Racial disparities in preterm birth rates and short inter-pregnancy interval: an overview

Carol Hogue, *Emory University*
Ramkumar Menon, *University of Texas*
Anne Dunlop, *Emory University*
Michael Kramer, *Emory University*

Journal Title: Acta Obstetricia et Gynecologica Scandinavica
Volume: Volume 90, Number 12
Publisher: Wiley: 12 months | 2011-12, Pages 1317-1324
Type of Work: Article | Post-print: After Peer Review
Publisher DOI: 10.1111/j.1600-0412.2011.01081.x
Permanent URL: https://pid.emory.edu/ark:/25593/s4r51

Final published version: http://dx.doi.org/10.1111/j.1600-0412.2011.01081.x

HHS Public Access
Author manuscript
Acta Obstet Gynecol Scand. Author manuscript; available in PMC 2017 August 30.

Published in final edited form as:
Acta Obstet Gynecol Scand. 2011 December ; 90(12): 1317–1324. doi:10.1111/j.1600-0412.2011.01081.x.

Racial disparities in preterm birth rates and short inter-pregnancy interval: an overview

CAROL J. HOGUE[1], **RAMKUMAR MENON**[2], **ANNE L. DUNLOP**[3], and **MICHAEL R. KRAMER**[1]

[1]Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, GA

[2]Department of Obstetrics & Gynecology, Division of Maternal-Fetal Medicine Perinatal Research, The University of Texas Medical Branch at Galveston, Galveston, TX

[3]Department of Family and Preventive Medicine, School of Medicine, Emory University, Atlanta, GA, USA

Abstract

Objective—We seek to expand on a biopsychosocial framework underlying the etiology of excess preterm birth experienced by African-American women by exploring short inter-pregnancy intervals as a partial explanatory factor.

Design—We conducted a qualitative analyses of published studies that met specified criteria for assessing the association of inter-pregnancy interval and preterm birth.

Methods—We determine whether inter-pregnancy interval is associated with preterm birth, what the underlying causal mechanism may be, whether African-American women are more likely than Caucasian women to have short intervals, and whether achieving an optimal interval will result in reduced African-American–Caucasian gap in preterm births.

Main Outcome Measures—Crude and adjusted odds ratios for preterm birth, with the referent group being the interval closest to the ‘ideal’ of 18–23 months and the exposed group having intervals <12 months or some subset of that inter-pregnancy interval.

Results—Inter-pregnancy interval less than six months increases preterm birth by about 40%. The mechanism may be through failure to replenish maternal nutritional stores. While there may not be an interaction between race and short inter-pregnancy interval, short intervals can explain about 4% of the African-American–Caucasian gap in preterm birth because African-American women are approximately 1.8 times as likely to have inter-pregnancy intervals of less than six months. Limited studies indicate that optimal intervals can be achieved through appropriate counseling and health care.

Conclusions—Excess risk for preterm birth may be reduced by up to 8% among African-Americans and up to 4% among Caucasians through increasing inter-pregnancy intervals to the optimal length of 18–23 months.

Correspondence: Carol J. Hogue, PhD, MPH, Women’s and Children’s Center, Department of Epidemiology, Rollins School of Public Health, Emory University, 1518 Clifton Road NE, Atlanta, GA 30322, USA., chogue@emory.edu.

Conflict of interest
The authors have stated explicitly that there are no conflicts of interest in connection with this article.

Keywords

Inter-pregnancy interval; African-American; preterm; health disparities; infant health

Introduction

Preterm birth (<37 completed weeks' gestation) accounts for nearly half (46%) of non-Hispanic African-American infant deaths (1) and more than 80% of the excess infant mortality of African-American as compared with Caucasian infants (2). Since 2006, when the preterm birth rate reached its peak in the USA, there has been a slight decline in the preterm birth rate, from 12.8% to 12.3% in 2008 (3). While this decline, which was observed for all racial and ethnic groups, may portend a reduced infant mortality rate, the continued alarmingly high African-American preterm birth rate demands increased attention. In 2008, 11.1% of non-Hispanic white and 17.5% of non-Hispanic black infants were born preterm (3). Among very preterm births (<32 weeks' gestation), there was a nearly 2.4-fold excess for non-Hispanic African-American (3.8%) compared with non-Hispanic white (1.6%) births. These rates have not declined, and deaths among very preterm infants now account for half of the excess deaths among African-American as compared with Caucasian infants (2).

Recent efforts to understand the African-American–Caucasian racial disparity in preterm and very preterm births has focused on complex interrelations among biopsychosocial factors that are known or suspected to be greater among African-Americans (4). We recognize that these factors may work in concert and cannot be examined fully in isolation. Rather, a comprehensive understanding and ultimate elimination of excess preterm birth for African-Americans will require studies that include understanding of interactions among relevant factors. It is likely, as well, that effective interventions will encompass actions on more than one factor at a time. Nevertheless, it is useful to examine specific risk factors, particularly ones that can be prevented with known interventions, to develop priorities for action. One of these risk factors is inter-pregnancy interval, i.e. the time between the end of one pregnancy and conception of the next, which has been studied as a risk factor for preterm birth in second-and higher-order births.

Women with short inter-pregnancy intervals may or may not have intended to become pregnant again soon after their index pregnancy. In this article, we describe the possible etiologic role of a short inter-pregnancy interval per se on racial disparity in preterm birth. We distinguish this from a population-level explanation of excess preterm birth and infant mortality attributable to different rates of births from unwanted conceptions (5). At the population level, unwanted fertility contributes to racial disparity because women who have unwanted pregnancies are more likely to be at risk of preterm birth for reasons unrelated to the desirability of the pregnancy. While reducing unwanted fertility through improved contraception would undoubtedly reduce the African-American–Caucasian gap in preterm birth, the route of improvement is not an etiologic one. The questions for this article are whether a short inter-pregnancy is a true risk factor for preterm risk and, if so, whether differences in length of inter-pregnancy interval between racial groups in the USA may contribute to the black–white gap in preterm birth.

Material and methods

Our methodology was first to determine whether a short inter-pregnancy interval (variously defined as less than three months, less than six months, <12 months or <18 months, with 18–23 months defined as the lowest risk or ideal inter-pregnancy interval) is associated with preterm birth and, if so, what the underlying causal mechanism may be. Second, we assessed whether African-American women are more likely than Caucasian women to have short inter-pregnancy intervals. Finally, we examined what evidence exists to indicate that extending all inter-pregnancy intervals to at least 18 months will result in reducing the racial gap in preterm birth rates.

In an earlier systematic review, Conde-Agudelo and colleagues (6) selected cohort, cross-sectional or case–control studies that specified the exposure as birth-to-conception (i.e. inter-pregnancy intervals). To be included in the meta-analysis, studies also were required to have reported results for at least four inter-pregnancy interval strata and to have controlled statistically for maternal age and at least one measure of socio-economic status.

We updated the review by Conde-Agudelo et al. using similar criteria to review studies published since 2006. We chose studies that were entered into PubMed by January 2010. Our search terms were ‘birth spacing’ or ‘birth interval’ or ‘inter-pregnancy interval’ and ‘preterm’ or ‘low birthweight’. In addition, we examined references of relevant studies in a ‘snowball’ to identify other studies that might have been missed in the initial search. We did not limit our search to any specific language or country. We did not require the studies to report at least four intervals, as done by Conde-Agudelo et al.; rather, we included any study that compared intervals <18 months with intervals ≥18 months. The principal summary measures used were the crude and adjusted odds ratios.

As this is an overview and not designed to be a systematic review, we conducted a qualitative analysis rather than a quantitative meta-analysis of the six studies that met the following criteria: presentation of odds ratios for inter-pregnancy interval, control for maternal age and control for at least one socio-demographic or socio-economic factor. We assessed risk of bias at the level of individual studies through how they defined the outcome level of gestational age. Studies varied by their definition of preterm birth and also by the minimum and maximum gestational age of their comparison group. Studies were considered to be higher quality if they compared very preterm birth (<32 or <34 weeks) with full-term birth (37–41 weeks) control subjects. Studies that limited analyses to singleton pregnancies, excluded pregnancies with congenital anomalies and limited cases to spontaneous preterm delivery were also considered to have less bias than studies that were less exclusive. We assessed risk of bias at the study level by their choice of control variables and presentation of adjusted odds ratios.

We further reviewed the literature for hypotheses regarding causal mechanisms. We used the same search strategy as described above, except that we did not limit the publication date to later than 2006. For intervention studies, we searched PubMed for ‘intervention’ or ‘prevention’ and ‘inter-pregnancy interval’. For both pathophysiology and intervention searches, we made use of the snowball method as well.

Results

The association between a short inter-pregnancy interval and subsequent preterm birth

More than 50 years ago, Yerushalmy et al. observed that infants born to women giving birth in Kauai who had inter-pregnancy intervals of less than 11 months had an increased risk of neonatal death (7). It is likely that this association was related to their increased risk of preterm birth. Twenty-five years later, Winikoff et al. published a systematic review of the effects of inter-pregnancy interval on maternal and child health (8). While noting many methodological problems and limitations of these early studies, Winikoff et al. concluded that very short inter-pregnancy intervals may result in a higher risk of preterm births. These early reviews did not produce quantitative estimates of the effect of short inter-pregnancy intervals on preterm birth risk, but a more recent systematic review and meta-analysis did provide quantitative effect estimates (6). Of the 67 studies that met reviewers’ criteria, 30 reported results on preterm birth. Twenty-one of the 30 studies found an association between short intervals and preterm birth. In a meta-analysis performed on 16 of these studies, Conde-Agudelo and colleagues found that risk of preterm birth was associated with very short and very long inter-pregnancy intervals (6). Compared with the lowest risk interval of 18–23 months, inter-pregnancy intervals of less than six months had a pooled unadjusted odds ratio (with 95% confidence interval) of 1.77 (1.54–2.04) and a pooled adjusted odds ratio of 1.40 (1.24–1.58). Intervals of 6–17 months had a smaller increased risk of preterm birth [pooled adjusted odds ratio of 1.11 (1.03–1.20) compared with interval of 18–23 months].

The studies reviewed by Conde-Agudelo et al. (6) provide strong evidence of a true risk of very short (less than six months) inter-pregnancy intervals on preterm birth of the next child. However, their conclusions cannot be considered definitive. Study results were heterogeneous, and the pooled adjusted odds ratio was reduced to 1.30 (1.23–1.38) when the most extreme study result was removed. Their analysis has also been criticized for failing to control for potential confounders that vary by country (such as breastfeeding, which has an impact on postpartum fertility) and which might help to explain the heterogeneity of results (9). Since publication of this systematic review, several investigations of the association of inter-pregnancy interval and subsequent preterm birth have contributed additional and, in some instances, more refined information about this relation (10–20). Studies that met Conde-Agudelo and colleagues’ inclusion criteria, but which were published after their review, are summarized in Table 1, along with the key results from the Conde-Agudelo review for comparison.

Each of the six studies summarized in Table 1 has methodological issues. Some issues are common across studies, while others pertain to fewer studies. One common problem pertains to the definition of ‘exposed’ and ‘unexposed’. Exposure is defined by the length of the inter-pregnancy intervals. There is heterogeneity in the categorization of the inter-pregnancy interval defined as exposed. Three investigators used less than six months as the definition for short intervals (14,15,17), one used less than seven months (18), one divided the less than six month interval into two subintervals (16), while one used <18 months (19). There is also heterogeneity in the categorization of the inter-pregnancy interval defined as unexposed. There is a well-documented 'J-shaped' curve of preterm birth associated with inter-pregnancy intervals, with the increased preterm birth risk for longer intervals possibly associated with underlying subfecundity and other maternal morbidities (6,14). None of the studies used the 'ideal' inter-pregnancy interval of 18–23 months for the comparison with short inter-pregnancy intervals. Three chose to compare short intervals with intervals >18 or ≥18 months (14,16,19). The advantage to this approach is to increase the sample size of control subjects, but the greater disadvantage is lumping longer intervals with the ideal intervals. Thus, including births with longer intervals in the comparison group would tend to underestimate the effect of short intervals. One study compared intervals of less than seven to seven months or more (18). This would exacerbate the underestimation issue by including some shorter intervals at presumably higher risk along with the longer intervals. The only study that approximated an ideal comparison used 12–23 months (17).

Case definition, i.e. preterm birth, also varied among studies, with some examining only the larger category of <37 weeks (16,19), while others chose <35 weeks (14) and others made a distinction between early preterm birth and moderate or later preterm birth (14,15,17,18). Making valid comparisons across studies using the same case definition also requires that they use the same control definition. Unfortunately, the studies varied in their definition of control group as well. One used births >35 weeks' gestation (14), while another used >36 weeks (18), and three used >37 weeks (15,17,19). When subcategories of preterm birth are analyzed within a study, it is preferable to use the same comparison group for all subanalyses. However, two of the three studies with subgroup analyses chose to compare with all other births, making it difficult to assess a dose–response relation (14,17).

All studies limited their analysis to the inter-pregnancy interval between the first and second birth. Also, all excluded late fetal deaths and multiple gestations. However, other study exclusions varied across studies. Live births <20 weeks' gestation were excluded from two studies (14,16). Congenital anomalies were excluded in two studies (14,19). Only one study examined spontaneous preterm births (18), while the other investigations included all preterm births.

Special populations in the USA were investigated, including women whose first birth was >35 weeks' gestation (14), women who were at least 20 years old at the time of their first birth (15), and women whose first and second births occurred before they reached 20 years of age (16). Other studies were conducted in Israel (17), Portugal (18) and Sudan (19). The latter two studies were hospital based, whereas the rest were population-based analyses of vital records data. There is also a considerable difference in variables chosen to control for confounding as well as in the comparison groups (Table 1 footnotes). Finally, despite these considerable differences, the results were remarkably similar. In Missouri, inter-pregnancy interval of less than six months appeared to be an independent risk factor for preterm birth (14,15,20), with adjusted odds ratios around 1.5 and possibly increasing with decreasing gestational age. Likewise, women with no previous preterm birth were at 50% increased risk of preterm birth of their next pregnancy if the inter-pregnancy interval was less than six months (14). Conversely, there appeared to be a doubling of risk for teenagers in Milwaukee (WI, USA) who have a short interval between two births prior to reaching their twentieth birthday (16). For an interval less than three months, the odds ratio was 2.04. For an interval of three to five months the odds ratio was 2.36.

Outside the USA, the observed excess risk of preterm birth following short inter-pregnancy intervals varies from 20% in Israel (17) to 360% for early, spontaneous preterm births in Portugal (18). The study by Adam et al. (19), with a broader interval of <18 months, reported an adjusted odds ratio of 2.3. This study emphasized the need to assess the impact of inter-pregnancy intervals in low-resource countries, such as Sudan, within the context of overall maternal health.

Viewed overall, it appears that the increased risk for preterm birth associated with an inter-pregnancy interval of less than six months is at least 40%, as previously reported (6,21).

Discussion

Hypothesized mechanisms to explain the increased risk of preterm birth associated with very short inter-pregnancy intervals

For over 20 years, investigators have been attempting to determine whether the observed associations between poor pregnancy outcomes and prior short inter-pregnancy intervals are causal or rather merely co-associated, with other, causal agents (22). It is widely recognized that women who experience miscarriage, late fetal death or neonatal loss are motivated to ‘replace’ the loss quickly (23,24). Also, women who are at risk of poor pregnancy outcomes because of socioeconomic factors are more likely to experience a shorter inter-pregnancy interval because of an unplanned pregnancy. If short intervals are due exclusively to replacement of prior pregnancy loss or to socio-demographic factors that would not be mitigated by increasing the inter-pregnancy interval, the observed association between intervals less than six months and subsequent preterm birth would not have public health relevance. However, as shown in Table 1, results of studies that limit analyses to women with no poor prior pregnancy outcomes and that control for maternal age, parity, social factors and other hypothesized confounders show a consistent residual effect of the short interval of at least 40%. In an earlier study, after controlling for explanatory variables in a study of Scottish women delivering from 1992 to 1998, Smith and colleagues estimated the population attributable risk for inter-pregnancy intervals less than six months to be 6.1% for very preterm birth (24–32 weeks) and 3.9% for moderate preterm birth (33–35 weeks) (23).

One causal hypothesis for this residual effect is that women are nutritionally depleted by pregnancy and require a certain amount of time to replenish their nutritional stores (25–27). In particular, folate (27) or iron (26) stores may require longer than six months to become replenished post-delivery. As inadequate stores of these and other essential nutrients are associated with increased risk of preterm birth (28), failure to allow sufficient time to replenish essential nutrients may help to explain why women with short inter-pregnancy intervals are at increased risk of preterm birth. Moreover, the association between short inter-pregnancy intervals and USA racial groups may help to explain why African-American women enter pregnancy with a higher risk of reduced essential nutrients (28).

Other causal hypotheses for the residual effect of inter-pregnancy interval on risk of preterm birth that have been proposed include increased maternal stress, possibly related to the mother's postpartum state and the demands of the young infant (29), as well as infections. Infections that contributed to the index preterm birth (30) or the risk of acquiring such infections are more likely to be present with a short inter-pregnancy interval. Also, poorly controlled chronic health conditions that may have contributed to the index preterm birth are more likely to remain poorly controlled in the setting of a short inter-pregnancy interval. Even with medical attention, there may be inadequate time for the recovery of physiological mediators related to hormonal and other changes associated with the previous pregnancy or birth. However, none of these hypotheses has been adequately evaluated via appropriate research studies at this time.

The association between short inter-pregnancy interval and risk of preterm birth among African-American women

Most investigators report that when compared with Caucasian women, African-American women have shorter inter-pregnancy intervals and, in particular, intervals of less than six months. Among women in the military from 1983 to 1993, African-American women were 4.4 times as likely as Caucasian women to conceive within six months of their previous birth (31). In the USA as a whole from 1989 to 1991, African-American women were 1.8 times as likely as all women to have an inter-pregnancy interval of less than six months (32). About 25% of non-Hispanic black women had inter-pregnancy intervals <12 months, compared with about 18.5% of non-Hispanic white women. For intervals less than six months, the black–white gap was greater: 10.5% of non-Hispanic blacks but only 5.7% of non-Hispanic whites have intervals less than six months. The difference between these estimates and those of Rawlings and colleagues (31) was largely due to a much larger proportion of African-American women in the military (29.9%) compared with in the nation as a whole (10.5%) with inter-pregnancy intervals of less than six months' duration.

Prevalence of short inter-pregnancy intervals appears to vary by state of residence, but the black–white prevalence ratio appears to be more similar. In Michigan from 1993 to 1998, inter-pregnancy intervals of less than six months were documented for 10.3% of African-Americans' second births, but only 5.8% of Caucasians' second births, a risk ratio of 1.8 (33). In contrast, in Missouri from 1989 to 1997, less than six-month inter-pregnancy intervals for second births were 16.7% of African-Americans and 8.4% of Caucasians, for a risk ratio of 1.99 (14). Among low-risk women in Georgia, with second-born infants delivered from 1989 to 1992, African-American women were 1.89 times as likely as Caucasian women to conceive within six months of the first birth (34). More recently, second births in California between 1999 and 2004 were assessed for racial differences in inter-pregnancy interval (12). First-to-second intervals for African-American as compared with Caucasian women were 1.17 times as likely to be less than six months (95% confidence interval 1.04–1.32). For the even shorter inter-pregnancy interval of less than three months, the African-American/Caucasian odds ratio was 1.44 (1.16–1.79). Whether the lower odds ratios for the California study are related to a temporal reduction in the African-American/Caucasian ratio for shorter intervals or a reflection of geospatial differences is not known.

Among women with short inter-pregnancy intervals, African-American and Caucasian women may be at equivalent risk for preterm birth in the subsequent pregnancy, although the evidence is somewhat inconsistent. Three studies reviewed by Conde-Agudelo et al. (6) tested for interaction between race and inter-pregnancy interval (33–35). In all three, the test for interaction was not significant. While the overall preterm risk for African-American infants was elevated in all studies, there were no significant racial differences in inter-pregnancy-specific odds ratios for preterm birth. Likewise, Bryant and Madden (13) found that for second-born infants in California, born between 1999 and 2004, there was no interaction for preterm birth risk by race and inter-pregnancy interval, while controlling for preterm birth of the first-born infant. Conversely, in their study of military women, Rawlings and colleagues found that low birth-weight and preterm birth rates were higher among infants born to Caucasian women only if the inter-pregnancy interval was less than three months (11.6%, vs. 4.4% for longer inter-pregnancy intervals, $p=0.02$), whereas for African-American women, rates were elevated for infants conceived within nine months of the previous delivery (11.8 vs. 2.8%, $p<0.001$) (31).

In summary, compared with inter-pregnancy intervals of Caucasian women, the inter-pregnancy intervals of African-American women tend to be shorter and are about twice as likely to fall within the higher-risk ranges of less than six or <12 months. Khoshnood and colleagues estimated that approximately 8% of preterm birth among African-Americans, but only about 4% of preterm birth among Caucasians, can be attributed to inter-pregnancy intervals <12 months (32). Among women with shorter inter-pregnancy intervals, there may or may not be an interactive risk associated with African-American as compared with Caucasian women.

The potential impact of intervention to extend the interval between pregnancies on reducing the gap in preterm birth

Since African-American women are more likely to have short inter-pregnancy intervals, interventions to assist women to achieve an optimal inter-pregnancy interval should reduce both the overall risk of preterm birth for African-American infants and the African-American–Caucasian gap in preterm birth. There is some evidence that targeted care for high-risk women will increase their inter-pregnancy intervals. Olds and colleagues conducted a randomized clinical trial of prenatal and infant home visits by nurses for 473, mainly African-American, parous women who had at least two socio-demographic risk factors (i.e. unmarried, education <12 years or unemployed) (36). Women in the treatment group had significantly longer inter-pregnancy intervals (average 40.73 vs. 34.09 months, $p=0.002$) and were signifi-cantly less likely to conceive again within two years of the index pregnancy. In a more recent pilot study, Dunlop and colleagues provided inter-pregnancy care for 29 African-American women who delivered a very-low-birthweight infant at Grady Memorial Hospital in Atlanta (the main indigent-care hospital in the metropolitan Atlanta area) (37). One-third of the 21 women who completed the 24-month intervention were diagnosed and treated for previously unrecognized chronic disease, and one-fourth were diagnosed and treated for iron-deficiency anemia. Compared with five of 58 women in an historical cohort, none of the original 29 women conceived within nine months of the index pregnancy, and only five (compared with 29) conceived between nine and 18 months postpartum.

These small studies suggest that interventions for high-risk African-American women can reduce their risk of short inter-pregnancy intervals. Whether there is a concomitant reduction in subsequent preterm risk is not known. Larger randomized trials are needed to address this question.

Conclusion

To summarize the literature to date, conception within six months after birth increases the risk of preterm birth of the subsequent pregnancy, irrespective of the underlying risk profile for preterm birth. The evidence, while based on studies of mixed quality (none of the recent studies being highest quality), is compelling. An inter-pregnancy interval less than six months increases the risk of preterm birth of the subsequent pregnancy by about 40% over what can be expected for 18–23 months within groups of women categorized by socioeconomic and racial/ethnic status. An inter-pregnancy interval of 6–11 months increases the preterm birth risk by about 25% over the 18- to 23-month preterm birth risk. The mechanism may be through failure to replenish maternal nutritional stores or to re-establish an immune balance/tolerance or reprogramming of the uterine tissues. Approximately 8% of preterm births among African-Americans and 4% of births among Caucasians in the USA can be attributed to inter-pregnancy intervals <12 months. Almost twice as many African-American as Caucasian women have intervals less than six months and about one-fourth of African-American inter-pregnancy intervals are <12 months (vs. 18.5% of non-Hispanic white intervals). This means that even without an interaction between race and inter-pregnancy interval, an intervention that could extend inter-pregnancy intervals to the optimum 18–23 months would not only decrease preterm birth rates overall but also decrease the black–white gap in preterm birth rates.

Acknowledgments

Funding

The seminar series on which this article is based and this work are supported in part by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Reproductive, Perinatal, and Pediatric Health Training grant T32 HD052460.

This article followed from a four-part seminar series on causes of racial disparities in preterm birth held in the fall of 2009 at the Rollins School of Public Health, Emory University, Atlanta, GA, USA.

References

1. MacDorman MF, Callaghan WM, Mathews TJ, Hoyert DL, Kochanek KD. Trends in preterm-related infant mortality by race and ethnicity, United States, 1999–2004. Int J Health Serv. 2007; 37:635–41. [PubMed: 18072312]
2. Schempf AH, Branum AM, Lukacs SL, Schoendorf KC. The contribution of preterm birth to the Black–White infant mortality gap, 1990 and 2000. Am J Public Health. 2007; 97:1255–60. [PubMed: 17538050]
3. Hamilton BE, Martin JA, Ventura SJ. Births: preliminary data for 2008. Natl Vital Stat Rep. 2010; 58:1–17.

4. Kramer MR, Hogue CR. What causes racial disparities in very preterm birth? A bio-social perspective. Epidemiol Rev. 2009; 31:84–98. [PubMed: 19477907]
5. Collier S, Hogue C. Modifiable risk factors for low birth weight and their effect on cerebral palsy and mental retardation. Matern Child Health J. 2007; 11:65–71. [PubMed: 16802187]
6. Conde-Agudelo A, Rosas-Bermúdez A, Kafury-Goeta AC. Birth spacing and risk of adverse perinatal outcomes: a meta-analysis. JAMA. 2006; 295:1809–23. [PubMed: 16622143]
7. Yerushalmy J, Bierman JM, Kemp DH, Connor A, French FE. Longitudinal studies of pregnancy on the island of Kauai, Territory of Hawaii. I. Analysis of previous reproductive history. Am J Obstet Gynecol. 1956; 71:80–96. [PubMed: 13282976]
8. Winikoff B. The effects of birth spacing on child and maternal health. Stud Fam Plann. 1983; 14:231–45. [PubMed: 6648993]
9. Royce RA. Birth spacing: the long and short of it. JAMA. 2006; 295:1837–8. [PubMed: 16622147]
10. Hamad KA, Abed Y, Hamad BA. Risk factors associated with preterm birth in the Gaza Strip: hospital-based case-control study. La Revue de Santé de la Méditerranée orientale. 2007; 13:1132–41.
11. Mohsin M, Jalaludin B. Influence of previous pregnancy outcomes and continued smoking on subsequent pregnancy outcomes: an exploratory study in Australia. BJOG. 2008; 115:1428–35. [PubMed: 18700893]
12. Bryant A, Madden E. Risk of short inter-pregnancy intervals among women in California (poster session abstract #579). Am J Obstet Gynecol. 2009; 201:S214.
13. Bryant A, Madden E. How short is too short? The risk of preterm birth with inadequate birth spacing (poster session abstract #580). Am J Obstet Gynecol. 2009; 201:S214.
14. DeFranco EA, Stamilio DM, Boslaugh SE, Gross GA, Muglia LJ. A short inter-pregnancy interval is a risk factor for preterm birth and its recurrence. Am J Obstet Gynecol. 2007; 197:264.e1–6. [PubMed: 17826413]
15. Nabukera SK, Wingate MS, Kirby RS, Owen J, Swaminathan S, Alexander GR, et al. Inter-pregnancy interval and subsequent perinatal outcomes among women delaying initiation of childbearing. J Obstet Gynaecol Res. 2008; 34:941–7. [PubMed: 19012690]
16. Partington SN, Steber DL, Blair KA, Cisler RA. Second births to teenage mothers: risk factors for low birth weight and preterm birth. Perspect Sex Reprod Health. 2009; 41:101–9. [PubMed: 19493219]
17. Grisaru-Granovsky S, Gordon E-S, Haklai Z, Samuloff A, Schimmel MM. Effect of inter-pregnancy interval on adverse perinatal outcomes – a national study. Contraception. 2009; 80:512–8. [PubMed: 19913144]
18. Rodrigues T, Barros H. Short inter-pregnancy interval and risk of spontaneous preterm birth. Eur J Obstet Gynecol Reprod Biol. 2008; 136:184–8. [PubMed: 17490802]
19. Adam I, Ismail MH, Nasr AM, Prins MH, Smits LJM. Low birth weight, preterm birth and short inter-pregnancy interval in Sudan. J Matern Fetal Med. 2009; 22:1068–71.
20. Nabukera SK, Wingate ML, Owen J, Salihu HM, Swaminathan S, Alexander GR, et al. Racial disparities in perinatal outcomes and pregnancy spacing among women delaying initiation of childbearing. Matern Child Health J. 2009; 13:81–9. [PubMed: 18317891]
21. Zhu B-P. Effect of inter-pregnancy interval on birth outcomes: findings from three recent US studies. Int J Gynaecol Obstet. 2005; 89:S25–S33. [PubMed: 15820365]
22. Miller JE. Birth intervals and perinatal health: an investigation of three hypotheses. Fam Plann Perspect. 1991; 23:62–70. [PubMed: 2060613]
23. Smith GCS, Pell JP, Dobbie R. Inter-pregnancy interval and risk of preterm birth and neonatal death: retrospective cohort study. BMJ. 2003; 327:313–8. [PubMed: 12907483]
24. Stephansson O, Dickman PW, Cnattingius S. The influence of inter-pregnancy interval on the subsequent risk of stillbirth and early neonatal death. Obstet Gynecol. 2003; 102:101–8. [PubMed: 12850614]
25. Winkvist A, Rasmussen K, Habicht J-P. A new definition of maternal depletion syndrome. Am J Public Health. 1992; 82:691–4. [PubMed: 1566948]

26. Singh K, Fong YF, Arulkumaran S. Anaemia in pregnancy – a cross-sectional study in Singapore. Eur J Clin Nutr. 1998; 52:65–70. [PubMed: 9481535]
27. Smits LJM, Essed GGM. Short inter-pregnancy intervals and unfavourable pregnancy outcome: role of folate depletion. Lancet. 2001; 358:2074–7. [PubMed: 11755634]
28. Dunlop AL, Kramer MR, Hogue CJR, Menon R, Ramakrishnan U. Racial disparities in preterm birth: an overview of the potential role of nutrient deficiencies. Acta Obstet Gynecol Scand. 2011; 90:1332–1341. [PubMed: 21910693]
29. Kramer MR, Hogue CJ, Dunlop AL, Menon R. Preconceptional stress and racial disparities in preterm birth: an overview. Acta Obstet Gynecol Scand. 2011; 90:1307–1316. [PubMed: 21446927]
30. Menon R, Dunlop AL, Kramer MR, Fortunato SJ, Hogue CJ. An overview of racial disparities in preterm birth rates: caused by infection or inflammatory response? Acta Obstet Gynecol Scand. 2011; 90:1325–1331. [PubMed: 21615712]
31. Rawlings JS, Rawlings VB, Read JA. Prevalence of low birth weight and preterm birth in relation to the interval between pregnancies among white and black women. N Engl J Med. 1995; 332:69–74. [PubMed: 7990903]
32. Khoshnood B, Lee KS, Wall S, Hsieh HL, Mittendorf R. Short inter-pregnancy intervals and the risk of adverse birth outcome among five racial/ethnic groups in the United States. Am J Epidemiol. 1998; 148:798–805. [PubMed: 9786235]
33. Zhu B-P, Haines KM, McGrath-Miller K, Boulton ML. Effect of the interval between pregnancies on perinatal outcomes among white and black women. Am J Obstet Gynecol. 2001; 185:1403–10. [PubMed: 11744916]
34. Adams MM, Kelaney KM, Stupp PW, McCarthy BJ, Rawlings JS. The relationship of inter-pregnancy interval to infant birthweight and length of gestation among low-risk women, Georgia. Paediatr Perinat Epidemiol. 1997; 11(Suppl 1):48–62. [PubMed: 9018715]
35. Kallan JE. Effects of inter-pregnancy intervals on preterm birth, intrauterine growth retardation, and fetal loss. Soc Biol. 1992; 39:231–45. [PubMed: 1340042]
36. Olds DL, Kitzman H, Hanks C, Cole R, Anson E, Sidora-Arcoleo K, et al. Effects of nurse home visiting on maternal and child functioning: age-9 follow-up of a randomized trial. Pediatrics. 2007; 120:e832–45. [PubMed: 17908740]
37. Dunlop AL, Dubin C, Raynor BD, Bugg GW Jr, Schmotzer B, Brann AW Jr. Inter-pregnancy primary care and social support for African-American women at risk for recurrent very-low-birthweight delivery: a pilot evaluation. Matern Child Health J. 2008; 12:461–8. [PubMed: 17712612]

Table 1

Selected studies of preterm birth associated with short inter-pregnancy intervals published since 2006, with comparative data from the meta-analysis published in 2006.

Source	Place, time and study type	Number in sample of shortest intervals	Shortest inter-pregnancy interval	Variables controlled[a]	Preterm birth definition (weeks' gestation)	Crude odds ratio (95% confidence interval)	Adjusted odds ratio (95% confidence interval)
Conde-Agudelo et al. (6)	Meta-analysis	8 studies	<6 vs. 18–23 months	Variable (4 or more)	Not specified	Pooled 1.77 (1.54–2.04)	Pooled 1.40 (1.24–1.58)
		9 studies	6–11 vs. 18–23 months	Variable (4 or more)	Not specified	Pooled 1.23 (1.16–1.31)	Pooled 1.14 (1.10–1.17)
		9 studies	12–17 vs. 18–23 months	Variable (4 or more)	Not specified	Pooled 1.11 (1.03–1.20)	Pooled 1.07 (1.03–1.11)
DeFranco et al. (14)	Missouri, 1989–1997, longitudinal	15 200	<6 vs. >18 months	1, 2, 3, 4, 5	<35	2.28 (2.12–2.48)	1.48 (1.37–1.61)
					32–35	2.11 (1.92–2.31)	1.46 (1.32–1.62)
					28–32	2.62 (2.28–3.02)	1.57 (1.35–1.83)
					20–28	2.55 (2.09–3.10)	1.41 (1.13–1.76)
	Subanalysis: preceding birth >35 weeks' gestation	14,196	<6 vs. >18 months	2, 3, 4, 5	<35	2.19 (2.01–2.37)	1.50 (1.37–1.64)
Nabukera et al. (15)	Missouri, 1978–1997, longitudinal, age at first birth >20 years	13 708[b]	<6 vs. >6 months	2, 3, 10, 11, 13, 14, 17, 18, 21	<37	1.34 (1.26–1.42)	1.12 (1.05–1.20)
					32–36	1.29 (1.21–1.38)	1.10 (1.02–1.170)
					28–31	1.87 (1.46–2.41)	1.48 (1.13–1.93)
					24–27	1.95 (1.42–2.66)	1.38 (0.97–1.95)
Partington et al. (16)	Milwaukee, WI, USA, 1993–2002, longitudinal, 1st and 2nd births to teenagers	293 <3 months, 568 3–5 months	<3 vs. >18 months	2, 3, 5, 10, 11, 12, 14, 18, 19, 20	<37	1.9[c]	2.04[c]
			3–5 vs. >18 months		<37	2.16[c]	2.36[c]
Grisaru-Granovsky et al. (17)	Israel, 1993–2005, longitudinal,	36 020	<6 vs. 12–23 months	5, 6, 7, 8, 9	<37		1.23 (1.17–1.29)
					<33		1.22 (1.08–1.37)
Rodrigues & Barros (18)	Portugal, 25 units, case–control		<7 vs. >7 months	2, 5, 10, 11, 12, 13, 14	Spontaneous preterm delivery: 34–36, *n*=172	0.8 (0.32–1.83)	Not provided
					32–34, *n*=91	3.9 (1.91–8.10)	3.6 (1.41–8.98)
Adam et al. 2009 (19)	Sudan, Khartoum, one hospital, 2007–2008, cross-sectional	388	<18 vs. >18 months	2, 5, 7, 15, 16	<37		2.3 (1.1–4.7)

Note:

[a]Variables controlled: 1, previous preterm birth <35 weeks' gestation; 2, prenatal care; 3, black race; 4, Medicaid; 5, maternal age; 6, ethnicity; 7, parity; 8, previous infant <2500g; 9, previous infant >3800g; 10, marital status; 11, education; 12, previous poor outcome; 13, pre-pregnancy body mass index; 14, smoking; 15, urban/rural; 16, anemia; 17, maternal complications; 18, year of birth; 19, weekly prenatal weight gain; 20, household income; and 21, age at first birth 20–29 cf. 30–50 years.

[b]Estimated from tables in Nabukera et al. (20).

[c]Confidence intervals not provided; p<0.001.