Maternal alcohol use and medically indicated vs. spontaneous preterm birth outcomes: a population-based study

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Received 15 September 2009, accepted 8 March 2010

Background: The aetiology of preterm birth remains poorly understood. The purpose of this study is to investigate if an association exists between prenatal alcohol consumption and preterm birth and to determine if such an association differs by subcategories of preterm birth. Methods: We employed vital statistics data from the state of Missouri covering the period 1989–2005 (n = 1,221,677 singleton records). The outcome of interest was preterm birth, subclassified into medically indicated and spontaneous phenotypes. Multivariate logistic regression was used to generate adjusted odds ratios, with non-drinking mothers as the referent category. Results: Prenatal alcohol use was associated with elevated risk for preterm birth. The strength of association was more prominent for spontaneous preterm delivery (adjusted odds ratio [AOR] [95% confidence interval (CI)] = 1.34 (1.28–1.41)) than for medically indicated preterm birth [AOR (95% CI) = 1.16 (1.05–1.28)]. The overall risk for drinking-related spontaneous preterm birth increased with incremental rise in the number of drinks consumed per week (P for trend < 0.01). Conclusions: Prenatal alcohol use is a risk factor for preterm delivery, and especially for spontaneous preterm birth. These findings enhance our understanding of the aetiology of preterm birth and could be utilized in the development of appropriate prevention strategies that will assist in decreasing perinatal mortality and morbidity associated with preterm delivery.

Keywords: alcohol, medically indicated preterm birth, population-based study, pregnancy, singletons, spontaneous preterm birth

Introduction

Preterm birth is a leading cause of neonatal mortality and morbidity, with more than three quarters of perinatal deaths attributable to this condition in the USA.1 The search for preventable causes of preterm birth remains elusive, despite the extensive research efforts targeted to this area. Among the risk factors for preterm birth that have been investigated is maternal alcohol use in pregnancy. The association between alcohol use in pregnancy and occurrence of preterm birth remains contentious, with investigators reporting conflicting findings.2–5 Several reasons have been advanced to explain this lack of agreement, including inadequate sample size, imperfect recall, errors in classification of exposure, different intake levels and failure to account for important confounding factors, such as smoking, socio-economic status and ethnicity.5–9

An important reason that could also explain the differences in results among studies of alcohol use and preterm birth is failure to examine preterm birth as a heterogeneous entity comprising distinct categories of spontaneous and medically indicated preterm delivery. The few studies that examined the association between prenatal alcohol use and preterm birth phenotypes had small numbers and were especially underpowered at high levels of maternal alcohol use. The conclusions from those studies were also divergent. While Kesmodel et al. found no difference in the effect of alcohol on incidence of spontaneous or medically indicated preterm birth,3 two other studies showed raised risks for induced preterm birth with prenatal alcohol consumption.10,11

The purpose of this article is to examine the association between maternal alcohol consumption during pregnancy and the risk of medically indicated and spontaneous preterm (<37 weeks) and very preterm (<33 weeks) delivery in a large population-based sample of singleton deliveries in the USA. We hypothesize a priori that: (i) in utero exposure to alcohol is associated with preterm birth, regardless of the subcategory of preterm delivery; (ii) a threshold level exists at which alcohol will result in preterm birth; and (iii) a dose–response relationship can be demonstrated between the quantity of alcohol ingested and the risk of medically indicated and spontaneous preterm birth.

Methods

We utilized the Missouri maternally linked cohort data files covering the period 1989 through 2005. The Missouri vital record system is a reliable one that has been adopted as 'gold
standard to validate US national datasets that involve matching and linking procedures. The dataset used for this study has previously been validated through a linkage system that we describe as follows:

A probabilistic linkage method was used in the linking process of the Missouri data files longitudinally using a multi-stage algorithm. The method is dependent on the calculation of a weighted score for every possible pair of records that reflects the likelihood that they belong to the same person. A computer program was employed to compare a combination of variables from two files, giving a separate weight to each value that matches or mismatches. The weights for a pair of records are summed up and this represents the relative likelihood of both records belonging to the same person. Although the summing assumes that the weights for each field are independent, there is usually some dependence between fields. Initially, the linkage weights were calculated using two training datasets. The weights for a correct match came from the exact linkage of first and family name, month and year of birth in a training data set of 52,683 pairs of births with a previous live birth in 1983 or 1985. These exact links were assumed to be correct. The weights for an incorrect match came from a computer-generated random linkage of a training data set of 52,683 pairs of records. Weights of an individual variable were calculated as follows:

\[
W_a = \log_2 \left( \frac{N_1}{N_2} \right)
\]

where \(W_a\) = weight for agreement, \(N_1\) = agreement in the first training dataset, \(N_2\) = number in the first training dataset, \(N_3\) = number in the second training dataset.

\[
W_d = \log_2 \left( \frac{N_1}{N_2} \right)
\]

where \(W_d\) = weight for disagreement, \(N_1\) = disagreement in the first training dataset, \(N_2\) = number in the first training dataset, \(N_3\) = number in the second training dataset.

Correct and incorrect match weights were assigned to each pair of records and then summed up. Linkages with a score \(<-5\) were rejected. A quality of agreement indicator, based on the level of agreement of birth outcome, maternal first and family name, year and month of birth and race, was then assigned to the remaining linkages and a priority indicator was then assigned. The highest priority was given to records with a high linkage weight that matched exactly on month and year of birth, maternal family and first names. The lowest priority was given to records with no agreement on maternal first and family names, and intermediate priority levels for linkage for those records in between. The quality of agreement and priority indicators were used to assess the validity of potential linkages, especially those to multiple earlier births. For multiple linkages, the most likely potential linkage based on the score and quality of agreement indicator was accepted. Paternal last name and zip code of residence could change between pregnancies and two summary weights were accepted. Paternal last name and zip code of residence was assumed to be correct. The weights for an incorrect match were calculated: one with paternal name and zip code and one without; the higher sum was used. A family indicator variable was then assigned. The highest priority was given to records with a high linkage weight that matched exactly on month and year of birth, maternal family and first names, \(N_1\) = agreement in the second training dataset, \(N_2\) = number in the second training dataset, \(N_3\) = number in the second training dataset.

The main outcome of interest was preterm birth (defined as birth at <37 weeks of gestation) and very preterm (defined as <33 weeks). Gestational age was largely based on the interval between the last menstrual period and the date of delivery of the baby (95% of cases). When the menstrual estimate of gestational age was inconsistent with the birth weight (e.g. very low birth weight at term), a clinical estimate of gestational age on the vital records was used instead.

We examined preterm births based on two clinical subtypes: spontaneous and medically indicated preterm birth. Since the data did not denote whether women experienced labour, we therefore considered labour to have been present if the birth record contained the presence of one or more of the following, as we previously reported: vaginal birth without an induction of labour; tocolysis; cephalopelvic disproportion; precipitated, prolonged, or dysfunctional labour; or vaginal birth after caesarean. If labour was present and if the woman delivered preterm, then we classified that preterm birth as spontaneous. Additionally, if women experienced premature rupture of membranes, they were also combined with the spontaneous labour group. We then defined a medically indicated preterm birth as one that required either an induction of labour or prelabour caesarean or both.

The distribution of the following selected maternal socio-demographic characteristics was compared between drinking and non-drinking mothers to assess differences in baseline characteristics: maternal age, parity, race, education, marital status and adequacy of prenatal care. Adequacy of prenatal care was assessed using the revised graduated index algorithm, which has been found to be more accurate than several others, especially in describing the level of prenatal care utilization among groups that are at high risk. This index assesses the adequacy of care based on when the trimester prenatal care began, number of visits, and the gestational age of the infant at birth. In this study, inadequate prenatal care utilization refers to women who either had missing prenatal care information, had prenatal care but the level was considered sub-optimal, or mothers who had no prenatal care at all. We performed crude frequency comparisons between the two groups for the presence of common obstetric complications, namely, anaemia, insulin-dependent diabetes mellitus, other types of diabetes mellitus, chronic hypertension, preeclampsia, eclampsia, abruptio placenta and placenta previa.

**Statistical analysis**
Chi-square test was used to assess differences in socio-demographic characteristics and maternal pregnancy complications between the two groups (drinking/non-drinking). We used logistic regression models to generate adjusted odds ratios and their 95% confidence intervals. The covariates included in our model are: maternal pregnancy complications, namely, anaemia, insulin-dependent diabetes mellitus, other types of diabetes mellitus, chronic hypertension, preeclampsia, eclampsia, abruptio placenta and placenta previa.
age, maternal education, marital status, maternal race, adequacy of prenatal care, gender of the infant and year of birth. We constructed the regression models and assessed goodness-of-fit of the regression models using the $-2$ log likelihood ratio test. We estimated the significance of main effects by means of the Wald test, and assessed dose-response using the chi-square test for linear trend.\textsuperscript{21}

Adjusted estimates were derived in all cases by using non-drinking gravidas as the referent category. All tests of hypothesis were two-tailed with a type I error rate fixed at 5%. SAS version 9.1 (SAS Institute, Cary, NC) was used to perform all analyses. This study was approved by the Office of the Institutional Review Board at the University of South Florida.

Results

A total of 1 304 557 singleton births were available for analysis. We excluded pregnancies before 20 weeks or beyond 44 weeks of gestation (69 424 or 5.3\%) and records for which prenatal drinking (6897), gestational age (6343) and birth weight (216) were missing (total = 13 456 or 1.1\%). The final dataset comprised a total of 1 221 677 singleton records consisting of drinkers (15 914 or 1.3\%) and non-drinkers (1 205 763 or 98.7\%; the referent group).

There was approximately an 8-fold decline in alcohol consumption over the study period in the total sample (data not shown). The average prevalence of drinking over the duration of the study was 1.3\%. Table 1 shows frequency comparison between drinking and non-drinking mothers with respect to selected socio-demographic characteristics. Drinking gravidas were more likely to be older, black, multiparous and to have smoked. Drinking mothers were also less likely to be married, to have received adequate prenatal care and to have at least twelve years of education than their non-drinking counterparts.

Table 2 displays the prevalence of common medical and obstetric complications among mothers in the study. The overall prevalence of pregnancy complication was 10.4\% ($N = 127\,226$) distributed as follows: drinkers ($n = 1337$ or 1.1\%) and non-drinkers ($n = 126\,132$ or 98.9\%). Of the obstetric complications, placenta previa and placental abruption were more likely among drinkers while pre-eclampsia, insulin dependent diabetes, other forms of diabetes and chronic hypertension were more common among mothers who were non-drinkers during pregnancy. However, there was no statistical difference between the two groups with respect to anaemia and eclampsia. Infants born to non-drinking mothers had slightly greater mean gestational age (mean = 38.9 weeks, standard deviation $\pm$ 2.4) than those born to drinking mothers (mean = 38.7 $\pm$ 2.9) ($P < 0.01$). Infants of non-drinking mothers were also found to have higher mean birth weight (g) (3347 $\pm$ 582 vs. 3210 $\pm$ 646) ($P < 0.01$).

There were 132 670 (10.9\%) infants born preterm in the study population, of which 106 766 (80.5\%) were classifiable as spontaneous preterm births while the remaining 25 904 (19.5\%) were medically indicated preterm deliveries. Additionally, there were 24 881 (2.0\%) infants born very preterm. Of these, 18 811 (75.9\%) were spontaneous while 5981 (24.1\%) were medically indicated very preterm. Figure 1 is an illustration of the distribution of rates of preterm and very preterm phenotypes by prenatal drinking status.

The adjusted estimates for the association between prenatal drinking and preterm and very preterm phenotypes are summarized in table 3. Prenatal ethanol consumption was associated with elevated risk for all preterm and spontaneous preterm regardless of the severity of drinking. Also, the overall risk for spontaneous preterm birth associated with prenatal drinking was doubled that for medically indicated preterm [odds ratio (OR) = 1.34 vs. 1.16]. The risk for drinking-related preterm birth increased as the number of drinks consumed per week increased in a dose-dependent fashion for all preterm and spontaneous preterm phenotypes ($P$ for trend $< 0.01$).

Although, there was an increased risk for medically indicated preterm birth among Class 3 drinkers, the elevated risk did not reach statistical significance for Classes 1 and 2 drinkers.

For very preterm birth, the overall risk associated with prenatal drinking for all very preterm birth and very preterm phenotypes were appreciably stronger than for all preterm and preterm phenotypes except for Class 2 drinkers who showed a non-significant reduction in risk for medically indicated preterm birth. It is noteworthy that risk estimates were significant for all very preterm and spontaneous very preterm birth regardless of the severity of drinking during pregnancy. However, for medically indicated very preterm birth the risk with prenatal ethanol consumption was only significant for heavy drinkers (Class 3).

### Table 1

<table>
<thead>
<tr>
<th>Maternal age $\geq$ 35 years (%)</th>
<th>Non-drinker ($N = 1,205,763$)</th>
<th>Drinker ($N = 15,914$)</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age $\geq$ 35 years (%)</td>
<td>9.8</td>
<td>18.5</td>
<td>$&lt; 0.01$</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiparous</td>
<td>58.8</td>
<td>68.7</td>
<td>$&lt; 0.01$</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>15.0</td>
<td>21.2</td>
<td>$&lt; 0.01$</td>
</tr>
<tr>
<td>White</td>
<td>82.6</td>
<td>77.5</td>
<td></td>
</tr>
<tr>
<td>Education $\geq$ 12 years (%)</td>
<td>80.5</td>
<td>78.0</td>
<td>$&lt; 0.01$</td>
</tr>
<tr>
<td>Smoke</td>
<td>19.4</td>
<td>52.4</td>
<td>$&lt; 0.01$</td>
</tr>
<tr>
<td>Married</td>
<td>67.8</td>
<td>59.5</td>
<td>$&lt; 0.01$</td>
</tr>
<tr>
<td>Adequate prenatal care (%)</td>
<td>51.0</td>
<td>39.4</td>
<td>$&lt; 0.01$</td>
</tr>
</tbody>
</table>

### Table 2

<table>
<thead>
<tr>
<th>Maternal age $\geq$ 35 years (%)</th>
<th>Non-drinker ($N = 1,205,763$)</th>
<th>Drinker ($N = 15,914$)</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>17 425 (1.45)</td>
<td>252 (1.58)</td>
<td>0.13</td>
</tr>
<tr>
<td>Insulin-dependent diabetes</td>
<td>8864 (0.74)</td>
<td>49 (0.31)</td>
<td>$&lt; 0.01$</td>
</tr>
<tr>
<td>Other forms of diabetes</td>
<td>27 366 (2.27)</td>
<td>258 (1.62)</td>
<td>$&lt; 0.01$</td>
</tr>
<tr>
<td>Chronic hypertension</td>
<td>11 422 (0.93)</td>
<td>119 (0.74)</td>
<td>0.01</td>
</tr>
<tr>
<td>Pre-eclampsia</td>
<td>55 615 (4.61)</td>
<td>473 (2.97)</td>
<td>$&lt; 0.01$</td>
</tr>
<tr>
<td>Eclampsia</td>
<td>1194 (0.10)</td>
<td>10 (0.10)</td>
<td>0.10</td>
</tr>
<tr>
<td>Placental abruption</td>
<td>9152 (0.76)</td>
<td>197 (1.24)</td>
<td>$&lt; 0.01$</td>
</tr>
<tr>
<td>Placenta previa</td>
<td>4496 (0.37)</td>
<td>86 (0.54)</td>
<td>$&lt; 0.01$</td>
</tr>
</tbody>
</table>
We report an increased risk of all preterm and spontaneous preterm birth among a large population-based cohort of mothers who drink alcohol in pregnancy. This association showed a dose–response gradient with increasing number of drinks consumed by the mother. On the other hand, the strength of association between medically indicated preterm birth and prenatal alcohol use was not as prominent, and a dose response gradient was not evident. Similar findings were apparent in the case of very preterm birth, with very preterm spontaneous birth being more strongly associated with maternal alcohol use in pregnancy than medically indicated very preterm birth. Our results support the assertion that preterm birth is a heterogeneous entity with separate causal pathways. Researchers have advocated consideration of subcategories of preterm birth in studies of aetiology and prevention. The development of effective preventive approaches to preterm birth will require an understanding of the risk factors underlying the pathophysiologic basis for these subcategories.

To our knowledge, only three other studies have examined the association between subcategories of preterm delivery and prenatal alcohol use. In contrast to our report, two of those studies reported elevated risks for induced preterm birth, but only a slight or decreased risk of spontaneous preterm delivery. Kesmodel et al. found no difference in the association between alcohol and the occurrence of different categories of preterm birth among a cohort of Danish mothers (N = 18 228). These findings are in conflict with our report. However, our study cohort is substantially larger than all of the three studies described above (N = 1 221 677), and was drawn from a more representative group. Other explanations for the disparity in findings could include variation in classification (e.g. we grouped PROM with spontaneous labour) and differences in the process of recording mode of initiation of labour.

The mechanism by which alcohol predisposes to preterm birth has been attributed to prostaglandins and other inflammatory cytokines. Increased secretion of prostaglandins and thromboxanes has been described in alcoholics and their offspring, and mothers with preterm birth have elevated levels of proinflammatory markers, e.g. serum C-reactive protein, interleukin (IL)-1, IL-6 and IL-8. Alcohol increases the production of prostaglandins E2 and F2α which in turn increases cyclic 3',5'-adenosine monophosphate activity thereby decreasing cell division and possibly

![Figure 1](https://academic.oup.com/eurpub/article-abstract/20/5/582/607968)

**Table 3** Adjusted OR (AOR) for the association between prenatal drinking vs. all preterm, spontaneous and medically indicated preterm births, Missouri, USA, 1989–2005

<table>
<thead>
<tr>
<th>Preterm birth</th>
<th>Spontaneous preterm</th>
<th>Medically indicated preterm</th>
</tr>
</thead>
<tbody>
<tr>
<td>(N=132 670)</td>
<td>(N=106 766)</td>
<td>(N=25 904)</td>
</tr>
<tr>
<td>Non-drinker</td>
<td>Referent</td>
<td>Referent</td>
</tr>
<tr>
<td>Drinker</td>
<td>1.32 (1.26–1.38)</td>
<td>1.34 (1.28–1.41)</td>
</tr>
<tr>
<td>Class 1</td>
<td>1.74 (1.60–1.89)</td>
<td>1.77 (1.64–1.91)</td>
</tr>
<tr>
<td>Class 2</td>
<td>1.86 (1.74–2.00)</td>
<td>1.93 (1.81–2.05)</td>
</tr>
<tr>
<td>Class 3</td>
<td>2.12 (1.97–2.28)</td>
<td>2.19 (2.04–2.34)</td>
</tr>
</tbody>
</table>

| Very preterm birth | (N=24 881) | (N=18 885) | (N=5 996) |
| Non-drinker | Referent | Referent | Referent |
| Drinker | 1.61 (1.48–1.75) | 1.70 (1.67–1.73) | 1.25 (1.10–1.43) |
| Class 1 | 1.71 (1.59–1.84) | 1.80 (1.65–1.95) | 1.38 (1.16–1.64) |
| Class 2 | 2.15 (1.97–2.34) | 2.52 (2.31–2.75) | 0.78 (0.61–1.00) |
| Class 3 | 3.14 (2.80–3.50) | 3.25 (2.75–3.78) | 2.52 (2.04–3.09) |

CI = confidence interval; non-drinker: number of drinks per week = 0; drinker: number of drinks per week >0; Class 1: number of drinks per week = (1–2); Class 2: number of drinks per week = (3–4); Class 3: number of drinks per week ≥5.

a: Adjusted estimates were generated after controlling for the effects of maternal age, parity, race, smoking, education, marital status, adequacy of prenatal care, maternal height, gender of the infant and year of birth.

P for trend <0.01 in all cases except for medically indicated very preterm.

### Discussion

We report an increased risk of all preterm and spontaneous preterm birth among a large population-based cohort of mothers who drink alcohol in pregnancy. This association showed a dose–response gradient with increasing number of drinks consumed by the mother. On the other hand, the strength of association between medically indicated preterm birth and prenatal alcohol use was not as prominent, and a dose response gradient was not evident. Similar findings were apparent in the case of very preterm birth, with very preterm spontaneous birth being more strongly associated with maternal alcohol use in pregnancy than medically indicated very preterm birth. Our results support the assertion that preterm birth is a heterogeneous entity with separate causal pathways. Researchers have advocated consideration of subcategories of preterm birth in studies of aetiology and prevention. The development of effective preventive approaches to preterm birth will require an understanding of the risk factors underlying the pathophysiologic basis for these subcategories.

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predisposing to preterm birth.\textsuperscript{3,16,27,28} It is particularly interesting that elevated CRP levels have been reported to be more strongly associated with spontaneous preterm birth than medically indicated preterm birth.\textsuperscript{29} Although this result is not in agreement with another recent report,\textsuperscript{23} it is deserving of further investigation, as it could explain why prenatal alcohol use was more strongly related to spontaneous than to medically indicated preterm birth in this study.

The prevalence of drinking during pregnancy among our study population is significantly lower than nation-wide numbers reported by the Behavioral Risk Factor Surveillance Surveys (BRFSS), where the average annual percentage of any alcohol use among pregnant women was 12.2% (range 10.2–16.2%).\textsuperscript{30} However, our numbers are close to those reported by prior statewide drug prevalence studies to determine the extent of tobacco, alcohol and illegal substance use during pregnancy in Missouri (the Missouri Prenatal Drug Prevalence Study).\textsuperscript{31} In 1997, the estimated prevalence of alcohol usage during pregnancy from the Missouri Prenatal Drug Prevalence study was estimated at 3.6 and 1.6% based on chart abstraction and urine testing, respectively. Our study population comprised of only singleton births in a single state. In addition, we excluded pregnancies before 20 weeks or beyond 44 weeks of gestation (5.3%) and records for which prenatal drinking, gestational age and birth weight values were missing (1.1%). We can therefore safely state that our study population is not exactly identical to the BRFSS population of pregnant women surveyed in 1991–2005. Furthermore, BRFSS surveys comprise nation-wide data and exclude households without landline telephones, so their results might not be representative of certain segments of the U.S. population. In addition, the median response rate for BRFSS surveys is not 100% (ranged from 71.4% in 1993 to 51.1% in 2005) and the small numbers of pregnant women sampled in each state for the BRFSS surveys preclude accurate state-specific prevalence rates for alcohol consumption among pregnant women. In summary, differences in study design and exposure ascertainment makes it difficult to compare our findings with those of nation-wide surveys (such as the BRFSS) and it is possible that our figures reflect under-ascertainment associated with alcohol exposure assessment in pregnancy.

There are limitations to our study. Underreporting of alcohol intake is an acknowledged phenomenon in pregnant women, especially if ascertainment of alcohol use was based on history obtained in the postnatal period.\textsuperscript{6,32} It is widely known that self-report of alcohol ingestion could represent under-estimates in the absence of a biomarker, however rigorous the questioning is. It is therefore likely that differential misclassification could have influenced our results although the actual magnitude and direction will remain unknown in the absence of biomarker ascertainment, a procedure that is not routinely performed in population-based data collection process. This limitation is, however, not uniquely associated with our study but affects any study on alcohol consumption and birth outcomes in which biomarkers are not employed. However, misclassification of prenatal alcohol use because of retrospective data collection is uncommon.\textsuperscript{33–36} In addition, the net effect of underreporting in this study would have been to bias our results toward the null. That we still report elevated risks of preterm birth further strengthens the validity of our findings. Another limitation is our database did not include information on the timing of alcohol use and of certain consumption patterns, such as binge drinking. We are therefore unable to comment on the effect of these factors on risk of preterm delivery in our cohort.

The strengths of this study include the population-based design and the high response rate (nearly 100% complete information on the exposure variable—only 0.5% of our study population lack data on alcohol consumption during pregnancy over a 16-year period). The effect of this is enhanced external validity of our findings and a reduced risk of bias arising from sample selection, a source of concern in data derived from individual health facilities. Another strength is our adjustment to a wide range of known confounding factors, thereby ensuring that any associations we detect in this study represent independent relationships between the exposure variable (prenatal alcohol use) and our defined outcomes.

In conclusion, we found that prenatal alcohol use is more strongly related to spontaneous preterm delivery than to medically indicated preterm birth, and this pattern of association extended to very preterm birth. Our findings highlight the importance of stratifying analyses of studies on preterm birth by etiologic subcategories (e.g. whether medically indicated or spontaneous). Future adequately powered studies which take into account timing of alcohol use during pregnancy and certain drinking patterns (e.g. binge drinking) will assist in further shedding light on the aetiology of this important cause of perinatal mortality and morbidity.

Funding
Roger Zoorob MD, MPH is partly supported by the Southeastern Fetal Alcohol Syndrome Regional Training Center grant # U84/CCU425037-02 awarded by the Centers for Disease Control and Prevention. The funding agency did not play any role in the conception, design or execution of this study.

Conflicts of interest: None declared.

Key points
- Preterm birth is a leading cause of neonatal mortality and morbidity worldwide, but its aetiology remains poorly understood.
- The consumption of alcohol during pregnancy is a risk factor for preterm and very preterm birth.
- The strength of association between alcohol use and preterm birth varies by subcategory of preterm delivery.
- Prenatal alcohol use is more strongly related to spontaneous preterm delivery than to medically indicated preterm birth.
- Future studies of preterm birth need to take into consideration the aetiologic heterogeneity of the condition.

References
Prenatal alcohol use and preterm delivery

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