Adverse Birth Outcomes

The period of gestation is a crucial determinant of an infant's health and survival for years to come. Two measures that may be used to understand the quality of an infant's gestation are 1) length of gestation (pregnancy length) and 2) birth weight. Normal term pregnancies last between 37 and 41 completed weeks, allowing for more complete development of an infant's organs and systems.[1] Preterm birth is defined as a live birth before 37 completed weeks of gestation.[1] Birth weight is determined by two factors: length of gestation and fetal growth (the rate at which an infant develops and increases in size). Low birth weight infants are defined as weighing less than 2,500 grams (about 5 pounds, 8 ounces).[2] Infants may be born with a low birth weight because they were born early, because their growth while in utero has been restricted, or both. Because they have had sufficient time to develop, infants born at term with low birth weight are usually considered growth restricted. Because birth weight alone does not always indicate whether an infant's fetal growth has been restricted, other measurements such as birth length, head circumference, and abdominal circumference are also used.

Other adverse birth outcomes that are not discussed here include post-term birth, high birth weight, neonatal mortality, and birth defects, a specific group of adverse birth outcomes that include structural and functional abnormalities.

Preterm and low birth weight infants are at greater risk for mortality and a variety of health and developmental problems. As a result, the birth of a preterm or low birth weight infant can have significant emotional and economic effects on the infant's family.[3] Conditions related to preterm birth and low birth weight are the second leading cause of infant death in the United States (after birth defects).[4] The infant mortality rate for low birth weight infants is about 25 times that of the infant mortality rate for normal weight babies. Likewise, the infant mortality rate for late preterm babies (34–36 weeks of gestation) is about three times the infant mortality rate for term babies, and the infant mortality rate for very preterm babies (less than 32 weeks of gestation) is 75 times that of term babies.[4] Preterm infants may experience complications such as acute respiratory, gastrointestinal, immunologic, and central nervous system problems. Longer-term effects of preterm birth, including motor, cognitive, visual, hearing, behavioral, social-emotional, health, and growth problems, may not become apparent for years and may persist throughout a child's life into adulthood. It is important to recognize that not all infants born before 37 completed weeks have the same risk of adverse health outcomes. As gestational age decreases, the risk of morbidity and mortality increases greatly. Also, recent research suggests that even early term births, those at 37 or 38 weeks, are at increased risk of respiratory and other adverse neonatal outcomes.[5-7]

Because many of the effects of low birth weight are due to being born immature and unprepared for life outside the womb, morbidities associated with low birth weight often overlap with those of preterm birth. Low birth weight infants are more likely to have underdeveloped lungs and breathing problems; heart problems (which can lead to heart failure); immature and improperly functioning livers; too many or too few red blood cells

(polycythemia or anemia); inadequate body fat, leading to trouble maintaining a normal body temperature; feeding problems; and increased risk of infection.[2] Furthermore, the process of growth restriction may exert its own negative effects aside from often producing low birth weight infants. Data suggest that fetuses with a declining growth rate may make adaptations, such as preserving brain growth, in order to survive adverse intrauterine conditions. Such adaptations can have physiological costs, and may have effects on fetal brain development, cardiac and renal function, and adult health.[8] The theory of fetal origins of adult disease postulates that certain types of chemical, nutritional, or stress-related exposures in utero can alter the programming of fetal cells in ways that are not apparent at birth, but are predictive of disease risk later in life. Birth weight and measures of growth restriction are used as proxies for these changes and have been associated with diseases in adulthood, including cardiovascular disease, obesity, metabolic disorders, and cancer.[9]

For many years, the rates of both preterm birth and low birth weight have been increasing;[10] however, starting in 2006 this pattern seems to be partially reversing as the rate of preterm birth is now declining. A number of factors may contribute to increasing rates of preterm birth and low birth weight, including increases in maternal age, rates of multiple births (e.g., twins, triplets), use of early Cesarean sections and labor inductions, changes in neonatal technology, and use of assisted reproductive technologies (e.g., *in vitro* fertilization).[3] Multiple births run a higher risk of preterm birth and low birth weight, and the rates of multiple births have increased in recent decades. The rate of twin births increased 70% from 1980–2004, but has been essentially stable since that time. The rate of triplet and higher-order births increased 400% from 1980 to 1998, but since that time has been trending downward.[11] Advances in medical technology that allow for resuscitation of infants born at increasingly early gestational ages may also contribute to the increase in percentage of births that are preterm, since many of those infants would not have survived previously and thus would have be characterized as fetal deaths. Other factors linked to preterm birth and low birth weight include birth defects; chronic maternal health problems (e.g., high blood pressure); maternal use of tobacco, alcohol, and illicit drugs; maternal and fetal infections; placental problems; inadequate maternal weight gain; and socioeconomic factors (e.g., low income and poor education).[12-16]

Rates of low birth weight and preterm birth can vary greatly by maternal race/ethnicity. Black women have consistently had higher rates of preterm and low birth weight babies.[17] While it has been suggested that race is a proxy for differences in socioeconomic status (SES), most studies that have controlled for differences in SES continue to find persistent birth outcomes differences between Black and White women.[17-20] Similarly, studies that have adjusted for other risk factors, such as risky behavior during pregnancy and use of prenatal care, have found these persistent Black-White differences in birth outcomes as well.[4,21,22]

While maternal characteristics and obstetric practices play an important role in preterm birth and low birth weight, other factors—including environmental contaminants—may also contribute to adverse birth outcomes.[23] A growing number of studies have examined the possible role that exposure to environmental contaminants may play in the causation of preterm birth and low birth weight. The evidence is particularly strong for environmental

tobacco smoke (ETS) and lead. The Surgeon General has determined that exposure of pregnant women to ETS causes a small reduction in mean birth weight, and that the evidence is suggestive (but not sufficient to infer causation) of a relationship between maternal exposure to environmental tobacco smoke during pregnancy and preterm delivery.[24] The National Toxicology Program has concluded that maternal exposure to lead is known to cause reduced fetal growth, and that there is limited evidence of an association with preterm birth.[25]

In recent years, the potential effects of common air pollutants on adverse birth outcomes have received more attention. A number of large epidemiological studies (many with 10,000+ participants) from several countries have identified potential links between elevated levels of exposure to particulate matter (PM), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), and carbon monoxide (CO) exposure and outcomes such as decreased fetal growth, low birth weight, and preterm birth.[26-40] Several of these studies have identified such links to adverse birth outcomes even in regions with relatively low ambient air pollution levels.[27,29,33,36] In such epidemiological studies, researchers make an effort, when data are available, to adjust for other factors that may also lead to an increased risk of low birth weight or preterm birth, such as mother's age, smoking status, race, and income.[41] Articles reviewing the findings from these studies have generally concluded that these air pollutants likely have an adverse effect on birth outcomes, although methodological inconsistencies across studies have made definitive conclusions difficult.[42-45] In addition, studies have reported associations between elevated levels of exposure to airborne polycyclic aromatic hydrocarbons (PAHs), generated largely by fossil fuel combustion, and reduced birth weight and fetal growth restriction, especially when in combination with ETS exposure.[46-49] Other studies have reported associations between living in proximity to traffic during pregnancy and increased risk of preterm birth and low birth weight, although an extensive review study concluded that there is inadequate and insufficient evidence to infer a causal relationship.[50-54]

In addition to air pollutants, several other environmental chemicals have been studied for possible roles in contributing to adverse birth outcomes. A handful of studies with typical population-level exposure levels have reported associations between prenatal exposure to some phthalates and preterm birth, shorter gestational length, and low birth weight; however, one study reported phthalate exposure to be associated with longer gestational length and increased risk of delivery by Cesarean section.[55-59]

A limited number of studies suggest that prenatal exposure to another class of chemicals, polychlorinated biphenyls (PCBs), may lead to preterm birth and low birth weight or otherwise restrict fetal growth.[60-63] One study examining women from the Danish National Birth Cohort reported that elevated exposure to PCBs from fatty fish consumption was associated with lower birth weight. The study found that infants born to highly exposed women weighed, on average, about 5.5 ounces less than infants born to women with relatively low PCB exposure.[64] Another study looked at a historical cohort of women who were pregnant prior to the 1979 ban of PCBs, and did not observe any relation between levels of PCB exposure and low birth weight or shorter pregnancy length.[65] Some human health studies have reported associations between prenatal exposure to perfluorinated compounds (PFCs)—particularly perfluorooctane sulfonic

acid (PFOS) and perfluorooctanoic acid (PFOA)—and a range of adverse birth outcomes, such as low birth weight, decreased head circumference, reduced birth length, and smaller abdominal circumference.[66-70] However, there are inconsistencies in the results of these studies, and two other studies did not find an association between prenatal PFC exposure and birth weight.[71,72] The participants in all of these studies had PFC blood serum levels comparable to levels in the general population. Studies of disinfection byproducts in drinking water as possible causes of adverse birth outcomes are also conflicting, with recent evidence indicating that there may be no effect on preterm birth.[73-75] Studies of arsenic in drinking water and birth outcomes have produced similarly mixed results.[76-78] For the following environmental contaminants, there is some evidence from animal studies and a limited number of studies in humans of possible associations with adverse birth outcomes, particularly reduced fetal growth: benzene,[79] herbicides,[80] bisphenol A (BPA),[81] dioxins and dioxin-like chemicals,[82] and manganese.[83]

This section presents two indicators of adverse birth outcomes: Indicator H12 presents the rate of preterm birth, and Indicator H13 presents the rate of term low birth weight. These two indicators were chosen because for each there is a wealth of quality data available.

Indicator H12: Percentage of babies born preterm, by race/ethnicity, 1993–2017

Indicator H13: Percentage of babies born at term with low birth weight, by race/ethnicity, 1993–2017

About the Indicator: Indicator H12 shows the percentage of babies born preterm, and Indicator H13 shows the percentage of babies who are born at term with low birth weight. Both graphs show separate lines for the different race/ethnicity groups. The data come from a national data system that collects data from birth certificates for virtually every baby born in the United States each year. Indicators H12 and H13 show the change in preterm and term low birth weight over time.

The National Vital Statistics System

The National Vital Statistics System (NVSS), operated by the National Center for Health Statistics (NCHS), provides national data on gestational ages and birth weights. The NVSS data are provided through contracts between the NCHS and vital registration systems operated in each state, which are legally responsible for the registration of vital events including births, deaths, marriages, divorces, and fetal deaths. The collection and publication of this information is mandated by federal law. Together NCHS and the states have developed standard forms and procedures to use for the data collection. The NVSS captures virtually all of the births occurring in the United States. The most current NVSS data available are for 2017.

Birth certificates provide information on characteristics of both the infant and his/her parents, including the weight of the infant and the length of gestation. Length of gestation is recorded in completed weeks, so for example a pregnancy of 36 weeks and 6 days would be recorded as 36 weeks, and would therefore be considered preterm.[3] Pregnancy duration is often estimated from the date of a woman's last menstrual period. Many factors, including age, levels of physical activity, and body mass, can cause variation in menstrual cycle timing, making this method of estimating gestational length subject to some error.[3] NVSS data also report pregnancy duration based on a clinical estimation, often determined using ultrasound, if information on last menstrual period is unavailable or is inconsistent with the reported birth weight. Because ultrasound measurements tend to give lower gestational age estimates than last menstrual period (LMP),[3] the slight increase in use of ultrasound data in recent years could contribute to any increase in the rate of preterm birth. In 2014, the National Center for Health Statistics transitioned to a new standard for estimating the gestational age of the newborn. The new standard is based on the obstetric estimate (OE), replacing the former standard that was based on the LMP. National data based on the OE are available only from the data year 2007 forward.[i]

[i] Martin, J.A., M.J.K. Osterman, S.E. Kirmeyer, and E.C.W. Gregory. 2015. Measuring gestational age in vital statistics data: Transitioning to the obstetric estimate. *National Vital Statistics Reports*, vol 64, no. 5.

Data Presented in the Indicators

Indicator H12 displays the trend in the percentage of preterm births for all births (singletons, as well as multiples), with a separate line for each maternal race/ethnicity group and a single line for all maternal races and ethnicities combined for the years 1993–2017. Values for 1993 to 2006 use the LMP gestational age estimate. Values for 2007 and later use the OE gestational estimate.

Indicator H13 displays the trend in the percentage of low birth weight births at term among all births (singletons, as well as multiples), with a separate line for each maternal race/ethnicity group and a single line for all maternal races and ethnicities combined for the years 1993–2017. Values for 1993 to 2006 use the LMP gestational age estimate. Values for 2007 and later use the OE gestational estimate. Presentation of low birth weight data for only term births (babies with a gestational age of 37 completed weeks or more) is intended to identify trends in growth restriction separate from trends in gestational duration. This indicator does not include all infants with low birth weight, nor does it include all infants who are growth-restricted; therefore, it is designed as a surveillance tool and not as a way to identify a group of infants that are particularly at risk for adverse health effects.

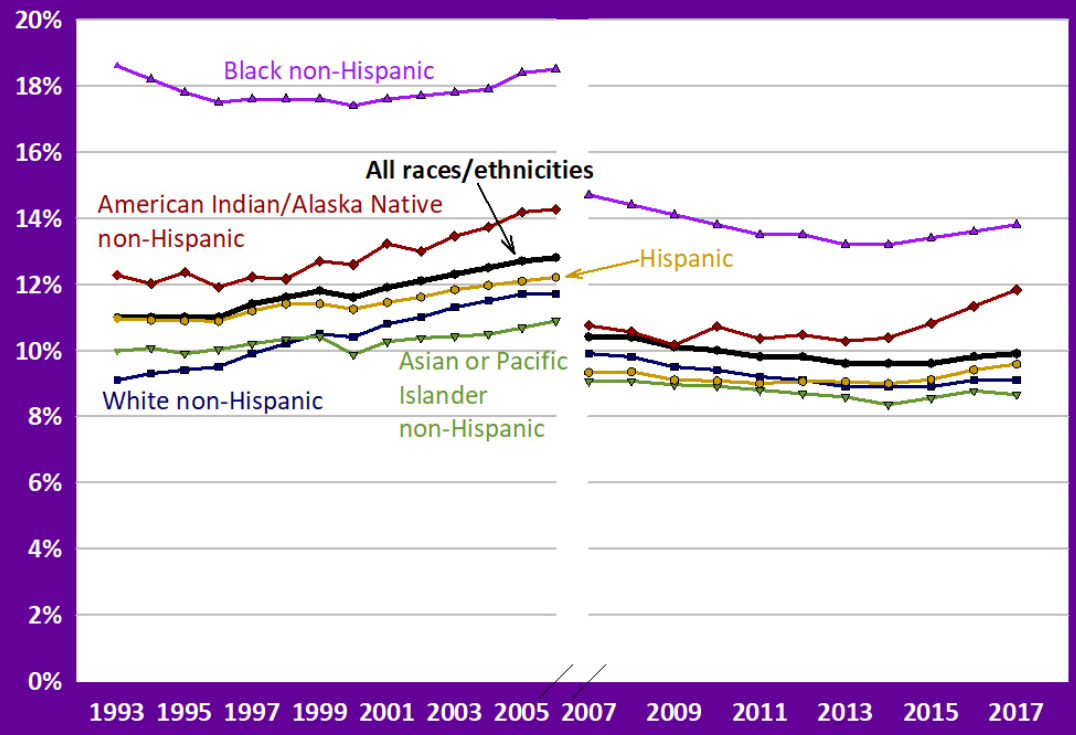
Five maternal race/ethnicity groups are presented in these indicators: White non-Hispanic, Black non-Hispanic, Hispanic, American Indian/Alaska Native non-Hispanic, and Asian Pacific Islander non-Hispanic. Prior to the year 1993, not all states recorded Hispanic origin on birth certificates; for this reason, both Indicator H12 and H13 begin with data from 1993. Birth certificates do not include information on family or maternal income, so it is not possible to examine differences or trends by income level.

The indicator graphs show data for all births, singletons and multiples combined. The rates for singletons and multiples are provided in supplemental data tables. Additional supplemental tables highlight differences in rates of preterm birth and term low birth weight by age of the mother.

Please see the Introduction to the Health section for discussion of statistical significance testing applied to these indicators. The NVSS records virtually all births in the United States—approximately 4 million per year. Because of this very large sample size, differences in birth outcomes that appear to be small in magnitude may be found to be statistically significant. Extensive research has been conducted with NVSS data to assess the presence of statistically significant trends and demographic differences, including analyses with much more detail than the one conducted here.[23,84,85]

Indicator H12

Percentage of babies born preterm, by race/ethnicity, 1993-2017



Data: Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System

Note: Values from 2007 to the present are not comparable to those for earlier years due to a change in the measure for estimating gestational age.

America's Children and the Environment, Third Edition, Updated August 2019

Data characterization

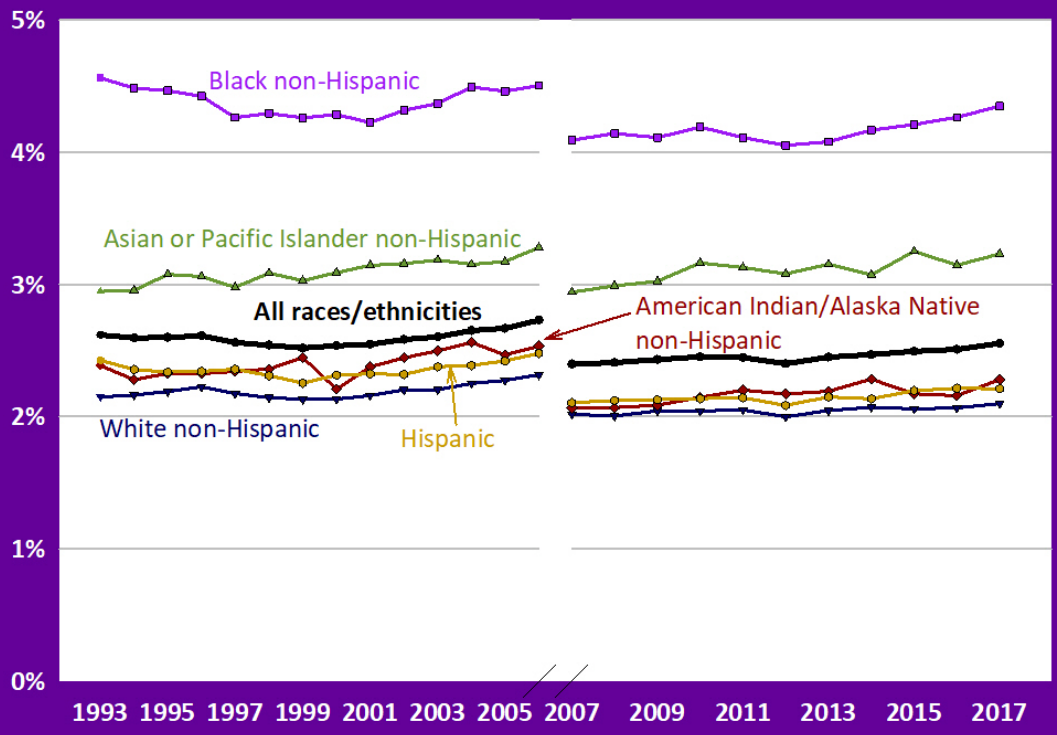
- Data from this indicator are obtained from a database maintained by the National Center for Health Statistics.
- The database collects information from birth certificates for virtually all births in the United States.
- Length of gestation is recorded on each birth certificate.

- Between 1993 and 2006, the rate of preterm birth increased from 11.0% in 1993 to its highest value of 12.8% in 2006. This increasing trend was statistically significant. The rate of preterm birth decreased from 10.4% in 2007 to 9.6% in 2014, and was 9.9% in 2017. The overall decreasing trend from 2007 to 2017 was statistically significant.
  - Values from 2007 to the present are not comparable to those for earlier years due to a change in the measure for estimating gestational age.

  - In 2017, Black non-Hispanic women had the highest rate of preterm birth, compared with women of other races/ethnicities. About 1 in 7 infants born to Black non-Hispanic women were born prematurely in that year.
    - The differences between the rate of preterm birth for Black non-Hispanic women and the rates for the other race/ethnicity groups were statistically significant.
- Between 2007 and 2017, the preterm birth rate showed a decreasing trend for each race/ethnicity group except American Indian Alaska Native non-Hispanic women. The preterm birth rate for American Indian Alaska Native non-Hispanic women showed an increasing trend.
  - These trends in the rate of preterm birth were statistically significant for each race/ethnicity group.
- The preterm birth rate varies depending on the age of the mother. Women ages 20 to 39 years have the lowest rate of preterm birth, compared with women under 20 years and women 40 years and older.
  - The differences between the preterm birth rates for the different age groups were statistically significant. The decreasing trends from 2007 to 2017 in the rate of preterm birth for women were statistically significant for each age group.
- Twins, triplets, and other higher-order multiple birth babies are more than 5 times as likely to be born preterm compared with singleton babies (e.g., 53.1% vs. 9.9% in 1993 and 60.6% vs. 8.1% in 2017). The preterm birth rates for both singletons and multiples showed an increasing trend from 1993 to 2006 followed by a decreasing trend from 2007 to 2017; however, the trends for multiples were larger than for singletons. (See Table H12b.)
  - These trends for both singleton and multiple births were statistically significant.

Indicator H13

Percentage of babies born at term with low birth weight, by race/ethnicity, 1993-2017



Data: Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System

Note: Values from 2007 to the present are not comparable to those for earlier years due to a change in the measure for estimating gestational age.

America's Children and the Environment, Third Edition, Updated August 2019

Data characterization

- Data from this indicator are obtained from a database maintained by the National Center for Health Statistics.
- The database collects information from birth certificates for virtually all births in the United States.
- Birth weight and length of gestation are recorded on each birth certificate.

- Between 1993 and 2006, the rate of term low birth weight for all races/ethnicities stayed relatively constant, ranging between 2.5% and 2.7%. Between 2007 and 2017, the rate of term low birth weight for women of all race/ethnicities increased from 2.4% to 2.6%. This increasing trend was statistically significant.
  - Values from 2007 to the present are not comparable to those for earlier years due to a change in the measure for estimating gestational age.

- Between 2007 and 2017, the rates of term low birth weight increased for each race/ethnicity group except for women of unknown ethnicity. Each of these increasing trends was statistically significant.
- The rate of term low birth weight varies by race/ethnicity. In 2017, the rate was highest for Black non-Hispanic women (4.3%), and next highest for Asian or Pacific Islander non-Hispanic women (3.2%). The rate of term low birth weight is lowest for White non-Hispanic women (2.1%), Mexican women (2.0%), and Hispanic women (2.2%).
  - The rate of term low birth weight for Black non-Hispanic women was statistically significantly higher than for all other race/ethnicity groups. The rate of term low birth weight for Asian or Pacific Islander non-Hispanic women was significantly lower than for Black non-Hispanic women but significantly higher than the other race/ethnicity groups.
- Term low birth weight rates vary by the age of the mother. In 2017, women ages 20 to 39 years had the lowest rate of term low birth weight infants, while women under 20 years had the highest rate of term low birth weight infants. These differences were statistically significant. (See Table H13a.)
- Between 2007 and 2017, the rates of term low birth weight for women under 20 and women ages 20 to 39 years showed increasing trends. These trends were statistically significant. (See Table H13a.)
- Twins, triplets, and other higher-order multiple birth babies are more than 4 times as likely to be born at term with low birth weight compared with singleton babies (e.g., 13.4% vs 2.3% in 1993 and 9.6% vs. 2.3% in 2017). The rate of term low birth weight for singleton babies stayed relatively constant over the period 2007–2017. The rate of term low birth weight for multiple birth babies also stayed constant over the period 2007–2017. (See Table H13b.)

References

1. Centers for Disease Control and Prevention. 2009. *Maternal and Infant Health Research: Preterm Birth*. CDC. Retrieved October 10, 2010 from http://www.cdc.gov/reproductivehealth/maternalinfanthealth/PBP.htm.

2. JAMA. 2002. JAMA patient page: Low birth weight. *Journal of the American Medical Association* 287 (2):270.

3. Institute of Medicine. 2007. *Preterm Birth: Causes, Consequences, and Prevention*. Edited by R. E. Behrman and A. S. Butler. Washington, DC: The National Academies Press.

4. Mathews, T.J., and M.F. MacDorman. 2008. Infant mortality statistics from the 2005 period linked birth/infant death data set. *National Vital Statistics Reports* 57 (2).

5. Clark, S.L., D.D. Miller, M.A. Belfort, G.A. Dildy, D.K. Frye, and J.A. Meyers. 2009. Neonatal and maternal outcomes associated with elective term delivery. *American Journal of Obstetrics and Gynecology* 200 (2):156 e1-4.

6. Moster, D., A.J. Wilcox, S.E. Vollset, T. Markestad, and R.T. Lie. 2010. Cerebral Palsy Among Term and Postterm Births. *Journal of the American Medical Association* 304 (9):976-982.

7. Tita, A.T., M.B. Landon, C.Y. Spong, Y. Lai, K.J. Leveno, M.W. Varner, A.H. Moawad, S.N. Caritis, P.J. Meis, R.J. Wapner, et al. 2009. Timing of elective repeat cesarean delivery at term and neonatal outcomes. *New England Journal of Medicine* 360 (2):111-20.

8. Cosmi, E., T. Fanelli, S. Visentin, D. Trevisanuto, and V. Zanardo. 2011. Consequences in infants that were intrauterine growth restricted. *Journal of Pregnancy* 2011:Article ID 364381.

9. Rinaudo, P.F., and J. Lamb. 2008. Fetal origins of perinatal morbidity and/or adult disease. *Seminars in Reproductive Medicine* 26 (5):436-45.

10. Martin, J.A., B.E. Hamilton, P.D. Sutton, S.J. Ventura, P.H. Menacker, S. Kirmeyer, and T.J. Mathews. 2009. Births: Final Data for 2006. *National Vital Statistics Reports* 57 (7).

11. Martin, J.A., B.E. Hamilton, P.D. Sutton, S.J. Ventura, T.J. Mathews, S. Kirmeyer, and M.J.K. Osterman. 2010. Births: Final Data for 2007. *National Vital Statistics Reports* 58 (24).

12. American College of Obstetricians and Gynecologists (ACOG). 2000. Intrauterine growth restriction. ACOG practice bulletin, number 12. *Obstetrics and Gynecology* 95 (1).

13. Berghella, V. 2007. Prevention of recurrent fetal growth restriction. *Obstetrics and Gynecology* 110 (4):904-12.

14. Honein, M.A., R.S. Kirby, R.E. Meyer, J. Xing, N.I. Skerrette, N. Yuskiv, L. Marengo, J.R. Petrini, M.J. Davidoff, C.T. Mai, et al. 2009. The association between major birth defects and preterm birth. *Maternal and Child Health Journal* 13 (2):164-75.

15. U.S. Department of Health and Human Services. 2004. *The Health Consequences of Smoking: A Report of the Surgeon General*. Atlanta, GA: Centers for Disease Control and Prevention, Office on Smoking and Health.

16. Goldenberg, R.L., and J.F. Culhane. 2007. Low birth weight in the United States. *American Journal of Clinical Nutrition* 85 (2):584S-590S.

17. Lu, M.C., and N. Halfon. 2003. Racial and ethnic disparities in birth outcomes: a life-course perspective. *Maternal and Child Health Journal* 7 (1):13-30.

18. Collins, J.W., Jr., and A.G. Butler. 1997. Racial differences in the prevalence of small-for-dates infants among college-educated women. *Epidemiology* 8 (3):315-7.

19. McGrady, G.A., J.F. Sung, D.L. Rowley, and C.J. Hogue. 1992. Preterm delivery and low birth weight among first-born infants of black and white college graduates. *American Journal of Epidemiology* 136 (3):266-76.

20. Schoendorf, K.C., C.J. Hogue, J.C. Kleinman, and D. Rowley. 1992. Mortality among infants of black as compared with white college-educated parents. *New England Journal of Medicine* 326 (23):1522-6.

21. Goldenberg, R.L., S.P. Cliver, F.X. Mulvihill, C.A. Hickey, H.J. Hoffman, L.V. Klerman, and M.J. Johnson. 1996. Medical, psychosocial, and behavioral risk factors do not explain the increased risk for low birth weight among black women. *American Journal of Obstetrics & Gynecology* 175 (5):1317-24.

22. Singh, G.K., and S.M. Yu. 1995. Infant mortality in the United States: trends, differentials, and projections, 1950 through 2010. *American Journal of Public Health* 85 (7):957-64.

23. Donahue, S.M., K.P. Kleinman, M.W. Gillman, and E. Oken. 2010. Trends in birth weight and gestational length among singleton term births in the United States: 1990-2005. *Obstetrics and Gynecology* 115 (2 Pt 1):357-64.

24. U.S. Department of Health and Human Services. 2006. *The Health Consequences of Involuntary Exposure to Tobacco Smoke: A Report of the Surgeon General*. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

25. National Toxicology Program. 2012. *NTP Monograph on Health Effects of Low-Level Lead*. Research Triangle Park, NC: National Institute of Environmental Health Sciences, National Toxicology Program. http://ntp.niehs.nih.gov/go/36443.

26. Bobak, M. 2000. Outdoor air pollution, low birth weight, and prematurity. *Environmental Health Perspectives* 108 (2):173-6.

27. Dugandzic, R., L. Dodds, D. Stieb, and M. Smith-Doiron. 2006. The association between low level exposures to ambient air pollution and term low birth weight: a retrospective cohort study. *Environmental Health* 5:3.

28. Ha, E.H., Y.C. Hong, B.E. Lee, B.H. Woo, J. Schwartz, and D.C. Christiani. 2001. Is air pollution a risk factor for low birth weight in Seoul? *Epidemiology* 12 (6):643-8.

29. Huynh, M., T.J. Woodruff, J.D. Parker, and K.C. Schoendorf. 2006. Relationships between air pollution and preterm birth in California. *Paediatric and Perinatal Epidemiology* 20 (6):454-61.

30. Lin, C.M., C.Y. Li, G.Y. Yang, and I.F. Mao. 2004. Association between maternal exposure to elevated ambient sulfur dioxide during pregnancy and term low birth weight. *Environmental Research* 96 (1):41-50.

31. Liu, S., D. Krewski, Y. Shi, Y. Chen, and R.T. Burnett. 2003. Association between gaseous ambient air pollutants and adverse pregnancy outcomes in Vancouver, Canada. *Environmental Health Perspectives* 111 (14):1773-8.

32. Maisonet, M., T.J. Bush, A. Correa, and J.J. Jaakkola. 2001. Relation between ambient air pollution and low birth weight in the Northeastern United States. *Environmental Health Perspectives* 109 (Suppl 3):351-6.

33. Maroziene, L., and R. Grazuleviciene. 2002. Maternal exposure to low-level air pollution and pregnancy outcomes: a population-based study. *Environmental Health* 1 (1):6.

34. Parker, J.D., T.J. Woodruff, R. Basu, and K.C. Schoendorf. 2005. Air pollution and birth weight among term infants in California. *Pediatrics* 115 (1):121-8.

35. Sagiv, S.K., P. Mendola, D. Loomis, A.H. Herring, L.M. Neas, D.A. Savitz, and C. Poole. 2005. A time-series analysis of air pollution and preterm birth in Pennsylvania, 1997-2001. *Environmental Health Perspectives* 113 (5):602-6.

36. U.S. Environmental Protection Agency. 2009. *Integrated Science Assessment for Particulate Matter (Final Report)*. Washington, DC: U.S. EPA. EPA/600/R-08/139F. http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=216546.

37. Wang, X., H. Ding, L. Ryan, and X. Xu. 1997. Association between air pollution and low birth weight: a community-based study. *Environmental Health Perspectives* 105 (5):514-20.

38. Wilhelm, M., and B. Ritz. 2005. Local variations in CO and particulate air pollution and adverse birth outcomes in Los Angeles County, California, USA. *Environmental Health Perspectives* 113 (9):1212-21.

39. Xu, X., H. Ding, and X. Wang. 1995. Acute effects of total suspended particles and sulfur dioxides on preterm delivery: a community-based cohort study. *Archives of Environmental Health* 50 (6):407-15.

40. Liu, S., D. Krewski, Y. Shi, Y. Chen, and R.T. Burnett. 2007. Association between maternal exposure to ambient air pollutants during pregnancy and fetal growth restriction. *Journal of Exposure Science and Environmental Epidemiology* 17 (5):426-32.

41. Stillerman, K.P., D.R. Mattison, L.C. Giudice, and T.J. Woodruff. 2008. Environmental exposures and adverse pregnancy outcomes: a review of the science. *Reproductive Sciences* 15 (7):631-50.

42. Glinianaia, S.V., J. Rankin, R. Bell, T. Pless-Mulloli, and D. Howel. 2004. Particulate air pollution and fetal health: a systematic review of the epidemiologic evidence. *Epidemiology* 15 (1):36-45.

43. Parker, J.D., D.Q. Rich, S.V. Glinianaia, J.H. Leem, D. Wartenberg, M.L. Bell, M. Bonzini, M. Brauer, L. Darrow, U. Gehring, et al. 2011. The International Collaboration on Air Pollution and Pregnancy Outcomes: initial results. *Environmental Health Perspectives* 119 (7):1023-8.

44. Ritz, B., and M. Wilhelm. 2008. Ambient air pollution and adverse birth outcomes: methodologic issues in an emerging field. *Basic and Clinical Pharmacology and Toxicology* 102 (2):182-90.

45. Sram, R.J., B. Binkova, J. Dejmek, and M. Bobak. 2005. Ambient air pollution and pregnancy outcomes: a review of the literature. *Environmental Health Perspectives* 113 (4):375-82.

46. Choi, H., W. Jedrychowski, J. Spengler, D.E. Camann, R.M. Whyatt, V. Rauh, W.Y. Tsai, and F.P. Perera. 2006. International studies of prenatal exposure to polycyclic aromatic hydrocarbons and fetal growth. *Environmental Health Perspectives* 114 (11):1744-50.

47. Choi, H., V. Rauh, R. Garfinkel, Y. Tu, and F.P. Perera. 2008. Prenatal exposure to airborne polycyclic aromatic hydrocarbons and risk of intrauterine growth restriction. *Environmental Health Perspectives* 116 (5):658-65.

48. Perera, F.P., V. Rauh, R.M. Whyatt, W.Y. Tsai, J.T. Bernert, Y.H. Tu, H. Andrews, J. Ramirez, L. Qu, and D. Tang. 2004. Molecular evidence of an interaction between prenatal environmental exposures and birth outcomes in a multiethnic population. *Environmental Health Perspectives* 112 (5):626-30.

49. Perera, F.P., D. Tang, V. Rauh, K. Lester, W.Y. Tsai, Y.H. Tu, L. Weiss, L. Hoepner, J. King, G. Del Priore, et al. 2005. Relationships among polycyclic aromatic hydrocarbon-DNA adducts, proximity to the World Trade Center, and effects on fetal growth. *Environmental Health Perspectives* 113 (8):1062-7.

50. Brauer, M., C. Lencar, L. Tamburic, M. Koehoorn, P. Demers, and C. Karr. 2008. A cohort study of traffic-related air pollution impacts on birth outcomes. *Environmental Health Perspectives* 116 (5):680-6.

51. Genereux, M., N. Auger, M. Goneau, and M. Daniel. 2008. Neighbourhood socioeconomic status, maternal education and adverse birth outcomes among mothers living near highways. *Journal of Epidemiology and Community Health* 62 (8):695-700.

52. Health Effects Institute. 2010. *HEI Panel on the Health Effects of Traffic-Related Air Pollution: A Critical Review of the Literature on Emissions, Exposure, and Health Effects*. Boston, MA. HEI Special Report 17. http://pubs.healtheffects.org/view.php?id=334

53. Ponce, N.A., K.J. Hoggatt, M. Wilhelm, and B. Ritz. 2005. Preterm birth: the interaction of traffic-related air pollution with economic hardship in Los Angeles neighborhoods. *American Journal of Epidemiology* 162 (2):140-8.

54. Wilhelm, M., and B. Ritz. 2003. Residential proximity to traffic and adverse birth outcomes in Los Angeles county, California, 1994-1996. *Environmental Health Perspectives* 111 (2):207-16.

55. Adibi, J.J., R. Hauser, P.L. Williams, R.M. Whyatt, A.M. Calafat, H. Nelson, R. Herrick, and S.H. Swan. 2009. Maternal urinary metabolites of Di-(2-Ethylhexyl) phthalate in relation to the timing of labor in a US multicenter pregnancy cohort study. *American Journal of Epidemiology* 169 (8):1015-24.

56. Latini, G., C. De Felice, G. Presta, A. Del Vecchio, I. Paris, F. Ruggieri, and P. Mazzeo. 2003. In utero exposure to di-(2-ethylhexyl)phthalate and duration of human pregnancy. *Environmental Health Perspectives* 111 (14):1783-5.

57. Meeker, J.D., H. Hu, D.E. Cantonwine, H. Lamadrid-Figueroa, A.M. Calafat, A.S. Ettinger, M. Hernandez-Avila, R. Loch-Caruso, and M.M. Tellez-Rojo. 2009. Urinary phthalate metabolites in relation to preterm birth in Mexico City. *Environmental Health Perspectives* 117 (10):1587-92.

58. Whyatt, R.M., J.J. Adibi, A.M. Calafat, D.E. Camann, V. Rauh, H.K. Bhat, F.P. Perera, H. Andrews, A.C. Just, L. Hoepner, et al. 2009. Prenatal di(2-ethylhexyl)phthalate exposure and length of gestation among an inner-city cohort. *Pediatrics* 124 (6):e1213-20.

59. Zhang, Y., L. Lin, Y. Cao, B. Chen, L. Zheng, and R.S. Ge. 2009. Phthalate levels and low birth weight: a nested case-control study of Chinese newborns. *Journal of Pediatrics* 155 (4):500-4.

60. Murphy, L.E., A.L. Gollenberg, G.M. Buck Louis, P.J. Kostyniak, and R. Sundaram. 2010. Maternal serum preconception polychlorinated biphenyl concentrations and infant birth weight. *Environmental Health Perspectives* 118 (2):297-302.

61. Wigle, D.T., T.E. Arbuckle, M.C. Turner, A. Berube, Q. Yang, S. Liu, and D. Krewski. 2008. Epidemiologic evidence of relationships between reproductive and child health outcomes and environmental chemical contaminants. *Journal of Toxicology and Environmental Health Part B Crit Reviews* 11 (5-6):373-517.

62. Hertz-Picciotto, I., M.J. Charles, R.A. James, J.A. Keller, E. Willman, and S. Teplin. 2005. In utero polychlorinated biphenyl exposures in relation to fetal and early childhood growth. *Epidemiology* 16 (5):648-56.

63. Baibergenova, A., R. Kudyakov, M. Zdeb, and D.O. Carpenter. 2003. Low birth weight and residential proximity to PCB-contaminated waste sites. *Environmental Health Perspectives* 111 (10):1352-7.

64. Halldorsson, T.I., I. Thorsdottir, H.M. Meltzer, F. Nielsen, and S.F. Olsen. 2008. Linking exposure to polychlorinated biphenyls with fatty fish consumption and reduced fetal growth among Danish pregnant women: a cause for concern? *American Journal of Epidemiology* 168 (8):958-65.

65. Longnecker, M.P., M.A. Klebanoff, J.W. Brock, and X. Guo. 2005. Maternal levels of polychlorinated biphenyls in relation to preterm and small-for-gestational-age birth. *Epidemiology* 16 (5):641-7.

66. Apelberg, B.J., F.R. Witter, J.B. Herbstman, A.M. Calafat, R.U. Halden, L.L. Needham, and L.R. Goldman. 2007. Cord serum concentrations of perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) in relation to weight and size at birth. *Environmental Health Perspectives* 115 (11):1670-6.

67. Fei, C., J.K. McLaughlin, R.E. Tarone, and J. Olsen. 2007. Perfluorinated chemicals and fetal growth: a study within the Danish National Birth Cohort. *Environmental Health Perspectives* 115 (11):1677-82.

68. Fei, C., J.K. McLaughlin, R.E. Tarone, and J. Olsen. 2008. Fetal growth indicators and perfluorinated chemicals: a study in the Danish National Birth Cohort. *American Journal of Epidemiology* 168 (1):66-72.

69. Stein, C.R., D.A. Savitz, and M. Dougan. 2009. Serum levels of perfluorooctanoic acid and perfluorooctane sulfonate and pregnancy outcome. *American Journal of Epidemiology* 170 (7):837-46.

70. Washino, N., Y. Saijo, S. Sasaki, S. Kato, S. Ban, K. Konishi, R. Ito, A. Nakata, Y. Iwasaki, K. Saito, et al. 2009. Correlations between prenatal exposure to perfluorinated chemicals and reduced fetal growth. *Environmental Health Perspectives* 117 (4):660-7.

71. Hamm, M.P., N.M. Cherry, E. Chan, J.W. Martin, and I. Burstyn. 2010. Maternal exposure to perfluorinated acids and fetal growth. *Journal of Exposure Science and Environmental Epidemiology* 20 (7):589-97.

72. Monroy, R., K. Morrison, K. Teo, S. Atkinson, C. Kubwabo, B. Stewart, and W.G. Foster. 2008. Serum levels of perfluoroalkyl compounds in human maternal and umbilical cord blood samples. *Environmental Research* 108 (1):56-62.

73. Bove, F., Y. Shim, and P. Zeitz. 2002. Drinking water contaminants and adverse pregnancy outcomes: a review. *Environmental Health Perspectives* 110 (Suppl 1):61-74.

74. Hoffman, C.S., P. Mendola, D.A. Savitz, A.H. Herring, D. Loomis, K.E. Hartmann, P.C. Singer, H.S. Weinberg, and A.F. Olshan. 2008. Drinking water disinfection by-product exposure and fetal growth. *Epidemiology* 19 (5):729-37.

75. Hoffman, C.S., P. Mendola, D.A. Savitz, A.H. Herring, D. Loomis, K.E. Hartmann, P.C. Singer, H.S. Weinberg, and A.F. Olshan. 2008. Drinking water disinfection by-product exposure and duration of gestation. *Epidemiology* 19 (5):738-46.

76. Myers, S.L., D.T. Lobdell, Z. Liu, Y. Xia, H. Ren, Y. Li, R.K. Kwok, J.L. Mumford, and P. Mendola. 2010. Maternal drinking water arsenic exposure and perinatal outcomes in inner Mongolia, China. *Journal of Epidemiology and Community Health* 64 (4):325-9.

77. Rahman, A., M. Vahter, A.H. Smith, B. Nermell, M. Yunus, S. El Arifeen, L.A. Persson, and E.C. Ekstrom. 2009. Arsenic exposure during pregnancy and size at birth: a prospective cohort study in Bangladesh. *American Journal of Epidemiology* 169 (3):304-12.

78. Smith, A.H., and C.M. Steinmaus. 2009. Health effects of arsenic and chromium in drinking water: recent human findings. *Annual Review of Public Health* 30:107-22.

79. Slama, R., O. Thiebaugeorges, V. Goua, L. Aussel, P. Sacco, A. Bohet, A. Forhan, B. Ducot, I. Annesi-Maesano, J. Heinrich, et al. 2009. Maternal personal exposure to airborne benzene and intrauterine growth. *Environmental Health Perspectives* 117 (8):1313-21.

80. Ochoa-Acuna, H., J. Frankenberger, L. Hahn, and C. Carbajo. 2009. Drinking-water herbicide exposure in Indiana and prevalence of small-for-gestational-age and preterm delivery. *Environmental Health Perspectives* 117 (10):1619-24.

81. Ranjit, N., K. Siefert, and V. Padmanabhan. 2010. Bisphenol-A and disparities in birth outcomes: a review and directions for future research. *Journal of Perinatology* 30 (1):2-9.

82. Konishi, K., S. Sasaki, S. Kato, S. Ban, N. Washino, J. Kajiwara, T. Todaka, H. Hirakawa, T. Hori, D. Yasutake, et al. 2009. Prenatal exposure to PCDDs/PCDFs and dioxin-like PCBs in relation to birth weight. *Environmental Research* 109 (7):906-13.

83. Zota, A.R., A.S. Ettinger, M. Bouchard, C.J. Amarasiriwardena, J. Schwartz, H. Hu, and R.O. Wright. 2009. Maternal blood manganese levels and infant birth weight. *Epidemiology* 20 (3):367-73.

84. Davidoff, M.J., T. Dias, K. Damus, R. Russell, V.R. Bettegowda, S. Dolan, R.H. Schwarz, N.S. Green, and J. Petrini. 2006. Changes in the gestational age distribution among U.S. singleton births: impact on rates of late preterm birth, 1992 to 2002. *Seminars in Perinatology* 30 (1):8-15.

85. Heron, M., P.D. Sutton, J. Xu, S.J. Ventura, D.M. Strobino, and B. Guyer. 2010. Annual summary of vital statistics: 2007. *Pediatrics* 125 (1):4-15.