A Population-based Matched Sibling Analysis Estimating the Association between First Interpregnancy Interval and Birth Outcomes

Annette K. Regan, Stephen J. Ball, Joshua L. Warren, Eva Malacova, Amy Padula, Cicely Marston, Natasha Nassar, Fiona Stanley, Helen Leonard, Nicholas de Klerk, and Gavin Pereira[1]

Correspondence to:

Dr Annette Regan, School of Public Health, Curtin University, GPO Box U1987, Perth WA 6845 (e-mail: annette.regan@curtin.edu.au)

Author Affiliations: School of Public Health, Curtin University, Bentley, Western Australia, Australia (Annette K. Regan, Eva Malacova, and Gavin Pereira)**;** School of Nursing, Midwifery and Paramedicine, Curtin University, Bentley, Western Australia, Australia (Stephen J. Ball)**;** School of Public Health, Yale University, New Haven, Connecticut, United States (Joshua L. Warren)**;** School of Medicine, University of California San Francisco, San Francisco, California, United States (Amy Padula)**;** London School of Hygiene and Tropical Medicine, London, United Kingdom (Cicely Marston)**;** School of Public Health, University of Sydney, Sydney, New South Wales, Australia (Natasha Nassar); and Telethon Kids Institute, University of Western Australia, Subiaco, Western Australia, Australia (Fiona Stanley, Helen Leonard, Nicholas de Klerk)

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Abstract

The association between a single interpregnancy interval (IPI) on birth outcomes has not yet been explored using matched methods. We modelled the odds of preterm birth, small-for-gestational age and low birthweight in a second, liveborn infant in a cohort of 192,041 sibling pairs born in Western Australia between 1980 and 2010. The association between IPI and birth outcomes was estimated from the interaction between birth order and IPI (with 18–23 months as the reference category), using conditional logistic regression. Matched analysis showed the odds of preterm birth were higher for siblings born following an IPI <6 month (adjusted Interaction Odds Ratio [IOR]: 1.22; 95% CI: 1.06, 1.38) compared with 18–23 month IPI. There were no significant differences for IPI <6 months for other outcomes (small-for-gestational age or low birthweight). This is the first study to use matched analyses to investigate the association between a single IPI on birth outcomes. IPI <6 months were associated with increased odds of preterm birth in secondborn infants, although the association is likely smaller than previously estimated by unmatched studies.

Keywords

Birth Intervals; Family Planning; Siblings; Preterm Birth; Pregnancy Outcome

Abbreviations

IPI, interpregnancy interval

Adverse birth outcomes remain a leading cause of infant death, neonatal morbidity and childhood illness in high-income countries.[1] Epidemiological studies have shown the interval between pregnancies may be linked to length of gestation, fetal growth, and birthweight.[2] Notably, intervals <6 months have been associated with increased odds of preterm birth,[3,4] low birthweight,[2] small-for-gestational age,[5] congenital anomalies,[5] and perinatal death.[4,6] Considering this, the World Health Organization recommends at least two years between pregnancies in order to minimize the risk of adverse perinatal outcomes.[7]

While several hypotheses have been proposed, including nutritional depletion and anemia post-birth,[7,8] a causal mechanism for the association between birth spacing and adverse birth outcomes has not yet been confirmed. It is also unclear how much of the association between interpregnancy interval (IPI) and perinatal outcomes is causal, and how much is due to other factors associated with interpregnancy interval resulting in confounding. IPI is correlated with many potential confounders, including socioeconomic status, age, obstetric history, and race,[9,10] all of which relate to maternal characteristics. For example, in the US, short IPIs are more common among mothers with higher education and non-Hispanic black mothers.[10]

Previous research into the association between IPI and birth outcomes has largely relied on traditional retrospective cohort studies.[2,4-6] This raises the possibility that, despite efforts to adjust for confounders, the association between IPI and birth outcomes could be induced by unmeasured or poorly measured maternal characteristics rather than being caused by the interval itself. Several recent studies have addressed the potential for unmeasured confounding by applying a sibling-matched (also known as 'maternally-matched') design.[11,12] These studies have controlled for maternal factors that remain constant between pregnancies, such as genetic factors and some aspects of lifestyle, by comparing two IPIs per mother. For all three studies that applied a matched design, effect estimates were attenuated in comparison

to results from an unmatched design, implying that there may have been consistent, unmeasured confounding occurring.[3,11,12]

A key limitation of the sibling-matched designs applied previously is that they utilize information on three or more consecutive pregnancies per mother in order to provide two IPIs per mother required for matching. Considering that 35-42% of multiparous women in Australia and other high-income countries have only two children[13,14] and maternal characteristics are known to vary by parity,[15] the results of previous matched studies may not be representative of the entire population of multiparous women. This study aims to investigate the association between the first IPI and birth outcomes using a sibling matched design and to compare these results with a traditional unmatched cohort analysis.

METHODS

We created a retrospective cohort of first and secondborn singleton births in Western Australia between 1980 and 2010. We aimed to measure the association between adverse birth outcomes and the interval between first and second liveborn pregnancies, accounting for individual predisposition to these outcomes.

Data source and definitions

Maternal and infant information was derived from the Midwives Notification System, a statutory data collection of all births in Western Australia ≥20 weeks gestation. This data collection covers >99% of births in Western Australia.[16] For consistency with previously published studies,[3,11,12] we restricted the dataset to include consecutive liveborn singleton infants. Date of birth, infant weight, gestation, and sex are variables included in this data collection. The accuracy of these variables is estimated to exceed 98%.[16] IPI was defined as the time between birth of the first infant and estimated conception of the second infant. Consistent with previous studies,[3,11,12] intervals were grouped into seven categories: <6

months, 6–11 months, 12–17 months, 18–23 months, 24–59 months, and ≥60 months, with 18–23 months as the referent interval. Birth outcomes included preterm birth (gestation <37 weeks), low birthweight (<2500 grams), and small-for-gestational age (<10th percentile for birthweight by sex and gestation based on the birthweight distribution in five calendar-year blocks). We performed additional supplemental analyses which accounted for categories of preterm brith, including spontaneous and iatrogenic, moderate (gestational age of 33–36 weeks), very (gestational age of 28–32 weeks), and extreme (gestational age of <28 weeks) preterm birth. Information on potential confounding factors including maternal age, race (Caucasian or non-Caucasian), and residence (Perth metropolitan or non-metropolitan), as recorded by the medical professional attending the birth was also ascertained. Socioeconomic status was derived from the mother's Statistical Local Area of residence based on the Index of Relative Socioeconomic Advantage and Disadvantage provided by Australian Bureau of Statistics. These scores were grouped by quintiles relative to the population in Western Australia.[17]

Statistical analysis

Characteristics of women were compared by first IPI, using chi-square tests for independence. We then used a sibling-matched design that requires only a single IPI per mother, based on a method previously applied by Cheslack-Postava et al[18] which measured the association between IPI and the incidence of autism. In traditional cohort studies, the first birth would not be included in the model and is therefore non-informative. However, in a sibling-matched analysis, information from the first birth is included in the model, and a conditional logistic regression model can be used to estimate the association between IPI and outcomes in the second birth accounting for covariate information within clusters.[19] In a sibling-matched analysis, more information on the mother is included which can allow for more comprehensive adjustment of maternal factors.

In our traditional cohort analysis, which does not account for sibling pairs, we estimated the unmatched odds of adverse birth outcomes in the second birth, as a function of IPI category, using logistic regression. As part of this unmatched model, we adjusted for age, race, socioeconomic status, and birth year. The statistical model is given as $Y_i|p_i \sim \text{Bernoulli}(p_i), i = 1, \ldots n,$ where

$$\text{logit}(p_i) = \text{x}_i^{\text{T}}\beta + \sum_{j=1}^{5} \theta_j I(\text{IPI}_i \in c_j).$$

In this model, only second births are of interest, the first birth does not contribute any information. Y_i is equal to one if the second birth from birth pair *i* results in the adverse outcome of interest; *n* is the total number of birth pairs in the study; p_i is the probability that the second birth from pair *i* results in the adverse outcome of interest; x_i is a vector of covariates specific to the second birth of pair *i* including an intercept term, maternal age at delivery, maternal race, maternal socioeconomic status, and year of birth; and β is a vector of unknown regression coefficients describing the association between the covariates and the probability of an adverse outcome.

For the sibling-matched design, we applied a conditional logistic regression model which estimated the odds of adverse birth outcomes in the second birth with an interaction term for IPI and birth order. We adjusted for maternal age, birth year and socioeconomic status, as these factors may potentially vary over time. This statistical model is given as $Y_{ij}|p_{ij} \sim \text{Bernoulli}(p_{ij}), i = 1, \ldots n_d;\ j = 1,2,$ where

$$\text{logit}(p_{ij}) = \alpha_i + \text{x}_{ij}^{\text{T}}\beta + \sum_{k=1}^{5} \theta_k I(\text{IPI}_i \in c_k) I(j = 2) + \lambda I(j = 2).$$

Y_{ij} is equal to one if birth *j* (*j=1*, first birth; *j=2*, second birth) from birth pair *i* results in the adverse outcome of interest; n_d is the total number of discordant birth pairs in the study (i.e.,

exactly one birth in the pair resulted in an adverse outcome); α_i is the birth pair specific intercept; p_{ij} is the probability that birth *j* from pair *i* results in the adverse outcome of interest; x_{ij} is a vector of covariates specific to birth *j* of pair *i* including maternal age at delivery, maternal race, maternal socioeconomic status, and year of birth; β is a vector of unknown regression coefficients describing the association between the covariates and the probability of an adverse outcome; and λ is an unknown regression parameter describing the association between second births and the adverse outcome of interest.

In both models, the association between IPI for birth pair *i* (IPI_i; measured in months) and the probability of an adverse outcome for the second birth is described by the unknown parameters, $\theta_1, \ldots, \theta_5$. IPI is modeled as a categorical variable where $c_1 = [0,6), c_2 = [6,12), c_3 = [12,18), c_4 = [24,60)$, and $c_5 = [60, \infty)$ months; where [18,24) months represents the reference category and $I(.)$ is the indicator function taking a value of one if the input statement is true and the value of zero if the input statement is false. In the sibling-matched design model, we ensure that only second births ($j = 2$) are used to estimate the IPI associations through use of the indicator function in the IPI formula, $I(\text{IPI}_i \in c_j) I(j = 2)$.

Analyses were performed in SAS version 9.4 (SAS Institute, Cary, North Carolina, USA) (Web Appendix).

Supplemental analysis

To explore the potential influence of random measurement error, which would have occurred more commonly during the earlier years of the cohort (e.g., when there was a lower likelihood that births had ultrasound-confirmed gestation), we performed supplementary analyses, in which our matched analysis of sibling pairs was restricted to those born after 1995. To allow further comparison with matched analyses, an unmatched analysis restricted to discordant sibling pairs was also performed.

Ethics

This study was approved by the Department of Health Western Australia Human Research Ethics Committee (RA#2011/64) and the Curtin University Human Research Ethics Committee (RA#RDHS-30-16).

RESULTS

In Western Australia, a total of 961,312 singleton, live births were identified with a date of birth between 1980 and 2010. Of these, 946,499 had complete information on maternal and birth characteristics; 177,510 non-consecutive births were excluded, leaving 768,989 consecutive live births for analysis. Of these, we identified 192,041 firstborn and secondborn sibling pairs (Figure 1).

Interpregnancy interval between first and second birth

There was considerable variation in maternal characteristics by IPI between first and second pregnancy (Table 1). One-third of secondborn infants (34%) were born 24–59 months after their sibling. A small percent of secondborn infants were born following either shorter IPIs <6 months (3%) or longer IPIs of ≥60 months (8%). Short IPIs (<6 months) were more frequently observed for mothers who were younger at first birth (<20 years) (Table 1). IPIs of 18–23 months and 24–59 months were most frequently observed for women with the greatest relative socioeconomic advantage and least frequently for women with the greatest relative socioeconomic disadvantage (P<.001). In general, higher parity was associated with shorter IPIs and lower parity was associated with longer IPIs (P<.001).

Unmatched, cohort study results

Of the 192,041 secondborn, live singleton births, a total of 24,375 (13%) infants had an outcome of interest: 10,530 (5%) were born preterm, 14,574 (8%) were small-for-gestational age, and 6,849 (4%) were low birthweight. Of the preterm births, 4,097 (39%) were iatrogenic

and 6,433 (61%) were spontaneous. Compared to infants born 18–23 months after their firstborn sibling, infants born after shorter IPIs (<12 months after their firstborn sibling) had greater odds of preterm birth, with the highest odds of preterm birth associated with the shortest IPIs (<6 months; aOR: 1.67; 95% CI: 1.50, 1.85) (Table 2). While we observed similar results for spontaneous preterm births, we did not observe this association for iatrogenic preterm births (Web Table 1). The strongest association between short IPI <6 months and preterm birth was observed for very preterm births (aOR: 2.54; 95% CI; 1.95, 3.31).

Low birthweight was similarly associated with the shortest IPIs (<6 months: aOR: 1.51; 95% CI: 1.32, 1.71; and 6–11 months: aOR: 1.09; 95% CI: 1.00, 1.19). Infants born after IPIs ≥24 months also had greater odds of preterm birth (24–59 months: aOR: 1.14; 95% CI: 1.07, 1.21; and ≥60 months: aOR: 1.61; 95% CI: 1.49, 1.74) and low birthweight (24–59 months: aOR: 1.22; 95% CI: 1.13, 1.31; and ≥60 months: aOR: 2.02; 95% CI: 1.84, 2.22) compared to infants born after an 18–23 month IPI. Infants born after long IPIs (≥60 months) had greater odds of being born small-for-gestational age compared with infants born after an 18–23 month IPI (≥60 interval: aOR: 1.72; 95% CI: 1.61, 1.84). Shorter IPIs (<18 months) were not associated with any differences in the odds of small-for-gestational age (Table 2).

Matched, sibling-pair study results

In the matched anaysis of sibling pairs, the odds of preterm birth among secondborn siblings was significantly greater among siblings born after a short IPI (<6 months) or long IPI (≥60 months) in comparison to the odds of preterm birth among siblings born after an 18–23 month IPI (IOR: 1.22; 95% CI: 1.06, 1.38; IOR: 1.73; 95% CI: 1.58, 1.89) (*P*-value for interaction < .001) (Table 3). We observed no major differences in the odds of preterm birth for other IPIs in comparison to the odds of preterm birth for the reference category of 18–23 month IPI.

When we examined the association between IPI and categories of preterm birth, we found siblings born after a short IPI <6 months had higher odds of spontaneous preterm birth (IOR: 1.43; 95% CI: 1.23, 1.62) and preterm birth at a gestational age of 33–36 weeks (IOR: 1.37; 95% CI: 1.19, 1.55); however, there was no association between short IPI <6 months and iatrogenic preterm birth or between short IPI and very or extreme preterm birth (Web Table 2). Long IPI ≥60 months was consistently associated with increased odds of all categories of preterm birth.

Siblings born after an IPI ≥60 months had greater odds of being small-for-gestational age (IOR: 1.21; 95% CI: 1.08, 1.34) compared to siblings born after an 18–23 month IPI (*P*-value for interaction = .01). We observed no difference in the relative odds of small-for-gestational age for shorter IPIs. The odds of low birthweight in secondborn siblings was significantly greater among sibling born after an IPI ≥60 months (IOR: 1.52; 95% CI: 1.34, 1.70) compared to siblings born after an 18–23 months IPI (*P*-value for interaction < .001). No other difference was observed in the odds of low birthweight for siblings following shorter IPIs (Table 3).

Supplemental Analysis

For comparison, results of unmatched analyses restricted to the sample of discordant sibling pairs are presented in Web Table 3.

When we restricted the cohort to siblings with a date of birth after 1995 (n=87,100), we observed similar results to those of the primary analysis (Web Table 4). However, the confidence intervals for the adjusted interaction odds ratio measuring the association between short IPI <6 months and preterm birth crossed the null (IOR: 1.19; 95% CI: 0.96, 1.42; *P*=0.13).

DISCUSSION

Our study shows that short IPIs between first and second pregnancies are associated with higher odds of preterm birth, specifically spontaneous preterm birth at 33–36 weeks, but not with small-for-gestational age or low birthweight. To our knowledge, this is the first study using matched analysis to examine the association between a single IPI occuring between first and second liveborn siblings and birth outcomes. This sibling-matched design offers several benefits in that: i) information from the first birth is informative to the model; and ii) mothers who do not go on to have a third birth can be included in the analysis, extending the generalizability of study findings to all multiparous women.

There are several strengths to our study. First, because the epidemiological method we employed allowed us to include a first birth in the model, we had additional information available in the analysis and were potentially able to restrict some residual confounding present when only the second birth is considered. If uncontrolled, such confounding may artificially inflate risk estimates relating to the interpregnancy interval.[3,11,12] This is an important consideration, as our study, as well as previous studies,[20,21] found that women with shorter IPIs were more likely to be in sociodemographic groups that have an increased likelihood of adverse birth outcomes, even at first birth. Women with prior adverse birth outcomes are at greater risk of a future adverse outcome compared to women with prior healthy birth outcomes.[22] While these findings underscore the importance of well-controlled analyses for reliable measurement of the impact of IPI, no previous epidemiologic investigation has used a matched study design to explore the association of the first IPI exclusively. In addition, the coverage and validity of our data source is considered high.[16] As a result, our study would have included nearly all births to women with two or more live, consecutive singleton births with ≥20 weeks gestation in the State between 1980 and 2010.

Our matched analysis, which would have restricted uncontrolled confounding, identified attenuated estimates of the association between IPI and birth outcomes in comparison to unmatched analysis. Using the traditional approach of unmatched models, we observed a 1.5–2-fold increase in the odds of preterm birth and low birthweight associated with an IPI of <12 months in unmatched models compared to an 18–23 month IPI. In contrast, our results from matched models showed reduced non-significant associations between IPI <12 months and all these birth outcomes, with exception to a 1.2-fold increase in the odds of preterm birth associated with the shortest IPI (<6 months) and preterm birth. This attenuated association has been documented in previously published studies. Unmatched analyses elsewhere have reported similar results to our unmatched analysis, documenting a two-fold increase in the risk of preterm birth,[3,11,12,21,23] and a 1.3–1.7-fold increase in the odds of low birthweight[21] and small-for-gestational age[5] associated with interpregnancy intervals <6 months.[3,5,21,23] They have also shown intervals ≥60 months are associated with a 1.2–1.5-fold increase in the odds of preterm birth[3,11,12] and a 1.3–1.9-fold increase in the odds of small-for-gestational age[11,12] and low birthweight.[11,12] Previous studies using matched analyses have consistently shown that the the association between IPI and preterm birth, small-for-gestational age, and low birthweight is attenuated compared to unmatched studies,[3,11,12] thus suggesting that these measured associations might be due in part to unmeasured confounding. To date, only three matched studies have been conducted, two of which identified no significant increase in the risk of these adverse birth outcomes for births following intervals <12 months compared to an 18–23 month intervals.[11,12] The third matched study showed a 1.2-fold increase in the risk of preterm birth when there was less than six months between pregnancies, an estimate similar to our own.[3]

The potential impact of long IPIs on subsequent birth outcomes has been less commonly explored compared to short IPIs.[24] Although the associations between long IPI and birth

outcomes were mostly attenuated in matched analyses, we consistently observed higher odds of all adverse birth outcomes for long IPI ≥60 months in our matched models. These findings would be consistent with some of those from previous matched studies.[11,12] However, the evidence in this area is mixed, with inconsistent results published from matched studies. It is important to note that unlike short IPIs, long IPIs are much more prone to measurement error. Miscarriages and abortions are inherently difficult to capture in population-based studies, and the likelihood that these events occurred between pregnancies and are not accounted for in analyses is greatest for long IPIs. This would introduce some measurement error in the exposure variable for longer IPIs.[24] While we were able to account for stillbirths in our cohort and restrict our analyses to consecutive live births, we were not able to account for earlier pregnancy loss. Studies which can comprehensively measure pregnancy outcomes following a previous live birth would be useful for better evaluating the health impacts of long IPIs.

There are several other potential limitations to our study. First, there were a small number of sibling pairs with IPIs ≥120 months between pregnancies, which made evaluation of the impact of very long intervals on perinatal health not possible due to poorly powered analysis. Second, for consistency with the current WHO recommendations[7] and previously published studies, we restricted our dataset to live, singleton consecutive births, thus these results may not apply to women with a fetal death at any gestational age between births. Given there is currently no recommendation for the optimal IPI following a stillbirth,[7] future research on IPI should aim to include stillbirths. Third, although the sibling-matched design would have restricted time-invariant confounders, such as race and chronic medical conditions, it does not restrict some important time-varying confounders, such as maternal age and changes in risk behaviour. We have attempted to control for such confounders as adjustment variables in our models; however, we cannot discount the possibility that some temporal confounders (e.g., smoking cessation, interpregnancy weight gain) which we were unable to measure, may have

introduced residual confounding. Finally, an assumption of our approach was that the probability of the outcomes of the first and second birth are exchangeable conditional on the adjustment variables. The presence of unmeasured temporal confounders would violate this assumption. A related limitation is that parity, maternal age and birth year increase monotonically in time. This collinearity may induce additional uncertainty in the observed effect estimates.

For planning pregnancies, it is important to consider that IPIs <18 months may be associated with risk of preterm birth. Preterm birth rates are increasing in most countries,[25] and strategies for preventing preterm birth are high priority. Our findings are potentially valuable to clinicians when counseling around family planning and for families considering a second pregnancy. In our study and others,[3,11,12] the observed optimal IPI for infant health is 18-23 months, suggesting the current recommendation for at least two years between pregnancies for women in a high-income countries [7] may be too long.

Author affiliations: School of Public Health, Curtin University, Bentley, Western Australia, Australia (Annette K Regan, Eva Malacova, Gavin Pereira); School of Nursing, Midwifery and Paramedicine, Curtin University, Bentley, Western Australia, Australia (Stephen Ball); School of Public Health, Yale University, New Haven, Connecticut (Joshua L Warren); School of Medicine, University of California San Francisco, San Francisco, California (Amy Padula); London School of Hygiene and Tropical Medicine, London, United Kingdom (Cicely Marston); **S**chool of Public Health, University of Sydney, Sydney, New South Wales, Australia (Natasha Nassar); Telethon Kids Institute, University of Western Australia, Subiaco, Western Australia, Australia (Fiona Stanley, Nicholas de Klerk, Helen Leonard)

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Table 1. Characteristics of Women by Interval Between First and Second Live, Singleton Births in Western Australia 1980–2010 (N=192,041).

Characteristic	Interpregnancy interval												
	<6 months		6-–11 months		12–17 months		18–23 months		24–59 months		≥60 months		Chi square p-value
	No.	*Row %*	*No.*	*Row %*	*No.*	*Row %*	*No.*	*Row %*	*No.*	*Row %*	*No*	*Row %*	
Total	5,871	3	29,158	15	42,756	22	34,405	18	64,926	34	14,925	8	
Age at first birth													<0.001
14–19 years	1,354	5	3,648	15	4,049	16	3,224	13	8,727	35	4,141	16	
20–24 years	2,115	4	8,634	16	11,599	21	9,205	17	18,142	33	5,622	10	
25–29 years	1,499	2	9,865	15	15,967	24	13,084	19	23,231	34	3,717	6	
30–34 years	692	2	5,463	15	8,997	25	7,226	20	12,383	34	1,291	4	
≥35 years	211	3	1,548	19	2,144	26	1,666	20	2,443	30	154	2	
Race[a]													0.243
Caucasian	4,716	3	25,686	15	38,702	23	31,324	18	57,360	34	12,911	7	
Non-Caucasian	1,155	5	3,472	16	4,054	19	3,081	14	7,566	36	2,014	9	
Socioeconomic													<0.001

status[b]												
Lowest 20%	522	4	2,050	16	2,908	23	2,170	17	3,931	31	939	8
20–39%	538	3	2,484	16	3,524	23	2,700	17	4,946	32	1,241	8
40–59%	1,161	4	5,078	16	7,018	22	5,660	17	10,690	33	2,820	9
60–79%	2,132	3	10,209	15	14,817	21	12,316	18	23,959	35	5,618	8
Highest 20%	1,518	2	9,337	15	14,489	23	11,559	18	21,400	34	4,307	7
Residence												<0.001
Metropolitan	4,030	3	20,394	15	30,201	22	24,833	18	47,925	35	10,727	8
Non-metropolitan	1,841	3	8,764	16	12,555	23	9,572	18	17,001	32	4,198	8
Parity												<0.001
Two children	2,745	2	15,495	13	25,221	21	22,133	18	45,810	38	10,404	8
Three children	1,809	4	8,843	18	12,524	25	9,167	18	14,334	28	3,506	7
Four or more children	1,317	7	4,820	24	5,011	25	3,105	15	4,782	24	1,015	5

[a] *Race was defined as Caucasian or non-Caucasian, which included Aboriginal and Torres Strait Islander, Asian, Indian, Black, Polynesian, Maori and other races.*

[b] *Socioeconomic status was defined based on the Statistical Local Area of the mother and the Socioeconomic Index for Areas (SEIFA) score for relative advantage and disadvantage produced by the Australian Bureau of Statistics.*[17]

Table 2. Odds of Adverse Birth Outcomes in Secondborn Child as Estimated by an Unmatched Cohort Study, by Interpregnancy Interval between First and Second Consecutive, Live Births – Western Australia, 1980–2010 (N=192,041).

Birth outcome, by Interpregnancy interval	Total	Secondborn with outcome				adjusted	
	N	No.	%	OR[a]	95% CI[a]	OR[b]	95% CI[b]
Preterm birth							
<6 months	5,871	516	8.8	1.90	1.71, 2.10	1.67	1.50, 1.85
6–11 months	29,158	1,608	5.5	1.15	1.08, 1.22	1.10	1.03, 1.18
12–17 months	42,756	2,028	4.7	0.98	0.92, 1.05	0.97	0.91, 1.04
18–23 months	34,405	1,664	4.8	1.00	Referent	1.00	Referent
24–59 months	64,926	3,585	5.5	1.15	1.08, 1.22	1.14	1.07, 1.21
≥60 months	14,925	1,129	7.6	1.61	1.49, 1.74	1.61	1.49, 1.74
Small-for-gestational age							
<6 months	5,871	484	8.2	1.20	1.09, 1.33	0.96	0.87, 1.07
6–11 months	29,158	2,093	7.2	1.03	0.97, 1.10	0.95	0.90, 1.01
12–17 months	42,756	2,924	6.8	0.98	0.93, 1.04	0.96	0.91, 1.01
18–23 months	344,05	2,395	7.0	1.00	Referent	1.00	Referent
24–59 months	64,926	5,075	7.8	1.13	1.08, 1.19	1.14	1.08, 1.20
≥60 months	14,925	1,603	10.7	1.61	1.51, 1.72	1.72	1.61, 1.84
Low birthweight							
<6 months	5,871	325	5.5	1.89	1.67, 2.15	1.51	1.32, 1.71
6–11 months	29,158	1,029	3.5	1.18	1.08, 1.29	1.09	1.00, 1.19
12–17 months	42,756	1,265	3.0	0.99	0.91, 1.07	0.96	0.89, 1.05
18–23 months	344,05	1,032	3.0	1.00	Referent	1.00	Referent
24–59 months	64,926	2,362	3.6	1.22	1.13, 1.31	1.22	1.13, 1.31
≥60 months	14,925	836	5.6	1.92	1.75, 2.11	2.02	1.84. 2.22

[a] *Odds ratio and corresponding 95% confidence interval based on logistic regression.*

[b] *Adjusted for age, race, socioeconomic status, and calendar year of birth.*

Table 3. Odds of Adverse Birth Outcomes in Secondborn Child as Estimated by Matched Sibling-Pair Analysis, by Interpregnancy Interval between First and Second Consecutive, Live Births – Western Australia between 1980 and 2010 (N=192,041).

Birth outcome, by Interpregnancy interval	Total number of sibling pairs	Number of discordant pairs in analysis	Unadjusted interaction odds ratios		Adjusted interaction odds ratios[a]	
			IOR	95% CI	IOR	95% CI
Preterm Birth						
<6 months	5,871	799	1.25	1.09, 1.41	1.22	1.06, 1.38
6–11 months	29,158	2,772	1.10	0.97, 1.21	1.08	0.98, 1.19
12–17 months	42,756	3,526	1.11	1.01, 1.21	1.10	1.00, 1.20
18–23 months	34,405	2,944	1.00	Referent	1.00	Referent
24–59 months	64,926	6,118	1.07	0.98, 1.16	1.09	1.00, 1.18
≥60 months	14,925	1,681	1.59	1.47, 1.71	1.73	1.58, 1.89
Small-for-gestational age						
<6 months	5,871	934	0.98	0.83, 1.14	1.01	0.86, 1.16
6–11 months	29,158	3,773	0.99	0.90, 1.08	1.01	0.92, 1.11
12–17 months	42,756	5,376	1.03	0.95, 1.12	1.05	0.96, 1.13
18–23 months	34,405	4,460	1.00	Referent	1.00	Referent
24–59 months	64,926	9,190	1.04	0.96, 1.11	0.99	0.91, 1.07
≥60 months	14,925	2,517	1.46	1.36, 1.56	1.21	1.08, 1.34
Low birthweight						
<6 months	5,871	599	1.00	0.81, 1.19	1.00	0.81, 1.29
6–11 months	29,158	1,971	1.10	0.97, 1.23	1.11	0.98, 1.24
12–17 months	42,756	2,471	1.06	0.93, 1.18	1.06	0.93, 1.18

18–23 months	34,405	2,019	1.00	Referent	1.00	Referent
24–59 months	64,926	4,653	1.02	0.91, 1.13	1.00	0.87, 1.11
≥60 months	14,925	1,334	1.62	1.47, 1.76	1.52	1.34, 1.70

[a] *Odds of secondborn being born with outcome under analysis compared with odds of firstborn being born with same outcome; Interaction odds ratios (IOR) and corresponding 95% confidence interval adjusted by maternal age, socioeconomic status and calendar year of birth, where 18-23 month intervals is the reference category.*

Figure 1. Study Flow Chart for Selection of First and Secondborn Infants from Birth Records in Western Australia, 1980–2010.

Figure 1 Legend. Births were excluded if they were missing either maternal age, infant's sex, birthweight or gestational age, or mother's socioeconononomic status or residence.

Births Identified in Western Australia between 1980 and 2010
(*n* = 961,312)

Births Excluded with Missing Information
(*n* = 14,813)

Births with Complete Information
(*n* = 946,499)

Births Excluded to Mothers with Incomplete Pregnancy History
(*n* = 177,510)

Consecutive Births to Mothers in Western Australia
(*n* = 768,989)

Third or Higher Parity Births Excluded
(*n* = 384,907)

Births Included in Primary Analysis
(*n* = 384,082 / 192,041 sibling pairs)

Births Excluded Occurring Prior to 1995
(*n* = 209,882)

Births with a Date of Birth after 1995 Included in Supplemental Analysis
(*n* = 174,200 / 87,100 sibling pairs)