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RESEARCH

Re-evaluation of link between interpregnancy interval and adverse birth outcomes: retrospective cohort study matching two intervals per mother

Stephen J Ball *scientist*[1], Gavin Pereira *postdoctoral associate*[1 2], Peter Jacoby *associate professor*[1], Nicholas de Klerk *professor*[1], Fiona J Stanley *professor*[1]

[1]Telethon Kids Institute, University of Western Australia, PO Box 855, West Perth, WA 6872, Australia; [2]Yale Center for Perinatal, Pediatric and Environmental Epidemiology, Yale University, New Haven, CT 06510, USA

Abstract

Objective To re-evaluate the causal effect of interpregnancy interval on adverse birth outcomes, on the basis that previous studies relying on between mother comparisons may have inadequately adjusted for confounding by maternal risk factors.

Design Retrospective cohort study using conditional logistic regression (matching two intervals per mother so each mother acts as her own control) to model the incidence of adverse birth outcomes as a function of interpregnancy interval; additional unconditional logistic regression with adjustment for confounders enabled comparison with the unmatched design of previous studies.

Setting Perth, Western Australia, 1980-2010.

Participants 40 441 mothers who each delivered three liveborn singleton neonates.

Main outcome measures Preterm birth (<37 weeks), small for gestational age birth (<10th centile of birth weight by sex and gestational age), and low birth weight (<2500 g).

Results Within mother analysis of interpregnancy intervals indicated a much weaker effect of short intervals on the odds of preterm birth and low birth weight compared with estimates generated using a traditional between mother analysis. The traditional unmatched design estimated an adjusted odds ratio for an interpregnancy interval of 0-5 months (relative to the reference category of 18-23 months) of 1.41 (95% confidence interval 1.31 to 1.51) for preterm birth, 1.26 (1.15 to 1.37) for low birth weight, and 0.98 (0.92 to 1.06) for small for gestational age birth. In comparison, the matched design showed a much weaker effect of short interpregnancy interval on preterm birth (odds ratio 1.07, 0.86 to 1.34) and low birth weight (1.03, 0.79 to 1.34), and the effect for small for gestational age birth remained small (1.08, 0.87 to 1.34). Both the unmatched and matched models estimated a high odds of small for gestational age birth and low birth weight for long interpregnancy intervals (longer than 59 months), but the estimated effect of long interpregnancy intervals on the odds of preterm birth was much weaker in the matched model than in the unmatched model.

Conclusion This study questions the causal effect of short interpregnancy intervals on adverse birth outcomes and points to the possibility of unmeasured or inadequately specified maternal factors in previous studies.

Introduction

The time interval between pregnancies is viewed as an important and modifiable risk factor for adverse birth outcomes.[1-3] The incidences of preterm birth, small for gestational age birth, and low birth weight have each been repeatedly shown to follow a strong J-shaped relation to the time interval between pregnancies.[1 2] Typically, short intervals (less than 18 months between previous birth and subsequent conception) and long intervals (more than 23 months) have a higher risk of these birth outcomes compared with intermediate intervals of 18-23 months.[1-4]

The causal effects of interpregnancy interval on birth outcomes have been vigorously debated.[1-11] In support of interpregnancy interval having a causal role, the "maternal depletion hypothesis" proposes that mothers with short interpregnancy intervals insufficiently recover from the physiological stresses of a previous pregnancy and subsequent lactation.[12] A mechanism proposed for the effects of long interpregnancy interval is that the benefits of a previous birth in terms of physiological adaptation are gradually lost, as though the mother returns toward an equivalent state to primigravida; this is known as the "physiological regression hypothesis."[1 13] Together, these hypotheses imply the existence of an optimal interval that affords enough time for recovery from a previous birth but is not so long that the benefits of adaptation are lost. The alternative view is that interpregnancy interval is not causal,

Correspondence to: S Ball stephen.ball@telethonkids.org.au

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and that the relation between interpregnancy interval and birth outcomes is entirely due to maternal factors that are correlated with interpregnancy interval and the birth outcome in question.[6 7] Such confounders could include various aspects of socioeconomic status, ethnicity, demographics, and lifestyle.[1] Erickson and Bjerkedal reasoned that if interpregnancy interval is causal it can only affect the second of the two births that define an interval between pregnancies,[6] yet they observed that both births shared a very similar relation between interpregnancy interval and mean birth weight. The logical inference from this result is that interpregnancy interval does not have a causal effect on birth weight. Proponents of interpregnancy interval having a causal effect point to the many studies that have shown a persistent J-shaped relation between interpregnancy interval and birth outcomes after adjustment for confounders.[1 2] Consistent results among studies in the magnitude and timing of effects of interpregnancy interval have led to strong assertions over the past decade that the effect of interpregnancy interval is indeed causal and therefore worthy of a public health message advocating optimal timing between births.[1 2] This message now includes a recommendation from the World Health Organization of a minimum birth to pregnancy spacing of two years.[14]

Although debate on interpregnancy interval has swung heavily towards the existence of a causal effect on birth outcomes, we considered that previous analyses based on between mother comparisons may have inadequately adjusted for important maternal factors that are difficult to measure or model. Much of the variation in birth outcomes might be explained by risk factors that vary greatly between women but tend to persist between pregnancies, such as genetic predisposition, lifestyle, or social conditions. We identified that among women who have had three births, we could use each mother as her own control for risk factors that might otherwise induce the J-shaped association between interpregnancy interval and birth outcomes seen in previous studies. Therefore, the purpose of this study was to test for an effect of interpregnancy interval after adjusting completely for persistent maternal factors by using a within mother analysis.

Methods

Study design and setting

This was a retrospective cohort study investigating the association between interpregnancy interval and the incidence of preterm birth, small for gestational age birth, and low birth weight among the second and third births of mothers in Perth, Western Australia, in the period 1980-2010.

Data source

We sourced birth data from the Midwives' Notification System, a population-wide database of all births in Western Australia (of at least 20 weeks' gestation, more than 400 g birth weight, or both), based on statutory collection since 1980.[15] Statistical linkage of births to the same mother was provided by Data Linkage Western Australia, located in the Western Australian Department of Health. We selected all mothers who had their first three births as liveborn singletons within the period 1 January 1980 to 31 December 2010 while resident in Perth at the time of each birth (figure⇓). We excluded births of 45 weeks' gestation or longer, as national reference data were unavailable for calculating small for gestational age.[16] We also excluded births to mothers younger than 14 years.

Of the 84 151 mothers whose third births were live singletons while mothers were resident in Perth in the study period, 40 443 had all their first three births as live singletons in the same period. Reasons for this reduction include mothers having at least one birth outside the study period or outside Western Australia (n=38 652), mothers being resident outside Perth but elsewhere in Western Australia for at least one birth (n=3900), mothers not having liveborn singletons for one or more pregnancies (n=631), and records missing data (for example, gestational age or birth weight) for one or more pregnancies (n=525). Interpregnancy interval was erroneously negative for two mothers, reducing the sample to 40 441. We were unable to determine whether these two records had erroneous birth dates or parities; we assume a low level of such errors in the database and a negligible effect on the precision and bias of results.

Variables

Outcome variables were preterm birth (gestational age less than 37 completed weeks), small for gestational age birth (less than the 10th centile of Australian national birth weight centiles by sex and gestational age in weeks[16]), and low birth weight (less than 2500 g). For consistency with previous studies,[1-5] we modelled interpregnancy interval as a categorical variable, classed as: 0-5 months, 6-11 months, 12-17 months, 18-23 months (as the reference category), 24-59 months, 60-119 months, and 120 months or longer. We calculated interpregnancy interval as the time between one birth and the estimated start of the pregnancy of the subsequent birth (birth date minus estimated gestational age). We also adjusted for possible confounders (see below). The proportion of records for which pregnancy dating, and hence gestational age, was estimated by ultrasonography (versus last menstrual period) increased to more than 70% throughout the study period. We expect the primary effects of this variation in method to be that some records have more precise estimates of prematurity and small for gestational age than others; we assume a very small effect on assignment of interpregnancy intervals given the scale of interpregnancy interval categories relative to uncertainties around pregnancy dating.

Statistical modelling

We used a maternally matched design to model the odds of preterm birth, small for gestational age birth, and low birth weight as a function of interpregnancy interval. Whereas previous studies have observed an association between interpregnancy interval and adverse birth outcomes as a comparison among women,[1 2] here we used conditional logistic regression to measure this association within individual women.[17] Conditional logistic regression is commonly used for matched case-control studies and longitudinal studies.[18-22] In the context of our study, in which we matched birth outcomes by mother, this conditional approach accounts for each woman's overall risk of adverse birth outcomes among all of her children included in the analysis. This design thereby removes the effects of measured or unmeasured maternal factors that are either fixed (such as genetic predisposition) or strongly correlated over time (such as long term health). Essentially, this enables inferences that are based purely on within mother effects. In comparison, the traditional approach of unconditional logistic regression is based on differences between women. In the absence of confounding by persistent maternal factors, the two models will report the same effects of interpregnancy interval. However, where unmeasured persistent confounders exist, the unconditional model will give biased estimates of the effects of interpregnancy interval.

The conditional model required data on three births per mother, with the first and second births defining the start of the

interpregnancy intervals of the second and third births. We explicitly controlled for factors that vary between births as possible within mother confounders of an effect of interpregnancy interval: maternal age (categorical variable: 14-19, 20-24, 25-29, 30-34, 35-39, and ≥40 years), parity, and birth year. We also controlled for socioeconomic status as a factor that potentially varies (using the area level Index of Relative Socio-Economic Disadvantage from the 1996 Australian Bureau of Statistics' Census of Population and Housing,[23] categorised as national fifths). The conditional model was fitted in R 2.15.1, using the clogit() function in R's Survival package.

For comparison with the unmatched design of previous studies, we also generated results by using an unconditional logistic regression model for each type of birth outcome, with interpregnancy interval as the predictor variable of interest. We also adjusted for possible confounders of an effect of interpregnancy interval: maternal age (in five year categories as for the conditional model), parity, birth year, socioeconomic status (in nationally defined fifths as for the conditional model), ethnicity (white versus non-white), and the outcome of the previous birth. Confidence intervals for the unconditional model were based on robust standard error estimates that take within mother clustering into account. The unconditional model was fitted in R 2.15.1, using lrm() and robcov() functions in R's rms package.

Throughout this paper, we use the term "matched" to refer to the within mother design based on conditional logistic regression and "unmatched" to refer to the between mother design based on unconditional logistic regression.

Results

The outcome data comprised 80 882 births, structured as 40 441 pairs of second and third births, matched by mother. Table 1⇓ shows the sociodemographic characteristics of the study population. Among second births, the mean incidence rates were 5.3% for preterm birth, 7.4% for small for gestational age birth, and 3.5% for low birth weight. Among third births, these rates were 5.8%, 6.3%, and 3.6%, respectively. Informative data for the matched design are those birth pairs with different outcomes between second and third births (for preterm birth, for example, this is when a mother's second child was term and her third child was preterm or vice versa). Of the 40 441 birth pairs, 3369 (8.3%) pairs were informative for preterm birth, 4001 (9.9%) for small for gestational age birth, and 2202 (5.4%) for low birth weight.

Unmatched model

Unconditional logistic regression suggested a strong effect of short interpregnancy interval on the incidence of preterm birth and low birth weight, but not on the incidence of small for gestational age birth, after adjustment for confounders (table 2⇓). Among interpregnancy intervals shorter than the reference category of 18-23 months, the highest odds ratios for preterm birth (adjusted odds ratio 1.41, 95% confidence interval 1.31 to 1.51) and low birth weight (1.26, 1.15 to 1.37) were for intervals of 0-5 months. The incidence of small for gestational age birth was similar across the range 0-23 months, with estimated odds ratios ranging from 0.98 to 1.03.

The unconditional model showed increased odds with long interpregnancy intervals for all three birth outcomes of interest, with the largest effect for small for gestational age birth. Among interpregnancy intervals longer than the reference category, the highest odds ratio of preterm birth (1.35, 1.26 to 1.45) was at intervals of 60-119 months, whereas the highest odds ratios of low birth weight (1.67, 1.42 to 1.97) and small for gestational age birth (1.98, 1.74 to 2.24) were for intervals longer than 119 months.

Matched model

The matched design of conditional logistic regression estimated small effects of short interpregnancy interval on all three types of birth outcomes (table 2⇓). Among interpregnancy intervals shorter than the reference category of 18-23 months, the highest odds ratio of preterm birth (1.07, 0.86 to 1.34) and low birth weight (1.03, 0.79 to 1.34) was for intervals of 0-5 months. The odds ratio of small for gestational age birth was estimated at 1.08 for all three categories of interpregnancy interval less than 18 months.

The matched model estimated a low odds ratio of preterm birth at interpregnancy intervals longer than 23 months, with odds ratios ranging from 1.01 (0.86 to 1.18) for intervals of 24-59 months to 0.88 (0.54 to 1.46) for intervals longer than 119 months. In contrast, the matched model estimated large effects of long interpregnancy intervals on the incidence of low birth weight and small for gestational age birth relative to the reference category. For intervals longer than 23 months, odds ratios for low birth weight ranged from 1.07 (0.88 to 1.30) for intervals of 24-59 months to 1.58 (0.82 to 3.06) for intervals longer than 119 months, and odds ratios for small for gestational age birth ranged from 1.11 (0.96 to 1.28) for intervals 24-59 months to 1.72 (1.04 to 2.85) for intervals longer than 119 months.

Discussion

Contrary to reports in the literature of strong causal effects of short interpregnancy interval on the risks of preterm birth, small for gestational age birth, and low birth weight,[1 2] we found small effects on the basis of a maternally matched design. Linking two intervals by mother allowed for adjustment of each woman's predisposition to have a preterm, small for gestational age, or low birthweight child. If short interpregnancy interval has strong causal effects on adverse birth outcomes, we expected these effects to be evident after such an adjustment. That we found small effects suggests that if this causal relation exists, it is a weak one.

At the same time, when analysed as a between mother model with adjustment for covariates, our data showed the typically strong relations reported in the literature between short interpregnancy interval and the incidences of preterm birth and low birth weight. With the unmatched model, pregnancies that followed a short interpregnancy interval had a relatively high incidence of preterm birth and low birth weight. However, the unmatched model showed almost no effect of short interpregnancy interval on the odds of small for gestational age birth. The difference between matched and unmatched models in the odds of preterm birth and low birth weight suggests that the associations of increased risk at short intervals reported in the literature may be an artefact of unmeasured or inadequately specified confounders, despite careful attempts to adjust models. Both models estimated a small effect of short interpregnancy interval on small for gestational age birth. This suggests that neither short interpregnancy interval nor unmeasured confounders of short interpregnancy interval strongly affected the incidence of small for gestational age birth in our study population.

Therefore, our study does not support the existence of a causal effect of short interpregnancy interval on adverse birth

outcomes, and we propose that the associations between short intervals and adverse birth outcomes in other studies may be due to unmeasured confounding by persistent maternal factors. This confounding may arise from misspecification of known factors—for example, area level indices or individual metrics of socioeconomic status may poorly represent aspects of individual circumstance.[24] Other confounders, such as lifestyle factors, may be excluded from analyses because they are difficult to measure.

The matched approach of conditional logistic regression showed little effect of long interpregnancy interval on the incidence of preterm birth, despite the unmatched model showing an increased risk. As with short interpregnancy intervals, this suggests that unmeasured confounding played a role in the unmatched model. Both models showed higher odds of small for gestational age birth and low birth weight following long interpregnancy intervals, with the effects only partially diminished in the matched model. This indicates an effect of long interpregnancy intervals that cannot be fully explained by persistent maternal factors. This is consistent with the hypothesis of physiological regression between pregnancies.[25] However, our accounting for persistent maternal factors does not in itself prove causality, as other confounders that vary between pregnancies within individual mothers may be present. Although we adjusted for maternal age, parity, birth year, and socioeconomic status, other potential confounders may include changes related to fertility, unplanned pregnancies,[7] maternal illness, and family/social disruptions.[26]

To our knowledge, our study is the first to apply within mother methods to examine the relation between interpregnancy interval and birth outcomes by matching more than one interval per mother. We acknowledge the large body of previous research that links interpregnancy interval with adverse birth outcomes and the importance of existing recommendations on spacing between births. We encourage further use of within mother analyses to assess the generalisability of our results across a variety of populations, as short interpregnancy interval could have context dependent effects. Whereas our study was conducted in a developed country, women in developing regions may, on average, be more susceptible to nutrient depletion during pregnancy and have slower recovery between pregnancies owing to poor access to nutrient rich foods.[10] Furthermore, beyond the birth outcomes considered in this study, interpregnancy interval may have effects on birth defects,[27] schizophrenia,[28] autism,[29] pregnancy complications, and risk of maternal death.[1]

Limitations of study

This study has several limitations. To facilitate a matched design, we based our analyses on the outcomes of second and third births to mothers who had their first three births as liveborn singletons. Although supplementary data (web appendix) suggest that these births were representative of the broader population of mothers in terms of a J-shaped relation between interpregnancy interval and unadjusted rates of adverse birth outcomes, clear sociodemographic differences existed between mothers of three or more children (that is, the records included in this study) and mothers with only two births (excluded from this study). Notably, mothers of three or more singletons tended to be younger at the birth of their second child and from areas with lower socioeconomic status, compared with mothers of only two singletons. We are unable to exclude the possibility that a causal effect of short interpregnancy interval on adverse birth outcomes applies to births excluded from this study. However, we are unaware of any hypotheses that predict how a causal effect of short intervals could apply to mothers of only two children but not to mothers of three or more children. Exploring this possibility was beyond the scope of our study.

The definition of interpregnancy interval used in our study was based on successful pregnancies. Calculating intervals relative to unsuccessful pregnancies may improve effect estimates, depending on the physiological effects, timing, and frequency of unsuccessful pregnancies. This study used a single threshold for each type of outcome: 37 weeks' gestation to define preterm birth, 10th centile of weight for gestational age to define small for gestational age birth, and 2500 g to define low birth weight. The use of lower thresholds to represent higher levels of outcome severity would help to extend the clinical significance of this research. However, the rarity of such outcomes would require a very large population database with a sufficient number of mothers with informative (that is, discordant) pairs of outcomes. Based on the confidence intervals generated in our analyses, we suggest that such a dataset would require a minimum of 2000 such mothers for each outcome.

Implications of findings

Regardless of causality, short interpregnancy interval remains a strong predictor of the risk of adverse birth outcomes. Irrespective of whether the risk of adverse birth outcomes is increased by short interpregnancy intervals or by the maternal factors correlated with short interpregnancy intervals, the association between short interpregnancy interval and adverse birth outcomes is strong and consistent across studies.[1-4] Our study suggests that adverse birth outcomes are not the result of short interpregnancy intervals in themselves but are due to correlated maternal risk factors. Furthermore, maternal factors that act as confounders may include those of which the effects are not easy to measure or model, such as socioeconomic and lifestyle factors. We therefore recommend that clinicians continue to treat short interpregnancy interval as a useful flag of increased risk of adverse birth outcomes but remain vigilant for maternal risk factors that may accompany the presentation of short interpregnancy interval.

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Contributors: SJB, PJ, GP, and NdK were responsible for the conception and design of the study. SJB did the literature review, data extraction, data manipulation, and data analysis. All authors contributed to interpreting the results. SJB and GP wrote the first draft of the paper, which all authors critically revised. SJB is the guarantor.

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Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: SJB, GP, and PJ had funding support from the Australian National Health and Medical Research Council; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

What is already known on this topic

Mothers with short (<18 months) and long (>23 months) intervals between pregnancies typically have a higher incidence of preterm birth, small for gestational age birth, and low birth weight

Consistent results among studies have led to public health messages advocating optimal timing between births

Previous studies have relied on between mother comparisons, which may inadequately account for maternal risk factors

What this study adds

This study applied a method that completely adjusts for all persistent maternal factors, by comparing birth outcomes between two interpregnancy intervals for every mother

When the analysis was based on within mother variation in interpregnancy interval, short intervals had very little effect on adverse birth outcomes and long interpregnancy intervals had very little effect on preterm birth

This study questions the causal effect of short interpregnancy intervals on adverse birth outcomes and of long intervals on the risk of preterm birth

Ethical approval: This study was approved by the Human Research Ethics Committee (#2011/64) at the Department of Health, Western Australia.

Transparency declaration: The lead author (the manuscript's guarantor) affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Data sharing: The authors do not have permission to share the data used in this project, which were sourced from the Data Linkage Branch and the Maternal and Child Health Unit (Western Australian Government Department of Health). The statistical code is available from the corresponding author at stephen.ball@telethonkids.org.au).

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Tables

Table 1| Characteristics of births analysed

Characteristics	Second births				Third births			
	Total	Preterm (%)	SGA (%)	Low birth weight (%)	Total	Preterm (%)	SGA (%)	Low birth weight (%)
Total No	40 441	2160 (5.3)	2976 (7.4)	1430 (3.5)	40 441	2365 (5.8)	2537 (6.3)	1456 (3.6)
Interpregnancy interval (months):								
0-5	2709	223 (8.2)	203 (7.5)	139 (5.1)	1990	179 (9.0)	160 (8.0)	114 (5.7)
6-11	8727	456 (5.2)	589 (6.7)	301 (3.4)	5899	357 (6.1)	348 (5.9)	192 (3.3)
12-17	9687	439 (4.5)	657 (6.8)	257 (2.7)	6971	356 (5.1)	409 (5.9)	245 (3.5)
18-23	6599	323 (4.9)	443 (6.7)	209 (3.2)	5809	294 (5.1)	330 (5.7)	179 (3.1)
24-59	10 309	552 (5.4)	837 (8.1)	397 (3.9)	14 989	861 (5.7)	903 (6.0)	509 (3.4)
60-119	2065	147 (7.1)	220 (10.7)	111 (5.4)	4144	273 (6.6)	324 (7.8)	184 (4.4)
≥120	345	20 (5.8)	27 (7.8)	16 (4.6)	639	45 (7.0)	63 (9.9)	33 (5.2)
Sex of child:								
Male	21 262	1214 (5.7)	1507 (7.1)	707 (3.3)	21 089	1302 (6.2)	1308 (6.2)	695 (3.3)
Female	19 179	946 (4.9)	1469 (7.7)	723 (3.8)	19 352	1063 (5.5)	1229 (6.4)	761 (3.9)
Birth year*:								
1980-84	3547	187 (5.3)	302 (8.5)	123 (3.5)	520	37 (7.1)	45 (8.7)	23 (4.4)
1985-89	7959	388 (4.9)	667 (8.4)	274 (3.4)	5587	255 (4.6)	408 (7.3)	175 (3.1)
1990-94	8275	413 (5.0)	666 (8.0)	284 (3.4)	7813	433 (5.5)	518 (6.6)	273 (3.5)
1995-99	8038	441 (5.5)	535 (6.7)	285 (3.5)	8089	430 (5.3)	517 (6.4)	278 (3.4)
2000-04	7666	440 (5.7)	525 (6.8)	292 (3.8)	7754	495 (6.4)	440 (5.7)	300 (3.9)
2005-10	4956	291 (5.9)	281 (5.7)	172 (3.5)	10 678	715 (6.7)	609 (5.7)	407 (3.8)
Maternal ethnicity†:								
White	36 457	1846 (5.1)	2506 (6.9)	1178 (3.2)	36 429	2024 (5.6)	2142 (5.9)	1215 (3.3)
Non-white	3984	314 (7.9)	470 (11.8)	252 (6.3)	4012	341 (8.5)	395 (9.8)	241 (6.0)
Maternal age (years)‡:								
14-19	1634	183 (11.2)	185 (11.3)	125 (7.6)	211	32 (15.2)	17 (8.1)	16 (7.6)
20-24	10 441	635 (6.1)	927 (8.9)	444 (4.3)	4478	402 (9.0)	422 (9.4)	283 (6.3)
25-29	15 887	716 (4.5)	1166 (7.3)	498 (3.1)	12 016	629 (5.2)	853 (7.1)	407 (3.4)
30-34	10 325	510 (4.9)	580 (5.6)	299 (2.9)	15 284	771 (5.0)	798 (5.2)	461 (3.0)
35-39	2055	107 (5.2)	111 (5.4)	57 (2.8)	7436	447 (6.0)	388 (5.2)	234 (3.1)
≥40	99	9 (9.1)	7 (7.1)	7 (7.1)	1016	84 (8.3)	59 (5.8)	55 (5.4)
Socioeconomic status fifth§:								
1	7816	519 (6.6)	808 (10.3)	413 (5.3)	6863	510 (7.4)	632 (9.2)	379 (5.5)
2	8084	463 (5.7)	634 (7.8)	307 (3.8)	7487	453 (6.1)	537 (7.2)	308 (4.1)
3	8838	442 (5.0)	660 (7.5)	283 (3.2)	8679	496 (5.7)	554 (6.4)	308 (3.5)
4	8269	404 (4.9)	493 (6.0)	238 (2.9)	8895	482 (5.4)	465 (5.2)	258 (2.9)
5	7434	332 (4.5)	381 (5.1)	189 (2.5)	8517	424 (5.0)	349 (4.1)	203 (2.4)

SGA=small for gestational age.

*Grouped here into five year categories (six years for last category) but analysed as single year data in all models; peak frequency of second births in middle of study period reflects study design, requiring preceding and subsequent birth within period 1980-2010; similarly, late peak of third births reflects need for two preceding births.

†Note slight change in ethnicity totals between second and third births; although maternal ethnicity itself cannot change, individual reporting may vary between births.

‡Refers to age at child's birth.

Table 1 (continued)

Characteristics	Second births				Third births			
	Total	Preterm (%)	SGA (%)	Low birth weight (%)	Total	Preterm (%)	SGA (%)	Low birth weight (%)

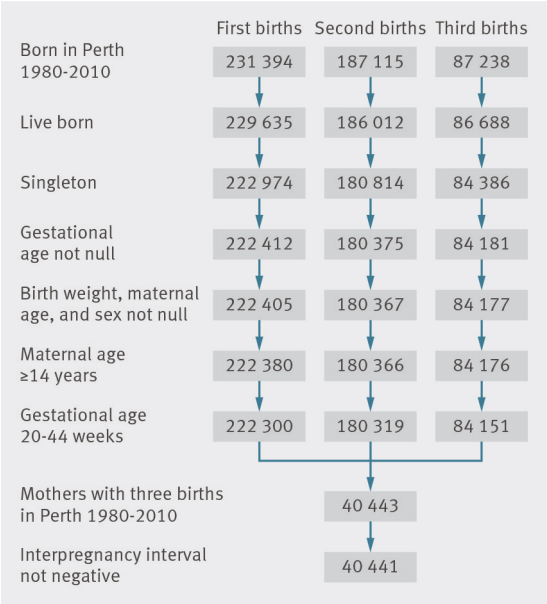
§Categorised as nationally defined fifths (1=most disadvantaged to 5=least disadvantaged); as fifths were defined nationally (rather than within study population), numbers within each category vary from 20% of total.

Table 2| **Relation between interpregnancy interval and adverse birth outcomes*. Values are odds ratios (95% CI)**

Interpregnancy interval (months)	Unmatched model		Matched model	
	Unadjusted	Adjusted†	Unadjusted	Adjusted‡
Preterm				
0-5	1.78 (1.66 to 1.90)	1.41 (1.31 to 1.51)	1.09 (0.88 to 1.36)	1.07 (0.86 to 1.34)
6-11	1.12 (1.06 to 1.18)	1.07 (1.01 to 1.13)	1.02 (0.86 to 1.22)	1.04 (0.87 to 1.23)
12-17	0.95 (0.90 to 1.00)	0.95 (0.90 to 1.01)	0.86 (0.73 to 1.02)	0.87 (0.73 to 1.03)
18-23	1.00	1.00	1.00	1.00
24-59	1.12 (1.07 to 1.18)	1.10 (1.05 to 1.16)	1.05 (0.90 to 1.23)	1.01 (0.86 to 1.18)
60-119	1.38 (1.29 to 1.47)	1.35 (1.26 to 1.45)	1.14 (0.93 to 1.39)	0.98 (0.76 to 1.25)
≥120	1.34 (1.18 to 1.54)	1.22 (1.06 to 1.40)	1.16 (0.77 to 1.74)	0.88 (0.54 to 1.46)
Small for gestational age				
0-5	1.26 (1.18 to 1.35)	0.98 (0.92 to 1.06)	1.06 (0.86 to 1.31)	1.08 (0.87 to 1.34)
6-11	1.03 (0.98 to 1.09)	0.97 (0.92 to 1.03)	1.09 (0.94 to 1.28)	1.08 (0.92 to 1.27)
12-17	1.04 (0.99 to 1.09)	1.03 (0.98 to 1.08)	1.10 (0.94 to 1.28)	1.08 (0.92 to 1.26)
18-23	1.00	1.00	1.00	1.00
24-59	1.12 (1.07 to 1.17)	1.15 (1.10 to 1.20)	1.06 (0.92 to 1.22)	1.11 (0.96 to 1.28)
60-119	1.45 (1.37 to 1.54)	1.61 (1.51 to 1.71)	1.27 (1.06 to 1.53)	1.40 (1.11 to 1.76)
≥120	1.52 (1.35 to 1.71)	1.98 (1.74 to 2.24)	1.53 (1.04 to 2.26)	1.72 (1.04 to 2.85)
Low birth weight				
0-5	1.76 (1.63 to 1.91)	1.26 (1.15 to 1.37)	1.01 (0.78 to 1.31)	1.03 (0.79 to 1.34)
6-11	1.08 (1.01 to 1.16)	0.99 (0.93 to 1.07)	1.00 (0.81 to 1.24)	1.01 (0.82 to 1.25)
12-17	0.96 (0.90 to 1.03)	0.95 (0.89 to 1.02)	1.01 (0.82 to 1.25)	1.02 (0.82 to 1.26)
18-23	1.00	1.00	1.00	1.00
24-59	1.15 (1.08 to 1.22)	1.12 (1.05 to 1.20)	1.09 (0.90 to 1.32)	1.07 (0.88 to 1.30)
60-119	1.55 (1.43 to 1.67)	1.55 (1.43 to 1.69)	1.30 (1.01 to 1.66)	1.14 (0.85 to 1.54)
≥120	1.63 (1.39 to 1.90)	1.67 (1.42 to 1.97)	2.10 (1.21 to 3.66)	1.58 (0.82 to 3.06)

*Shows odds ratios of preterm birth, small for gestational age birth, and low birth weight, as modelled by maternally unmatched and maternally matched logistic regression models for second and third births of mothers having three live singletons; odds ratio estimates are relative to reference category of 18-23 months.
†Adjusted unmatched model accounted for parity, socioeconomic status, birth year, maternal age, ethnicity, and previous birth outcome.
‡Adjusted matched model accounted for parity, socioeconomic status, birth year, and maternal age.

Figure



Selection of records used in study