

**Associations between interpregnancy interval and preterm birth by previous preterm birth status in four high-income countries: a cohort study**

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## ABSTRACT

**Objective:** To investigate the effect of interpregnancy interval (IPI) on preterm birth (PTB) according to whether the previous birth was preterm or term.

**Design:** Cohort study.

**Setting:** USA (California), Australia, Finland, Norway (1980-2017).

**Population:** Women who gave birth to first and second (N=3,213,855) singleton livebirths.

**Methods:** Odds ratios (ORs) for PTB according to IPIs were modelled using logistic regression with prognostic score stratification for potential confounders. Within-site ORs were pooled by random-effects meta-analysis.

**Outcome Measure:** PTB (gestational age < 37 weeks).

**Results:** Absolute risk of PTB for each IPI ranged from 3-6% after previous term and 17-22% after previous PTB. ORs for PTB differed between previous term and preterm births in all countries ( $P$ -for-interaction  $\leq 0.001$ ). For women with a previous term birth, pooled ORs were increased for IPI < 6 months (1.50, 95%CI 1.43-1.58); 6-11 months (1.10, 95%CI 1.04-1.16); 12-23 months (1.16, 95%CI 1.13-1.18); and  $\geq 24$  months (1.72, 95%CI 1.60-1.86), compared to 18-23 months. For previous PTB, ORs were increased for < 6 months (1.30, 95%CI 1.18-1.42) and  $\geq 24$  months (1.29, 95%CI 1.17-1.42), but were less than ORs among women with a previous term birth ( $P < 0.05$ ).

**Conclusions:** Associations between IPI and PTB are modified by whether the previous pregnancy was preterm. ORs for short and long IPIs were higher among women with a previous term birth than a previous PTB, which for short IPI is consistent with the maternal depletion hypothesis. Given high risk of recurrence and assuming a causal association

between IPI and PTB, IPI remains a potentially modifiable risk factor for women with previous PTB.

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**Keywords:** interpregnancy interval; preterm birth; effect modification.

**Tweetable Abstract:** Short, long interpregnancy intervals associated with higher ORs for preterm birth (PTB) after a previous PTB.

## Introduction

Interpregnancy interval (IPI), the length of time between pregnancies, has been identified as a potentially modifiable risk factor for adverse outcomes in infants and their mothers, with both short and long IPIs found to be associated with a range of adverse pregnancy outcomes.<sup>1,2</sup> To reduce the risk of adverse birth outcomes, the World Health Organization (WHO) recommends waiting at least two years following a live birth and six months following a miscarriage or induced abortion, before conceiving another child.<sup>3</sup> However, there is emerging evidence that the effects of IPI may differ according to obstetric history.<sup>1,4,5</sup> A meta-analysis of a million women with previous miscarriage found that IPI of <6 months was not associated with adverse outcomes in the subsequent pregnancy.<sup>1</sup> Recently, an international cohort study observed no increase in risk of adverse outcomes for short IPIs in women with a previous pregnancy ending in stillbirth.<sup>4</sup> These findings suggest that the current recommendations may oversimplify associations between IPI and adverse pregnancy outcomes; recommendations tailored according to obstetric history may be a more efficient way of communicating potential risks associated with birth spacing.

Studies examining the effect of IPI following live births<sup>6</sup> have indicated that short IPI (<6 months) was associated with a nearly two-fold increase in the odds of preterm birth (PTB). Given there is also a strong recurrence risk of PTB,<sup>7</sup> information on whether previous preterm birth may modify the association between IPI and risk of PTB in the subsequent pregnancy is sparse.<sup>8</sup> The aim of this study was to determine whether the association between IPI and PTB was modified by whether the previous birth was preterm. In addition, we planned to estimate absolute risks of PTB associated with short or long IPI, to better inform decision-making regarding birth spacing.

## Methods

We conducted a multi-country, longitudinal cohort study of women with consecutive singleton livebirths in California, USA (1991-2012); Western Australia (WA) (1980-2015); New South Wales (NSW), Australia (1995-2012); Norway (1980-2015); and Finland (1987-2017) (N=14,760,447 births). We obtained individual-level records from population-based birth and perinatal registries with >99% coverage in each site.<sup>9-13</sup> Data sources have been described in the previously published protocol.<sup>14</sup> Briefly, the extracted records included information on maternal age and infant's date of birth, gestational age, birthweight, birth order and vital status at birth. We excluded births with missing gestational age, birthweight, or date of birth. In addition, we excluded births where gestational age was recorded as <20 or  $\geq$ 45 weeks, and women aged <14 years.<sup>15</sup> Records with a negative IPI were also excluded.

### *Assessment of interpregnancy interval*

Interpregnancy interval was calculated as the time between the end of one pregnancy (birth date) and the start of the next pregnancy (birth date pertaining to next pregnancy minus gestational age at birth). Gestational age at birth was estimated based on ultrasound dating, or last menstrual period when ultrasound was not available. For comparison with WHO recommendations,<sup>3</sup> we defined six levels of IPI: <6 months ("short" IPI), 6-11 months, 12-17 months, 18-23 months, 24-59 months, and  $\geq$ 60 months ("long" IPI).

### *Birth outcome measures*

The primary outcome was PTB, defined as a pregnancy ending at <37 completed weeks' gestation. A literature search did not identify a core outcome set for IPI exposure. However, PTB was a primary outcome that informed the current WHO guidelines.

### *Statistical analyses*

Within-site analyses were first restricted to the cohort defined by the first and second consecutive livebirths (parity 0, 1), and repeated using the second and third consecutive livebirths (parity 1, 2). We used conditional (prognostic score-stratified) logistic regression to model PTB as the outcome, and IPI category, previous term or preterm birth status, and their multiplicative interaction as predictors. Statistical significance of the interaction was assessed by an overall Wald test. Prognostic scores<sup>16</sup> were derived from within-site logistic regression of PTB as the outcome on maternal age (14-19, 20-24, 25-29, 30-34, 35-39, or  $\geq 40$  years) and year of birth as predictors to account for confounder imbalance. Strata for conditional models were defined by five percentile increments in prognostic score.

Supplementary analyses included an additional variable for socioeconomic status (SES) in prognostic score models. For California, SES was assessed as level of education (some high school or less; high school diploma or equivalent; some college; college graduate or more). For Australia (WA, NSW), SES was derived from the Australian Bureau of Statistics Index of Relative Socioeconomic Disadvantage, a geographic area-level composite of education, skilled occupation status, and household income.<sup>17</sup> For Finland, SES was based on occupation during pregnancy recorded at birth (upper white collar; lower white collar; blue collar; others including students, housewives and unknown SES).<sup>18</sup> The Norwegian cohort did not have measures of SES and was therefore excluded from supplementary analyses.

Adjusted odds ratios (aORs) for PTB (at second birth) and their associated 95% confidence intervals (CIs) were estimated for each IPI category using an IPI of 18-23 months as the referent group, and calculated by previous preterm birth status (at first birth). Within-site aORs were pooled using the inverse variance method with random intercepts for countries (Revman 5.3).<sup>19</sup> The Cochrane Q statistic was used to test for differences in aORs between women with

previous term and preterm birth, within each IPI category.<sup>20</sup> Heterogeneity was quantified by the  $I^2$  statistic.<sup>21</sup> Crude absolute risks for PTB were derived within-countries for each IPI category, stratified by previous term birth (incident risk) and preterm birth (recurrence risk). Pooled absolute risks were computed using logistic regression models with random intercepts for countries (SAS 9.4, SAS Institute, Cary, NC). All tests were two-sided, and statistical significance was defined as  $P < 0.05$ .

#### *Patient involvement*

A reference group of consumer health representatives (*Healthy Pregnancies Reference Group*) was established, comprising women with lived experience of pregnancy with adverse birth outcomes. The group met twice-yearly to provide a community perspective on this research, providing advice regarding research aims; language, including lay summaries; links between consumers, the community, and the researchers; and advocacy on behalf of consumers and the community. The reference groups also contributed to interpretation of the findings by identifying factors that may influence IPI.<sup>14</sup>

#### *Details of study funding*

The study sponsors had no role in study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

## **Results**

#### *Cohort characteristics*

From a cohort of 14,760,447 births, we identified 3,574,889 women with their first two consecutive singleton births (parity 0, 1) in the study period (1980-2017); of these, 3,213,855 (89.9%) met eligibility criteria and were included in the analytic cohort (Table 1).

In all countries, the distribution of age at birth of the second child peaked between 25 and 34 years. For second births, 187,270 (5.8%) were PTBs, of which just over half (n=101,422) were spontaneous PTBs. The occurrence of PTB varied by study site, with the greatest incidence in California (7.9%, Table 1). Overall, 216,197 women (6.7%) had a PTB in their first pregnancy.

IPIs were most commonly within the WHO-recommended range of 24-59 months (37.0%) (Figure 1); 4.8% and 11.1% of women had IPIs <6 months and ≥60 months, respectively. Distributions of IPIs were similar for women with a previous preterm or previous term birth (Table S1).

As a supplementary analysis, we identified 1,332,854 women with second and third consecutive singleton livebirths (parity 1, 2), of which 1,146,545 (86.7%) met eligibility criteria (Table S2). For third births, 68,990 (6.0%) were PTBs, of which just over half (n=36,929) were spontaneous PTBs. Overall, 62,912 (5.5%) had a history of a PTB in the second pregnancy (Table S2). The most common IPI after a second birth was 24-59 months (39.1%) (Figure S1).

#### *Effect estimates of interpregnancy interval on preterm birth by previous preterm birth status*

##### Site-specific analyses

For all countries, the cohort analysis of first and second births showed an interaction between the effects of IPI and previous preterm birth on the odds of PTB (*P-for-interaction* ≤0.001 for all within-site analyses; Tables S3-S7). Qualitatively, there were similar relationships between IPI and odds of PTB in each site. For women with a previous term birth, there was a “U-shaped” association between IPI and the aOR of PTB, with greater aORs for IPIs of <6 months and ≥60

months compared with 18-23 months. For women whose prior pregnancy ended in a preterm birth, aORs in all countries were lower than for women with a previous term birth for IPIs of <6 months (except Norway, where the aORs were similar) and  $\geq 60$  months.

Site-specific analyses of second and third births were similar (Tables S3-S7). Greater instability among point estimates was observed in the latter analyses due to smaller numbers.

### Pooled analyses

When site-specific results were pooled for women with previous term birth, aORs for subsequent PTB were elevated for IPIs of <6 months (1.50, 95% CI 1.43-1.58); 6-11 months (1.10, 95% CI 1.04-1.16); 24-59 months (1.16, 95% CI 1.13-1.18); and  $\geq 60$  months (1.72, 95% CI 1.60-1.86), compared to 18-23 months (Figure 2, panel A; Table 2). For women with previous preterm birth, pooled aORs for IPIs of <6 months (1.30, 95% CI 1.18-1.42); 6-11 months (1.03, 95% CI 0.98-1.07); and  $\geq 60$  months (1.29, 95% CI 1.17-1.42) were lower than those for women with previous term births.

Results were similar when analyses were repeated using the cohort of second and third births (Table S8). The inclusion of SES in prognostic score stratification (when available) did not change the results. Odds ratios closely approximated relative risks for unadjusted analyses (Table S9).

### *Absolute risk of preterm birth by interpregnancy interval category and previous preterm birth status*

Within-site analyses of first and second births consistently found that for each IPI category, the absolute risk of a preterm second birth was higher for women with a previous preterm than a previous term birth (Tables S10-S14). For all IPIs, pooled absolute risks of PTB ranged between 3 and 6% (incidence) for previous term birth and 17 to 22% (recurrence) for previous preterm birth, with highest risks at IPIs <6 or >60 months and lowest at 18-23 months (Figure

2, panel B; Table 3). Compared with 18-23 months, absolute risk differences for IPIs of <6 and >60 months were 2.0% and 2.3% (respectively) for women with previous term births, and 5.4% and 4.0% for women with previous preterm births. Similar results were observed for third births (Tables S9-S13). Pooled absolute risks of preterm third birth were 4-6% in those with term second birth versus 22-29% if the previous birth was preterm (Table S15).

## **Discussion**

### *Main findings*

In this large international cohort assembled over an almost 40-year period (1980-2017), we observed an increase in the odds of PTB for both short and long intervals compared with an interval of 18-23 months. Previous studies have observed similar relative increases in risk for short<sup>1,2</sup> and long IPI<sup>15,22</sup>; however, our results showed that those relative increases are lower if the previous pregnancy was preterm. For IPIs <6 months and  $\geq$ 60 months, the OR of PTB was greater among women with a previous term birth compared with a previous preterm birth.

### *Strengths and limitations*

A strength of our analyses was that we included adjustment for some potential confounders by prognostic score stratification, allowing for tighter control of confounding than conventional adjustment, and ensuring that temporal covariates (e.g. birth year) do not recreate the IPI.<sup>23</sup> This approach also has the advantage of approximating a mother-matched design without restriction of the cohort to women with three or more births, and therefore has greater applicability to the population of women for whom IPI is relevant.<sup>24</sup> However, this design cannot account for time-invariant confounding as effectively as a mother-matched design (the latter was not possible for this study question due to the same PTB event being both an outcome for the first IPI and an effect modifier for the second IPI). To maintain comparability between sites, our analysis had a limitation in the number of covariates that could be included in

prognostic score models (maternal age, year of birth, SES). Furthermore, unmeasured variables such as pregnancy intention or smoking have the potential to confound the association between IPI and birth outcomes,<sup>25</sup> and may vary according to whether the preceding birth was preterm or term. Given that the distribution of gestational length may vary by racial or ethnic background, future research should explore whether this further modifies the observed associations.<sup>24</sup>

Our study was based on large individual participant data sets from four high-income countries. Although our published study protocol invited collaboration,<sup>14</sup> we did not attempt to include all data sets that may be relevant to addressing our question. It is possible that other data sources may have been informative. No previous studies have explored the interaction between IPI and previous preterm birth, and hence no additional study-level data was available to contribute to our estimates.

An additional limitation of our study relates to assessment of gestational age at birth. This was measured primarily by ultrasound, but the measurement method was recorded inconsistently in the source data sets, and hence we could not estimate the proportion of births without sonographic measurement. Misclassification of preterm birth is possible when gestational length was estimated by last menstrual period.

### *Interpretation*

A recent study investigated the effect of IPI on birth outcomes in a cohort of women with a previous spontaneous preterm birth.<sup>26</sup> Consistent with our study, odds of subsequent PTB in that restricted cohort were increased for both short (<6 months) and long ( $\geq 60$  months) IPIs relative to an IPI of 18-23 months. However, the magnitudes of association were greater than our estimates (OR 2.22 versus 1.30 for short IPI; OR 2.19 versus 1.72 for long IPI). This may reflect the cohort restricted to previous spontaneous PTB for whom the biological effect of IPI

may be greater than after any (spontaneous or iatrogenic) PTB. Nonetheless, that previous study did not allow the effect of IPI to be compared with women who had a previous term birth. By not applying such restriction, our study overcomes this limitation to investigate the interaction between IPI and previous preterm birth, showing lower odds ratios for short and long IPI in women with a previous preterm birth.

It is unclear the extent to which the reduction in relative associations observed for IPI after preterm birth reflect an underlying biological mechanism (as opposed to the alternative explanation of unmeasured confounding). The prevailing explanation for increased risk of adverse pregnancy outcomes after short IPI posits that shorter intervals allow insufficient time for women to recover from the physiological strain of the previous pregnancy (the *maternal depletion hypothesis*).<sup>27</sup> Previous studies have reported mixed results regarding the effect of birth spacing on anthropometric status, anaemia, and micronutrient status as markers of nutritional depletion; the evidence is stronger for folate depletion as a potential causal mechanism.<sup>28</sup> In the absence of biological measurements, our study is limited in its ability to assess maternal depletion as a causal mechanism; however, a greater relative association for short IPI after term birth is consistent with this hypothesis if longer gestation is associated with greater maternal depletion. Measurements of markers for physiological depletion (e.g. metabolic levels of folate) would be worthwhile in future studies of the interaction between IPI and previous gestational length to further explore this potential mechanism. Similarly, future research is required to identify potential biological mechanisms underlying a greater relative association of long IPI with PTB after a previous term birth.

Consistent with a well-documented recurrence effect,<sup>29</sup> women who had a previous preterm birth had a roughly four-fold increase in the absolute risks of PTB in the subsequent pregnancy (17-22% across IPIs) compared to women who had a previous term birth (3-6%) (Table 3). For women with a previous term birth, for whom we observed significantly larger odds ratios, low

baseline risk of PTB translated to a small increase in absolute risk associated with both short and long IPIs (2%). Conversely, for women with a previous preterm birth, smaller odds ratios translated to larger increases in absolute recurrence risk (4% for short IPIs; 5% for long IPIs). In other words, where relative measures showed a greater association between IPI and PTB for women with previous term birth, absolute increases in risk were greater for women with previous preterm birth. Based on the relative measures, our results translate to a population attributable fraction (PAF) of 17.1% of PTB attributable to IPI for women with a previous term birth and a PAF of 9.4% of PTB attributable to IPI for women with a previous preterm birth. Therefore, IPI explains proportionally more cases of PTB among women with previous term birth than previous preterm birth, possibly due to the relatively smaller role of IPI involved in recurrent PTB, and the relatively more dominant role of other causes of recurrent PTB such as genetic factors and health-related behaviours unrelated to IPI. However, the absolute risk reduction of PTB at a population level is greater for women with previous preterm birth due to the much larger absolute risk of PTB among these women.

## **Conclusion**

The literature documenting differences in the burden of adverse pregnancy outcomes associated with different IPIs is extensive.<sup>22</sup> In recent years, studies have focussed primarily on disentangling confounding inherent in observational study designs,<sup>15</sup> and on quantifying associations between IPI and a range of long-term outcomes.<sup>30</sup> Evidence from matched study designs, in which greater control of confounding is possible, suggest that at a population level, any effect of short IPI is likely to be less than estimated by previous studies.<sup>15,31</sup> However, there is also an increasing recognition of the need for studies of the effect of IPI in high-risk groups, given that differences between subgroups may be obscured by population level analyses.<sup>25</sup> A body of evidence evaluating differences in the associations according to obstetric context is emerging<sup>1,5,31</sup>, and may inform recommendations about IPI and reduce the

risk of harmful perinatal outcomes.<sup>3</sup> This large international study found that the relative association between IPI and PTB is less for women experiencing preterm birth in the previous pregnancy, which for short IPI is consistent with maternal depletion. Furthermore, our results indicate that recurrence, not IPI, is the primary determinant of absolute risk. However, given high risk of recurrence and assuming a causal association between IPI and PTB, IPI remains a potentially modifiable risk factor for women with previous preterm birth. For women with previous term birth, decisions about birth spacing should also include personal preferences and obstetric concerns in addition to IPI.<sup>8</sup>

## **DECLARATIONS**

### **Contributors**

MLM prepared data and performed statistical analyses for data from Western Australia and Norway; MG prepared data and performed statistical analyses for data from Finland; JAM prepared data and performed statistical analyses for data from California; JB prepared data and performed statistical analyses for data from New South Wales. MLM, SB, GP, MCM, SEH, MG, GMS, AMP, and JAM contributed to the study design and the development of the analytic plan. MLM drafted the technical protocol and statistical analysis plan, and undertook the meta-analysis. MLM, GP, SB, AKR, MG, MCM, SEH, AMP, JAM, GMS, JB, NN, ATG, CM, NdK and APB contributed to the interpretation of findings. MLM led the drafting of the report, and all co-authors contributed to revising of the report and approved the final version.

### **Declaration of interests**

MLM, GP and SB report grants from the National Health and Medical Research Council (NHMRC) during the conduct of the study. MCM reports grants from Research Council of Norway during the conduct of the study. The other authors declare no competing interests.

## **Ethics**

This study was approved by the Department of Health Western Australia Human Research Ethics Committee (2016/51; 14 September 2016); Curtin University Human Research Ethics Committee (RDHS-30-16; 23 February 2016); NSW Population and Health Services Research Ethics Committee (2017/HRE0705; 8 September 2017); Stanford University Institutional Review Board (24543; 30 September 2019); and the Norwegian Regional Committees for Medical and Health Research Ethics (2017/1066; 29 June 2017). Each committee provided a waiver of consent for participants. For Finland, ethical approval was not required since only anonymous register data were used and no registered person was contacted.

## **Consent for publication**

The authors confirm this work is original and has not been published elsewhere, in part or in whole.

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**Table 1: Characteristics at second birth of mothers with first two consecutive singleton livebirths.**

	USA		Australia				Norway		Finland		TOTAL	
	California		WA		NSW		(1980-2015)		(1987-2017)		(1980-2017)	
	(1991-2012)		(1980-2015)		(1995-2012)		(1980-2015)		(1987-2017)		(1980-2017)	
	N	%	N	%	N	%	N	%	N	%	N	%
<b>N</b>												
Total	8,141,687	-	964,015	-	1,710,128	-	2,094,171	-	1,850,446	-	14,760,447	-
Eligible*	1,809,836	22.2	254,511	26.4	387,244	22.6	601,413	28.7	521,885	28.2	3,574,889	24.2
Included**	1,619,394	19.9	252,473	26.2	386,357	22.6	546,118	26.1	409,513	22.1	3,213,855	21.8
<b>Maternal characteristics</b>												
<b>Age (years)</b>												
14-19	79,330	4.9	7,007	2.8	7,778	2.0	2,492	0.5	2,821	0.7	99,428	3.1
20-24	370,343	22.9	47,004	18.6	56,349	14.6	80,597	14.8	61,000	14.9	615,293	19.1
25-29	431,975	26.7	82,662	32.7	110,854	28.7	210,242	38.5	146,468	35.8	982,201	30.6
30-34	449,269	27.7	78,705	31.2	135,130	35.0	184,726	33.8	139,436	34.0	987,266	30.7
35-39	240,780	14.9	32,264	12.8	65,507	17.0	59,992	11.0	51,714	12.6	450,257	14.0
40 or older	47,697	2.9	4,831	1.9	10,739	2.8	8,069	1.5	8,074	2.0	79,410	2.5
<b>Year of second birth</b>												
1980-1984	-	-	15,019	5.9	-	-	23,369	4.3	-	-	38,388	1.2
1985-1989	-	-	32,775	13.0	-	-	68,402	12.5	8,973	2.2	110,150	3.4
1990-1994	105,252	6.5	35,339	14.0	-	-	80,390	14.7	67,803	16.6	288,784	9.0
1995-1999	377,276	23.3	36,488	14.5	70,431	18.2	82,846	15.2	72,801	17.8	639,842	19.9
2000-2004	422,619	26.1	35,998	14.3	112,344	29.1	86,341	15.8	69,210	16.9	726,512	22.6
2005-2009	446,930	27.6	41,494	16.4	125,355	32.4	91,448	16.7	74,226	18.1	779,453	24.3
2010-2014	267,317	16.5	45,923	18.2	78,227	20.2	94,570	17.3	75,950	18.5	561,987	17.5
2015-2017	-	-	9,437	3.7	-	-	18,752	3.4	40,550	9.9	68,739	2.1
<b>Outcome in second birth</b>												
Preterm birth	121,484	7.5	13,939	5.5	16,465	4.3	21,660	4.0	13,722	3.4	187,270	5.8
<b>Previous birth outcome (first birth)</b>												
Previous term	1,491,338	92.1	235,563	93.3	365,110	94.5	515,567	94.4	390,080	95.3	2,997,658	93.3
Previous preterm	128,056	7.9	16,910	6.7	21,247	5.5	30,551	5.6	19,433	4.7	216,197	6.7

*Abbreviations:* NSW = New South Wales; USA = United States of America; WA = Western Australia.

\* *Mothers with first two consecutive singleton livebirths.*

\*\* *Excludes births with missing gestational age, birthweight or date of birth; gestational age <20 or ≥45 weeks; mothers aged <14 years; or records with a negative IPI.*

**Table 2: Pooled adjusted odds ratios for the outcome of PTB for IPI categories, stratified by previous term or preterm birth (mothers with first and second births).**

Interval	Previous Term Birth		Previous Preterm Birth		P-value (difference in aORs)
	Pooled aOR* (95% CI)	I <sup>2</sup>	Pooled aOR* (95% CI)	I <sup>2</sup>	
<6 months	1.50 (1.43-1.58)	54%	1.30 (1.18-1.42)	58%	0.006
6-11 months	1.10 (1.04-1.16)	79%	1.03 (0.98-1.07)	0%	0.04
12-17 months	1.00 (0.95-1.06)	80%	1.02 (0.97-1.08)	23%	0.60
18-23 months (referent)	1	-	1	-	-
24-59 months	1.16 (1.13-1.18)	30%	1.12 (1.06-1.19)	49%	0.36
≥60 months	1.72 (1.60-1.86)	88%	1.29 (1.17-1.42)	69%	<0.001

\* Study-level odds ratios from prognostic score-stratified models. Prognostic score components: maternal age, birth year.

Abbreviations: aOR = adjusted odds ratio; IPI = interpregnancy interval; CI = confidence interval; PTB = preterm birth.

**Table 3: Pooled absolute risk of PTB for IPI categories, stratified by previous term or preterm birth (mothers with first and second births).**

Interval	Previous Term Birth		Previous Preterm Birth		Risk difference %, 95% CI (Preterm - Term)
	Pooled absolute risk %, 95% CI	Risk difference %, 95% CI (Interval - 18-23 months)	Pooled absolute risk %, 95% CI	Risk difference %, 95% CI (Interval - 18-23 months)	
<6 months	5.3 (3.4-8.0)	2.0 (-0.6-5.0)	22.4 (19.4-25.6)	5.4 (0.8-9.8)	17.1 (13.0-20.9)
6-11 months	3.7 (2.3-5.9)	0.4 (-1.9-2.9)	17.8 (14.6-21.5)	0.8 (-3.9-5.6)	14.1 (10.2-18.1)
12-17 months	3.3 (2.1-5.3)	0.0 (-2.1-2.3)	17.3 (14.4-20.6)	0.3 (-4.2-4.8)	14.0 (10.5-17.5)
18-23 months	3.3 (2.1-5.0)	-	17.0 (14.0-20.5)	-	13.7 (10.2-17.4)
24-59 months	3.8 (2.6-5.7)	0.5 (-1.6-2.7)	18.8 (16.3-21.6)	1.8 (-2.4-6.0)	15.0 (11.9-18.1)
≥60 months	5.6 (4.0-7.8)	2.3 (0.0-4.8)	21.0 (18.3-23.9)	4.0 (-0.4-8.2)	15.4 (11.9-18.6)

Abbreviations: CI = confidence interval; IPI = interpregnancy interval; PTB = preterm birth.