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Effect of interpregnancy interval on gestational diabetes: a retrospective matched cohort study

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ABSTRACT

Purpose: To examine the association between interpregnancy interval (IPI) and gestational diabetes using both within-mother and between-mother comparisons.
Methods: A retrospective cohort study of 103,909 women who delivered three or more consecutive singleton births (n = 358,046) between 1 January 1980 and 31 December 2015 in Western Australia. The association between IPI and gestational diabetes was estimated using conditional logistic regression, matching pregnancies to the same mother and adjusted for factors that vary within-mother across pregnancies. For comparison with previous studies, we also applied unmatched logistic regression (between-mother analysis).
Results: The conventional between-mother analysis resulted in adjusted odds ratios (aOR) of 1.13 (95% CI, 1.06–1.21) for intervals of 24–59 months and 1.51 (95% CI, 1.33–1.70) for intervals of 120 or more months, compared with IPI of 18–23 months. In addition, short IPIs were associated with lower odds of gestational diabetes with (aOR: 0.89; 95% CI, 0.82–0.97) for 6–11 months and (aOR: 0.92; 95% CI, 0.85–0.99) for 12–17-month. In comparison, the adjusted within-mother matched analyses showed no statistically significant association between IPIs and gestational diabetes. All effect estimates were attenuated using the within-mother matched model.
Conclusion: Our findings do not support the hypothesis that short IPI (<6 months) increases the risk of gestational diabetes and suggest that observed associations in previous research might be attributable to confounders that vary between mothers.

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Introduction

Gestational diabetes is one of the major pregnancy complications that affect 6%–13% of pregnancies worldwide [1]. Pregnancies complicated by gestational diabetes have an increased risk of caesarean section, high blood pressure and greater risk of perinatal complications including perinatal death [2–5].

The length of time between previous delivery and subsequent conception (interpregnancy interval [IPI]) has been extensively evaluated with respect to its association with birth outcomes [6–9]. However, there is relatively less research on its association with pregnancy complications.

It has previously been observed that both short and long IPIs increase the risk of gestational diabetes [10–14]. However, inference was limited due to small sample sizes, reliance on hospital-based cohorts, insufficient control for important confounders (e.g., socio-economic status [SES]) and biased IPI length measurements, such as the use of birth-to-birth intervals or birth-to-outcome intervals instead of birth to conception.

The World Health Organization (WHO) and the American College of Obstetricians and Gynecologists recommend that women should wait at least two years, and at least 18 months after live birth before commencing their next pregnancy, respectively [15,16]. However, the suitability of these recommendations for mothers in high-income countries is uncertain as the recommendations emanate from studies from low-income and middle-income settings conducted prior to the early 2000's.

Several hypotheses have been postulated, including the "maternal depletion" and "physiologic regression" hypotheses [8,17,18]; however, a causal effect of IPI on pregnancy complications has not yet been elucidated. Recently, researchers have posited that the association between IPI and increased risk of adverse perinatal outcomes might be attributed to confounding factors ("systematic bias" hypothesis) [9,14,19]. It remains plausible that the previously reported associations between IPI and gestational diabetes may be explained by risk factors that tend to persist within-mothers across pregnancies and potentially vary greatly between mothers [9,14]. Complementary within-mother matched analyses offer an opportunity to account for within-mother effects.

This study aimed to examine the association between IPI and gestational diabetes employing both matched pregnancies within the same mother and unmatched between-mother comparisons in a high-income setting.

Materials and methods

Data source and study population

We conducted a retrospective cohort study using matched and unmatched approaches to examine the association between IPI and risk of gestational diabetes for all mothers who gave birth between January 1st, 1980, and December 31st, 2015 in Western Australia (WA). We sourced maternal, infant and birth information from the Midwives Notification System (MNS), a population-wide registry of all births (>99%) with at least 20 weeks' gestation or with birthweight >400 grams if the gestational length is unknown [20]. Hospitalization records were identified from Hospital Morbidity Data Collection (HMDC), which includes information on all hospitalizations in the state, with the Australian Modification of International Classification of Diseases (ICD-10-AM) coded diagnostic information and procedures performed [21]. Ethics approval was obtained from the Human Research Ethics Committee (2016/51) of the Department of Health, WA.

Our analyses included all mothers with at least three consecutive singleton births (at least two IPIs) at 20–44 weeks of gestation in WA within the study period. Of the original total of 487,297 mothers who gave birth in the study period, we sequentially excluded mothers who delivered multiples (n = 4381); mothers who delivered only once during the study period (n = 189,269); and mothers for whom parity as recorded in the birth record was discordant with the order of the birth dates of her children (n = 5902). These exclusions resulted in a sample of 287,745 mothers with ≥2 consecutive births eligible for analysis (Fig. 1). We further excluded mothers who had missing information (e.g., gestational age, SES, maternal age, negative IPI) for one or more pregnancies (n = 7109). Finally, we excluded mothers with fewer than two intervals (n = 176,727), leaving 103,909 mothers included in the final analyses.

Measures

Outcome assessment

The outcome of interest, gestational diabetes was ascertained from the MNS notifications and hospital separation codes consistent with gestational diabetes (ICD-9-AM: 648.8, ICD-10-AM: O24.4).

Exposure

The exposure, IPI, was defined as the length of time between delivery date of the previous pregnancy and the estimated conception date of the subsequent pregnancy (date of birth minus gestational age at birth). Gestational age at birth was based on dating ultrasounds, or last menstrual period when ultrasound was not available. We used IPI as a categorical variable, grouped into seven categories (<6 months, 6–11 months, 12–17 months, 18–23 months (reference), 24–59 months, 60–119 months, or 120 or more months), which is consistent with WHO recommendations and categories used in past studies [9,14,22].

Independent variables

For the within-mother matched analyses, we adjusted for factors that can vary between births to the same mother. Specifically, we adjusted for maternal age at time of each delivery (categorical variable: 14–19, 20–24, 25–29, 30–34, 35–39, or 40 years or older), parity, birth year (continuous), SES, infant sex, marital status, history of obesity, known pre-existing hypertension and gestational hypertension. SES was derived by the Australian Bureau of Statistics as the Socio-Economic Index of Areas - Index of Relative Socio-economic Disadvantage at a geographic area for the maternal residence at the time of birth [23], which we categorized into quintiles.

Statistical analysis

We summarized the socio-demographic and medical conditions of the cohort at their first pregnancy during the study period. Conditional logistic regression (accounting for matching pregnancies to the same mother) was used to estimate odds of gestational diabetes as a function of IPI categories, comparing pregnancies within-mothers. Under this approach, effect estimates also controlled for unmeasured characteristics that remained stable or strongly correlated over time for mothers throughout their consecutive pregnancies. This enables inference that is based purely on within-mother effects [7,9,14]. To estimate the total effect of IPI, we repeated our matched analyses without adjustment for maternal age at time of each delivery and birth year. In the absence of residual time-varying confounding or selection bias, we would expect similar effects of IPI on gestational diabetes in both between-mother and within-mother comparisons. It is plausible that if unmeasured persistent confounders exist, the unconditional logistic regression may result in biased estimates [9]. For comparison with previous unmatched studies, we also applied unmatched logistic regression

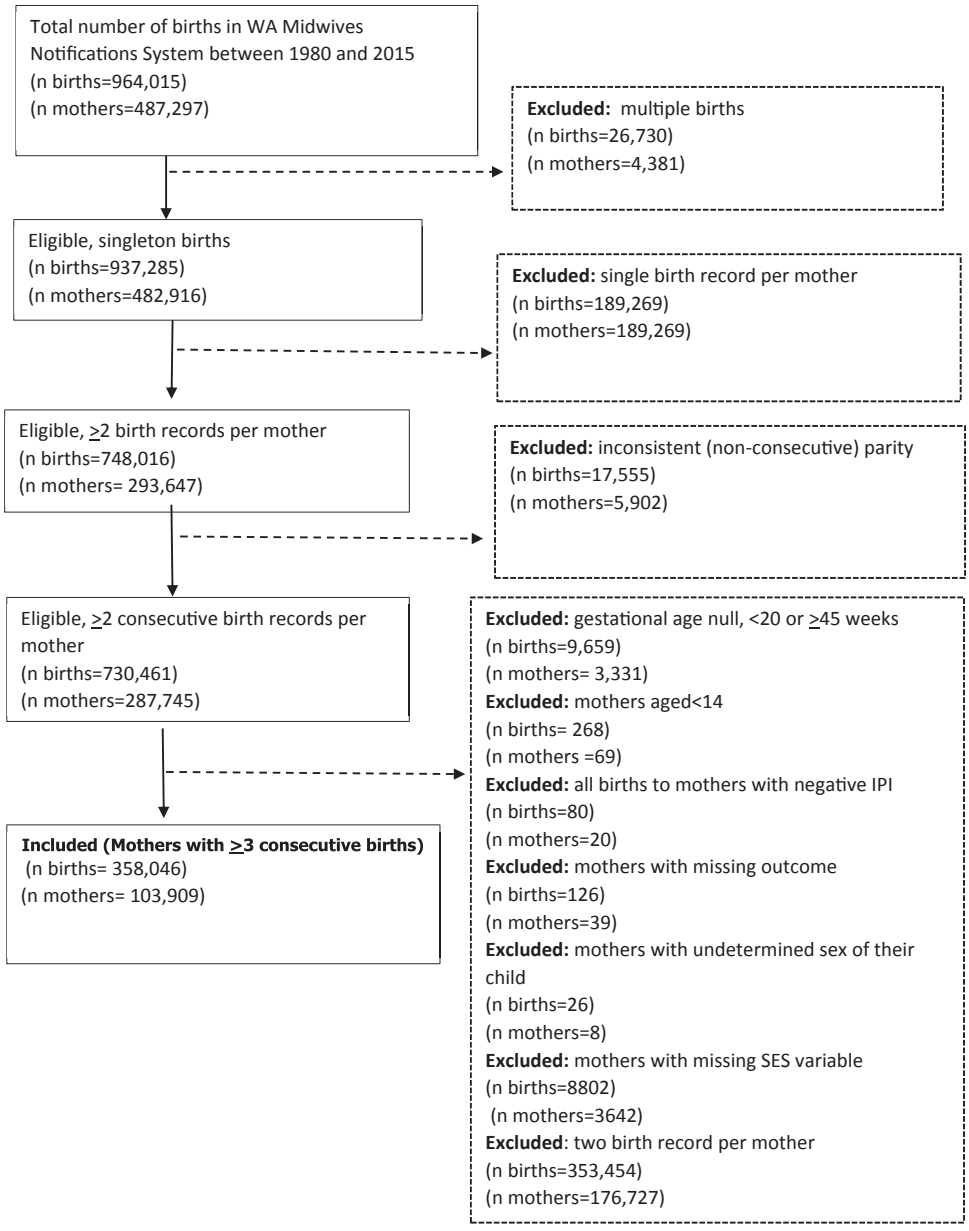

Fig. 1. Selection of eligible birth records included in this study – Western Australia, 1980–2015.

that additionally adjusted for measured covariates that vary between mothers, such as race/ethnicity. To minimize multicollinearity between time-varying covariates (such as maternal age at time of each delivery and birth year), our within-mother matched model was adjusted for a prognostic score defined as the logit of the probability of the outcome regressed on the adjustment variables from an unmatched model. This results in estimation of the direct effect of IPI and allows the whole cohort to contribute to the adjustment for the underlying risk of the outcome [24].

Supplementary analysis

We further estimated the association of gestational diabetes with post-birth IPI. In the absence of confounding factors, gestational diabetes should not be associated with the IPI that follows this birth. An observed association between gestational diabetes and this post-birth IPI indicates the presence of factors in a mother influencing both the risk of gestational diabetes and the IPI, potentially leading to bias estimates. Thus, the post-birth IPI serves as a "negative control" exposure that estimates the effect of mother-level confounding [19,25,26].

Sensitivity analysis

To ascertain the sensitivity of our results to higher-order parity, and inclusion of stillbirths, we conducted separate analyses restricted to the first three births for all mothers with births at parity 0, 1, and 2, and to mothers with at least three consecutive live births, respectively. To explore if our results are sensitive to the time period of the cohort, we restricted our further analyses to consecutive births after first of September 1997, after which smoking status and pre-existing chronic conditions were routinely recorded and ultrasound scans were more common (Appendix Table 2, Model 2a–c). Finally, we included a sensitivity analyses restricted to mothers who had no gestational diabetes in their first pregnancy, to ascertain if effect of IPI differs for those with and without gestational diabetes in the first pregnancy (Appendix Table 3).

Table 1
Socio-demographic characteristics and medical conditions of the study cohort of mothers at their first birth included during the study period (n = 103,909 mothers) in Western Australia, 1980–2015

Characteristics	Mothers, N (%)
Total number of mothers	103,909
Maternal age at first birth (y)	
<25	56,901 (54.8)
25–29	32,988 (31.7)
30–34	12,467 (12.0)
35–39	1521 (1.5)
40 or older	32 (0.03)
Marital status	
Married	83,875 (80.7)
Never married	19,221 (18.5)
Widowed, divorced, separated	618 (0.6)
Unknown	195 (0.2)
Race/ethnicity	
Caucasian	88,106 (84.8)
Aboriginal/Torres Strait Islander	8267 (7.9)
Asian*	1986 (1.9)
African	600 (0.6)
Others†	4950 (4.8)
Birth year	
1980–1984	20,264 (19.5)
1985–1989	17,681 (17.0)
1990–1994	16,811 (16.2)
1995–1999	16,053 (15.4)
2000–2004	15,538 (15.0)
2005–2009	14,448 (13.9)
2010–2015	3114 (3.0)
SES in quintiles	
<20th percentiles (most disadvantaged)	20,398 (19.6)
20–39th percentile	21,679 (20.8)
40–59th percentile	21,914 (21.1)
60–79th percentile	20,648 (19.9)
≥80th percentile (least disadvantaged)	19,270 (18.6)
Chronic conditions	
Known chronic hypertension	259 (0.3)
Known chronic diabetes	181 (0.2)
Known obesity history	237 (0.2)
Pregnancy characteristics	
Pregnancy complications	
Gestational diabetes	1716 (1.6)
Gestational hypertension	2400 (2.3)
Infant sex	
Male	54,132 (52.1)
Parity	
0	96,314 (92.7)
1	4977 (4.8)
2	1636 (1.6)
≥3	374 (1.0)

* Including Indian.
† Including Polynesian & Maori.

Table 2
Characteristics of study population of births by gestational diabetes status for all births to mothers with at least three consecutive births during the study period (n = 254,137 births) in Western Australia, 1980–2015

Characteristics	Total	Gestational diabetes
	Births (N)	Births, N (%)*
Total number of births	254,137	10,032 (4)
Interpregnancy interval (mo)		
0–5	16,548	539 (3.3)
6–11	45,076	1261 (2.8)
12–17	50,528	1509 (3.0)
18–23	37,352	1272 (3.4)
24–59	78,909	3526 (4.5)
60–119	21,780	1499 (6.9)
120 or more	3944	426 (10.8)
Maternal age at time of each delivery (y)		
<25	53,083	915 (1.7)
25–29	83,808	2430 (2.9)
30–34	77,280	3407 (4.4)
35–39	34,138	2603 (7.6)
40 or older	5828	677 (11.6)
Race/ethnicity		
Caucasian	209,073	6803 (3.3)
Non-Caucasian	45,064	3229 (7.2)
Birth year		
1980–1984	12,277	30 (0.3)
1985–1989	35,264	238 (0.7)
1990–1994	41,065	765 (1.9)
1995–1999	40,560	1353 (3.3)
2000–2004	39,082	1613 (4.1)
2005–2009	43,408	2098 (4.8)
2010–2015	42,481	3935 (9.3)
SES in quintiles		
<20th percentiles (most disadvantaged)	51,221	2232 (4.4)
20–39th percentile	49,930	1915 (3.8)
40–59th percentile	49,689	1846 (3.7)
60–79th percentile	50,968	2027 (4.0)
≥80th percentile (least disadvantaged)	52,329	2012 (3.8)
Marital status		
Married	229,549	8873 (3.8)
Never married	19,588	887 (4.5)
Widowed, divorced, separated	4156	225 (5.4)
Unknown	844	47 (5.6)

* Row percentages.

All analyses were performed using STATA version 15.1 (Stata Corporation, College Station, Texas). We reported unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (CIs) for each model.

Results

At study entry, defined as mothers' first birth occurring during the study period, the majority of women were generally free from chronic hypertension, diabetes and obesity. There were 1716 (1.6%) mothers who had a diagnosis of gestational diabetes at study entry (Table 1). For all births included in the cohort, the incidence of gestational diabetes during the study period was 4% (Table 2). There were 16,548 (6%) births which occurred after an IPI of 0–5 months, 45,076 (18%) after 6–11 months, 50,528 (20%) after 12–17 months; 37,352 (15%), after 18–23 months; 78,909 (31%) after IPI of 24–59 months, 21,780 (9%) births after 60–119 months and 3944 (1.6%) of births after 120 or more months. Gestational diabetes diagnoses were more common among mothers in the older age groups, and in mothers with longer IPIs (Table 2). Moreover, mothers with shorter IPIs tended to be younger and non-Caucasian. Observation of longer IPIs was more prevalent late in the study period (1995 onwards) Appendix Table 1.

Compared to an IPI of 18–23 months, unmatched adjusted analysis showed lower odds of gestational diabetes for 6–11-month intervals (adjusted odds ratio (aOR), 0.89; 95% CI, 0.82–0.97) and 12–17-month intervals (aOR: 0.92; 95% CI, 0.85–0.99) (Table 3). However, IPI of 24 months or more was associated with greater odds of gestational diabetes. The greatest adjusted effect was observed for IPIs of 120 or more months (aOR: 1.51; 95% CI, 1.33–1.70).

Conditional logistic regression restricts analyses to births from informative (non-concordant) strata (mothers), which in this study were mothers who experienced gestational diabetes for at least one, but not all of their births. There were 18,873 births to mothers with non-concordant gestational diabetes. The unadjusted within-mother matched comparison indicated that an IPI of 24 months or longer was associated with greater odds of gestational diabetes compared to an interval of 18–23 months, with OR ranging from 1.40 (95% CI, 1.26–1.55) for 24–59 months interval, to 3.65 (95% CI, 2.95–4.52) for IPI of 120 or more months. After full adjustment for covariates including, maternal age at time of each delivery and birth year, matched analyses showed a statistically non-significant lower odd of gestational diabetes for short IPIs as compared to

Table 3
Odds Ratios (ORs) and 95% confidence intervals for the association between interpregnancy interval and gestational diabetes for births to mothers with at least three consecutive births during the study period (n = 103,909 mothers, n = 254,137 births) in Western Australia, 1980–2015

IPI in months	Unmatched		Matched			
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)*	Informative strata, n (%)§	Unadjusted OR (95% CI)	Adjusted OR (95% CI)†	Adjusted OR (95% CI)‡
0–5	0.95 (0.86–1.05)	1.01 (0.91–1.12)	1305 (6.9)	**0.78 (0.67–0.91)**	**0.80 (0.68–0.95)**	0.88 (0.75–1.05)
6–11	**0.81 (0.75–0.88)**	**0.89 (0.82–0.97)**	2954 (15.7)	**0.79 (0.70–0.89)**	**0.84 (0.74–0.96)**	0.92 (0.80–1.05)
12–17	**0.87 (0.80–0.94)**	**0.92 (0.85–0.99)**	3297 (17.5)	**0.83 (0.74–0.93)**	**0.86 (0.76–0.98)**	0.90 (0.79–1.02)
18–23	1.00 (reference)	1.00 (reference)	2489 (13.2)	1.00 (reference)	1.00 (reference)	1.00 (reference)
24–59	**1.32 (1.24–1.41)**	**1.13 (1.06–1.21)**	6096 (32.3)	**1.40 (1.26–1.55)**	**1.29 (1.15–1.44)**	1.07 (0.95–1.20)
60–119	**2.09 (1.94–2.26)**	**1.32 (1.22–1.43)**	2216 (11.7)	**2.28 (2.01–2.57)**	**1.96 (1.71–2.23)**	1.08 (0.93–1.25)
120 or more	**3.42 (3.06–3.85)**	**1.51 (1.33–1.70)**	516 (2.7)	**3.65 (2.95–4.52)**	**3.02 (2.41–3.80)**	1.02 (0.77–1.34)

Bold indicates statistical significance at the 5% level.
Models adjusted for the following variables.
* Maternal age at time of each delivery (categorical), parity, birth year, SES, race/ethnicity, marital status, infant sex, history of obesity, gestational hypertension and known chronic hypertension.
† Prognostic score for gestational diabetes by parity, SES, marital status, infant sex, history of obesity, gestational hypertension, and known chronic hypertension.
‡ Prognostic score for gestational diabetes by maternal age at time of each delivery (categorical), birth year, parity, SES, marital status, infant sex, history of obesity, gestational hypertension and known chronic hypertension.
§ Number and percentage of informative strata of gestational diabetes for each IPI category for births to mothers with at least three consecutive births.

reference category of 18–23 months, with aOR of 0.88 (95% CI, 0.75–1.05) for IPI lower than 6 months and 0.90 (95% CI, 0.79–1.02) for IPI of 12–17 months. However, we observed a statistically non-significant increased odds of gestational diabetes for long IPI compared to an 18–23-month IPI, with aORs ranging from 1.07 (95% CI, 0.95–1.20) for IPI of 24–59 months to 1.08 (95% CI, 0.93–1.25) for IPI of 60 months or longer.

The results of our sensitivity analyses Appendix Table 2 restricted to mothers with their first three consecutive births [Model 2a], and a cohort that only included live births [Model 2b] were consistent with the effect estimates obtained from our main analyses. However, statistically significant lower odds of gestational diabetes were observed for shorter IPIs of 0–5 months and 12–17 months in the model that excluded stillbirths [Model 2b]. Additionally, we observed a negligible difference in the association between IPI and gestational diabetes when we restricted our cohort to births from September 1997 onwards, for which more information was available for adjustment, although this induced a 65% reduction in sample size [Model 2c]. We observed a little difference in the effect estimates with and without exclusion of mothers with gestational diabetes in their first pregnancy Appendix Table 3. In general, our sensitivity analyses collectively supported a weak adverse association of long IPIs and gestational diabetes, similar to those reported in the main analyses.

The adjusted model from the supplementary analyses indicated that the short post-birth IPI of 6 months or less was statistically significantly associated with gestational diabetes in the previous pregnancy (aOR: 1.25; 95% CI, 1.03–1.52). However, the long post-birth IPIs of 24 or more months were not associated with gestational diabetes in this model with aOR of 1.04 (95% CI, 0.91–1.18) for post-birth IPI of 24–59 months and 1.18 (95% CI, 0.78–1.79) for 120 or more months (Appendix Table 4).

Discussion

Principal findings

Both the between-mother adjusted model and within-mother unadjusted model indicate that IPIs of 24 months or longer were associated with greater odds of gestational diabetes compared to an interval of 18–23 months. In contrast, pregnancies that followed IPIs shorter than 18–23 months had lower odds of gestational diabetes. However, the fully adjusted within-mother matched analyses showed no statistically significant association between short and long IPIs and gestational diabetes.

Meaning of the findings

Point estimates from within-mother analyses were lower than those from between-mother analyses; and estimates from the within-mother analyses were attenuated after full adjustment for covariates, indicating that the influence of IPI could be partially explained by the pathway through time-varying confounders, most notably maternal age. Longer IPIs are inherently linked to increasing maternal age, which is a well-established risk factor for gestational diabetes [2,27]. Contrary to the findings of previous between-mother comparisons [13,14], which showed that short IPIs were statistically significantly associated with increased risk of gestational diabetes, our results did not support the existence of an adverse association between short IPIs and gestational diabetes. This finding is consistent with previous unmatched cohort studies [6,28] as well as recent case-control study [29]. However, our findings for long IPIs are consistent with findings of other studies [12,14,29].

The associations observed in the unmatched between-mother comparisons were attenuated in the within-mother matched comparisons. This suggests that the observed effects of short and long IPIs in the unmatched between-mother comparison and previous similar unmatched studies likely were influenced by factors that remain stable for mothers throughout their pregnancies (e.g., persistent lifestyle factors, SES) but vary much more between women. Our long IPI findings are consistent with those from a recent matched study of a Canadian cohort [14], which reported that matched analyses resulted in statistically non-significant associations between long IPIs and gestational diabetes. However, our findings differ for short IPIs, as the Canadian study reported greater odds of gestational diabetes for short IPIs lower than 6 months. The observed differences may be due to unmeasured confounding that could arise from the lack of adjustment for known risk factors (SES, parity) or differences in susceptibility of the study populations to IPI in the Canadian study [14]. Future research would benefit from exploring the role of pregnancy complications at mothers first birth, as it remains possible that the effect of IPI might be modified by gestational diabetes in first birth. In our cohort, there were 3906 total pregnancies among mothers who had gestational diabetes during their first pregnancy, and 1525 (39%) pregnancies were complicated by recurrent gestational diabetes.

Our supplementary analyses using post-birth IPI established the presence of confounding of the association between IPI and gestational diabetes by factors that vary between women (Appendix Table 4). Specifically, short post-birth IPIs (<6 months)

were associated with increased odds of gestational diabetes in the previous pregnancy. Intuitively, a pregnancy complication cannot be caused by an exposure that occurs after that complication. This result provides justification for the within-mother design because it demonstrates confounding at the mother-level [19,25]. The lack of association between long post-birth IPI and gestational diabetes might indicate that such confounding is less of a concern for longer intervals.

Strengths and limitations

We sourced our cohort from highly reliable population-based perinatal information ascertained from hospital separations and midwives' notifications. To our knowledge this is the largest population-based study to examine the association between IPIs and gestational diabetes among mothers with at least three consecutive births (two intervals) using within-mother comparison (matching pregnancies of the same mother). The within-mother matched design provides estimates based on a cohort of mothers who have experienced pregnancies with and without the complication of interest (gestational diabetes). The premise of this design is that it accounts to a larger extent for environmental and genetic confounders that can vary between mothers.

There were some limitations to our study. Firstly, we restricted our analyses to the outcomes of more than two births for each mother to enable matching of at least two IPIs. Thus, although our design achieves greater interval validity, there remains the possibility of selection-bias. Secondly, we attempted to control time-varying confounders but were unable to measure some variables that may have significance (e.g., pre-pregnancy weight change). However, matched analyses were statistically non-significant and adjustment for such variables would have likely attenuated effect estimates further, and our conclusions would have remained unchanged. Thirdly, it should be acknowledged that chronic conditions were not routinely collected until 1997 and without good capture until 2000. However, our sensitivity analyses suggested that the effect estimates were consistent between the main analyses, and births restricted to 1997 onwards with complete information. Finally, as with all retrospective cohort studies that use comprehensive perinatal records, we were unable to identify pregnancy loss before 20 weeks of gestation. However, gestational diabetes usually occurs later in pregnancy and if any bias is introduced by truncation of pregnancies after 20 weeks of gestation, this is likely to be limited to survivor bias. Even though, information on pregnancy loss may be relevant to consider, findings from a recent study reported insufficient evidence for differences in pregnancy losses by IPI [30].

In conclusion, there was insufficient statistical evidence for a harmful association between short IPI (<6 months) and gestational diabetes in our cohort. Our findings do not support the hypothesis that short IPI (<6 months) increases risk of gestational diabetes and suggests that observed associations in previous studies were possibly attributable to residual confounding.

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Appendix

Appendix Table 1
Characteristics of the study population of all births to mothers with at least three consecutive births during the study period (n = 254,137 births) in Western Australia, 1980–2015

Characteristics	Interpregnancy interval (months)						
	<6	6–11	12–17	18–23	24–59	60–119	120 or more
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Total (n = 254,137)	16,548 (6.5)	45,076 (17.7)	50,528 (19.9)	37,352 (14.7)	78,909 (31.1)	21,780 (8.6)	3944 (1.6)
Gestational diabetes (GDM), n (%): 10,032 (4)							
Yes	539 (3.3)	1261 (2.8)	1509 (3.0)	1272 (3.4)	3526 (4.5)	1499 (6.9)	426 (10.8)
Maternal age at time of each delivery (y)							
<25	6656 (40.2)	13,032 (28.9)	11,872 (23.5)	7747 (20.7)	12,871 (16.3)	905 (4.2)	0 (0.0)
25–29	5395 (32.6)	15,905 (35.3)	17,822 (35.3)	13,023 (34.9)	25,743 (32.6)	5733 (26.3)	187 (4.7)
30–34	3220 (19.5)	11,627 (25.8)	14,883 (29.5)	11,610 (31.1)	26,394 (33.5)	8378 (38.5)	1168 (29.6)
35–39	1130 (6.8)	4024 (8.9)	5290 (10.5)	4397 (11.8)	12,040 (15.3)	5528 (25.4)	1729 (43.8)
40 or older	147 (0.9)	488 (1.1)	661 (1.3)	575 (1.5)	1861 (2.4)	1236 (5.7)	860 (21.8)
Marital status							
Married	14,263 (86.2)	41,118 (91.2)	46,825 (92.7)	34,438 (92.2)	70,892 (89.8)	18,705 (85.9)	3308 (83.9)
Never married	1948 (11.8)	3303 (7.3)	3074 (6.1)	2382 (6.4)	6312 (8.0)	2178 (10.0)	391 (9.9)
Widowed, divorced, separated	282 (1.7)	545 (1.2)	497 (1.0)	419 (1.1)	1429 (1.8)	772 (3.5)	212 (5.4)
Unknown	55 (0.3)	110 (0.2)	132 (0.3)	113 (0.3)	276 (0.4)	125 (0.6)	33 (0.8)
Race/ethnicity							
Caucasian	12,299 (74.3)	37,050 (82.2)	42,262 (83.6)	31,413 (84.1)	64,944 (82.3)	17,801 (81.7)	3304 (83.8)
Non-Caucasian	4249 (25.7)	8026 (17.8)	8266 (16.4)	5939 (15.9)	13,965 (17.7)	3979 (18.3)	640 (16.2)
Birth year							
1980–1984	1452 (8.8)	3698 (8.2)	3545 (7.0)	1973 (5.3)	1609 (2.0)	0 (0.0)	0 (0.0)
1985–1989	2460 (14.9)	7173 (15.9)	8132 (16.1)	5862 (15.7)	10,641 (13.5)	996 (4.6)	0 (0.0)
1990–1994	2569 (15.5)	7315 (16.2)	8381 (16.6)	6260 (16.8)	13,059 (16.6)	3275 (15.0)	206 (5.2)
1995–1999	2433 (14.7)	6807 (15.1)	7725 (15.3)	5787 (15.5)	13,192 (16.7)	3931 (18.1)	685 (17.4)
2000–2004	2327 (14.1)	6367 (14.1)	7201 (14.3)	5545 (14.9)	12,652 (16.0)	4125 (18.9)	865 (21.9)
2005–2009	2828 (17.1)	7398 (16.4)	8023 (15.9)	5943 (15.9)	13,443 (17.0)	4686 (21.5)	1087 (27.6)
2010–2015	2479 (15.0)	6318 (14.0)	7521 (14.9)	5982 (16.0)	14,313 (18.1)	4767 (21.9)	1101 (27.9)
SES*							
1	4602 (27.8)	9386 (20.8)	9482 (18.8)	6905 (18.5)	15,507 (19.7)	4603 (21.1)	736 (18.7)
2	3712 (22.4)	9070 (20.1)	9563 (18.9)	7096 (19.0)	15,245 (19.3)	4445 (20.4)	799 (20.3)
3	3283 (19.8)	8994 (20.0)	9909 (19.6)	7367 (19.7)	15,073 (19.1)	4276 (19.6)	787 (20.0)
4	2749 (16.6)	8938 (19.8)	10,450 (20.7)	7684 (20.6)	15,976 (20.3)	4328 (19.9)	843 (21.4)
5	2202 (13.3)	8688 (19.3)	11,124 (22.0)	8300 (22.2)	17,108 (21.7)	4128 (19.0)	779 (19.8)

* Categorized as quintiles (1 = most disadvantaged to 5 = least disadvantaged).

Appendix Table 2
Odds Ratios (OR) and 95% confidence intervals for the association between interpregnancy interval and gestational diabetes for births to (Model 2a) mothers with three consecutive births (parity 0, 1, 2); (Model 2b) mothers with at least three consecutive live births; (Model 2c) mothers with at least three consecutive births during the end of the study period (Sept 1997 onwards) in Western Australia, 1980–2015

IPI in months	Unmatched		Matched		
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)*	Unadjusted OR (95% CI)	Adjusted OR (95% CI)†	Adjusted OR (95% CI)‡
Gestational diabetes					
Model 2a: (n = 96,354 mothers, n = 192,708 births)					
0–5	0.99 (0.87–1.12)	**1.14 (1.00–1.30)**	0.82 (0.66–1.03	0.83 (0.66–1.05)	0.94 (0.75–1.19)
6–11	**0.86 (0.78–0.95)**	0.97 (0.87–1.07)	0.89 (0.75–1.05)	0.93 (0.78–1.11)	1.01 (0.84–1.20)
12–17	**0.88 (0.79–0.96)**	0.94 (0.85–1.03)	**0.82 (0.70–0.96)**	**0.86 (0.73–1.01)**	0.91 (0.76–1.07)
18–23	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
24–59	**1.34 (1.24–1.45)**	**1.14 (1.05–1.24)**	**1.44 (1.25–1.65)**	1.37 (1.18–1.58)	1.11 (0.95–1.29)
60–119	**2.16 (1.97–2.38)**	**1.36 (1.23–1.50)**	**2.42 (2.03–2.88)**	2.22 (1.85–2.66)	1.19 (0.97–1.45)
120 or more	**3.82 (3.32–4.38)**	**1.60 (1.38–1.86)**	**3.13 (2.39–4.10)**	2.72 (2.06–3.59)	0.92 (0.65–1.30)
Model 2b: (n = 100,286 mothers, n = 244,125 births)					
0–5	0.90 (0.81–1.01)	0.96 (0.86–1.07)	**0.74 (0.63–0.88)**	**0.75 (0.62–0.90)**	**0.82 (0.68–0.98)**
6–11	**0.80 (0.74–0.87)**	**0.88 (0.81–0.96)**	**0.75 (0.66–0.85)**	**0.82 (0.71–0.94)**	0.87 (0.76–1.01)
12–17	**0.85 (0.79–0.92)**	**0.91 (0.83–0.98)**	**0.79 (0.70–0.89)**	**0.83 (0.73–0.95)**	**0.86 (0.76–0.99)**
18–23	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
24–59	**1.33 (1.25–1.42)**	**1.14 (1.07–1.22)**	**1.40 (1.26–1.55)**	**1.28 (1.14–1.43)**	1.10 (0.97–1.23)
60–119	**2.11 (1.95–2.29)**	**1.34 (1.23–1.45)**	**2.26 (1.99–2.56)**	**1.90 (1.65–2.18)**	1.13 (0.97–1.31)
120 or more	**3.45 (3.08–3.88)**	**1.52 (1.34–1.72)**	**3.66 (2.93–4.56)**	**2.95 (2.32–3.73)**	1.13 (0.86–1.50)
Model 2c: (n = 40,405 mothers, n = 93,716 births)					
0–5	0.91 (0.79–1.04)	1.05 (0.91–1.21)	**0.77 (0.62–0.95)**	0.83 (0.66–1.04)	0.91 (0.72–1.15)
6–11	**0.82 (0.74–0.91)**	0.93 (0.84–1.03)	**0.74 (0.63–0.87)**	0.84 (0.70–1.00)	0.90 (0.75–1.07)
12–17	0.91 (0.82–1.01)	0.97 (0.88–1.07)	**0.79 (0.67–0.92)**	0.89 (0.75–1.06)	0.92 (0.77–1.09)
18–23	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
24–59	**1.32 (1.20–1.44)**	**1.15 (1.07–1.27)**	**1.41 (1.22–1.62)**	**1.32 (1.13–1.54)**	1.07 (0.91–1.25)
60–119	**2.01 (1.80–2.25)**	1.33 (1.19–1.49)	**2.18 (1.81–2.63)**	**2.05 (1.67–2.51)**	1.05 (0.84–1.31)
120 or more	**2.78 (2.07–3.74)**	**1.28 (0.95–1.74)**	**1.94 (1.16–3.26)**	**2.03 (1.16–3.55)**	0.61 (0.30–1.24)

Bold indicates significance at the 5% level.
Model 2a and 2b were adjusted for the following variables.
* Maternal age at time of each delivery (categorical), birth year, parity, SES, race/ethnicity, marital status, infant sex, history of obesity; gestational hypertension and known chronic hypertension.
† Prognostic score for GDM of parity, SES, marital status, infant sex, history of obesity; gestational hypertension, and known chronic hypertension.
‡ Prognostic score for GDM of maternal age at time of each delivery (categorical), parity, birth year, SES, marital status, infant sex, history of obesity; gestational hypertension and known chronic hypertension; Model 2c: includes all variables in Model 2a plus smoking during pregnancy.

Appendix Table 3
Odds Ratios (OR) and 95% confidence intervals for the association between interpregnancy interval and gestational diabetes for births to (Model-A) mothers with at least three consecutive births during the study period (n = 103,909 mothers, n = 254,137 births); (Model-B) mothers with at least three consecutive births during the study period, excluding mothers with gestational diabetes in first pregnancy (n = 102,193 mothers, n = 250,231 births) in Western Australia, 1980–2015

IPI in months	Unmatched			
	Unadjusted OR (95% CI)		Adjusted OR (95% CI)*	
	Model A	Model B	Model A	Model B
0–5	0.95 (0.86–1.05)	0.97 (0.86–1.08)	1.01 (0.91–1.12)	1.00 (0.89–1.13)
6–11	**0.81 (0.75–0.88)**	**0.79 (0.72–0.87)**	**0.89 (0.82–0.97)**	**0.86 (0.79–0.95)**
12–17	**0.87 (0.80–0.94)**	**0.84 (0.77–0.91)**	**0.92 (0.85–0.99)**	**0.88 (0.81–0.96)**
18–23	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
24–59	**1.32 (1.24–1.41)**	**1.42 (1.32–1.52)**	**1.13 (1.06–1.21)**	**1.21 (1.13–1.30)**
60–119	**2.09 (1.94–2.26)**	**2.40 (2.21–2.61)**	**1.32 (1.22–1.43)**	**1.52 (1.40–1.66)**
≥120	**3.42 (3.06–3.85)**	**4.07 (3.61–4.58)**	**1.51 (1.33–1.70)**	**1.83 (1.61–2.08)**

IPI in months	Matched							
	Informative strata, n (%)§		Unadjusted OR (95% CI)		Adjusted OR (95% CI)†		Adjusted OR (95% CI)‡	
	Model A	Model B	Model A	Model B	Model A	Model B	Model A	Model B
0–5	1305 (6.9)	1202 (6.9)	**0.78 (0.67–0.91)**	**0.77 (0.65–0.91)**	**0.80 (0.68–0.95)**	**0.79 (0.67–0.95)**	0.88 (0.75–1.05)	0.87 (0.73–1.05)
6–11	2954 (15.7)	2665 (15.3)	**0.79 (0.70–0.89)**	**0.79 (0.70–0.89)**	**0.84 (0.74–0.96)**	**0.84 (0.73–0.96)**	0.92 (0.80–1.05)	0.91 (0.79–1.05)
12–17	3297 (17.5)	3004 (17.2)	**0.83 (0.74–0.93)**	**0.82 (0.72–0.93)**	**0.86 (0.76–0.98)**	**0.84 (0.74–0.96)**	0.90 (0.79–1.02)	0.87 (0.76–1.00)
18–23	2489 (13.2)	2262 (12.9)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
24–59	6096 (32.3)	5685 (32.6)	**1.40 (1.26–1.55)**	**1.43 (1.29–1.60)**	**1.29 (1.15–1.44)**	**1.33 (1.19–1.50)**	1.07 (0.95–1.20)	1.10 (0.97–1.24)
60–119	2216 (11.7)	2128 (12.2)	**2.28 (2.01–2.57)**	**2.37 (2.08–2.69)**	**1.96 (1.71–2.23)**	**2.04 (1.77–2.34)**	1.08 (0.93–1.25)	1.11 (0.95–1.29)
≥120	516 (2.7)	504 (2.9)	**3.65 (2.95–4.52)**	**3.75 (3.02–4.67)**	**3.02 (2.41–3.80)**	**3.07 (2.43–3.88)**	1.02 (0.77–1.34)	1.01 (0.75–1.34)

Bold indicates significance at the 95% confidence level.
Models adjusted for the following variables.
* Maternal age at time of each delivery (categorical), parity, birth year, SES, race/ethnicity, marital status, infant sex, history of obesity, gestational hypertension and known chronic hypertension.
† Prognostic score for gestational diabetes by parity, SES, marital status, infant sex, history of obesity, gestational hypertension, and known chronic hypertension.
‡ Prognostic score for gestational diabetes by maternal age at time of each delivery (categorical), birth year, parity, SES, marital status, infant sex, history of obesity, gestational hypertension and known chronic hypertension.
§ Number and percentage of informative strata of gestational diabetes for each IPI category for births to mothers with at least three consecutive births.

Appendix Table 4

Odds Ratios (ORs) and 95% confidence intervals for the association between post-birth interpregnancy interval (interval between second and third births) and gestational diabetes in the second birth for mothers with three consecutive births during the study period (n = 96,354 births) in Western Australia, 1980–2015

IPI in months	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[†]
Gestational diabetes[*]		
0–5	**1.36 (1.13–1.65)**	**1.25 (1.03–1.52)**
6–11	**1.00 (0.86–1.16)**	0.94 (0.81–1.10)
12–17	1.05 (0.91–1.22)	1.02 (0.88–1.18)
18–23	1.00 (reference)	1.00 (reference)
24–59	0.93 (0.82–1.06)	1.04 (0.91–1.18)
60–119	**0.67 (0.55–0.81)**	0.96 (0.79–1.16)
120 or more	**0.54 (0.36–0.81)**	1.18 (0.78–1.79)

[*] Predicting gestational diabetes of second born (parity 1 births) using post-pregnancy IPI (interval between second born and third born births).

[†] Model adjusted for maternal age (categorical), birth year, parity, SES, race/ethnicity, marital status, infant sex, history of obesity, gestational hypertension and known chronic hypertension.