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Does caffeine and alcohol intake before pregnancy predict the occurrence of spontaneous abortion?

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BACKGROUND: Consumption of caffeine and alcohol is suspected to affect pregnancy outcome. Use of both stimulants is widespread and even minor effects on fetal viability are of public health interest. METHODS: We performed a nested case–control study using prospective data from a population-based cohort comprising 11 088 women aged 20–29 years. From this cohort, women who experienced either a spontaneous abortion (n = 303) or who gave birth (n = 1381) during follow-up [mean time: 2.1 years (range: 1.6–3.4)] were selected. Associations between self-reported exposures to caffeine and/or alcohol at enrolment and spontaneous abortion were analysed by means of logistic regression. RESULTS: Compared with women with a pre-pregnancy intake of <75 mg caffeine per day, the adjusted odds ratio (95% confidence interval) for spontaneous abortion was 1.26 (0.77–2.06), 1.45 (0.87–2.41), 1.44 (0.87–2.37) and 1.72 (1.00–2.96) for a pre-pregnancy intake on 75–300, 301–500, 501–900 and >900 mg caffeine per day respectively (P = 0.05 for trend). A pre-pregnancy intake of alcohol was not a predictor for spontaneous abortion. CONCLUSIONS: A high intake of caffeine prior to pregnancy seems to be associated with an increased risk of spontaneous abortion, whereas a low-to-moderate alcohol intake does not influence the risk.

Key words: alcohol drinking/caffeine/epidemiology/risk factors/spontaneous abortion

Introduction

Numerous studies of the association between caffeine intake and spontaneous abortions have been conducted. However, results are not entirely consistent (Kline *et al*., 1991; Armstrong *et al*., 1992; Infante-Rivard *et al*., 1993; Mills *et al*., 1993; Dominguez-Rojas *et al*., 1994; Dlugosz *et al*., 1996; Fenster *et al*., 1997; Klebanoff *et al*., 1999; Cnattingius *et al*., 2000; Wen *et al*., 2001). Several studies have also addressed the subject of alcohol and spontaneous abortion. Some North American studies point towards an increased risk of spontaneous abortion among women with a moderate alcohol intake compared with non-drinkers (Harlap *et al*., 1980; Anokute, 1986; Armstrong *et al*., 1992; Windham *et al*., 1997) whereas the majority of European studies have shown no harmful effect (Grisso *et al*., 1984; Halmesmaki *et al*., 1989; Dominguez-Rojas *et al*., 1994; Parazzini *et al*., 1994; Cavallo *et al*., 1995; reviewed by Abel, 1997). Many of these studies have been limited by small sample size or have a retrospective design with the potential risk of recall bias. Furthermore, most prospective studies on the subject have followed women from their first antenatal visit, which mostly takes place in late first trimester (Harlap *et al*., 1980; Grisso *et al*., 1984; Anokute, 1986; Dlugosz *et al*., 1996; Windham *et al*., 1997; Fenster *et al*., 1997; Kesmodel *et al*., 2002). Only the risk of spontaneous abortion occurring after this time in pregnancy is evaluated in these studies and early fetal loss is not accounted for. In addition, pregnant women may tend to reduce their intake of alcohol, especially, upon recognition of a conception, meaning that information on intake obtained before pregnancy may be a valid measure for the consumption in early and still unrecognized pregnancy. A few of the studies have included pre-pregnancy exposures of caffeine and alcohol, but only one smaller study has obtained this information prospectively.

In the present study, pre-pregnancy intake of caffeine and alcohol was assessed prospectively in a population with a high proportion of moderate-to-heavy alcohol and coffee drinkers and this information was related to pregnancy outcome in the following 2–3 years.

Materials and methods

Study population

The study population was selected from a prospective cohort study comprising 11 088 women, 20–29 years old, randomly sampled from the general population of Copenhagen, Denmark. This cohort was established from May 1991 to January 1993 with the purpose of studying the natural history of human papillomavirus infection and cervical intraepithelial neoplasia. After 2 years (September 1993 to January 1995), a second interview was conducted which included 8655 subjects (78%). The study was approved by the Ethical Committee of Copenhagen and Frederiksberg Municipality, Denmark (V.100.1665/90). The enrolment and data collection procedures are described in detail elsewhere (Kjaer *et al*., 1996).

First interview

Trained female nurses interviewed all women personally at enrolment. The interview included questions about socio-demographic variables, sexual and contraceptive habits, previous sexually transmitted diseases, cervix dysplasia screening history, and smoking habits. The participants also filled in a food frequency questionnaire where information on caffeine and alcohol intake was obtained. Consumption of coffee and tea was reported as number of cups. Caffeine intake was estimated by assuming one cup of tea to be equivalent to 34 mg and one cup of coffee to be equivalent to 107 mg (Bunker and McWilliams, 1979). Alcohol consumption was reported as the intake of beer (bottles), wine (glasses) and spirits (units). One bottle of beer contains 12 g of alcohol and this is considered also to be the average amount of alcohol in the other types of drinks. The total alcohol intake was calculated by summing the intake of beer, wine and spirits.

Second interview

The women were again interviewed personally with the same questions for the enrolment interview. The women were also asked if they had been pregnant, and, if so, to state the birth outcome(s).

Follow-up

We selected all women who either gave birth or experienced a spontaneous abortion during the period between the two interviews [mean observation time: 2.1 years (range: 1.6–3.4)]. Women who were already pregnant at the enrolment interview were excluded (n = 202). For women who did not participate in the second interview, the observation period was defined as the mean time between the two interviews among women who participated in both interviews.

In the present study, spontaneous abortion was defined as a non-deliberate fetal loss occurring before the 28th week of gestation. This information was collected using multiple sources, namely information obtained through the personal interviews and by linking the cohort to the Danish Hospital Discharge Register. In Denmark, all citizens have a unique personal identification number, which is used universally in Danish society and ensures correct linkage of the different types of registers available in Denmark. The Danish Hospital Discharge Register is a population-based register, which has kept record of all somatic hospitalizations in Denmark since 1977 (Jürgensen *et al*., 1986; National Board of Health, 1993). The diagnoses are classified according to the World Health Organization's *International Classification of Diseases,* Eighth and Tenth Revision (ICD-8 and -10). The diagnoses for spontaneous abortions include the following ICD-8 codes: 634.61, 643, 644, 645.1 and 645.7, and ICD-10 codes: O01.1, O02.0, O02.1, O02.9 and O03. The birth diagnoses include the following ICD-8 codes: 650 to 666; and ICD-10 codes: O60, O63 to O70, and O80 to O84.

Cases included women who at the second interview reported that they had experienced a spontaneous abortion and/or had been registered in the Danish Hospital Discharge Register with a diagnosis of spontaneous abortion during the observation period. Likewise, non-cases were defined as women who at the second interview reported that they had given birth or were pregnant >28 weeks of gestation, or had been registered in the Danish Hospital Discharge Register with a birth diagnosis during the observation period or during the following 12 weeks after the time of the second interview, corresponding to being ⩾28 weeks pregnant at the time of the second interview. Women who had not participated in the second examination were followed up by register linkage only. If a woman experienced both a spontaneous abortion and a livebirth, the first occurring event defined her case/non-case status.

Exposures and potential confounders

All measures of exposures and confounders were taken from the interview at enrolment. Age at baseline was tested for linearity (log likelihood ratio test) at the 5% level and after acceptance entered as a continuous variable. Marital status was defined in three levels (married, cohabiting or living alone), but since there was no significant difference in the odds ratios (OR) for spontaneous abortion between being married and being cohabiting, this variable was entered in two levels (married/cohabiting versus living alone). Smoking status was entered in four categories (non-smoker, 1–10, 11–20 and ⩾21 cigarettes per day). Pregnancy history was evaluated in four levels (no previous pregnancies, no previous spontaneous abortions, one previous spontaneous abortion, and two or more previous abortions). School education was entered in two levels (<10 years or ⩾11 years of education).

Statistical analysis

The associations between caffeine and alcohol intake and spontaneous abortion were analysed by means of multiple logistic regression with simultaneous adjustment for potentially confounding factors (SAS/STAT version 8.0). If a covariate altered the estimates of variables of interests by >5%, it was added in the adjusted statistical model. Interactions between alcohol and caffeine, alcohol and smoking, and caffeine and smoking were examined by a nested log likelihood test; a model containing the exposure variables as single terms was compared with a model also including interaction terms (conducted separately for each interaction). The criterion for a significant interaction was 5%. Baseline characteristics were compared by the Kruskal–Wallis test or by χ^2-test (dichotomous variables). The time of conception was calculated for women registered in the Danish Hospital Discharge Register as time of the spontaneous abortion minus 9 weeks or date of birth minus 40 weeks (Andersen *et al*., 2000). The exact gestational week at the time of miscarriage could not be obtained, since this information is not included in the Danish Hospital Discharge register.

Results

In the period between the two interviews, 1381 pregnancies had been completed to the 28th gestational week and 303 had ended with a spontaneous abortion (18%). Among women who participated in both interviews, there were 253 cases of spontaneous abortions of which 60 cases were found only from self-report, 24 cases only from the Danish Hospital Discharge Register and 169 cases from both sources. Among women who did not participate in the second interview, 211 livebirths and 50 spontaneous abortions were identified from the Danish Hospital Discharge Register. The mean (SD) time interval

Table I. Baseline characteristics of the study population on caffeine and alcohol consumption, Copenhagen, Denmark, 1991–1995

	Mean age (years)	Living alone (%)	Smokers (%)	Education <11 years (%)	Never pregnant (%)	Previous SAB[a] (%)
Caffeine (mg per day)						
<75	24.5	20	30	53	50	11
75–300	25.6	19	31	31	53	8
301–500	26.0	17	39	28	47	9
501–900	25.9	23	51	28	49	9
>900	26.0	25	68	45	49	10
P[b]	<0.01	0.11	<0.01	<0.01	0.15	0.83
Alcohol (drinks/week[c])						
<1	24.9	17	41	59	39	14
1–3	25.5	19	42	34	52	7
4–6	26.2	21	40	27	48	10
7–13	26.2	25	48	23	55	6
>13	26.4	30	60	21	49	14
P[b]	<0.01	0.01	<0.01	<0.01	0.01	0.01

[a]Percentage of ever-pregnant women.
[b]*P* for Kruskal–Wallis test.
[c]Rounded up to the nearest integer, e.g. 4 include 3.5 drinks.
SAB = spontaneous abortion.

Table II. Adjusted odds ratios for caffeine consumption and spontaneous abortion among the study population, Copenhagen, Denmark, 1991–1995

Caffeine (mg per day)	SAB (%)	Odds ratio (crude)	95% CI	Odds ratio[a]	95% CI
<75[b]	26 (14)	1.00	–	1.00	–
75–300	74 (16)	1.18	0.72, 1.91	1.26	0.77, 2.06
301–500	69 (18)	1.32	0.81, 2.15	1.45	0.87, 2.41
501–900	81 (18)	1.35	0.84, 2.19	1.44	0.87, 2.37
>900	53 (23)	1.74	1.04, 2.91	1.72	1.00, 2.96

[a]Adjusted for maternal age, marital status, smoking, and alcohol intake.
[b]Reference category.
P for linear trend = 0.05.
SAB = spontaneous abortion; CI = confidence interval.

between interview and estimated time of conception was 9.3 (6.5) months.

Women with a pregnancy who did not participate in the second interview ($n = 261$) tended to drink a little less alcohol and to be younger than women with a pregnancy who participated in both interviews ($n = 1423$) ($P < 0.05$). For the other characteristics, there was no difference. Women who were lost from the second interview ($n = 2433$) tended to drink a little less alcohol, to be younger, more often smoking and better educated than women who participated in both interviews ($n = 8655$). For the other characteristics, there was no difference.

Women in the high caffeine categories were more frequently smokers than women in the lower categories (Table I). Mean daily caffeine intake was 508 mg corresponding to 4.7 cups of coffee. Only 16 women reported never drinking any coffee or tea (<1%). The reference group for caffeine intake was set to <75 mg per day, which included 206 women (11%). Women in the high alcohol categories were more often living alone, smoking and were more educated than women in the lighter drinking categories. Mean alcohol intake was 4.6 drinks per week and 333 people (20%) were reported to consume less than one drink weekly.

Among women who experienced a spontaneous abortion during follow-up, a larger fraction was living alone compared with women who gave birth ($P < 0.01$). For age, smoking and education, there was no significant difference between women who had a spontaneous abortion and women who had a live birth.

School education was omitted in the final analyses because it had no statistical influence in itself or on the other estimates. Maternal age, marital status and smoking were added in the adjusted logistic regression model. The occurrence of previous spontaneous abortions before baseline was significantly associated with having spontaneous abortions during follow-up, but had no influence on the caffeine and alcohol estimates and was not included in the adjusted model. No significant interaction was found between alcohol intake and caffeine, alcohol and smoking or caffeine and smoking.

Compared to women with a pre-pregnancy intake of <75 mg caffeine per day, the adjusted OR for spontaneous abortion was 1.26, 1.45, 1.44 and 1.72 for a pre-pregnancy intake on 75–300, 301–500, 501–900 and >900 mg caffeine per day respectively ($P = 0.05$ for trend) (Table II). We examined this result to see if this association was confined to coffee drinking. The coffee estimates showed the same tendency as for total caffeine, though somewhat attenuated and with lower statistical power (data not shown).

The adjusted OR for spontaneous abortion in women drinking >13 alcoholic drinks per week was 1.28 (95% confidence interval: 0.76, 2.51) compared with women drinking less than one drink per week (Table III). For women consuming lower amounts of alcohol, the OR was not increased and no statistically significant trend was observed.

No significant interaction was found between alcohol intake and caffeine ($P > 0.20$), alcohol and smoking ($P > 0.20$) or caffeine and smoking ($P > 0.2$).

Repeating the analysis on women who participated in both examinations ($n = 1423$), the association between spontaneous abortion and caffeine intake was marginally strengthened and

Table III. Odds ratios for alcohol consumption and spontaneous abortion among the study population, Copenhagen, Denmark, 1991–1995

Alcohol (drinks per week[a])	SAB (%) (*n*)	Odds ratio (crude)	95% CI	Odds ratio[b]	95% CI
<1[c]	62 (14)	1.00	–	1.00	–
1–3	96 (16)	0.93	0.65, 1.32	0.92	0.64, 1.32
4–6	75 (18)	0.99	0.68, 1.43	0.98	0.67, 1.45
7–13	50 (18)	0.82	0.55, 1.24	0.79	0.51, 1.20
>13	20 (23)	1.46	0.82, 2.59	1.28	0.71, 2.32

[a]Rounded up to the nearest integer.
[b]Adjusted for maternal age, marital status, smoking, and caffeine intake.
[c]Reference category.
P for linear trend = 0.60.
SAB = spontaneous abortion; CI = confidence interval.

Table IV. Odds ratios for caffeine consumption and spontaneous abortion among the study population according to time interval between interview and estimated time of conception, Copenhagen, Denmark 1991–1995

Caffeine (mg per day)	Time between interview and conception					
	<12 months			⩾12 months		
	SAB/livebirths (*n*)	Odds ratio[a]	95% CI	SAB/livebirths (*n*)	Odds ratio[a]	95% CI
<75[b]	12/100	1.00	–	9/51	1.00	–
75–300	28/237	1.03	0.50, 2.13	33/119	1.67	0.73, 3.82
301–500	29/182	1.44	0.69, 3.01	25/121	1.25	0.53, 2.93
501–900	39/211	1.63	0.80, 3.36	27/132	1.24	0.53, 2.92
>900	19/110	1.41	0.63, 3.19	22/69	1.91	0.77, 4.72

[a]Adjusted for maternal age, marital status, smoking, and alcohol intake.
[b]Reference category.
SAB = spontaneous abortion; CI = confidence interval.

the statistical power was increased ($P = 0.02$ for trend). The estimate for alcohol was virtually unchanged in this subpopulation and the statistical power was the same ($P = 0.60$).

For women whose pregnancy outcome was recovered from the National Discharge Register ($n = 1575$, 94%), the time of conception was estimated and analyses were repeated, stratified according to the time interval between interview and estimated time of conception (<12 months, ⩾12 months). No consistent differences with regard to the caffeine (Table IV) and alcohol estimates (data not shown) were found in the group with <12 months between interview and estimated date of conception and those with an interval of >12 months.

Discussion

In this study, a high daily intake of caffeine prior to pregnancy suggested an increased risk of spontaneous abortion. This association seemed more related to caffeine than to coffee drinking since the association with coffee drinking alone was weaker than for total caffeine. For alcohol, we found no increased risk of spontaneous abortion in women with a moderate alcohol intake (1–13 weekly drinks) compared with non-drinkers, while our data cannot rule out that a higher intake may imply an increased risk.

The former finding is in line with some previous studies using measures of pre-pregnancy caffeine exposures (Axelsson *et al*., 1989; Infante-Rivard *et al*., 1993) where the risk estimates obtained were similar to our results, but Fenster *et al*. (1997) only found a slightly increased risk (OR = 1.25; 95% CI: 0.90–1.73) for an intake of >300 mg per day (versus no intake), and Wen *et al*. (2001) found no relationship (Table V). However, these studies could not look at caffeine levels as high as in the present study, so the findings may be fairly consistent, especially since only the OR for an intake of >900 mg caffeine per day was significantly increased in the present study.

The results regarding the association between spontaneous abortion and caffeine intake during pregnancy are not entirely consistent either; both the earlier studies (summarized by Fenster *et al*., 1997) and those more recently published (Table V). The majority (Fernandes *et al*., 1998; Klebanoff *et al*., 1999; Cnattingius *et al*., 2000; Wen *et al*., 2001) but not all (Fenster *et al*., 1997) show a relationship between caffeine intake during pregnancy and spontaneous abortion. For example, Cnattingius *et al.* found an association, but only among non-smokers, and the study by Wen *et al.* showed that caffeine intake after the start of nausea in the first trimester was associated with an increased risk of spontaneous abortion.

It is not known whether the association between the pre-pregnancy caffeine intake and spontaneous abortion found in this and other studies reflects a causal relationship due to a true adverse effect of caffeine on female reproductive health through a still unknown mechanism. Alternatively, caffeine intake before pregnancy may not in itself be a risk factor, but may rather be an indicator for caffeine intake during pregnancy, which has been suggested to be a risk factor for spontaneous abortion. Finally, it could be that a high pre-pregnancy caffeine intake may be only a proxy measure of other risk factors present before or during pregnancy. Indeed,

Table V. Recent studies of the association between caffeine intake and risk of spontaneous abortion

Author	Study design	Study population	Measure of association	OR (95% CI)			Comments
				Before pregnancy	During pregnancy		
Fenster *et al.* (1997)	Prospective[a]	5144 women	Caffeine (mg/day):				13 had a caffeine intake of >300 mg/day before pregnancy
		⩽13 weeks pregnant	0[b]	1.00	1.00		Adjustment for age, gestational age, pregnancy history, alcohol intake, smoking, marital status, ethnicity, employment, socio-economic status
			1–150	1.05 (0.82–1.35)	1.01 (0.82–1.25)		
			151–300	1.04 (0.77–1.39)	1.18 (0.84–1.66)		
			>300	1.25 (0.90–1.73)	1.29 (0.80–2.06)		
Fernandes *et al.* (1998)	Meta-analysis of five studies	42 889 pregnancies	Caffeine (mg/day)				No confounder control
			0–150†		1.00		
			>150		1.36 (1.29–1.45)		
Klebanoff *et al.* (1999)	Nested case–control	591 women with spontaneous abortion (<140 days of gestation) and 2558 women, who gave birth	Serum paraxanthine (ng/ml):				Adjustment for age, smoking, and ethnicity. Estimates were not affected when vomiting since last menstrual period was taken into account
			<50[b]		1.0		
			50–1845		No increased risk[c]		
			>1845		1.9 (1.2–2.8)		
Cnattingius *et al.* (2000)	Case–control	562 women with spontaneous abortion (6–12 weeks gestation)	Caffeine (mg/day):		Smokers:	Non-smokers:	Adjustment for age, pregnancy history, alcohol intake, nausea, vomiting, and fatigue
		953 women seeking antenatal care	0–99[b]		1.0	1.0	Increased risk confined to fetuses of normal/unknown karyotype
			100–299		0.9 (0.3–2.5)	1.3 (0.9–1.8)	
			300–499		1.7 (0.6–4.6)	1.4 (0.9–2.0)	
			⩾500		0.7 (0.3–1.9)	2.2 (1.3–3.8)	
Wen *et al.* (2001)	Prospective	75 women who had spontaneous abortion	Caffeine (mg/day):				17% of cases and 16% of controls had a caffeine intake of ⩾300 mg/day
			<20[b]	1.0	1.0		Only unadjusted estimates were available
			20–99	1.0 (0.5–1.9)	1.5 (0.8–2.7)		
		575 women delivering singleton live births	100–299	1.1 (0.6–2.1)	2.0 (1.0–4.1)		
			⩾300	1.1 (0.5–2.4)	2.5 (1.0–6.4)		

[a]Information on pre-pregnancy caffeine intake obtained retrospectively.
[b]Reference category.
[c]No exact value for odds ratios available.

coffee drinking is related to smoking, for example, and Danish women are known for being heavy smokers. However, alcohol is also related to smoking, and no increased risk was observed for alcohol intake in the present study.

In the case of alcohol use, the same tendency exists for inconsistent results as some studies show a significant increase in risk for spontaneous abortion in moderate drinkers compared with abstainers (Harlap *et al*., 1980; Anokute, 1986; Armstrong *et al*., 1992; Windham *et al*., 1997; Kesmodel *et al*., 2002) while others do not (Grisso *et al*., 1984; Halmesmaki *et al*., 1989; Parazzini *et al*., 1994; Dominguez-Rojas *et al*., 1994; Cavallo *et al*., 1995). We find no place to review this subject extensively, but as with intake of caffeine, suggested explanations for the varying results include differences in study populations, definition of outcome, and inadequate or no control for confounders.

The findings of this study should be interpreted with caution. We used data on pre-pregnancy consumption of caffeine and alcohol, which may not reflect the appropriate exposure period (early pregnancy). This may explain the lack of association with alcohol.

The association between the pre-pregnancy exposure and the risk of spontaneous abortion may depend on the length of the interval between assessment of exposure and conception, since women might change their habits over time. We repeated the analyses stratified according to the time interval between interview and estimated time of conception, and no consistent differences in results between the group of women with an interval of <12 months and the group of women with a longer interval (≥12 months) were found. Time of conception was estimated as date of birth minus 40 weeks or date of the spontaneous abortion minus 9 weeks, since information on exact gestational age could not be obtained. By this procedure, the time of conception is probably more inaccurately defined for spontaneous abortions than it is for live births. However, since this information is solely used for the time-stratified analysis and the results are in agreement, we do not consider this to be a major problem.

An advantage of this study is that we assessed the intake of caffeine and alcohol prospectively and independently of pregnancy, thus minimizing information bias. In our study, 24% of the spontaneous abortions were identified only from the interview, i.e. they were not registered in the Hospital Discharge Register. The majority of these are most likely early spontaneous abortions that were not treated at a hospital, even though some may represent misinterpreted heavy menstruations.

Women who did not participate in the second interview (22% of the total study population) were followed by register linkage only. Since ~75% of all spontaneous abortions and 99% of all births are registered in the patient registers, there will be a greater loss to follow-up of women who did not participate in the second examination than of women who participated in both examinations. However, if this loss is independent of exposure status, the estimates presented are still valid.

Other strengths of the study include that it is population-based and that the spectrum of both alcohol and caffeine intake was wide with a high proportion of heavy coffee drinkers. Only 12% of the women had a daily intake of <100 mg caffeine and 20% reported drinking less than one drink per week. The mean daily caffeine intake was found to be almost 500 mg, which is more than twice the intake of American women (Barone and Roberts, 1996). More than 62% of the women in this study had a daily intake of caffeine >300 mg. The corresponding figures in the most recently published studies of caffeine intake before pregnancy were respectively 13% (Fenster *et al*., 1997) and 17% (Wen *et al*., 2001) (Table V).

Caffeine intake was only calculated from consumption of tea and coffee. Information on caffeine from other sources such as cola and chocolate was unfortunately not given. The daily intake of caffeine for women in the low and middle caffeine categories is therefore probably underestimated. If, however, such a misclassification were independent of pregnancy outcome, the risk estimates would be shifted in the direction of unity.

Nausea in early pregnancy is shown to modify the association between caffeine intake and spontaneous abortion so that only heavy caffeine consumers reporting nausea had an increased risk of spontaneous abortion (Fenster *et al*., 1991). Since the present study is on alcohol and caffeine intake before pregnancy, we do not have information on nausea during pregnancy, and hence we have no opportunity to examine whether nausea is modifying our results. If results from the Fenster study apply to our study, then the estimates would be conservative estimates for heavy caffeine users with nausea and exaggerated estimates for heavy caffeine users without nausea.

In summary, we obtained information on intake of caffeine and alcohol in younger women before pregnancy and followed them until pregnancy outcome for 2–3 years. For caffeine, an increasing risk of spontaneous abortion was found with a moderate-to-high pre-pregnancy intake. Moderate pre-pregnancy alcohol intake does not seem to be associated with spontaneous abortion.

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