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Low to moderate prenatal alcohol consumption and the risk of selected birth outcomes: a prospective cohort study

Lisbet S. Lundsberg, PhD, MPH[a], **Jessica L. Illuzzi, MD, MS**[a], **Kathleen Belanger, PhD**[b,†], **Elizabeth W. Triche, PhD**[c], and **Michael B. Bracken, PhD, MPH**[a,b]

Lisbet S. Lundsberg: lisbet.lundsberg@yale.edu; Jessica L. Illuzzi: jessica.illuzzi@yale.edu; Elizabeth W. Triche: Elizabeth_Triche@brown.edu; Michael B. Bracken: michael.bracken@yale.edu

[a]Yale University School of Medicine, Department of Obstetrics, Gynecology and Reproductive Sciences, 333 Cedar Street, New Haven, CT 06520 USA Phone: 1 (203) 785-4294, Fax: 1 (203) 785-6586

[b]Yale University School of Public Health, Center for Perinatal, Pediatric and Environmental Epidemiology, 1 Church Street, 6thfloor, New Haven, CT 06510 USA Phone: 1 (203) 764-9375, Fax: 1 (203) 764-9378

[c]Brown University School of Medicine, Dept. of Community Health/Epidemiology, 121 S. Main St., 2nd floor, Providence, RI 02912 USA Phone: 1 (401) 863-1987

Abstract

Purpose—Estimate whether low to moderate prenatal alcohol exposure is associated with selected birth outcomes.

Methods—Low to moderate prenatal alcohol drinking and effects on low birth weight, preterm delivery, intrauterine growth restriction (IUGR), and selected neonatal outcomes were evaluated among 4,496 women and singleton infants. Odds ratios (OR) and 95% confidence intervals (CI) were calculated using multivariable logistic regression, controlling for confounding variables.

Results—Early pregnancy drinking was associated with reduced odds of low birth weight, OR 0.66 (95% CI 0.46, 0.96) and birth length < 10th percentile, OR 0.74 (95% CI 0.56, 0.97). Drinking during the first 3 months showed lower odds for birth length and head circumference <

Corresponding author: Michael B. Bracken, PhD, MPH, Yale University School of Public Health, Yale Center for Perinatal, Pediatric and Environmental Epidemiology, One Church Street, 6th floor, New Haven, CT 06510 USA; Phone: 1 (203) 764-9375, Fax: 1 (203) 764-9378, michael.bracken@yale.edu.
†deceased

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10^{th} percentile, OR 0.56 (95% CI 0.36, 0.87) and OR 0.69 (95% CI 0.50, 0.96), respectively. Third trimester drinking was associated with lower odds for low birth weight, OR 0.56 (95% CI 0.34, 0.94) and preterm delivery, OR 0.60 (95% CI 0.42, 0.87).

Conclusions—Our results suggest low to moderate alcohol exposure during early and late gestation is not associated with increased risk of low birth weight, preterm delivery, IUGR and most selected perinatal outcomes.

Keywords

alcohol; birth outcomes; low birth weight; preterm delivery; IUGR

Introduction

Alcohol use during pregnancy has historically been associated with a range of negative birth outcomes and developmental effects that include fetal alcohol syndrome (FAS), alcohol related birth defects (ARBD) and alcohol related neurodevelopmental disorders (ARND) [1, 2], often characterized at birth by facial dysmorphology, poor growth, and neurologic functional and structural abnormalities, including reduced head circumference [3]. While epidemiological research has delineated adverse effects of heavy or chronic drinking on the fetus, reported effects of low to moderate prenatal alcohol which represents the majority of exposures, are inconsistent. Previous studies have documented increased risks between alcohol and infertility [4], miscarriage [5], stillbirth and infant mortality [6, 7], congenital anomalies [8], low birth weight [9], reduced gestational age [10], preterm delivery [11], and intrauterine growth restriction (IUGR) or small-for-gestational age (SGA) [8, 12, 13], but at relatively higher consumption levels. Conversely, other research demonstrated no increase in risk from light to moderate alcohol consumption for selected perinatal or developmental outcomes [14–18], and several studies have reported *reductions* in risk of adverse pregnancy outcomes, including a curvilinear effect for increasing levels of prenatal alcohol exposure [9, 19–21]. A systematic review of low to moderate prenatal drinking reported lacking evidence of increased risk for selected birth outcomes including IUGR, prematurity, birth weight, and malformations [22] yet results overall were inconclusive.

Methodological difficulties related to study design, including retrospective exposure assessment, potential exposure misclassification, and inadequate control for potential confounders have resulted in limited high-quality analyses of low to moderate prenatal alcohol drinking. The current study is a prospective investigation of alcohol use during pregnancy and IUGR, low birth weight, preterm delivery, and other selected neonatal outcomes among a cohort of 4,496 women and their newborns.

Materials and Methods

Sample

The study population included women enrolled in two related and almost concurrent prospective longitudinal cohorts: one examining prenatal caffeine exposure and the other investigating asthma in pregnancy; see Figure 1. Pregnant women were recruited from 56 obstetric practices and 15 clinics associated with six hospitals in Connecticut and

Massachusetts during the period of September 1996 to June 2000. Study design for each cohort was similar with respect to methodology, timing and content of structured interviews [23, 24]. The final sample was restricted to singleton live births, yielding a total study sample of N=4,496 for the current analyses.

All women completed a baseline interview prior to 24 weeks gestation. Information was collected on multiple risk factors through the pregnancy, including comprehensive maternal characteristics and potential confounding variables. Detailed pregnancy history was collected, including pre-existing medical conditions. The postpartum interview was conducted following delivery, typically in the hospital during the postpartum stay or within 1 month of delivery. Medical records for both the mother and infant were reviewed to collect detailed information related to labor and delivery, selected medical risk factors and potential confounders.

Exposure ascertainment

Alcohol consumption information was collected for specific months of pregnancy during two study visits: baseline prenatal interview and postpartum interview. In the baseline prenatal interview, participants were asked in detail about alcohol use during months 1–3 of gestation, in addition to any alcohol exposure up to the baseline interview; median gestational age at baseline interview was 14 weeks (range 6–24 weeks). During the postpartum interview an assessment of drinking was completed for gestational month 7 and the third trimester. Second trimester alcohol use was not assessed. For each beverage type (wine, beer, liquor), women were asked how often they drank alcohol and how many drinks they consumed during the specific time period. Using a previously established algorithm [25], alcohol content values for each beverage were summed for a total exposure score expressed as daily ounces of absolute alcohol (oz AA/day) for each month/trimester. Drinking levels were categorized as: abstinent, <0.1 oz AA/day, 0.1<0.25 oz/AA day, 0.25<0.50 oz AA/day, 0.50<1.0 oz AA/day, and ≥1.0 oz AA/day. It is estimated that 0.5 oz (14g) AA/day is approximately equal to 1 standard drink; therefore, alcohol exposure categories correspond approximately to: 0 drinks, <1.5 drinks/week, 1.5<3.5 drinks/week, 3.5<7 drinks/week, 7<14 drinks/week, and 14+ drinks/week. First trimester exposure was categorized into: abstinent, drinking in month 1 only (with no subsequent drinking in months 2 or 3), and other alcohol exposure during months 1–3. Binge drinking was classified as consuming 4+ drinks at one time [26].

Outcomes of interest

Birth weight obtained from the delivery log was used to categorize infants considered low birth weight (<2,500 g). Gestational age was based on last menstrual period (LMP) or an ultrasound estimate if LMP was uncertain or inaccurate: 55.3% were confirmed by early ultrasound, 37.2% based on LMP, and 7.5% based on a newborn clinical exam. Preterm delivery was defined as <37 weeks. IUGR was classified as <10^{th} percentile of birth weight for gestational age according to 1999 US birth standards [27], adjusted for gender and mother's ethnicity. Birth length and head circumference were analyzed as continuous outcomes using the lowest 10^{th} percentile according to Centers for Disease Control and Prevention (CDC) standards [28] to define low birth length and reduced head circumference.

Additional clinical outcomes included: major selected congenital malformations [29]; Apgar score <7 at 1 and 5 minutes; ventilation (including need for continuous positive airway pressure, CPAP); placement in the neonatal intensive care unit, NICU (observation or admission); and neonatal jaundice.

Potential Confounding Variables

Demographic covariates included maternal age, ethnicity, marital status, education, parity, and employment. Smoking, caffeine intake, prenatal and multivitamin use, passive smoke exposure, illicit drug use prior to conception, pre-pregnancy body mass index, work, and exercise before and during pregnancy were also evaluated. Obstetric and medical variables assessed included hypertension, preterm labor, bleeding during pregnancy, placental problems, gestational diabetes, incompetent cervix, respiratory disease, maternal asthma, induction or augmentation of labor, and infant gender.

Statistical Analysis

Analysis focused on patterns of drinking throughout pregnancy in first and third trimesters. Bivariate analyses were performed for selected maternal characteristics and alcohol exposure compared to primary dichotomous outcomes of interest using the χ^2 statistic. Multivariable analysis of prenatal alcohol exposure and birth outcomes was performed using logistic regression modeling in PC-SAS 9.3 (SAS Institute, Cary, NC). Odds ratio (OR) estimates for alcohol exposure were obtained for each assessment period and each outcome of interest. Models were developed using multiple logistic regression with backwards selection at α=0.10 level of significance, including the exposure of interest, potential confounders, and independent risk factors. Final models included the selected measure of alcohol exposure, indicator variable for study cohort, as well as confounding variables that changed alcohol β estimates more than 10%. Continuous outcomes were analyzed using generalized linear modeling and backwards selection at α=0.10 level of significance, with transformation of the response variable using log base 10 to account for lack of normal distribution.

Protocols for both investigations were approved by the Human Investigations Committee at Yale University and all participating institutions. Written or oral consent was obtained from each participant per the guidelines of the local human investigations committee.

Results

Maternal alcohol exposure was most prevalent during the first month of pregnancy (29%), and declined in the second and third months to 9% and 7%, respectively; median exposure among women who drank during months 1, 2, and 3 was 0.07oz AA/day (about 1 drink/week), 0.03oz AA/day (slightly less half a drink/week), and 0.02oz AA/day (slightly less than one-third of a drink/week), respectively. Alcohol consumption demonstrated a curvilinear pattern, becoming less frequent following recognition of pregnancy, and then modestly increasing through the third trimester, to 11% in month 7 (median consumption of 0.02oz AA/day among drinkers, slightly less than one-third of a drink/week) and reaching 27% with any alcohol exposure during the third trimester.

Selected maternal characteristics and first gestational month alcohol exposure are presented in Table 1. Women drinking in month 1 of pregnancy were more likely to be nulliparous, over age 25, Caucasian, married, normal pre-pregnancy body mass index (BMI) (18.5–24.9), and completed higher education. A strong relationship is shown between caffeine (mg/day) and alcohol consumption in month 1. Similarly, women smoking during pregnancy were more likely to be drinking alcohol compared to non-smokers. Women who exercise, work and take multivitamins are more likely to have consumed alcohol in month 1. Additional associated maternal variables are presented in Supplemental Table 1.

The association between maternal characteristics and birth weight, preterm delivery, and IUGR are presented in Table 2. Among the study cohort, 4.7% of infants were low birth weight, 6.9% were delivered preterm, and 7.9% were diagnosed with IUGR. Risks of low birth weight, preterm delivery and IUGR were increased among women who were nulliparous, under age 25, with less than high school education, and smoked during pregnancy; married and Caucasian women had decreased risk for these birth outcomes. Women who were underweight (pre-pregnancy BMI <18.5) or reported caffeine consumption, were at increased risk for low birth weight, preterm delivery and IUGR, while exercise decreased the risk of low birth weight, and early prenatal vitamin use decreased the risk of each outcome. Additional associations are presented in Supplemental Table 2.

Analyses to estimate the effect for early pregnancy drinking and birth outcomes are presented in Table 3. Alcohol consumption among low to moderate drinkers in month 1, evaluated as discrete levels of daily drinking (oz AA/day), does not confer any increased risk compared to the non-drinking group. For first trimester exposure, drinking in month 1 only had a significantly lower odds for low birth weight, odds ratio (OR) 0.63 (95% confidence interval (CI) 0.43, 0.94). Tests for trend across level of drinking and low birth weight were statistically significant for month 1 drinking (P=0.03) and first trimester drinking (P=0.007). Low to moderate prenatal drinking up to the baseline interview was associated with significantly reduced odds of low birth weight, OR 0.58 (95% CI 0.42, 0.80). Low to moderate drinking in early pregnancy was not associated with preterm delivery or IUGR.

Following multivariable analysis, no increased risk from low to moderate levels of alcohol drinking in the first trimester on selected birth outcomes was observed. Month 1 estimates for levels ≥0.10 oz AA/day were stronger after adjustment, and early pregnancy drinking showed a significant, yet attenuated, odds for low birth weight, OR 0.66 (95% CI 0.46, 0.96). Estimates do not demonstrate any increase in risk for preterm delivery or IUGR.

Third trimester drinking estimates were modeled to determine any differences in risk based on timing of alcohol exposure (Table 4). Due to small cell numbers, analysis was limited to evaluation of alcohol as a bivariate exposure: mothers who abstained or drank. Drinking in month 7 demonstrated significant reduced odds of low birth weight; following multivariate adjustment, the estimate is attenuated and non-significant. Third trimester drinking was associated with a significant reduction in odds of low birth weight, and was statistically significant following multivariate adjustment, OR 0.56 (95% CI 0.34, 0.94). Month 7 drinking did not appear to be associated with preterm delivery and adjusted estimates for

third trimester drinking showed a decreased risk with preterm delivery, OR 0.60 (95% CI 0.42, 0.87). No increased risk of IUGR is observed for month 7 or third trimester drinking.

Table 5 presents adjusted odds ratio estimates for early pregnancy alcohol use and selected neonatal outcomes. Following multivariable analysis, alcohol exposure was not associated with a significant increased risk for major congenital malformations, Apgar score <7 at 5 minutes, admission or observation in the NICU, or jaundice. In addition, low to moderate drinking was not associated with an increased risk for reduced head circumference or reduced birth length, markers often associated with fetal alcohol spectrum disorders. However, month 1 drinking at ≥0.25 oz AA/day was associated with an increased risk of need for ventilation, OR 2.10 (95% CI 1.16–3.79). Analysis of neonatal ventilation and month 1 drinking stratified into higher drinking levels demonstrated that while drinking 0.25<0.50oz AA/day showed a significantly increased risk, estimates for higher levels (0.50<1.00 oz AA/day and ≥1.00 oz AA/day) were attenuated and not significant. Apgar score <7 at 5 minutes, as well as 1 minute Apgar (not presented) show similar but statistically nonsignificant increases. First trimester drinking in months 1–3 or drinking ever in early pregnancy was associated with reduced risk of short birth length, OR 0.56 (95% CI 0.36–0.87) and OR 0.74 (95% CI 0.56–0.97), respectively. Lower odds ratio estimates were observed for drinking in months 1–3 and small head circumference, OR 0.69 (95% CI 0.50–0.96). Analysis of continuous outcomes demonstrated longer infant birth length among those women drinking in the first 3 months than among those who were abstinent, 20.3cm vs. 20.1cm (β=0.0031; p=0.02); newborns of women who consumed 0.10<0.25 oz AA/day in month 1 had mean head circumference of 34.04cm compared to 33.77cm among those who were abstinent (β=0.0034; p=0.03); see Supplemental Table 3.

Binge drinking was also analyzed in this cohort. During month 1, 139 women (3%) reported drinking 4+ servings on one occasion, and 159 (3.5%) reporting binge drinking during the first trimester. Adjusted models for binge drinking in the first trimester, while imprecise, did not suggest an increased risk for low birth weight, OR=0.64 (0.24, 1.69), preterm delivery, OR=0.55 (0.22, 1.38), or IUGR, OR=0.75 (0.39, 1.44) compared to non-drinkers.

Discussion

Our findings provide no support for an increased risk for low birth weight, preterm delivery, IUGR, and selected birth outcomes, consistent with earlier studies of low to moderate alcohol exposure [14, 16, 17, 30] and a systematic review of low to moderate drinking [22]. Similar to a previous meta-analysis of low to moderate prenatal drinking and malformations [30] we did not observe an increase in the risk for major congenital malformations. Risk for reduced birth length, reduced head circumference, and lower Apgar scores was not increased with low to moderate drinking in this cohort, consistent with an earlier analysis [17]. Previous studies have also reported significant reductions in risk of preterm delivery, low birth weight, and IUGR with low to moderate prenatal drinking and a curvilinear effect [19–21]. In the current analysis, significant reductions in risk were observed for low birth weight, head circumference <10th percentile, and birth length <10th percentile with low to moderate drinking. While an increased risk for neonatal ventilation was observed, stratified analysis of drinking levels ≥0.50 did not demonstrate a dose-response effect. Whether this is a real

association or owed to multiple comparisons is unclear. Previous report of an increased risk for jaundice with maternal drinking [31] was not observed in our analysis; while rates of jaundice in our cohort were lower than some literature reports [32], almost one-third of the newborns were jaundiced overall. Earlier investigation using record linkage data demonstrated increased newborn care admission among infants born to mothers with alcohol-related diagnoses, however this represented a high-risk group [33]. We observed no significant increase in NICU admission with low to moderate prenatal alcohol exposure.

Comprehensive analysis of alcohol exposure throughout the first and third trimesters of pregnancy is a major strength of this study. Alcohol exposure was assessed in the first trimester prospective to birth outcomes, avoiding potential recall bias. Second trimester exposure was not assessed but is unlikely to have deviated in a meaningful way from the first and third trimester assessments. Third trimester exposures were measured retrospectively but concordance of results across trimesters suggests that recall bias was not a major factor in third trimester reporting. Exposure assessment was objectively quantified, included alcohol type, frequency, and volume, from which a validated alcohol score could be constructed to determine daily absolute alcohol exposure [25]. In addition, we adjusted for numerous potential confounders, collected primarily during prospective interviews.

There are several study limitations. The cohort was primarily of women reporting lower levels of drinking during pregnancy, precluding evaluation of risk estimates for higher levels of drinking. However, analysis of this cohort is important as it permits interpretation of effects attributable to more typical levels of low to moderate alcohol exposure among women of childbearing age. The cohort included a diverse population of urban and suburban pregnant women from hospital clinics, community clinics, and private obstetrical offices, supporting the generalizability of findings. Underreporting is a concern in studies involving maternal alcohol exposure [34]; however 29% of women in this cohort reported some alcohol exposure in month 1 which does not suggest underreporting, and exposure was lower in months 2 (9%) and 3 (7%), reflective of drinking patterns prior to and following pregnancy recognition. Prospective ascertainment of maternal drinking, including beverage type, frequency, and amount, may improve validity of self-reported drinking [35, 36]; with the current cohort, we assessed alcohol exposure both prospectively and by beverage type, frequency and amount. Cohort follow-up continued until immediately postpartum, thus evaluation of neurodevelopmental and pediatric outcomes previously reported [18, 37, 38] was not performed.

Different standards used to define IUGR make it difficult to draw comparisons across existing studies of prenatal drinking and fetal growth restriction. We constructed the most widely used formulation: the lowest 10^{th} percentile of birth weight for gestational age, and did so according to the 1999 US birth standards [27], aligning with cohort recruitment from 1997–2001; percentiles were further adjusted for gender and ethnicity to refine population standards. CDC standards (2000) establishing the lowest 10^{th} percentile of birth length and head circumference [28] were appropriate for the study period. While the potential for misclassification exists, further multivariable analysis of birth length and head circumference as a continuous outcome confirmed no risk increase with low to moderate

levels of prenatal alcohol. Additional adjustment for gestational age within these models did not materially affect risk estimates.

We also performed a sensitivity analysis for first trimester drinking and alcohol exposure up to the baseline interview, to account for participants entering the study at different weeks during early gestation. This analysis excluded those who completed the baseline interview less than 9 weeks gestation and therefore could not provide exposure information for month 3. Both unadjusted and adjusted odds ratio estimates were similar in magnitude and statistical significance was unchanged for all outcomes.

Reported lower odds ratio estimates may be attributable to a “healthy lifestyle” effect where low levels of drinking are associated with specific lifestyles or behaviors. We observed that low to moderate drinkers in month 1 were significantly more likely to consume multivitamins and prenatal vitamins during the first trimester, work, exercise, and have normal pre-pregnancy BMI. Women may abstain from alcohol for medical reasons (which could increase risk); however, our analysis evaluated potential confounders in detail, including maternal medical history and obstetrical factors. While the observed effect may be due to unmeasured confounders, they would need to be protective and independent of variables included in our multivariable models. Effects due to beverage type have been of interest; previous analysis of supermarket transactions found an association between wine and healthier food purchases [39]. Among the current cohort, wine was the predominant source of alcohol, consumed by 68% of women drinking in month 1. Multivariable modeling for beverage type did not demonstrate a significant increase in risk for low birth weight, IUGR, or preterm delivery.

Specific birth outcomes investigated in this analysis, including IUGR, birth length, and reduced head circumference can be hallmark features of FAS. We found no association of low to moderate alcohol with these outcomes. Evaluation of infant medical records identified two newborns with ICD-9 diagnostic code 760.7, defined as “Noxious influences affecting fetus or newborn via placenta or breast milk.” One had no adverse birth outcomes and exposure to 0.25<0.50oz AA/day (approximately 3.5 to 7 drinks per week) in the first trimester; the other newborn had IUGR, with head circumference and birth length below the 10^{th} percentile, yet no first trimester alcohol exposure. However, due to lack of systematic evaluation of specific structural features and longitudinal follow-up to assess cognitive, motor and neurological functioning, we were not able to specifically evaluate FAS or ARND in this cohort.

Conclusions

National and international guidelines advise women to abstain from drinking during pregnancy [40–43]. As lower level drinking represents a more prevalent exposure among pregnant women especially before pregnancy recognition, scientific research regarding lower level exposures is a priority; yet published study findings remain inconsistent and qualitatively varied. This study adds to accumulating evidence regarding a lack of increased risk from low to moderate maternal alcohol consumption during pregnancy, selected perinatal outcomes and measures of fetal growth.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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LIST OF ABBREVIATIONS AND ACRONYMS

AA	absolute alcohol
ADH1B	alcohol dehydrogenase 1B
ARBD	alcohol related birth defects
ARND	alcohol related neurodevelopmental disorders
BMI	body mass index
CDC	Centers for Disease Control and Prevention
CI	confidence interval
CPAP	continuous positive airway pressure
FAS	fetal alcohol syndrome
ICD-9	International Classification of Diseases, Ninth Revision
IUGR	intrauterine growth restriction
LMP	last menstrual period
NICU	neonatal intensive care unit
OR	odds ratio
SGA	small-for-gestational age;

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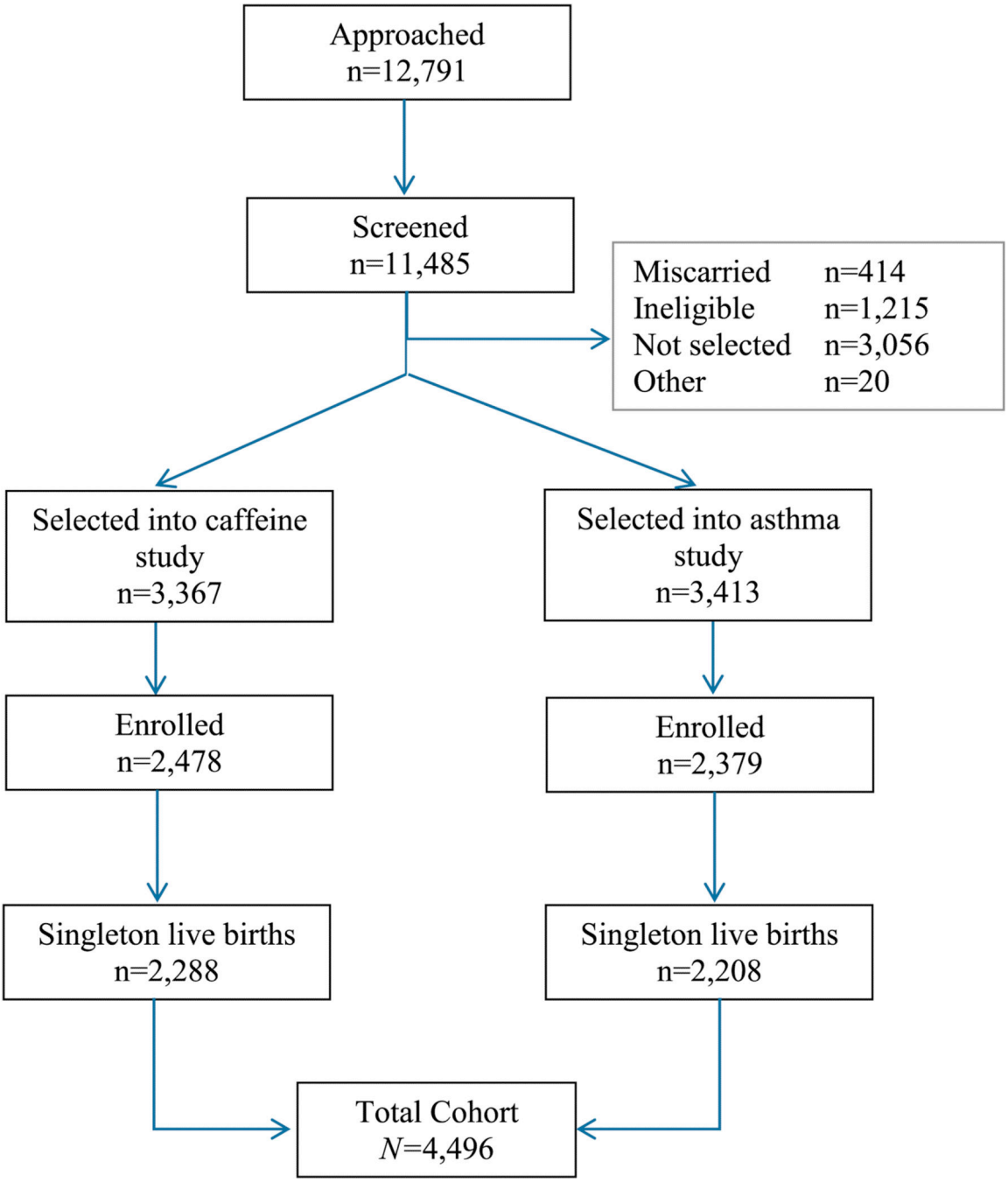

Figure 1.
Number of subjects approached, screened, and enrolled into the total cohort. Low to moderate alcohol use in pregnancy and birth outcomes: Connecticut/Massachusetts, 1996–2000.

Table 1

Selected Characteristics of the Study Cohort by Absolute Alcohol (AA) Drinking Month 1 – n (%)

Characteristic	N[a]	Levels of alcohol exposure						p-value
oz AA/day[b]		**0**	**<0.10**	**0.10<.25**	**0.25<0.50**	**0.50<1.00**	**≥1.00**	
(drinks/week)		**0**	**(<1.5)**	**(1.5<3.5)**	**(3.5<7.0)**	**(7.0<14.0)**	**(≥14.00)**	
	4,496	3183 (71.2)	733 (16.4)	245 (5.5)	155 (3.5)	96 (2.2)	59 (1.3)	
Parity								
0	1981	1363 (68.8)	328 (16.6)	129 (6.5)	80 (4.0)	47 (2.4)	34 (1.7)	*P*=0.0294
1	1553	1128 (72.6)	253 (16.3)	79 (5.1)	40 (2.6)	37 (2.4)	16 (1.0)	
2	663	491 (74.1)	105 (15.8)	26 (3.9)	27 (4.1)	8 (1.2)	6 (0.9)	
3+	270	200 (74.1)	45 (16.7)	11 (4.1)	8 (3.0)	4 (1.5)	2 (0.7)	
Age								
<25	1052	872 (82.9)	83 (7.9)	35 (3.3)	21 (2.0)	22 (2.1)	19 (1.8)	*P*<0.0001
25<30	1150	826 (71.8)	193 (16.8)	66 (5.7)	38 (3.3)	17 (1.5)	10 (0.9)	
30<35	1465	976 (66.6)	295 (20.1)	94 (6.4)	50 (3.4)	34 (2.3)	16 (1.1)	
≥35	803	509 (63.4)	162 (20.1)	50 (6.2)	46 (5.7)	23 (2.9)	13 (1.6)	
Education								
< 12 yrs	627	542 (86.4)	46 (7.3)	11 (1.8)	8 (1.3)	8 (1.3)	12 (1.9)	*P*<0.0001
12 years	792	611 (77.2)	91 (11.5)	36 (4.6)	17 (2.2)	18 (2.3)	19 (2.4)	
13–16 yrs	2131	1425 (66.9)	389 (18.3)	148 (6.9)	94 (4.4)	54 (2.5)	21 (1.0)	
17+ yrs	916	603 (65.9)	205 (22.4)	50 (5.5)	36 (3.9)	16 (1.7)	6 (0.7)	
BMI[c] (kg/m²)								
Underweight	231	169 (73.2)	38 (16.5)	9 (3.9)	5 (2.2)	8 (3.5)	2 (0.9)	*P*=0.0088
Normal weight	2617	1791 (68.44)	471 (18.0)	158 (6.0)	104 (4.0)	61 (2.3)	32 (1.2)	
Overweight	927	677 (73.0)	133 (14.4)	51 (5.5)	32 (3.5)	19 (2.1)	15 (1.6)	
Obese	583	450 (77.2)	82 (14.1)	24 (4.1)	12 (2.1)	7 (1.2)	8 (1.4)	
Marital Status								
Married	3114	2119 (68.1)	590 (19.0)	190 (6.1)	122 (3.9)	67 (2.2)	26 (0.8)	*P*<0.0001
Single	1164	927 (79.6)	115 (9.9)	46 (4.0)	24 (2.1)	25 (2.2)	27 (2.3)	
Divorced, separated	191	136 (71.2)	28 (14.7)	9 (4.7)	9 (4.7)	4 (2.1)	5 (2.6)	

Characteristic	N[a]	Levels of alcohol exposure						p-value
oz AA/day[b]		**0**	**<0.10**	**0.10<.25**	**0.25<0.50**	**0.50<1.00**	**≥1.00**	
(drinks/week)		**0**	**(<1.5)**	**(1.5<3.5)**	**(3.5<7.0)**	**(7.0<14.0)**	**(≥14.00)**	
Ethnicity - mother								
Caucasian	3048	1982 (65.0)	605 (19.9)	207 (6.8)	131 (4.3)	82 (2.7)	41 (1.4)	*P*<0.0001
Black, African American	399	329 (82.5)	44 (11.0)	11 (2.8)	8 (2.0)	5 (1.3)	2 (0.5)	
Hispanic	842	719 (85.4)	70 (8.3)	19 (2.3)	13 (1.5)	9 (1.1)	12 (1.4)	
Asian	77	64 (83.1)	9 (11.7)	2 (2.6)	2 (2.6)	0 (0.0)	0 (0.0)	
Other	96	82 (85.4)	5 (5.2)	6 (6.3)	0 (0.0)	0 (0.0)	3 (3.1)	
Caffeine (mgs/day) - first trimester								
0	1888	1463 (77.5)	285 (15.1)	81 (4.3)	32 (1.7)	20 (1.1)	7 (0.4)	*P*<0.0001
1–149 mgs/day	2193	1458 (66.5)	391 (17.8)	144 (6.6)	104 (4.7)	62 (2.8)	34 (1.6)	
150–299 mgs/day	265	177 (66.8)	43 (16.2)	14 (5.3)	11 (4.2)	7 (2.6)	13 (4.9)	
300+ mgs/day	123	85 (69.1)	13 (10.6)	6 (4.9)	8 (6.5)	7 (5.7)	4 (3.3)	
Smoking History								
Never	2754	2046 (74.3)	453 (16.5)	128 (4.7)	74 (2.7)	39 (1.4)	14 (0.5)	*P*<0.0001
Quit before pregnancy	945	642 (67.9)	168 (17.8)	61 (6.5)	45 (4.8)	21 (2.2)	8 (0.9)	
First trimester only	475	290 (61.1)	77 (16.2)	35 (7.4)	29 (6.1)	20 (4.2)	24 (5.1)	
First and third trimester	293	202 (68.9)	35 (11.5)	21 (7.2)	7 (2.4)	16 (5.5)	12 (4.1)	
Exercise since becoming pregnant								
No	2058	1553 (75.5)	302 (14.7)	95 (4.6)	52 (2.5)	32 (1.6)	24 (1.2)	*P*<0.0001
Yes	2410	1628 (67.6)	431 (17.9)	150 (6.2)	103 (4.3)	64 (2.7)	34 (1.4)	
Worked since becoming pregnant								
No	1121	892 (79.6)	131 (11.7)	38 (3.4)	29 (2.6)	17 (1.5)	14 (1.3)	*P*<0.0001
Yes	3349	2291 (68.4)	602 (18.0)	207 (6.2)	126 (3.8)	79 (2.4)	44 (1.3)	
Prenatal vitamin use month 1								
No	2650	1858 (70.1)	426 (16.1)	157 (5.9)	94 (3.6)	67 (2.5)	48 (1.8)	*P*=0.0006
Yes	1820	1325 (72.8)	307 (16.9)	88 (4.8)	61 (3.4)	29 (1.6)	10 (0.6)	
Multivitamin use month 1								
No	3579	2639 (73.7)	549 (15.3)	169 (4.7)	104 (2.9)	74 (2.1)	44 (1.2)	*P*<0.0001
Yes	871	525 (60.3)	183 (21.0)	76 (8.7)	51 (5.9)	22 (2.5)	14 (1.6)	

Characteristic	N[a]	Levels of alcohol exposure						p-value
oz AA/day[b]		**0**	**<0.10**	**0.10<.25**	**0.25<0.50**	**0.50<1.00**	**≥1.00**	
(drinks/week)		**0**	**(<1.5)**	**(1.5<3.5)**	**(3.5<7.0)**	**(7.0<14.0)**	**(≥14.00)**	
Nausea/vomiting 1st trimester								
No	790	520 (65.8)	136 (17.2)	64 (8.1)	30 (3.8)	21 (2.7)	19 (2.4)	*P<0.0001*
Yes	3679	2663 (72.4)	596 (16.2)	181 (4.9)	125 (3.4)	75 (2.0)	39 (1.1)	
Bleeding/spotting								
No	3522	2485 (70.6)	601 (17.1)	191 (5.4)	129 (3.7)	72 (2.0)	44 (1.3)	P=0.1759
Yes	751	555 (73.9)	102 (13.6)	44 (5.9)	21 (2.8)	18 (2.4)	11 (1.5)	
Hypertension								
No	3880	2760 (71.1)	641 (16.5)	217 (5.6)	131 (3.4)	86 (2.2)	45 (1.2)	P=0.0811
Yes	409	293 (71.6)	63 (15.4)	20 (4.9)	19 (4.6)	4 (1.0)	10 (2.4)	
Gestational diabetes								
No	3547	2519 (71.0)	575 (16.2)	198 (5.6)	131 (3.7)	82 (2.3)	42 (1.2)	P=0.1119
Yes	736	533 (72.4)	126 (17.1)	37 (5.0)	19 (2.6)	8 (1.1)	13 (1.8)	
Preterm labor								
No	3831	2689 (70.2)	648 (16.9)	219 (5.7)	142 (3.7)	81 (2.1)	52 (1.4)	*P=0.0103*
Yes	426	335 (78.6)	52 (12.2)	19 (4.5)	8 (1.9)	9 (2.1)	3 (0.7)	
Beverage type								
Wine only	478		366 (76.6)	59 (12.3)	36 (7.5)	12 (2.5)	5 (1.1)	*P*<0.0001
Beer only	204		143 (70.1)	27 (13.2)	18 (8.8)	11 (5.4)	5 (2.5)	
Liquor only	136		83 (61.0)	34 (25.0)	7 (5.2)	6 (4.4)	6 (4.4)	
Drinks in combination	469		141 (30.1)	125 (26.7)	94 (20.0)	67 (14.3)	42 (9.0)	

[a] Numbers may not sum to total N due to missing values

[b] AA= absolute alcohol ounces; 0.5 oz AA is approximately equal to 1 standard drink

[c] BMI: Underweight(<18.5); normal weight (18.5–24.9); overweight (25–29.9); obese (30+)

Table 2

Maternal Characteristics and Low Birth Weight, Preterm Delivery, and IUGR

	N[a]	LBW (%)	p value	N	PTD (%)	p value	N	IUGR (%)[b]	p-value
	4488	209 (4.7)		4495	310 (6.9)		4486	353 (7.9)	
Parity									
0	1988	119 (6.0)	*P*=0.0010	1990	160 (8.0)	*P*=0.0112	1978	214 (10.8)	*P*<0.0001
1	1561	56 (3.6)		1564	97 (6.2)		1556	81 (5.2)	
2	666	20 (3.0)		667	31 (4.7)		664	40 (6.0)	
3+	270	14 (5.2)		271	22 (8.1)		270	20 (7.4)	
Age									
<25	1048	70 (6.7)	*P*=0.0032	1054	92 (8.7)	*P*=0.0453	1044	96 (9.2)	*P*=0.1284
25<30	1153	48 (4.2)		1154	67 (5.8)		1146	99 (8.6)	
30<35	1479	64 (4.3)		1479	96 (6.5)		1476	103 (7.0)	
35+	807	27 (3.4)		807	55 (6.8)		804	57 (7.1)	
Education									
< 12 yrs	625	60 (9.6)	*P*<0.0001	629	74 (11.8)	*P*<0.0001	624	73 (11.7)	*P*=0.0024
12 years	794	35 (4.4)		796	54 (6.8)		788	59 (7.5)	
13–16 yrs	2143	80 (3.7)		2143	126 (5.9)		2135	152 (7.1)	
17+ yrs	921	33 (3.6)		922	56 (6.1)		919	70 (7.6)	
BMI[c] (kg/m²)									
Underweight	230	16 (7.0)	*P*=0.2965	231	25 (10.8)	*P*=0.0045	229	27 (11.8)	*P*=0.0047
Normal weight	2637	118 (4.5)		2640	159 (6.0)		2629	2124 (8.5)	
Overweight	927	39 (4.2)		928	65 (7.0)		922	68 (7.4)	
Obese	582	30 (5.2)		583	53 (9.1)		579	29 (5.0)	
Marital Status									
Married	3133	103 (3.3)	*P*<0.0001	3135	177 (5.7)	*P*<0.0001	3126	221 (7.1)	*P*=0.0037
Single	1161	87 (7.5)		1166	112 (9.6)		1152	113 (9.8)	
Divorced, separated	192	19 (9.9)		192	21 (10.9)		191	21 (11.0)	
Ethnicity - mother									
White, Caucasian	3065	97 (3.2)	*P*<0.0001	3068	179 (5.8)	*P*=0.0001	3061	227 (7.4)	*P*=0.3474
Black, African-American	401	33 (8.2)		401	31 (7.7)		399	36 (9.0)	

	N[a]	LBW (%)	p value	N	PTD (%)	p value	N	IUGR (%)[b]	p-value
Hispanic	841	68 (8.1)		844	83 (9.8)		838	75 (9.0)	
Asian	77	4 (5.2)		77	4 (5.2)		77	9 (11.7)	
Other	96	7 (7.3)		97	13 (13.4)		96	8 (8.3)	
Caffeine (mgs/day) - first trimester									
0	1897	73 (3.9)	*P*=0.0051	1901	117 (6.2)	*P*=0.0060	1893	134 (7.1)	*P*=0.0061
1–149 mgs/day	21990	106 (4.8)		2201	152 (6.9)		2187	183 (8.4)	
150–299 mgs/day	266	18 (6.8)		266	24 (9.0)		266	19 (7.1)	
300+ mgs/day	123	12 (9.8)		124	17 (13.7)		122	19 (15.6)	
Smoking History									
Never	2764	112 (4.1)	*P*<0.0001	2770	169 (6.1)	*P*=0.0040	2754	197 (7.2)	*P*<0.0001
Quit before pregnancy	949	35 (3.7)		950	66 (7.0)		946	61 (6.5)	
First trimester only	477	33 (7.0)		477	43 (9.0)		473	38 (8.0)	
First and third trimester	294	29 (9.9)		294	32 (10.9)		294	59 (20.1)	
Exercise since becoming pregnant									
No	2057	109 (5.3)	*P*=0.0621	2063	156 (7.6)	*P*=0.1082	2052	160 (7.8)	*P*=0.7328
Yes	2427	100 (4.1)		2428	154 (6.3)		2415	195 (8.1)	
Worked since becoming pregnant									
No	1123	63 (5.6)	*P*=0.0804	1127	81 (7.2)	*P*=0.6581	1119	100 (8.9)	*P*=0.1552
Yes	3364	146 (4.3)		3367	229 (6.8)		3351	255 (7.6)	
Prenatal vitamin use month 1									
No	2653	146 (5.5)	*P*=0.0012	2658	198 (7.5)	*P*=0.0794	2642	235 (8.9)	*P*=0.0046
Yes	1834	63 (3.4)		1836	112 (6.1)		1828	120 (6.6)	
Multivitamin use month 1									
No	3590	171 (4.8)	*P*=0.4969	3597	260 (7.2)	*P*=0.0871	3574	289 (8.1)	*P*=0.5194
Yes	876	37 (4.2)		876	49 (5.6)		875	65 (7.4)	
Nausea/vomiting 1st trimester									
No	793	37 (4.7)	P=0.9907	794	48 (6.1)	P=0.2960	788	65 (8.3)	P=0.7255
Yes	3694	172 (4.7)		3700	263 (7.1)		3682	290 (7.9)	
Bleeding/spotting									
No	3546	135 (3.8)	*P<0.0001*	3546	185 (5.2)	*P<0.0001*	3535	279 (7.9)	P=0.9965
Yes	753	64 (8.5)		753	101 (13.4)		748	59 (7.9)	

		N[a]	LBW (%)	p value	N	PTD (%)	p value	N	IUGR (%)[b]	p-value
Hypertension										
	No	3904	159 (4.1)	*P<0.0001*	3904	244 (6.3)	*P<0.0001*	3887	288 (7.4)	*P<0.0001*
	Yes	411	44 (10.7)		411	47 (11.4)		411	53 (12.9)	
Gestational diabetes										
	No	3573	164 (4.6)	P=0.5030	3573	228 (6.4)	*P=0.0440*	3558	282 (7.9)	P=0.8836
	Yes	736	38 (5.2)		736	62 (8.4)		734	57 (7.8)	
Preterm Labor										
	No	3853	109 (2.8)	*P*<0.0001	3853	117 (3.0)	*P*<0.0001	3842	292 (7.6)	*P*=0.0268
	Yes	428	92 (21.5)		428	171 (40.0)		422	45 (10.7)	

[a] numbers may not sum to total N due to missing values

[b] IUGR based on 1999 US singletons adjusted for gender and ethnicity

[c] Underweight(<18.5); normal weight (18.5–24.9); overweight (25–29.9); obese (30+)

Table 3

Unadjusted and Adjusted Estimates for Early Pregnancy Drinking and Low Birth Weight, Preterm Delivery, and IUGR

		Low birth weight					Preterm delivery					IUGR			
	N (%)	OR	95% CI	aOR	95% CI	N (%)	OR	95% CI	aOR	95% CI	N (%)	OR	95% CI	aOR	95% CI
Month 1															
None	163 (5.1)	1.00		1.00[a]		226 (7.1)	1.00		1.00[d]		257 (8.1)	1.00		1.00[g]	
<0.10 oz AA/day	28 (3.8)	0.74	0.49–1.10	0.96	0.61–1.52	48 (6.6)	0.92	0.66–1.27	1.05	0.74–1.51	58 (7.9)	0.97	0.72–1.31	0.98	0.71–1.35
0.10<0.25oz AA/day	8 (3.3)	0.62	0.30–1.28	0.57	0.24–1.36	17 (6.9)	0.98	0.59–1.63	0.79	0.42–1.47	13 (5.3)	0.64	0.36–1.13	0.60	0.33–1.08
≥0.25oz AA/day	10 (3.2)	0.62	0.32–1.18	0.52	0.24–1.12	19 (6.2)	0.86	0.53–1.39	0.79	0.46–1.36	23 (7.5)	0.91	0.59–1.42	0.69	0.42–1.13
First trimester															
Abstinent	157 (5.3)	1.00		1.00[b]		215 (7.3)	1.00		1.00[e]		240 (8.2)	1.00		1.00[h]	
1st month only	31 (3.4)	0.63	0.43–0.94	0.67	0.43–1.06	58 (6.4)	0.88	0.65–1.18	0.89	0.63–1.25	63 (7.0)	0.84	0.63–1.13	0.79	0.57–1.08
Drinking months 1–3	21 (3.6)	0.66	0.41–1.04	0.78	0.47–1.31	37 (6.4)	0.87	0.60–1.24	0.79	0.51–1.20	46 (7.8)	0.95	0.69–1.32	0.83	0.58–1.20
To baseline interview															
Abstinent	156 (5.5)	1.00		1.00[c]		212 (7.4)	1.00		1.00[f]		236 (8.3)	1.00		1.00[i]	
Drinking	53 (3.3)	0.58	0.42–0.80	0.66	0.46–0.96	98 (6.0)	0.80	0.62–1.02	0.79	0.60–1.05	119 (7.3)	0.87	0.69–1.10	0.81	0.63–1.04

[a] n=4116, adjusted for parity, age, ethnicity, study cohort, height, marital status, smoking, exercise (before/during pregnancy), multivitamin use, preterm labor, hypertension, anomalies

[b] n=4105; adjusted for parity, age, ethnicity, study cohort, height, marital status, education, smoking, exercise (before/during pregnancy), hypertension, preterm labor, anomalies, incompetent cervix, placental problems, infant gender, induction

[c] n=4157; adjusted for parity, age, ethnicity, study cohort, height, smoking, exercise (before/during pregnancy), hypertension, preterm labor, anomalies, incompetent cervix, placental problems, infant gender, induction

[d] n=4090; adjusted for parity, age, ethnicity, study cohort, education, BMI, smoking, caffeine, marijuana use, bleeding, hypertension, nausea/vomiting, incompetent cervix, placental problem, STD, diabetes

[e] n=4028; adjusted for parity, age, ethnicity, study cohort, BMI, smoking, caffeine, bleeding, hypertension, nausea/vomiting, incompetent cervix, placental problem, STD, anomalies, induction

[f] n=4115; adjusted for parity, age, ethnicity, study cohort, BMI, smoking, bleeding, hypertension, nausea/vomiting, incompetent cervix, placental problems, STD, diabetes, induction

[g] n=4053; adjusted for parity, age, ethnicity, study cohort, marital status, exercise during pregnancy, caffeine, smoking, work, prenatal vitamins/multivitamins (month 1), hypertension, preterm labor, anomalies

[h] n=4035; adjusted for parity, age, ethnicity, study cohort, BMI, smoking, prenatal vitamins (month 1), work, caffeine, hypertension, preterm labor, anomalies

[i] n=4122; adjusted for parity, age, ethnicity, study cohort, BMI, smoking, prenatal vitamins (month 1), work, hypertension, preterm labor

Table 4

Unadjusted and Adjusted Estimates for Third Trimester Drinking and Low Birth Weight, Preterm Delivery, and IUGR

		Low birth weight					Preterm delivery					IUGR			
	N (%)	OR	95% CI	aOR	95% CI	N (%)	OR	95% CI	aOR	95% CI	N (%)	OR	95% CI	aOR	95% CI
Month 7															
Abstinent	154 (4.4)	1.00		1.00[a]		227 (6.5)	1.00		1.00[c]		284 (8.2)	1.00		1.00[e]	
Drinking	9 (2.1)	0.45	0.23–0.89	0.67	0.33–1.39	24 (5.5)	0.83	0.54–1.28	0.89	0.55–1.44	31 (7.1)	0.85	0.58–1.26	0.91	0.60–1.38
Third trimester															
Abstinent	143 (5.0)	1.00		1.00[b]		209 (7.3)	1.00		1.00[d]		238 (8.3)	1.00		1.00[f]	
Drinking	20 (1.9)	0.36	0.22–0.58	0.56	0.34–0.94	42 (3.9)	0.52	0.37–0.72	0.60	0.42–0.87	78 (7.3)	0.86	0.66–1.12	0.91	0.68–1.22

[a] n=3726; adjusted for parity, ethnicity, marital status, height, study cohort, smoking, exercise (before/during pregnancy), bleeding, hypertension, preterm labor, placental problems, infant gender, induction

[b] n=3672; adjusted for parity, ethnicity, marital status, height, study cohort, smoking, exercise (before/during pregnancy), hypertension, preterm labor, placental problems, infant gender, induction

[c] n=3746; adjusted for parity, ethnicity, age, marital status, education, study cohort, smoking, bleeding, hypertension, nausea/vomiting, incompetent, cervix, placental problems, diabetes, maternal asthma, STD, induction

[d] n=3773; adjusted for parity, education, study cohort, smoking bleeding, hypertension, incompetent cervix, placental problem, STD, diabetes, induction

[e] n=3641; adjusted for parity, ethnicity, education, BMI, study cohort, smoking, work, bleeding, hypertension, preterm labor, maternal asthma, anomalies

[f] n=3689; adjusted for parity, age, education, BMI, study cohort, smoking, work, exercise during pregnancy, cocaine use (year before pregnancy), prenatal/multivitamin use (month 1), hypertension, maternal asthma, anomalies

Table 5

Adjusted estimates for selected clinical measures and early pregnancy drinking[a]

	Major congenital malformations[b]		Apgar 5 Min (<7)		Ventilation/CPAP[c]		NICU[d]		Jaundice		Birth Length[e]		Head Circumference[e]	
Outcome n (%):	**190 (4.4)**		**41 (1.0)**		**139 (3.3)**		**519 (12.3)**		**1230 (28.8)**		**338 (8.0)**		**576 (14.0)**	
Adjusted estimates:	**aOR**	**95% CI**	**aOR**	**95% CI**	**aOR**	**95% CI**	**aOR**	**95% CI**	**aOR**	**95% CI**	**aOR**	**95% CI**	**aOR**	**95% CI**
Month 1 drinking														
None	1.00		1.00		1.00		1.00		1.00		1.00		1.00	
< 0.10 oz AA/day	0.78	0.40–1.50	1.61	0.67–3.84	1.43	0.89–2.31	1.12	0.86–1.46	1.17	0.97–1.42	1.10	0.78–1.54	1.08	0.83–1.42
0.10<0.25oz AA/day	1.20	0.65–2.22	-	NAC	0.28	0.07–1.19	0.67	0.41–1.09	0.87	0.64–1.20	0.71	0.38–1.32	0.78	0.49–1.25
≥0.25 oz AA/day	1.15	0.77–1.71	2.32	0.86–6.28	2.10	1.16–3.79	1.25	0.87–1.79	1.01	0.79–1.37	0.70	0.41–1.20	0.83	0.56–1.24
First Trimester drinking														
Abstinent	1.00		1.00		1.00		1.00		1.00		1.00		1.00	
1st month only	1.07	0.73–1.57	1.12	0.47–2.66	1.27	0.81–2.00	1.08	0.84–1.38	1.01	0.85–1.21	0.92	0.67–1.27	0.99	0.77–1.28
Drinking months 1–3	1.28	0.83–1.96	1.28	0.48–3.43	1.12	0.64–1.97	0.96	0.70–1.31	1.09	0.88–1.35	0.56	0.36–0.87	0.69	0.50–0.96
Drinking up to baseline interview														
Abstinent	1.00		1.00		1.00		1.00		1.00		1.00		1.00	
Drinking	1.17	0.86–1.60	1.19	0.59–2.40	1.23	0.84–1.80	0.99	0.81–1.23	1.06	0.92–1.23	0.74	0.56–0.97	0.81	0.66–1.01

[a] Adjusted models included investigation of the following potential confounders and risk factors: parity, maternal age, education, BMI, marital status, ethnicity, caffeine, smoking, exercise, work, prenatal and multivitamin use, passive smoke exposure, marijuana use, cocaine use, study cohort, preterm labor, respiratory problem, infant gender, bleeding, nausea/vomiting, hypertension, incompetent cervix, placental problems, sexually transmitted disease, induction/augmentation, maternal asthma, gestational diabetes. Total observations included in adjusted multivariable models: Month 1 across (n=4047; n=4017; n=3988; n=3983; n=3999; n=3985; n=3892); First trimester across (n=4009; n=3979; n=3950; n=3945; n=3961; n=3947; n=3856); Drinking to baseline interview, across (n=4066; n=4036; n=4007; n=4002; n=4018; n=4003; n=3910)

[b] Based on definition of major congenital malformations [28]

[c] Includes both ventilation and continuous positive airway pressure (CPAP)

[d] Includes NICU observation and admission

[e] 10th percentile based on CDC 2000 growth standards [27]

NAC=Not able to calculate