7 (0.3–1.6)[c]	−0.1 (−0.4 to 0.3)[d]	18 (9.7)	410 (7.7)	1.0 (0.6–1.9)[e]
Non cigarette smokers	51	4557	−31 (−164 to 101)[f]	1 (2.0)	189 (4.1)	–	0.2 (−0.3 to 0.7)	3 (5.9)	335 (7.4)	0.6 (0.1–2.4)[g]
Cigarette smokers	134	785	−14 (−102 to 75)[f]	8 (6.0)	54 (6.9)	0.7 (0.3–2.0)[h]	−0.2 (−0.6 to 0.3)[i]	15 (11.2)	75 (9.6)	1.2 (0.7–2.1)
First trimester cannabis use	174	5343	−5 (−81 to 72)[j]	9 (5.2)	243 (4.5)	0.7 (0.3–1.7)[c]	−0.1 (−0.4 to 0.2)[k]	17 (9.8)	410 (7.7)	1.1 (0.6–1.9)[l]
Non cigarette smokers	48	4557	−9 (−150 to 131)[m]	1 (2.1)	189 (4.1)	–	0.2 (−0.3 to 0.8)	3 (6.2)	335 (7.4)	0.6 (0.1–2.6)[g]
Cigarette smokers	126	785	−4 (−95 to 86)[n]	8 (6.3)	54 (6.9)	0.7 (0.2–2.1)[o]	−0.2 (−0.7 to 0.2)[p]	14 (11.1)	75 (9.6)	1.2 (0.6–2.2)
Second trimester cannabis use	76	5343	−100 (−202 to 1)[q]	6 (7.9)	243 (4.5)	0.9 (0.3–2.8)[c]	−0.4 (−0.9 to 0.1)[e]	11 (14.5)	410 (7.7)	1.6 (0.8–3.3)[r]
Non cigarette smokers	19	4557	−41 (−257 to 175)[s]	1 (5.3)	189 (4.1)	–	−0.4 (−1.2 to 0.4)[g]	3 (15.8)	335 (7.4)	1.6 (0.4–7.2)[g]
Cigarette smokers	57	785	−136 (−253 to 18)[t]	5 (8.8)	54 (6.9)	1.0 (0.3–3.6)[h]	−0.3 (−1.0 to 0.3)[u]	8 (14.0)	75 (9.6)	1.5 (0.7–3.3)[v]
Third trimester cannabis use	53	5343	−89 (−209 to 30)[q]	4 (7.5)	243 (4.5)	0.9 (0.2–4.3)[w]	−0.5 (−1.1 to 0.1)[e]	8 (15.1)	410 (7.7)	1.8 (0.9–4.0)[l]
Non cigarette smokers	16	4557	−99 (−316 to 118)[x]	1 (6.2)	189 (4.1)	–	−0.5 (−1.4 to 0.4)[g]	3 (18.8)	335 (7.4)	2.0 (0.4–9.0)[g]
Cigarette smokers	37	785	−87 (−233 to 59)[y]	3 (8.1)	54 (6.9)	0.8 (0.1–4.7)[h]	−0.5 (−1.3 to 0.3)[u]	5 (13.5)	75 (9.6)	1.8 (0.6–5.5)[u]

[a] Regression coefficient, which represents the difference in birth weight (g) or gestational age (weeks) between exposed and non-exposed infants, with 95% confidence interval.
[b] Adjusted for gestational age, maternal age at delivery, race or ethnicity, cigarette smoking, binge drinking (≥4 drinks per sitting), prepregnancy BMI, and gestational weight gain.
[c] Adjusted for gestational age and cigarette smoking.
[d] Adjusted for maternal age at delivery, race or ethnicity, cigarette smoking, binge drinking, prepregnancy BMI, and gestational weight gain.
[e] Adjusted for cigarette smoking, binge drinking, and gestational weight gain.
[f] Adjusted for gestational age, maternal age at delivery, race or ethnicity, binge drinking, prepregnancy BMI, and gestational weight gain.
[g] Adjusted for gestational weight gain.
[h] Adjusted for gestational age.
[i] Adjusted for maternal age at delivery, race or ethnicity, binge drinking, prepregnancy BMI, and gestational weight gain.
[j] Adjusted for gestational age, maternal age at delivery, race or ethnicity, cigarette smoking, binge drinking, and gestational weight gain.
[k] Adjusted for cigarette smoking and binge drinking.
[l] Adjusted for cigarette smoking.
[m] Adjusted for gestational age, maternal age at delivery, race or ethnicity, binge drinking, and gestational weight gain.
[n] Adjusted for gestational age, maternal age at delivery, race or ethnicity, level of education, binge drinking, prepregnancy BMI, and gestational weight gain.
[o] Adjusted for gestational age and binge drinking.
[p] Adjusted for binge drinking, prepregnancy BMI, and gestational weight gain.
[q] Adjusted for gestational age, maternal age at delivery, and cigarette smoking.
[r] Adjusted for cigarette smoking and gestational weight gain.
[s] Adjusted for gestational age, maternal age at delivery, binge drinking, prepregnancy BMI, and gestational weight gain.
[t] Adjusted for gestational age, maternal age at delivery, and gestational weight gain.
[u] Adjusted for binge drinking.
[v] Adjusted for prepregnancy BMI.
[w] Adjusted for gestational age, cigarette smoking, and binge drinking.
[x] Adjusted for gestational age, maternal age at delivery, race or ethnicity, and prepregnancy BMI.
[y] Adjusted for gestational age and maternal age at delivery.

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Contributors

Authors van Gelder, Reefhuis, Caton, Werler, Druschel, and Roeleveld designed the study. Van Gelder, Reefhuis, and Roeleveld wrote the protocol. Van Gelder and Caton conducted statistical analyses. Van Gelder wrote the first draft of the manuscript, all authors contributed to and approved the final manuscript.

Conflict of interest

The authors report no conflicts of interest.

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