

Seasonality of Birth and Implications for Temporal Studies of Preterm Birth

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Background: A strength of time-series analyses is the inherent control of individual-level risk factors that do not vary temporally. However, in studies of adverse pregnancy outcomes, risk factors considered time-invariant at the individual level may vary seasonally when aggregated into a pregnancy risk set. To illustrate, we describe the seasonal patterns of birth in Atlanta and demonstrate how these patterns could lead to confounding in time-series studies of seasonally-varying exposures and preterm birth.

Methods: The study cohort included all births in 20-county metropolitan Atlanta delivered during the period 1994–2004 ($n = 715,875$). We assessed the seasonal patterns of estimated conception and birth for the full cohort and for subgroups stratified by socio-demographic factors. Based on the observed patterns, we quantified the degree of potential confounding created by (1) differences in the gestational age distribution in the risk set across calendar months and (2) differences in the sociodemographic composition of the risk set across calendar months.

Results: The overall seasonal pattern of birth was characterized by a peak in August–September and troughs in April–May and November–January. Seasonal patterns differed among racial and ethnic groups, maternal education levels, and marital status. As a consequence of these seasonal patterns, systematic seasonal differences in the gestational age distribution and the sociodemographic composition of the risk set led to differences in expected rates of preterm birth across calendar months.

Conclusions: Time-series investigations of seasonally-varying exposures and adverse pregnancy outcomes should consider the potential for bias due to seasonal heterogeneity in the risk set.

(*Epidemiology* 2009;20: 699–706)

Seasonal patterns of birth have been documented in human populations for almost 2 centuries.^{1,2} Cultural, biologic, and environmental factors are hypothesized to contribute to these seasonal patterns, which differ across locations and time. Over the past 50 years, the annual pattern of birth in the United States has been characterized by a peak during August–September and a trough during April–May, with southern latitudes showing more pronounced spring troughs.^{3–5} High summer temperatures may reduce conceptions through reduced coital frequency or decreased fecundability (eg, decreased sperm quality).^{4–6} Other factors that could contribute to the annual pattern of birth include photoperiod (day length), increases in coital frequency during holidays, seasonal patterns in fetal loss, and seasonal preferences in pregnancy planning.^{7–10} The factors thought to drive seasonality may differ among sociodemographic groups, leading to different seasonal patterns of birth among population subgroups. For example, less affluent groups might have less access to air conditioning, work in occupations with more exposure to outdoor light and temperature, and have different patterns of contraceptive use.^{11–14}

These seasonal patterns could have implications for time-series studies of preterm birth (birth at <37 weeks of gestation). Many hypothesized causes of preterm birth lend themselves well to a time-series approach; temporal spikes in various types of infection, air pollution levels, allergen levels, pesticide applications, water quality, and meteorologic factors can be examined in relation to short-term changes in the rate of preterm birth. Because associations are driven entirely by temporal contrasts, individual-level risk factors that do not vary across time cannot act as confounders. However, unlike most time-series applications, in which the population at risk remains relatively stable across short periods of time, the population at risk in a time-series analysis of pregnancy outcomes is constantly changing according to which women are currently pregnant or in a specific stage of pregnancy.

Submitted 23 June 2008; accepted 16 October 2008; posted 17 June 2009. From the ^aRollins School of Public Health, Emory University, Atlanta, Georgia; and ^bNational Center for Birth Defects and Developmental Disabilities, Centers for Disease Control, Atlanta, Georgia.

Supported by National Institute of Environmental Health Sciences, NIH for the STAR Fellowship Program of the United States Environmental Protection Agency grants (R01-ES-012967-02S2A1).

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention or the United States Environmental Protection Agency.

SDC Supplemental digital content is available through direct URL citations in the HTML and PDF versions of this article (www.epidem.com).

Editors' note: A related article appears on page 706.

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ISSN: 1044-3983/09/2005-0699
DOI: 10.1097/EDE.0b013e3181a66e96

This creates a potential for confounding when examining a seasonally-varying exposure because the underlying risk of preterm birth can differ across seasons due to changing distributions of risk factors in the pregnancy risk set.

It is well recognized that certain sociodemographic risk factors for preterm birth, such as race, should be controlled in studies comparing individual pregnant women with one another. When risks of preterm birth are contrasted across time, race (or other sociodemographic risk factors) could more subtly confound an association with a seasonally-varying exposure if the racial composition of fetuses at risk differed by season. This would occur if different racial groups tended to conceive at different times of the year. For example, in a time-series analysis of particulate matter (PM), if the months of highest pollution corresponded to the months when the fetuses at risk are most likely to be African American, PM would appear predictive of preterm birth only because African American race is a strong risk factor for preterm birth.

Similarly, confounding by gestational age caused by seasonal differences in the gestational age distribution of the fetuses at risk can be an issue in the time-series setting when the risk set includes fetuses at a range of gestational ages (ie, fetuses conceived at different times). Several previous studies have examined acute exposures hypothesized to trigger delivery and have defined exposure windows relative to birth, which is the precipitated event (eg, the week before birth). These studies have related daily (or monthly) counts of preterm birth (the numerator) to the number of ongoing gestations at risk for preterm birth (the denominator or risk set) without adjusting for the gestational age distribution in the denominator.^{15–18} Using this approach, the seasonality of conception would lead to different distributions of gestational age in the risk set at different times of year. Because gestational age is a strong predictor of imminent birth (eg, a fetus is more likely to be born at 36 weeks than at 24 weeks, despite both gestational ages being preterm), seasonal differences in the gestational age distribution of the fetuses at risk could confound studies of seasonally-varying exposures and preterm birth. Returning to the PM example, if the highest PM levels occur in months when the risk set of ongoing, not-yet-term gestations is weighted toward those who are 36 weeks, PM levels may spuriously appear predictive of preterm birth.

The objectives of this paper are both descriptive and methodologic. We first describe the seasonal patterns of birth and estimated conception in metropolitan Atlanta over the period 1994–2004. Then we explore the implications of these patterns for confounding by sociodemographic factors and gestational age in time-series investigations of seasonally-varying exposures and preterm birth. Although we focus on preterm birth, the potential for confounding that arises from a dynamic pregnancy risk set is also relevant to time-series studies of other adverse pregnancy outcomes, and for inves-

tigations of season of birth as a predictor of later health conditions (eg, schizophrenia, sudden infant death syndrome).

METHODS

We obtained vital records for births to residents of 20-county metropolitan Atlanta during the years 1994–2004 from the Georgia Division of Public Health, Office of Health Information and Policy. Birth records identified live births occurring at ≥ 20 weeks of gestation. Using this cohort, we considered 4 separate issues. First, we assessed the overall seasonality of estimated conception and birth in the full cohort. Second, we investigated possible differences in seasonal patterns among sociodemographic subgroups. Third, based on the seasonal patterns observed, we investigated whether changing distributions of gestational age in a time-series analysis could create seasonal patterns of preterm birth. Finally, we examined whether changes in the mix of sociodemographic characteristics of the pregnancies at risk could create seasonal patterns of preterm birth.

Overall Seasonality of Birth and Estimated Conception

To quantify the magnitude of seasonal fluctuation in birth rates, we created a ratio of the observed to expected number of births for each study month.^{4,5} The observed number of births per day was the average number of births per day in each study month across the 11-year study period. The expected number of births per day was calculated using a centered 12-month moving average comprising the month of interest and the 5.5 months before and the 5.5 months after that month. Thus, the expected count captured long-term trends (ie, the increasing number of births over time) but not seasonal trends. The observed-to-expected ratio allowed us to examine the seasonal variation in birth rates without forcing a specific shape to the seasonal patterns across calendar months.^{4,5} There were 120 study months analyzed, July 1994–June 2004; expected counts could not be calculated for the first or final 6 months of the study.

Although estimating conception date introduces measurement error, we also examined seasonality of conception for our cohort of live births. Only conceptions resulting in a live birth could be identified. For 98.2% of birth records, conception was estimated to be 2 weeks after the reported last menstrual period (LMP) date. Where the LMP date was missing or yielded an implausible gestational age (ie, < 20 or > 44 weeks), conception was estimated using the clinical estimate of gestational age (1.7%). For the remaining 0.1% of observations, we estimated conception using the gestational age assigned by the Georgia Division of Public Health based on the birth weight of the infant.

Seasonality of Birth and Estimated Conception by Sociodemographic Subgroup

We examined available sociodemographic factors known to be associated with preterm birth: infant race and ethnicity (non-Hispanic black, non-Hispanic white, Hispanic, Asian), maternal age (<20, 20–34, ≥35 years), maternal marital status (married, unmarried), maternal education (<12 years, 12–15 years, ≥16 years), and maternal parity (first birth, second or greater birth). To compare the seasonality of birth across levels of sociodemographic characteristics, the birth cohort was stratified by the characteristic of interest, and a ratio of observed-to-expected births per day was calculated for each study month (July 1994–June 2004) for each stratum. To assess whether seasonality of birth differed by infant race or ethnicity, we regressed the ratio of observed-to-expected births (log transformed) on calendar month indicator variables, indicator variables for race/ethnicity, and interaction terms between race/ethnicity and calendar month. We used an *F* test to assess the statistical significance of interaction terms after testing the independence of the residuals with the Durbin-Watson test. The model took the form:

$$\ln(Y_{kij}) = \alpha + \sum_{i=1}^{11} \beta_i(\text{month}_i) + \sum_{j=1}^3 \delta_j(\text{race}_j) + \sum_{i=1}^{11} \sum_{j=1}^3 \gamma_{ij}(\text{month}_i * \text{race}_j) + \varepsilon_{kij}$$

Y_{kij} represents the ratio of observed-to-expected births per day in study year *k* and calendar month *i* within race and ethnicity stratum *j*. The product terms allow for possible interaction between race and birth seasonality (ie, calendar month). We constructed analogous models for maternal age, maternal marital status, maternal educational status, and maternal parity. We also examined the seasonality of estimated conception for each sociodemographic group using the same approach. Differences in seasonal patterns between population subgroups would imply an association between these factors and season, creating a potential for confounding in studies of seasonally-varying exposures and preterm birth.

Confounding by Gestational Age in Time-series Assessment of Preterm Birth

To contrast rates of preterm birth over time in a time-series analysis when examining exposure windows defined relative to the birth date (eg, the last week of pregnancy), daily preterm birth counts must be related to an appropriate denominator. When the denominator includes in utero fetuses within a range of gestational ages (eg, ongoing gestations from 20 through 36 weeks),^{15–18} seasonal patterns of conception create a risk set more heavily weighted toward older,

36-week-old fetuses in some months and weighted toward younger, 20-week-old fetuses in other months. For example, if conceptions peaked around the December holiday season, 36 weeks later there would be a peak in 36-week-old fetuses. A higher rate of preterm birth would be expected to occur in months when the denominator was more heavily weighted toward the 36-week-old fetuses, who are more likely to deliver preterm. We emphasize that confounding by gestational age is possible only when the risk set includes a range of gestational ages. If exposures during a specific gestational period (eg, week 36 of gestation) are of interest, births are aggregated by conception cohort and confounding by gestational age is not possible.

Using the Atlanta data, we quantified the potential for seasonal differences in the gestational age distribution of the risk set to create artifactual seasonal differences in the rate of preterm birth. For each study day, we identified the risk set of all ongoing gestations between 20 and 36 weeks using the reported (or estimated) LMP date for each birth record.

To quantify the influence of the seasonally-changing gestational-age distribution among the fetuses at risk on expected rates of preterm birth, our approach was as follows:

1. We calculated the conditional probability of birth for each gestational week using the gestational age of each infant in the birth cohort (eg, probability of birth during week 21 = $P[21 \text{ weeks} \leq \text{birth} < 22 \text{ weeks} | \text{birth} \geq 21 \text{ weeks}]$).
2. For each study day, we enumerated the in utero fetuses at each gestational week from 20 through 36 weeks (ie, the daily risk set for preterm birth).
3. Based on the birth probabilities at each gestational age and the number of fetuses at each gestational age, we calculated a daily expected count of preterm births for each study day.
4. These expected daily counts of preterm birth and total fetus-days-at-risk were summed by calendar month (eg, across all Januaries), and an average expected rate of preterm birth in each calendar month was calculated.
5. Rate ratios comparing expected rates of preterm birth for each calendar month to the expected rate in May, the month with the lowest rate, were calculated to quantify the seasonal variation in rates of preterm birth attributable solely to seasonal differences in the gestational age distribution of the risk set.

Confounding by Sociodemographic Factors in Time-series Assessment of Preterm Birth

We conducted a similar analysis to investigate whether seasonal changes in the sociodemographic composition of the risk set could create artifactual seasonal patterns of preterm birth rates. We focused on race and ethnicity, although similar analyses could be conducted for other sociodemographic risk factors. We stratified the dataset according to infant race and ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, and Asian) and aggregated births according

to estimated conception date; unlike the gestational-age distribution issue, confounding by sociodemographic characteristics can be a problem regardless of aggregation method (ie, aggregation by birth date or by conception cohort). Using the daily conception counts for each race and the race-specific risks of preterm birth, we calculated the number of conceptions on each day expected to be born preterm based solely on the racial and ethnic distribution of the risk set. Because non-Hispanic black fetuses have a relatively high risk of preterm birth, a day with a higher proportion of non-Hispanic black conceptions would lead to a higher expected proportion of preterm births 7 or 8 months later. Average expected preterm birth rates were calculated for each conception month. Rate ratios comparing expected rates of preterm birth between calendar months were calculated to quantify the expected difference in the rate of preterm birth attributable to seasonal changes in the racial and ethnic composition of the risk set.

RESULTS

The 20-county metropolitan Atlanta 1994–2004 pregnancy cohort consisted of 715,875 births; characteristics of the population are presented in the Table. Because of missing data, we excluded 2.24% of births from the maternal education analysis, 0.02% from the marital status analysis, and 1.61% from the parity analysis. The 0.35% of births categorized as American Indian, Native Hawaiian or Other Pacific Islander, or multiracial were excluded because of insufficient numbers.

Overall Seasonality of Birth

Average numbers of births per day for each study month are shown in Figure 1; seasonal as well as long-term trends are apparent. The average ratios of observed-to-expected number of births and estimated conceptions by calendar month are presented in Figure 2A, B. Monthly ratios of observed-to-expected births for individual study years are also shown and demonstrate the consistency of the seasonal pattern. Birth rates during July, August, and September were 2%–5% higher than expected; birth rates during April, May, June, November, December, and January were 2%–3% lower than expected. The overall pattern of estimated conception was similar but shifted 8–9 months earlier.

Seasonality of Birth by Sociodemographic Subgroup

Model-based ratios of observed-to-expected births by sociodemographic group are presented in Figure 3; the seasonal patterns of estimated conception were very similar but shifted approximately 9 months earlier (Online Appendix, <http://links.lww.com/A1045>). Distinct seasonal patterns of estimated conception and birth were observed among infant racial and ethnic groups, maternal education levels, and maternal marital status. Notably, the college-educated group showed a peak in spring births (summer conceptions) as

TABLE. Maternal and Infant Characteristics in the 20-County Metropolitan Atlanta 1994–2004 Birth Cohort

	Births (n = 715,875) ^a No. (%)
Preterm (<37 weeks)	84,559 (12)
Singleton	693,159 (97)
Female	350,656 (49)
Race and ethnicity	
Non-Hispanic white	374,818 (52)
Non-Hispanic black	230,985 (32)
Hispanic	80,644 (11)
Asian	26,876 (4)
American Indian	156 (<1)
Native Hawaiian or other Pacific Islander	1217 (<1)
Multiracial	1179 (<1)
Maternal age (years)	
<20	75,377 (11)
20–34	539,112 (75)
≥35	101,386 (14)
Maternal education (years)	
<12	134,920 (19)
12	195,583 (28)
13–15	149,142 (21)
≥16	220,220 (32)
Married	484,952 (68)
Parity	
1	304,697 (43)
2	229,888 (33)
≥3	169,734 (24)

^a11,556 records missing parity; 16,010 records missing maternal education; 110 records missing marital status.

opposed to the trough seen among the less-educated groups. The largest April–May troughs in birth rates were observed among those who were unmarried, were Hispanic or non-Hispanic black, and had less than a high school education. The college-educated, married, and non-Hispanic white groups showed a trough in births during November–January following reduced estimated conceptions in spring. Of all the sociodemographic subgroups examined, the Hispanic group showed the largest seasonal amplitude in birth rate, with 7% fewer births than expected in May and 7% more births than expected in September. All sociodemographic strata examined showed higher than expected numbers of births during August and September. Differences in seasonality of estimated conception and birth between maternal age groups and between parity groups were less pronounced; however, *F* tests showed strong statistical evidence for interaction between each sociodemographic factor and calendar months ($P < 0.001$).

Confounding by Gestational Age in Time-series Assessment of Preterm Birth

Conditional probabilities of birth during gestational weeks 20–36 are displayed in Figure 4. The week-specific

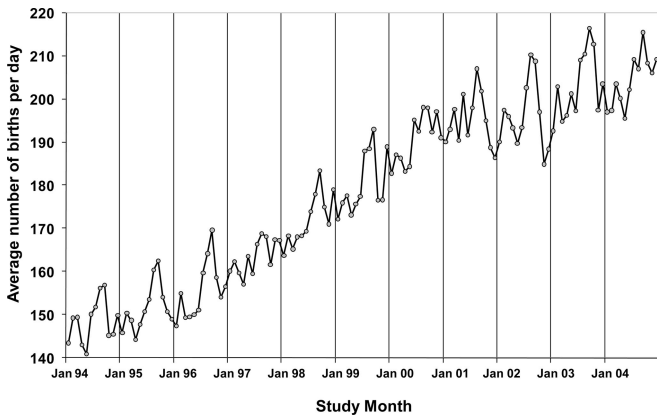
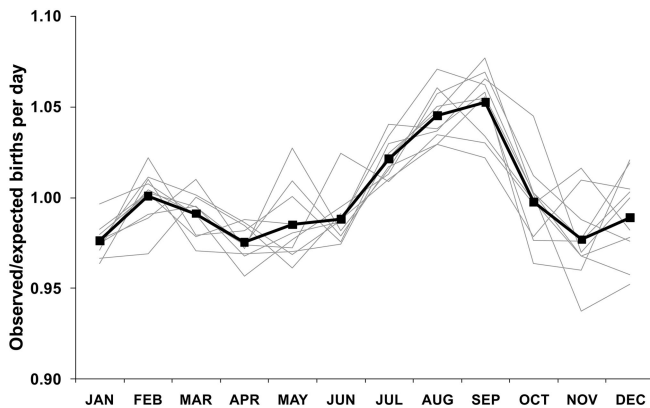


FIGURE 1. Average number of births per day by study month in the 20-county metropolitan Atlanta birth cohort, 1994–2004.

A Births



B Conceptions

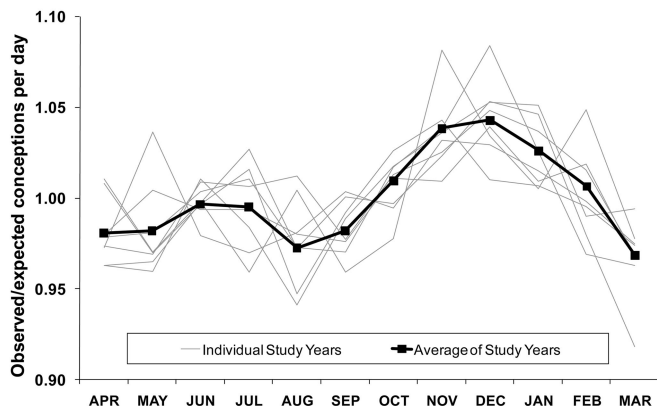


FIGURE 2. Seasonality of **A**, births and **B**, estimated conceptions in the 20-county metropolitan Atlanta 1994–2004 birth cohort: average observed-to-expected counts per day by calendar month and monthly observed-to-expected counts per day for individual study years.

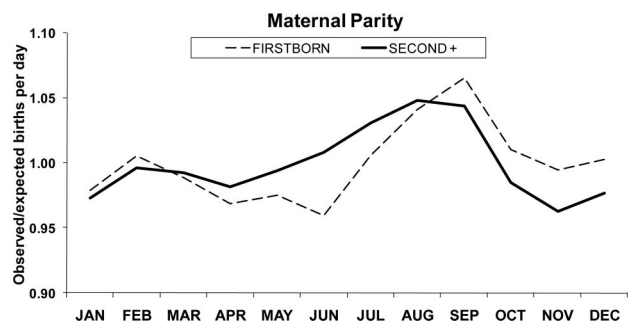
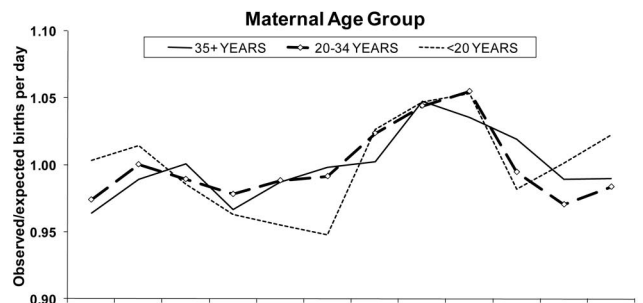
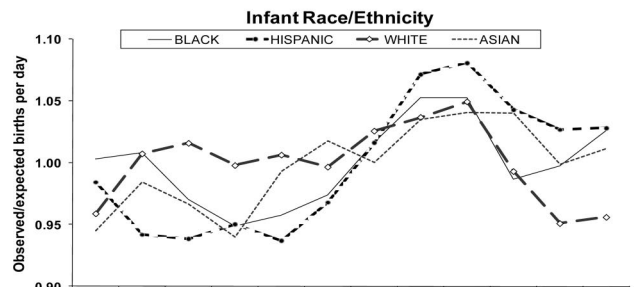
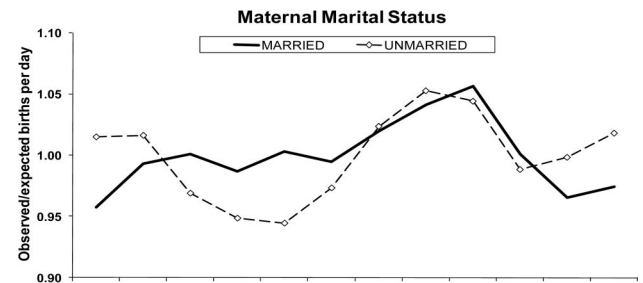
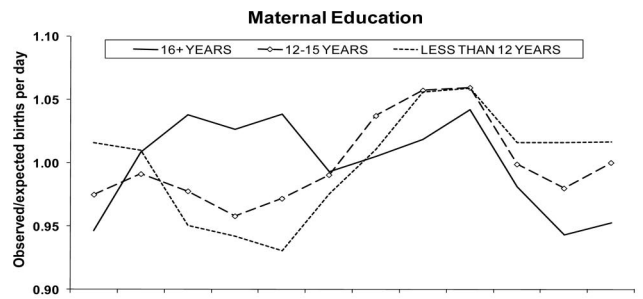


FIGURE 3. Model-based estimates of observed-to-expected births per day by calendar month, stratified by sociodemographic characteristics for the 20-county metropolitan Atlanta 1994–2004 birth cohort.

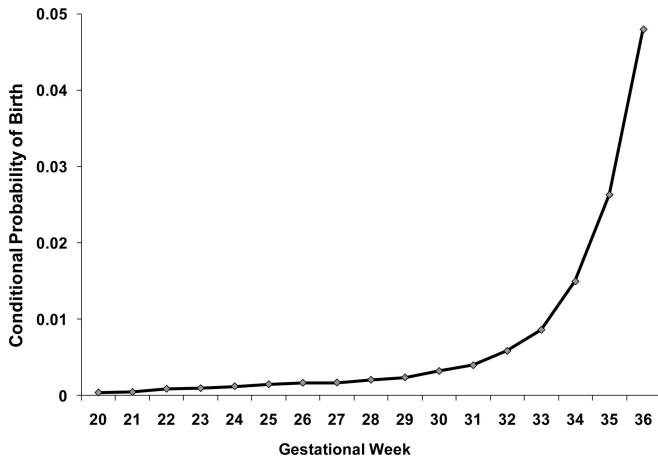


FIGURE 4. Week-specific conditional probabilities of birth for gestational weeks 20–36 for births in the 20-county metropolitan Atlanta 1994–2004 birth cohort (n = 715,875), eg, probability of birth during week 21 = $P(21 \text{ weeks} \leq \text{birth} < 22 \text{ weeks} | \text{birth} \geq 21 \text{ weeks})$.

probability of birth increases dramatically as the fetus approaches full term (37 weeks); risk of birth during week 36 is roughly 100-fold higher than risk of birth during week 20. Figure 5 shows the proportion of fetuses at risk (ie, 20–36 weeks gestation) that were in week 36 of gestation, averaged by calendar month. The proportion was highest in August and lowest in May. Also plotted in Figure 5 are the rate ratios comparing expected rates of preterm birth during each month versus the expected rate in May, the month with the lowest expected rate. Average expected rates of preterm birth were highest in August, when the risk set was more heavily weighted toward older gestational ages, and lowest in May, when a smaller proportion of fetuses were in late gestation. The ratio of expected rates comparing August with May was 1.08. In other words, simply failing to account for seasonal differences in the gestational age distribution of the risk set

would lead to an apparent 8% increase in rates of preterm birth in August compared with May.

Confounding by Sociodemographic Factors in Time-series Assessment of Preterm Birth

In the study cohort, risk of preterm birth varied by race and ethnicity (15.4% for non-Hispanic black infants, 10.3% for non-Hispanic white infants, 9.2% for Hispanic infants, and 9.6% for Asian infants). As our previous analyses demonstrated, the race and ethnicity groups also showed different seasonal patterns of estimated conception and birth. As shown in Figure 6, the proportion of infants conceived who were black was 2.7% higher in March compared with July. Because African Americans have an elevated risk of preterm birth, this translated into an average 1% increase in the expected rate of preterm birth for infants conceived in March compared with those conceived in July, based solely on the racial and ethnic composition of the risk set (Fig. 6).

DISCUSSION

We have described the seasonal patterns of estimated conception and birth in 20-county metropolitan Atlanta between 1994 and 2004 and have demonstrated a potential for confounding by these patterns in time-series studies of seasonally varying exposures and preterm birth. In this setting, we found that differences in the gestational-age distribution of the risk set across calendar months could explain an observed rate ratio of 1.08; differences in the racial composition of the risk set could explain an observed rate ratio of 1.01. Although the magnitude of these effects in Atlanta is of interest, more generally our findings illustrate the potential for confounding in time-series studies when examining seasonally-varying exposures in a dynamic risk set of pregnancies.

This study contributes to the descriptive literature on seasonal birth patterns using a contemporary cohort. In the overall cohort, birth rates peaked in late summer–early fall and fell in April–June and November–January. Lam and

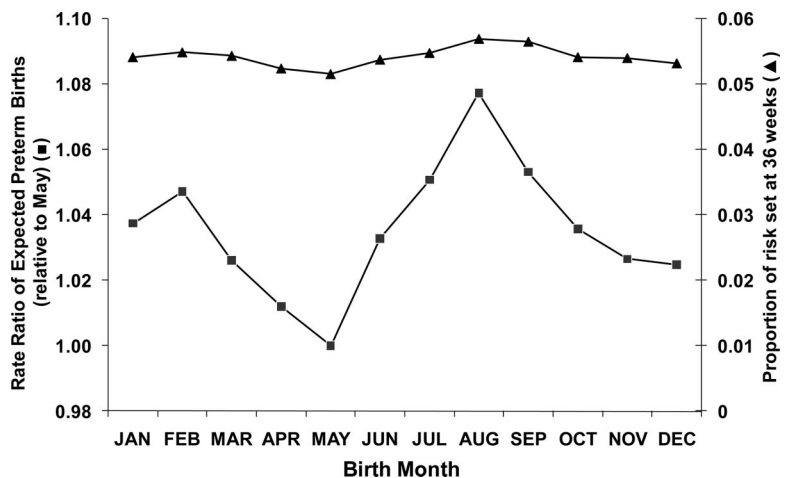


FIGURE 5. Proportion of all ongoing gestations 20–36 weeks that are in the 36th week, averaged by calendar month and rate ratios of preterm birth comparing expected rates in each calendar month relative to expected rates in May, based solely on the gestational age distribution of the risk set.

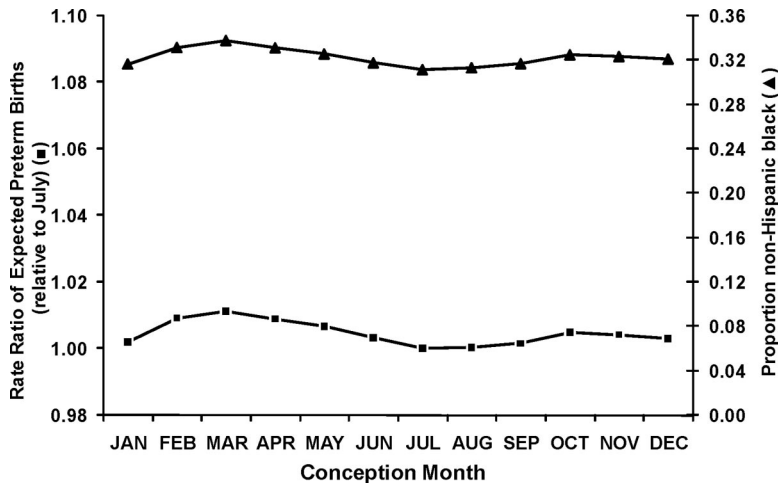


FIGURE 6. Proportion of conceptions that are non-Hispanic black, averaged by calendar month and rate ratios of preterm birth comparing expected rates of preterm birth for fetuses conceived in each month relative to expected rates for fetuses conceived in July, based solely on the racial composition of the risk set.

Miron (1996) previously reported a similar overall pattern of birth rates for Georgia for an earlier time period (1942–1988).⁴ Animal and human studies suggest that high temperatures interfere with spermatogenesis; lower sperm quality could reduce conceptions in the summer, leading to fewer spring births.^{6,19} The peak in birth rate in late summer–early fall may result from increased coital frequency during the winter holiday season, although this pattern has also been observed among populations not subject to the holiday effect.⁷ In contrast to the United States, birth rates in Europe peak in the spring and decline in the fall. It is possible that increased coital frequency during the long summer holidays in Europe counteract any decrease in fertility due to high temperatures.^{1,4} Photoperiodicity, may also play a role in places with large seasonal variations in day length.^{4,6,9,20} Furthermore, the seasonality of birth may be partially influenced by seasonal patterns in pregnancy loss or elective abortion, not just seasonal patterns of conception.¹⁰ Most studies conducted to date, including our own, could identify only conceptions that resulted in a live birth.

We observed the largest troughs in spring births (summer conceptions) in the unmarried, non-Hispanic black, Hispanic, and less than high school educated groups. Of the sociodemographic subgroups examined, Hispanics showed the strongest seasonal pattern of estimated conception and birth. In Atlanta, approximately 50% of Hispanic males work in the construction industry, an occupation involving high levels of exposure to outdoor temperature and light.²¹ The spring trough of births observed among the lowest educational stratum is consistent with previous findings in the United States suggesting lower income and less-educated women have a more pronounced seasonal pattern of birth.^{12,13} However, unlike previous studies, we also observed strong seasonality among the highest educational stratum, but with a markedly different pattern; these women showed a peak in spring births (summer conceptions). Because a greater percentage of births among this group are

planned, this pattern might reflect more closely the preferred timing of birth.^{8,22,23} Furthermore, if the preferred season of birth for pregnancy planners is spring, a higher proportion of planned pregnancies in Europe might explain the difference in seasonal patterns between Europe and the United States.^{24,25}

These seasonal patterns of conception and birth have methodologic implications for time-series studies of preterm birth. Although the expected seasonal differences in preterm rates resulting from these patterns were small, the magnitude is commensurate with several previously reported associations in time-series studies of preterm birth.^{16,17} Furthermore, the magnitude of bias is population-dependent, and could be more or less extreme in populations with different sociodemographic compositions or patterns of conception. In this analysis we examined only the racial composition of the risk set; the joint effects of all seasonal sociodemographic patterns may be larger, or these patterns may negate each other.

If season itself is not the exposure of interest, the degree of confounding by gestational age and sociodemographic factors will also depend on the seasonal pattern of the specific exposure being investigated. Failure to account for these seasonal differences in underlying risk of preterm birth could induce or obscure an association with a seasonally varying exposure. For example, in Atlanta, particulate matter (PM) is highest in late summer.²⁶ As a result, PM levels in the final weeks of pregnancy will appear predictive of preterm birth because the risk set for preterm birth during August is most heavily weighted toward the high-risk gestations.

This potential for confounding by gestational age in a time-series setting is created by aggregating fetuses at risk across a range of gestational ages, despite later gestational ages having exponentially higher risks of preterm birth. This issue arises only when exposures are defined relative to the birth date (eg, the week before birth) as opposed to a specific gestational window of vulnerability (eg, at conception). Thus, time-series investigations of exposures thought to trigger labor will require proper accounting for the gestational age

distribution of the risk set to avoid confounding by gestational age.

In contrast to the gestational age issue, seasonal differences in the sociodemographic composition of the risk set are an issue regardless of whether births are aggregated by birth date or conception cohort. If high- and low-risk population subgroups exhibit different seasonal patterns of conception, it may be necessary to temporally model counts of preterm birth separately for high- and low-risk strata. If season itself is not the exposure of interest, controlling for season as a proxy for unavailable seasonally-varying risk factors might be an option. However, the appropriate form of seasonal control is not always apparent; in our analyses, annual trends did not fit neatly into fall, winter, spring and summer categories. Ultimately, season is only a proxy for several potential confounders that, if available, should be handled directly in the analysis. Finally, we note that the degree of potential confounding by race we observed in the time-series setting is modest in comparison with what might be expected in an individual-level cohort analysis of preterm birth, a key strength of the time-series approach. Nonetheless, we have shown that temporal confounding by individual-level risk factors is possible in this context due to the dynamic nature of the pregnancy risk set.

Although the potential for confounding by gestational age is specific to time-series studies of preterm birth, differences in conception and birth patterns across sociodemographic groups could confound studies of seasonal exposures and other adverse pregnancy outcomes, as well as studies investigating season-of-birth as a predictor of later health (eg, sudden infant death syndrome, schizophrenia). Women delivering in April may be different than women delivering in December in ways that are related to the outcome of interest. Future studies examining seasonal exposures in the context of birth outcomes should consider the potential for confounding introduced by seasonal patterns of conception and birth.

ACKNOWLEDGMENTS

We thank Georgia Division of Public Health, Office of Health Information and Policy for providing the vital records data.

REFERENCES

1. Becker S. Seasonal patterns of births and conception throughout the world. *Adv Exp Med Biol*. 1991;286:59–72.
2. Roenneberg T, Aschoff J. Annual rhythm of human reproduction: I. Biology, sociology, or both? *J Biol Rhythms*. 1990;5:195–216.
3. Lam DA, Miron JA. Global patterns of seasonal variation in human fertility. *Ann NY Acad Sci*. 1994;709:9–28.
4. Lam DA, Miron JA. The effects of temperature on human fertility. *Demography*. 1996;33:291–305.
5. Seiver DA. Trend and variation in the seasonality of US fertility, 1947–1976. *Demography*. 1985;22:89–100.
6. Levine RJ. Seasonal variation of semen quality and fertility. *Scand J Work Environ Health*. 1999;25(suppl 1):34–37; discussion 76–78.
7. Greksa LP. Birth seasonality in the Old Order Amish. *J Biosoc Sci*. 2004;36:299–315.
8. Rodgers JL, Udry JR. The Season-of-Birth Paradox. *Soc Biol*. 1988;35:171–185.
9. Roenneberg T, Aschoff J. Annual rhythm of human reproduction: II. Environmental correlations. *J Biol Rhythms*. 1990;5:217–239.
10. Weinberg CR, Moledor E, Baird DD, Wilcox AJ. Is there a seasonal pattern in risk of early pregnancy loss? *Epidemiology*. 1994;5:484–489.
11. Chaudhury RH. Socioeconomic and seasonal variations in births: a replication. *Soc Biol*. 1972;19:65–68.
12. Warren CW, Tyler CW. Social status and season of birth: a study of a metropolitan area in the southeastern United States. *Soc Biol*. 1979;26:275–288.
13. Chandwani KD, Cech I, Smolensky MH, Burau K, Hermida RC. Annual pattern of human conception in the State of Texas. *Chronobiol Int*. 2004;21:73–93.
14. Bobak M, Gjonca A. The seasonality of live birth is strongly influenced by socio-demographic factors. *Hum Reprod*. 2001;16:1512–1517.
15. Keller CA, Nugent RP. Seasonal patterns in perinatal mortality and preterm delivery. *Am J Epidemiol*. 1983;118:689–698.
16. Lee SJ, Steer PJ, Filippi V. Seasonal patterns and preterm birth: a systematic review of the literature and an analysis in a London-based cohort. *BJOG*. 2006;113:1280–1288.
17. Sagiv SK, Mendola P, Loomis D, et al. A time-series analysis of air pollution and preterm birth in Pennsylvania, 1997–2001. *Environ Health Perspect*. 2005;113:602–606.
18. Lee SJ, Hajat S, Steer PJ, Filippi V. A time-series analysis of any short-term effects of meteorological and air pollution factors on preterm births in London, UK. *Environ Res*. 2008;106:185–194.
19. Thonneau P, Bujan L, Multigner L, Mieusset R. Occupational heat exposure and male fertility: a review. *Hum Reprod*. 1998;13:2122–2125.
20. Bronson FH. Are humans seasonally photoperiodic? *J Biol Rhythms*. 2004;19:180–192.
21. US Census Bureau. *Hispanic or Latino. Selected Population Profile*. Atlanta-Sandy Springs-Marietta, GA: Metropolitan Statistical Area 2005 American Community Survey; 2005. Report S0201.
22. Basso O, Olsen J, Bisanti L, Juul S, Boldsen J. Are seasonal preferences in pregnancy planning a source of bias in studies of seasonal variation in reproductive outcomes? The European Study Group on Infertility and Subfecundity. *Epidemiology*. 1995;6:520–524.
23. Mosher WD, Bachrach CA. Understanding US fertility: continuity and change in the National Survey of Family Growth, 1988–1995. *Fam Plann Perspect*. 1996;28:4–12.
24. Brown S, Eisenberg L. The Best Intentions: Unintended Pregnancy and the Well-Being of Children and Families. In: *Demography of Unintended Pregnancy*. Washington, DC: National Academies Press; 1995.
25. Trussell J, Wynn LL. Reducing unintended pregnancy in the United States. *Contraception*. 2008;77:1–5.
26. Vickery J. Conceptual models of PM for North American regions. In: McMurray P, Shepherd M, Vickery J, eds. *Particulate Matter Science For Policy Makers: A NARSTO Assessment*. New York: Cambridge University Press; 2003:379–383.