Title

The impact of diabetes during pregnancy on neonatal outcomes among the Aboriginal population in Western Australia: a whole-population study

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Word count: 4142 words (Paper); 240 words (Abstract)

Abstract

Background

Aboriginal and Torres Strait Islander (hereafter Aboriginal) women have high prevalence of diabetes in pregnancy (DIP), which includes pre-gestational diabetes (PGDM) and gestational diabetes (GDM). We aimed to characterise the impact of DIP in babies born to Aboriginal mothers.

Methods

A retrospective cohort study, using routinely collected linked health data, that included all singleton births (n= 510 761) in Western Australia between 1998-2015. Stratified by Aboriginal status, generalised linear mixed models quantified the impact of DIP on neonatal outcomes, estimating relative risks (RRs) with 95% confidence intervals (CI). Ratio of RRs (RRRs) examined whether RRs differed between Aboriginal and non-Aboriginal populations.

Results

Exposure to DIP increased the risk of adverse outcomes to a greater extent in Aboriginal babies. PGDM heightened the risk of large-for-gestational-age (LGA) (RR: 4.10, [95% CI: 3.56-4.72]; RRR: 1.25 [1.09-1.43]), macrosomia (RR: 2.03 [1.67-2.48]; RRR: 1.39 [1.14-1.69]), shoulder dystocia (RR: 4.51 [3.14-6.49]; RRR: 2.19 [1.44-3.33]) and major congenital anomalies (RR: 2.14 [1.68-2.74]; RRR: 1.62 [1.24-2.10]). GDM increased the risk of LGA (RR: 2.63 [2.36-2.94]; RRR: 2.00 [1.80-2.22]), macrosomia (RR: 1.95 [1.72-2.21]; RRR: 2.27 [2.01-2.56]) and shoulder dystocia (RR: 2.78 [2.12-3.63]; RRR: 2.11 [1.61-2.77]). Birthweight mediated about half of DIP effect on shoulder dystocia only in the Aboriginal babies.

Conclusions

DIP differentially increased risks of fetal overgrowth, shoulder dystocia and congenital anomalies in Aboriginal babies. Improving care for Aboriginal women with diabetes and further research on preventing shoulder dystocia among these women can reduce the disparities.

Key Words

Diabetes in pregnancy, Pre-gestational diabetes, Gestational diabetes, Aboriginal, Indigenous Australians, Neonatal outcomes

Key Messages

- In this population-wide, retrospective cohort study, diabetes in pregnancy heightened the risk of large-for-gestational age, macrosomia, shoulder dystocia (both gestational and pre-gestational diabetes) and congenital anomalies (pre-gestational diabetes) to a greater extent among Aboriginal babies.
- Birthweight mediated about half of the effect of diabetes in pregnancy on shoulder dystocia in Aboriginal mothers, and was protective in non-Aboriginal mothers.
- Disparities in these modifiable outcomes, which showed no improvement over time, can be potentially reduced by appropriate pre-pregnancy and prenatal management and by further investigations to identify modifiable factors that contribute to shoulder dystocia in pregnancies complicated by diabetes.

Introduction

The burden of diabetes in pregnancy (DIP), which includes pre-gestational diabetes mellitus (PGDM) and gestational diabetes mellitus (GDM), is increasing globally, primarily as a consequence of increasing rates of maternal overweight and obesity and older maternal ages (1). DIP is responsible for significant adverse neonatal outcomes including perinatal death, high birthweight (and subsequent birth trauma), preterm birth, fetal growth restriction, congenital anomalies and respiratory distress syndrome (2).

Indigenous populations worldwide suffer a disproportionately heavy burden of DIP (3). In Australia, a plethora of evidence highlights the substantially higher prevalence (and increasing trends) of DIP among Aboriginal and Torres Strait Islander (hereafter respectfully referred to as Aboriginal), compared with non-Aboriginal, women (4-6). This is consistent with the generally poorer profile of

cardio-metabolic health among Aboriginal peoples, which in part reflects a persistent colonial legacy that has impacted on all aspects of their wellbeing, and health behaviours and socioeconomic circumstances over generations (7, 8). The rates of type 2 diabetes mellitus (T2DM) among Aboriginal pregnant women increased ten-fold in the three decades to 2016 in Australia's Northern Territory, to what is believed to be the world highest prevalence of PGDM in pregnancy (6). Despite the robust evidence on DIP prevalence, the burden it exerts on Australian Aboriginal babies has not been properly quantified at the population level. There is thus a need for population-wide, sufficiently large, studies with potential to investigate wide range of neonatal outcomes to add to the existing evidence (9-16).

DIP-associated adverse neonatal outcomes can be greatly reduced (17), due to their well-established risk factor profiles that provide optimal targets for timely interventions over the pregnancy period. Therefore, we expected that characterising neonatal outcomes in babies born to Aboriginal mothers with diabetes would identify DIP-attributable, improvable, health disparities that can inform interventions and preventive measures. This study aimed to quantify the impact of PGDM and GDM on neonatal outcomes in the Western Australian Aboriginal population using total population data, linked administrative data from multiple sources.

Methods

Study design, data sources and study population

This is a whole-population, retrospective cohort study using population health datasets of Western Australia. Data from different sources have been linked by the Western Australian Data Linkage System using probabilistic matching techniques, with researchers receiving data without identifying information (18). The used linkage methods are internationally considered as best practice and proved to be highly reliable (19, 20). Linked datasets included data obtained from the Midwives Notification System (MNS), Hospital Morbidity Data Collection (HMDC), Western Australian Register of Developmental Anomalies (WARDA), Death Registrations and Births Registrations. MNS records

contain details on all births that occur in WA at ≥20 weeks' gestation. HMDC provides information related to all WA hospital admissions.

The study population (Figure 1) included all singleton births in Western Australia between January 1st, 1998 and December 31st, 2015. Of 526 319 births that occurred in WA during the study period, we excluded 15 558 (2.96%) multiple births.

Measures (Supplementary Tables S1 and S2, available as Supplementary data at IJE online, show the sources and ICD diagnosis codes of study variables)

Exposure

This study used the Indigenous status flag created using the algorithm of the *Getting Our Story Right* project (21). To identify Aboriginal individuals in linked administrative datasets, these guidelines recommend a multi-stage median approach to create a single consistent Aboriginal status for each individual. PGDM and GDM were ascertained from MNS and HMDC using relevant hospital separation codes.

Outcomes

Perinatal death was defined as stillbirth at ≥ 20 weeks gestation or neonatal death (death during the first 28 days of life). Post-neonatal death was defined as death between 28 and 365 days of life. Large-for-gestational age (LGA) was defined as birthweight higher than the 90th percentile and small-for-gestational age (SGA) as birthweight lower than the 10th percentile, using Australian gestational age- and sex-specific birthweight percentiles (22). Birthweight ≥ 4000-gram defined macrosomia and births before 37 weeks' gestation were considered preterm. WARDA includes births defects diagnosed during the first six years of life, and categorises a birth defect as major or minor depending on the severity (23). Shoulder dystocia was reported in the MNS when there was difficulty and delay in delivering the anterior shoulder at vaginal birth.

Covariates

The covariates were broadly classified into maternal sociodemographic and maternal morbidity factors. The sociodemographic factors included maternal age (years, continuous), parity group (categorical: 0, 1, 2 or ≥3), smoking during pregnancy (binary), marital status (binary: married or not), remoteness of residence (classified from metropolitan through to very remote, based on the Accessibility/Remoteness Index of Australia (ARIA) (24); used in the analyses in the binary form: Remote and Very remote, or not) and socioeconomic status (categorised into tertiles, based on Index of Relative Socioeconomic Disadvantage (25)). The morbidity factors included pre-existing hypertension, gestational hypertension, eclampsia/preeclampsia and urinary tract infections (all binary).

Missing data

The level of missing data was <1% for all variables included in this study, with the exception of remoteness (1.6%) and socioeconomic status (4.1%) (Supplementary Table S3, available as Supplementary data at IJE online), so multiple imputation was not done.

Statistical analysis

Counts and percentages were used to compare the distribution of maternal and pregnancy characteristics among the Aboriginal and non-Aboriginal populations. Absolute risks and crude relative risks (RRs) with 95% confidence intervals (CI) were estimated to describe the association between DIP (PGDM and GDM) and neonatal outcomes in the Aboriginal and non-Aboriginal populations.

To characterise the impact of DIP on neonatal outcomes, we quantified the strength of association between DIP and each outcome by estimating cluster- and covariate-adjusted RRs with 95% CI in analyses stratified by Aboriginal status. Covariates were selected based on prior knowledge of association with the outcome, and their associations with DIP in the cohort were then tested by bivariate analysis using Pearson's chi-squared test. The relationship between DIP and each outcome was characterised by fitting three models using different sets of covariates (Model 1 adjusted for

clustering effect; Model 2 adjusted for clustering effect and maternal sociodemographic characteristics; Model 3 adjusted for factors in Model 2 in addition to maternal morbidities). In our longitudinal cohort, a clustering effect reflects correlated outcomes among babies born to the same mother. The clustering effect (by mother) violates the "independence of observations" assumption of generalised linear models, reduces the effective sample size and results in inaccurate model estimates. It was important to account for the clustering effect as Aboriginal women had vastly different parity profiles to non-Aboriginal women. The mixed-effects models accommodate dependency among observations within a group and allow for a group-level random effect in the linear predictor, statistically accounting for clustering effect and preventing bias in the resultant estimates and their variances. We thus fitted generalised linear mixed models (GLMMs) using neonatal outcomes, separately, as the binary dependent variables. The linear predictor part of the model included fixed (DIP and covariates) and random (mother identifier) intercepts. As the purpose was to estimate the RRs, we specified Poisson as the distribution family of the dependent variable and log as the link function. We used the Huber-White sandwich estimator to obtain variance estimates that are robust to misspecifications.

To examine whether the estimated RRs from the stratified analysis differed by Aboriginal status, we incorporated an interaction term between Aboriginal status and DIP into pooled (non-stratified) models that also included their main effects along with the other covariates. The exponentiated coefficient of the interaction term provided the ratio of RRs (RRRs) for outcomes between Aboriginal and non-Aboriginal babies. We also investigated how the gap in outcomes (Aboriginal vs. non-Aboriginal) among babies born to diabetic mothers changed with time. Outcomes that showed significant RRRs were included in pooled GLMMs restricted to PGDM and GDM pregnancies, separately. These models also included an interaction term of Aboriginal status with time (year of birth divided by 10, as a continuous variable) in addition to the covariates. The exponentiated coefficient of the interaction term provided the change in RR (of neonatal outcomes in Aboriginal vs non-Aboriginal babies born to mothers with DIP) per decade.

High birthweight is an established risk factor for shoulder dystocia, and a consequence of DIP. To better characterise the impact of DIP on shoulder dystocia (without adjusting for the birthweight, which lies on the causal pathway between the exposure and outcome), we conducted a mediation analysis to decompose the total effect of DIP on shoulder dystocia into birthweight-mediated (indirect effect) and non-birthweight-mediated (direct effect) (Supplementary Figure S1, available as Supplementary data at IJE online). We estimated the proportion mediated in analyses stratified by Aboriginal status. We used a causal mediation analysis approach (described by VanderWeele) that accounts for possible exposure-mediator interaction and relies on the counterfactual framework (26). The mediation analysis, which was adjusted for maternal sociodemographic and morbidity factors, involved fitting logistic and linear regression models for shoulder dystocia (a binary outcome) and birthweight (a continuous mediator).

Stata version 16 (StataCorp. 2019) was used to perform all analyses. Stata commands "meglm" and "paramed" (27) were used to calculate the cluster- and covariate-adjusted RRs and the mediation estimates, respectively.

Bias

Clinical guidelines recommend screening for GDM at 24-28 weeks of gestation. The differences between GDM and non-diabetic pregnancies in the time of establishment of exposure status and in the start of follow-up introduce the risk of immortal time bias. We thus, conservatively, restricted GDM-related analyses to births at or after 28 weeks.

Results

There were 510 761 singleton births in WA during the study period. About 6.4 % of the births (n=32 845) were to Aboriginal mothers. PGDM was more prevalent in Aboriginal relative to non-Aboriginal pregnancies (2.8% vs 0.7%), whereas the prevalence estimates of GDM were comparable in the two populations (5.7% and 5.9%, respectively).

Aboriginal women were more likely to be younger, be of higher parity, live in a remote and low socio-economic area and to have smoked during pregnancy (Table 1). Both Aboriginal and non-Aboriginal women with DIP were more likely to be in the older age groups, less likely to smoke and more likely to have hypertensive disorders during pregnancy when compared to women without DIP (Table 1). Relative to those without DIP, mothers with DIP had higher proportions of caesarean section and labour induction and were more likely to be in the higher parity groups (to a greater extent in the Aboriginal population).

Unadjusted analysis (Table 2) revealed that PGDM increased the risk of perinatal death, post-neonatal death, LGA, preterm birth, major congenital anomalies, macrosomia and shoulder dystocia in both the Aboriginal and non-Aboriginal populations. GDM increased LGA and shoulder dystocia in both populations; increased preterm births and major congenital anomalies in the non-Aboriginal population; and heightened the risk of macrosomia among Aboriginal babies. Both PGDM and GDM decreased the risk of SGA among the Aboriginal and non-Aboriginal populations.

Pre-gestational diabetes

Adjusted analyses (Table 3: Model 3) showed that PGDM was associated with a 4.5-fold increased risk of shoulder dystocia (RR: 4.51, 95% CI: 3.14-6.49) and a 4-fold increased risk of LGA (RR: 4.10, 95% CI: 3.56-4.72) among the Aboriginal population. PGDM also doubled the risk of macrosomia (RR: 2.03, 95% CI: 1.67-2.48) and major congenital anomalies (RR: 2.14, 95% CI: 1.68-2.74). The impact of PGDM on shoulder dystocia, LGA, macrosomia, major congenital anomalies and preterm birth differed by Aboriginal status. The effect of PGDM on these outcomes was stronger in the Aboriginal relative to non-Aboriginal population (Table 4: Model 3) (shoulder dystocia [RRR: 2.19, 95% CI: 1.44-3.33]; LGA [RRR: 1.25, 95% CI: 1.09-1.43]; macrosomia [RRR: 1.39, 95% CI: 1.14-1.69]; major congenital anomalies [RRR: 1.62, 95% CI: 1.24-2.10]), while its impact on preterm birth was stronger among non-Aboriginal pregnancies (RRR: 0.60, 95% CI: 0.53-0.69).

The exponentiated interaction terms in Table 5 highlight that the disparities in Aboriginal and non-Aboriginal neonatal outcomes among mothers with PGDM did not decrease with time. The interaction term for LGA (1.26, 95% CI: 1.01-1.56) shows that its RR (LGA in Aboriginal vs non-Aboriginal babies born to mothers with PGDM) increased by 26% per decade, pointing to a widening in the gap between the two populations.

Gestational diabetes

GDM among Aboriginal mothers (Table 3: Model 3) increased the risk of shoulder dystocia (by about three-fold) (RR: 2.78, 95% CI: 2.12-3.63), LGA (RR: 2.63, 95% CI: 2.36-2.94) and macrosomia (RR: 1.95, 95% CI: 1.72-2.21), and reduced the risk of SGA (RR: 0.46, 95% CI: 0.39-0.55). GDM impacted shoulder dystocia, LGA, macrosomia, preterm birth and SGA differently in the Aboriginal and non-Aboriginal populations. Compared with non-Aboriginal neonates, GDM exerted significantly stronger effect on Aboriginal babies (Table 4) (shoulder dystocia [RRR: 2.11, 95% CI: 1.61-2.77]; LGA [RRR: 2.00, 95% CI: 1.80-2.22]; macrosomia [RRR: 2.27, 95% CI: 2.01-2.56]).The impact of GDM on preterm birth (RRR: 0.67, 95% CI: 0.58-0.76) and SGA (RRR: 0.49, 95% CI: 0.41-0.59) was stronger in non-Aboriginal pregnancies.

The disparities between Aboriginal and non-Aboriginal babies born to mothers with GDM did not change over time (Table 5: Model 3), except for SGA (the exponentiated interaction term [0.66, 95% CI: 0.47-0.92] which exhibited a 34% reduction per decade over the study period.

Mediation analysis

The causal mediation analysis (Table 6) revealed that, among the Aboriginal population, birthweight mediated 45% of the association between DIP and shoulder dystocia (natural indirect effect odds ratio [OR NIE] : 1.43, 95% CI: 1.29-1.58). In contrast, the mediation pathway (increase in birthweight) reduced the association among non-Aboriginal babies (OR NIE: 0.89, 95% CI: 0.87-0.91) (proportion mediated was not a valid measure since it took a negative value, reflecting opposite directions of direct and indirect effects).

Discussion

The present study includes several important findings. We found that DIP considerably and differentially heightened the risk of LGA, macrosomia, shoulder dystocia and major congenital anomalies (only PGDM) in the Aboriginal, relative to non-Aboriginal, population. The gap between these two populations did not improve over time. In Aboriginal mothers, birthweight mediated about half of the effect of DIP on shoulder dystocia while there was no evidence of mediation among non-Aboriginal population.

Our findings partly reflect the difficulties that Aboriginal mothers face in accessing timely, high quality, and culturally appropriate antenatal care. Data consistently highlight that these women typically have fewer and more delayed antenatal care visits (28). Recent evidence has highlighted the need to improve the care process for high risk Aboriginal pregnancies (29). Pregnancies complicated by diabetes are considered high risk and require special antenatal care to maintain appropriate glycemic control and improve neonatal outcomes (28). Improved antenatal care and targeted support of Aboriginal pregnancies complicated by diabetes can improve the outcomes from these pregnancies. Barriers to care for Aboriginal families remain a legacy of colonisation in Australia. Aboriginal people continue to experience racism, discrimination, marginalisation and exclusion in many forms (30). This can directly impact access to the health promotion and other resources required for optimal antenatal care, and has been shown to have a pronounced detrimental impact on the material circumstances that shape Aboriginal health more broadly (31).

To directly compare our findings with the available evidence, we extracted and synthesised related data from previous studies to estimate unadjusted RRs and RRRs (Tables S4-S9). One study featured in each of these tables is Pregnancy And Neonatal Diabetes Outcomes in Remote Australia (PANDORA)) by Maple-Brown et al., an important prospective cohort study with more than 1100 Aboriginal and non-Aboriginal pregnancies with and without DIP recruited from a clinical register, community midwifery programmes and antenatal clinics in the Australian Northern Territory (5).

PANDORA has a rich set of variables and biomarkers and thus provides pathophysiological explanations for many adverse neonatal outcomes.

Fetal overgrowth

Evidence from Australian studies shows that, in-line with our findings, PGDM and GDM are more strongly associated with fetal overgrowth in Aboriginal babies compared to their non-Aboriginal counterparts (5, 14) (Supplementary Tables S4 and S5, available as Supplementary data at IJE online). Among Canadian First Nations women, GDM exerted a similar directional effect, though smaller in magnitude (32, 33), while results from PGDM were inconsistent (32, 33) (Supplementary Tables S4 and S5, available as Supplementary data at IJE online).

There is a well-established, strong linear relationship between maternal hyperglycemia and fetal overgrowth (34), with the risk of high birthweight being a critical factor in setting the diagnostic thresholds for GDM (35). Poorer glycemic control among the Aboriginal population has been reported in primary care (36), and in pregnancies complicated by GDM and PGDM (5). The greater risk of fetal overgrowth among Aboriginal babies in this study may have been driven by suboptimal maternal glycemic control, but we did not have the data to investigate this further.

Fetal overgrowth increases the risk of many adverse perinatal outcomes, contributing to the health gap between the Aboriginal and non-Aboriginal populations. Among Canadian Indigenous women, having a high birthweight was associated with a higher risk of T2DM and GDM in later life, contributing to the intergenerational cycle of diabetes (37, 38) distinctive to Indigenous populations globally (30).

Proper glycemic control substantially reduces fetal overgrowth, and treatment of GDM considerably reduces the risk of fetal overgrowth (17). We recommend further research to identify the drivers and possibilities for improvement of fetal overgrowth in babies born to Aboriginal mothers with DIP. Another important gap in knowledge is the possible contribution of fetal overgrowth to the intergenerational cycle of diabetes among the Aboriginal Australian population. The PANDORA study

is planning to investigate the link between early life exposures and future risk of diabetes among the Aboriginal population (5).

Shoulder dystocia

Our findings of the differentially stronger risk of shoulder dystocia among Aboriginal than non-Aboriginal mothers with DIP contrast with those of the PANDORA study which showed no evidence of differences between the two populations (5) (Supplementary Tables S6 and S7, available as Supplementary data at IJE online). In Canada, GDM (32, 39) (but not PGDM (32)) increased the unadjusted risk of shoulder dystocia to a higher extent (though smaller in magnitude relative to our findings) in the Indigenous, compared with non-Indigenous, population (Supplementary Tables S6 and S7, available as Supplementary data at IJE online).

Hyperglycemia in pregnancy increases the risk for shoulder dystocia both independently and by increasing the risk of high birthweight (40). The association between shoulder dystocia and glycemic control as well as its improvability are supported by strong evidence. The risk of shoulder dystocia doubles with every 1 mmol elevation in fasting glucose levels (41), and treatment of GDM substantially reduces its risk (17). Therefore, shoulder dystocia, which is an obstetric emergency, and its detrimental implications on the neonate (fracture of humerus and clavicle, brachial plexus injury and even death) and mother (perineal and psychological trauma and postpartum haemorrhage) (42, 43) can potentially be reduced in diabetic pregnancies.

We also recommend further research to investigate specific risk factors (birthweight thresholds; intrapartum factors; type and remoteness of birth facility; and maternal reproductive history) and possible predictive models of shoulder dystocia in diabetic pregnancies. The strong mediatory effect of birthweight in the causal pathway between DIP and shoulder dystocia among Aboriginal mothers and absence of that effect in their non-Aboriginal counterparts add an extra layer of importance to the need for measures and research to prevent fetal overgrowth in Aboriginal pregnancies complicated by diabetes.

Congenital anomalies

The results from studies investigating the impact of DIP on congenital anomalies in Indigenous populations were inconsistent (5, 10, 15, 33, 44) (Supplementary Tables S8 and S9, available as Supplementary data at IJE online).

Hyperglycemia in early pregnancy is directly embryotoxic, with a nearly linear relationship between congenital anomalies and periconceptional glycemic control (45). Among Aboriginal women, the previously reported poorer glycemic control in primary care (36) implies higher risk of entering pregnancy with suboptimal glycemia. Supplementation of folic acid to prevent fetal anomalies is a key component of preconception care (46). The relatively late presentation of Aboriginal pregnant women to antenatal care (28) and their reported suboptimal folic acid supplementation (47) could have also contributed to the stronger impact of PGDM on congenital anomalies among the Aboriginal, relative to non-Aboriginal, populations. Our findings may also be partly explained by the suboptimal access to antenatal care in Aboriginal women (28) that can lead to low rates of termination of pregnancies with anomalies, magnifying the association between PGDM and congenital anomalies.

A meta-analysis reported that preconception care substantially reduced congenital anomalies among babies born to mothers with PGDM (48). A reduction in modifiable congenital anomalies is likely to reduce the rate of a range of complications, including infant death (49), hospitalisation, intensive care admissions and surgical interventions (50). Our findings point to the importance of early antenatal care, planned pregnancy and periconceptional euglycemia for Aboriginal women with diabetes.

Small for gestational age and preterm birth

Suboptimal glycemic control can, in addition to heightening LGA risk, lower the risk of SGA (51) and right shift the birthweight distribution (52). In the present study, GDM differentially shifted the distribution of birthweights to the right of the reference curve of non-diabetic pregnancies among

the Aboriginal mothers (Supplementary Figure S2, available as Supplementary data at IJE online). This explains our finding of the greater impact of GDM on SGA reduction among Aboriginal babies.

Our finding of a stronger effect of DIP on preterm birth among non-Aboriginal mothers may be an artefact of the high rates of preterm birth in Aboriginal non-diabetic pregnancies, which result in smaller RRs. DIP does not seem to differentially impact subtypes (medically indicated, spontaneous preterm labour and preterm premature rupture of membranes) nor severity of preterm birth in the Aboriginal and non-Aboriginal populations (Supplementary Tables S10 and S11, available as Supplementary data at IJE online).

Strengths and limitations

The utilisation of whole-population datasets linked from multiple sources is a strength of the present study. This maximises external validity, eliminates selection bias, minimises loss of participants by tracking them upon transfer, allows investigating a wider range of outcomes and improves the sensitivity of capturing conditions and procedures.

The limitation of this study is the use of retrospective administrative data (which lack information on the important variables of BMI and glycemic control biomarkers) instead of clinical or research data. Given the established associations between BMI and both diabetes and adverse neonatal outcomes (5), maternal overweight/obesity, as an unmeasured confounder, could have explained part of the reported association between DIP and neonatal outcomes. Although hyperglycemia is the defining characteristic of diabetes, absence of information on glycemic control and treatment of diabetes precluded direct attribution of the disparities between the Aboriginal and non-Aboriginal babies to maternal hyperglycemia. The used datasets have no information on the criteria and results for the screening and diagnosis of GDM. In Australia, these criteria have changed in 2013 (53). While the implementation of the new guidelines considerably increased the rates of GDM (54), we are not able to predict its directional implications on the RRRs for neonatal outcomes. Absence of glucose

screening and testing results raises the possibility that some women diagnosed with GDM could have had results suggestive of T2DM.

The data also did not distinguish between type 1 and type 2 pregestational diabetes, which can be differentially distributed between the Aboriginal and non-Aboriginal populations, posing questions on the interpretation of the PGDM-related RRRs. Viewing the fact that T2DM accounts for 95% of PGDM cases in Aboriginal mothers compared with 57% in their non-Aboriginal counterparts (55) in the light of the higher rates of fetal overgrowth (and similar rates of congenital anomalies) in type 1 diabetes relative to T2DM pregnancies (56), point to the conservativeness of our findings. Since Aboriginal women in remote areas are less likely to be screened for GDM (57), they may have different severity and outcome profiles of the disease, biasing our reported estimates. Adjusting for remoteness in the present study likely minimised this impact.

Conclusion

This population-wide study reported a stronger impact of DIP on fetal overgrowth, shoulder dystocia and major congenital anomalies among Aboriginal, compared with non-Aboriginal, babies. The risk for shoulder dystocia was largely mediated by birthweight only among Aboriginal babies. The disparities between the two populations showed no improvement over the study period.

Aboriginal-led initiatives and policies to prioritise and improve care, education and glycemic control in women with diabetes over the preconception, antenatal and inter-pregnancy periods are needed to reduce disparities in these outcomes. Future studies need to investigate the epidemiology of shoulder dystocia and the proximal risk factors for fetal overgrowth in Aboriginal babies born to mothers with DIP as well as the association of fetal overgrowth with the intergenerational transfer of diabetes.

Declarations

Ethics approval

The study was approved by the Western Australian Aboriginal Health Ethics Committee (Project 797), Western Australian DoH Human Research Ethics Committee (RGS0000003168) and the University of Western Australia Human Research Ethics Committee (RA/4/20/6161).

Author contributions

MAA, CCJS, KW and GP designed the Study; CCJS and HDB directed the study's implementation; MAA, CCJS, GP, KW and PR contributed to the statistical analysis; MAA, CCJS, HDB, SWW, PR, RM and BJM contributed to the interpretation of the findings; MAA drafted the manuscript; CCJS, HDB, GP, KW, SWW, PR, RM and BJM critically revised the manuscript. All authors approved the final version of the manuscript. CCJS will act as guarantor for the paper.

Data Availability

The datasets underlying this article were provided by the WA Data Linkage Branch. To access these datasets, researchers should refer to the Data Linkage Branch of the Western Australia Government Department of Health (www.datalinkage-wa.org.au).

Supplementary data

Supplementary data are available at IJE online.

Funding

MAA is supported by a University Postgraduate Award from the University of Western Australia, an Australian Government Research Training Program (RTP) Scholarship and the Peter and Anne Hector Award; CCJS and HDB are supported by an Australian National Health and Medical Research Council grant (APP 1127265); GP is supported with funding from the National Health and Medical Research Council Project and Investigator Grants #1099655 and #1173991, institutional funding for the WA Health and Artificial Intelligence Consortium, and the Research Council of Norway through its Centres of Excellence funding scheme #262700. The funders had no role in the study design, data analysis and interpretation or in writing the manuscript.

Acknowledgements

The authors would like to acknowledge the Western Australian Department of Health Data Linkage team, the Midwives' Notification System, Hospital Morbidity Database Collection, Western Australian Register of Developmental Anomalies, Death Registrations and Births Registrations for providing data for this project.

Conflict of interest

None declared.

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Figure 1: Flowchart of the study population

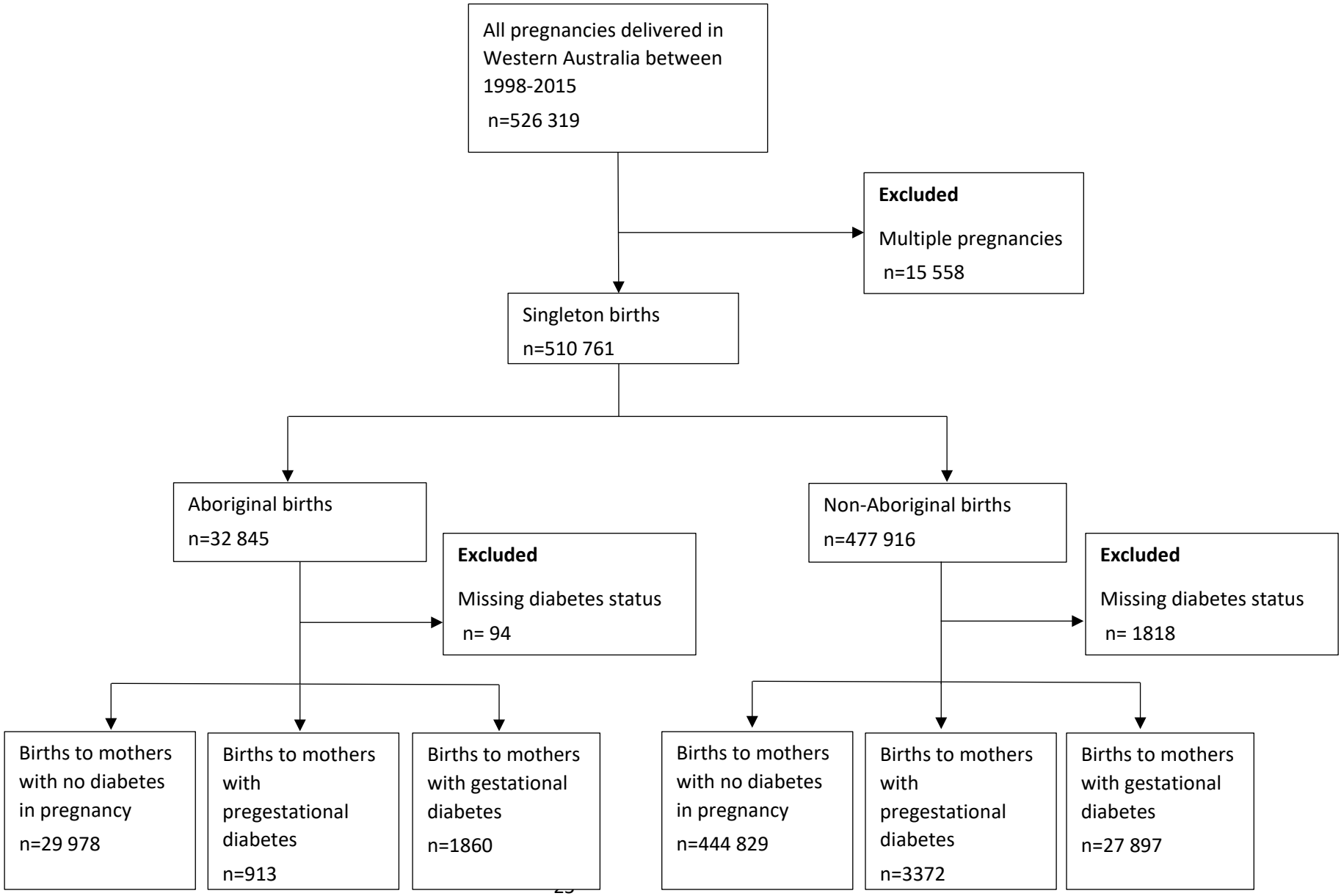

Table 1: Maternal and pregnancy characteristics of Aboriginal and non-Aboriginal mothers with and without diabetes in pregnancy in Western Australia, 1998-2015

Characteristics		Births to Aboriginal mothers		Births to non-Aboriginal mothers	
		No diabetes in pregnancy (n=29 978)	Diabetes in pregnancy (n= 2773)	No diabetes in pregnancy (n=444 829)	Diabetes in pregnancy (n=31 269)
Age group	25 or below	18779 (62.6%)	900 (32.5%)	102709 (23.1%)	3596 (11.5%)
	>25 to 35	9890 (33.0%)	1414 (51.0%)	277032 (62.3%)	19709 (63.0%)
	above 35	1309 (4.4%)	459 (16.6%)	65088 (14.6%)	7964 (25.5%)
Parity group	0	9188 (30.6%)	535 (19.3%)	188843 (42.5%)	12956 (41.5%)
	1	7237 (24.2%)	558 (20.1%)	154808 (34.8%)	10393 (33.3%)
	2	5263 (17.6%)	508 (18.3%)	66556 (15.0%)	4759 (15.3%)
	3 plus	8290 (27.7%)	1171 (42.2%)	34622 (7.8%)	3082 (9.9%)
Socioeconomic status	Low	21319 (76.6%)	1929 (76.2%)	140379 (32.8%)	10772 (35.6%)
	Middle	4961 (17.8%)	469 (18.5%)	146501 (34.3%)	10378 (34.3%)
	High	1536 (5.5%)	132 (5.2%)	140687 (32.9%)	9139 (30.2%)
Remoteness	Least remote	7918 (27.1%)	679 (25.2%)	265272 (60.5%)	21291 (69.0%)
	2	4562 (15.6%)	301 (11.2%)	106669 (24.3%)	6050 (19.6%)
	3	3676 (12.6%)	352 (13.1%)	30597 (7.0%)	1669 (5.4%)
	4	3613 (12.4%)	398 (14.8%)	16249 (3.7%)	894 (2.9%)
	Most remote	9425 (32.3%)	961 (35.7%)	19463 (4.4%)	971 (3.1%)
Marital status	Never married	10814 (36.1%)	843 (30.4%)	39387 (8.9%)	2247 (7.2%)
	Widowed	36 (0.1%)	<10 (<0.4%)[a]	288 (0.1%)	23 (0.1%)
	Divorced	65 (0.2%)	17 (0.6%)	1185 (0.3%)	125 (0.4%)
	Separated	582 (1.9%)	62 (2.2%)	2867 (0.6%)	240 (0.8%)
	Married, including defacto	17923 (59.8%)	1796 (64.8%)	397652 (89.4%)	28284 (90.7%)
	Unknown	558 (1.9%)	50 (1.8%)	3450 (0.8%)	271 (0.9%)

Smoking during pregnancy		14831 (49.5%)	1205 (43.5%)	60865 (13.7%)	3194 (10.3%)
Caesarean section		6142 (20.5%)	1197 (43.2%)	137691 (31.0%)	13547 (43.5%)
Onset of labour	Spontaneous	20821 (69.5%)	943 (34.0%)	231806 (52.1%)	9883 (31.8%)
	Induced	6177 (20.6%)	1105 (39.9%)	127547 (28.7%)	12598 (40.5%)
	No-labour	2980 (9.9%)	723 (26.1%)	85474 (19.2%)	8632 (27.7%)
Gestational age (weeks)	20 to 36	3991 (13.3%)	570 (20.6%)	29385 (6.6%)	3517 (11.3%)
	37 to 38	8876 (29.7%)	1266 (45.7%)	136006 (30.6%)	14757 (47.4%)
	39 to 40	13930 (46.6%)	849 (30.7%)	225226 (50.6%)	11983 (38.5%)
	41 and above	3105 (10.4%)	84 (3.0%)	54149 (12.2%)	854 (2.7%)
Pre-existing hypertension		274 (0.9%)	182 (6.6%)	4875 (1.1%)	948 (3.0%)
Gestational hypertension		1147 (3.8%)	258 (9.3%)	20937 (4.7%)	2082 (6.7%)
Preeclampsia or eclampsia		1529 (5.1%)	324 (11.7%)	19395 (4.4%)	2037 (6.5%)
Urinary tract infection		4184 (14.0%)	467 (16.9%)	17748 (4.0%)	1100 (3.5%)

[a]The number (percentage) is not shown for the small cell to maintain confidentiality.

Table 2: Comparisons of neonatal outcomes from pregnancies with pregestational diabetes, gestational diabetes and no diabetes among Aboriginal and non-Aboriginal births

	Rates in PGDM comparison groups		Rates in GDM[a] comparison groups (restricted to births ≥ 28 weeks)		PGDM versus no diabetes		GDM[a] versus no diabetes	
	PGDM	No DIP	GDM	No DIP	Risk Difference (95% CI)	Relative Risk (95% CI)	Risk Difference (95% CI)	Relative Risk (95% CI)
Aboriginal births								
Perinatal death (per 1000)	43.8	17.6	10.8	7.0	26.2 (12.8, 39.6)	2.49 (1.82, 3.41)	3.8 (-1.0, 8.6)	1.55 (0.98, 2.44)
Post-neonatal death (per 1000)	11.4	5.3	6.0	5.0	6.1 (-1.0, 13.1)	2.14 (1.13, 4.04)	1.0 (-2.6, 4.7)	1.21 (0.66, 2.22)
LGA (%)	33.5	7.0	23.3	7.0	26.5 (23.4, 29.6)	4.78 (4.32, 5.28)	16.3 (14.4, 18.3)	3.35 (3.05, 3.67)
SGA (%)	9.7	17.1	7.4	17.1	-7.4 (-9.4, -5.5)	0.57 (0.46, 0.69)	-9.7 (-11.0, -8.5)	0.43 (0.37, 0.51)
Preterm (%)	34.8	13.4	13.1	12.0	21.5 (18.3, 24.6)	2.61 (2.37, 2.86)	1.1 (-0.5, 2.7)	1.09 (0.97, 1.24)
Major congenital anomalies (%)	10.1	4.2	3.9	3.9	5.9 (3.9, 7.9)	2.40 (1.96, 2.94)	0.0 (-0.9, 0.9)	0.99 (0.79, 1.25)
Macrosomia (%)	16.2	7.0	17.3	7.2	9.2 (6.8, 11.6)	2.30 (1.98, 2.69)	10.1 (8.4, 11.9)	2.41 (2.16, 2.69)
Shoulder dystocia[b] (%)	9.0	1.8	5.4	1.8	7.2 (4.4, 10.0)	5.02 (3.63, 6.96)	3.6 (2.3, 4.9)	2.98 (2.30, 3.85)
Non-Aboriginal births								
Perinatal death (per 1000)	13.6	7.9	3.2	3.5	5.7 (1.8, 9.6)	1.72 (1.29, 2.29)	-0.3 (-1.0, 0.4)	0.92 (0.74, 1.13)
Post-neonatal death (per 1000)	2.1	1.0	0.8	0.9	1.1 (-0.5, 2.7)	2.13 (1.01, 4.48)	-0.1 (-0.4, 0.3)	0.90 (0.59, 1.37)
LGA (%)	35.9	10.4	15.4	10.5	25.4 (23.8, 27.1)	3.44 (3.28, 3.60)	4.9 (4.5, 5.4)	1.47 (1.43, 1.51)
SGA (%)	4.4	8.0	7.5	8.0	-3.7 (-4.4, -3.0)	0.54 (0.46, 0.64)	-0.4 (-0.7, -0.1)	0.95 (0.91, 0.99)
Preterm (%)	26.0	6.6	9.4	6.0	19.4 (17.9, 20.8)	3.93 (3.71, 4.16)	3.4 (3.1, 3.8)	1.57 (1.51, 1.63)
Major congenital anomalies (%)	6.6	4.5	4.9	4.3	2.0 (1.2, 2.9)	1.45 (1.28, 1.65)	0.6 (0.3, 0.8)	1.13 (1.07, 1.19)
Macrosomia (%)	17.8	11.1	10.8	11.1	6.8 (5.5, 8.1)	1.61 (1.50, 1.73)	-0.3 (-0.7, 0.0)	0.97 (0.94, 1.00)
Shoulder dystocia[b] (%)	5.0	2.2	3.1	2.2	2.8 (1.7, 4.0)	2.31 (1.83, 2.90)	0.9 (0.6, 1.2)	1.42 (1.29, 1.55)

GDM, gestational diabetes mellitus; LGA, large for gestational age; PGDM, pre-gestational diabetes mellitus; SGA, small for gestational age

[a]Analyses involving GDM were restricted to births at>=28 weeks to prevent immortal time bias (see Methods).

[b]Analyses for shoulder dystocia were restricted to vaginal deliveries.

Table 3: Adjusted RRs comparing neonatal outcomes from pregnancies with pre-gestational diabetes and gestational diabetes against pregnancies with no diabetes among Aboriginal and non-Aboriginal births

	PGDM versus no diabetes			GDM[a] versus no diabetes		
	Model 1[b]	Model 2[c]	Model 3[d]	Model 1[b]	Model 2[c]	Model 3[d]
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Aboriginal births						
Perinatal death	2.47 (1.79, 3.42)	2.40 (1.65, 3.48)	1.95 (1.30, 2.92)	1.34 (0.85, 2.11)	1.44 (0.89, 2.32)	1.38 (0.85, 2.23)
Post-neonatal death	2.11 (1.11, 4.01)	2.01 (0.97, 4.18)	1.73 (0.78, 3.82)	1.19 (0.65, 2.20)	1.46 (0.76, 2.80)	1.39 (0.72, 2.68)
LGA	4.68 (4.16, 5.27)	3.95 (3.44, 4.54)	4.10 (3.56, 4.72)	3.17 (2.87, 3.50)	2.64 (2.36, 2.94)	2.63 (2.36, 2.94)
SGA	0.56 (0.45, 0.70)	0.57 (0.45, 0.72)	0.53 (0.42, 0.68)	0.44 (0.37, 0.52)	0.46 (0.39, 0.55)	0.46 (0.39, 0.55)
Preterm	2.64 (2.37, 2.93)	2.60 (2.30, 2.93)	2.17 (1.91, 2.46)	1.12 (0.99, 1.27)	1.12 (0.98, 1.27)	1.06 (0.93, 1.20)
Major congenital anomalies	2.40 (1.95, 2.96)	2.16 (1.7, 2.75)	2.14 (1.68, 2.74)	0.98 (0.78, 1.24)	0.86 (0.66, 1.11)	0.86 (0.66, 1.11)
Macrosomia	2.20 (1.84, 2.63)	1.93 (1.59, 2.34)	2.03 (1.67, 2.48)	2.29 (2.05, 2.57)	1.94 (1.71, 2.20)	1.95 (1.72, 2.21)
Shoulder dystocia[e]	5.05 (3.58, 7.11)	4.51 (3.14, 6.49)	-	2.92 (2.25, 3.78)	2.78 (2.12, 3.63)	-
Non-Aboriginal births						
Perinatal death	1.70 (1.27, 2.28)	1.66 (1.23, 2.22)	1.59 (1.18, 2.16)	0.90 (0.73, 1.12)	0.90 (0.73, 1.12)	0.90 (0.73, 1.12)
Post-neonatal death	2.12 (1.01, 4.46)	2.26 (1.08, 4.74)	2.34 (1.11, 4.92)	0.90 (0.59, 1.37)	1.14 (0.74, 1.75)	1.15 (0.75, 1.76)
LGA	3.45 (3.27, 3.63)	3.30 (3.13, 3.49)	3.25 (3.08, 3.44)	1.44 (1.40, 1.49)	1.42 (1.38, 1.47)	1.42 (1.38, 1.46)
SGA	0.55 (0.46, 0.64)	0.56 (0.47, 0.66)	0.52 (0.44, 0.62)	0.95 (0.91, 0.99)	0.96 (0.92, 1.01)	0.95 (0.91, 1.00)
Preterm	3.95 (3.69, 4.22)	3.88 (3.62, 4.15)	3.10 (2.90, 3.31)	1.57 (1.51, 1.63)	1.53 (1.47, 1.59)	1.48 (1.42, 1.54)
Major congenital anomalies	1.45 (1.27, 1.65)	1.46 (1.28, 1.67)	1.43 (1.26, 1.64)	1.13 (1.07, 1.19)	1.08 (1.02, 1.14)	1.08 (1.02, 1.14)
Macrosomia	1.61 (1.49, 1.74)	1.58 (1.45, 1.71)	1.62 (1.5, 1.76)	0.96 (0.92, 0.99)	0.96 (0.93, 1.00)	0.97 (0.94, 1.01)
Shoulder dystocia[e]	2.32 (1.84, 2.93)	2.31 (1.82, 2.92)	-	1.41 (1.29, 1.54)	1.45 (1.33, 1.59)	-

GDM, gestational diabetes mellitus; LGA, large for gestational age; PGDM, pre-gestational diabetes mellitus; RR, relative risk; SGA, small for gestational age
Values across different columns should be interpreted independently as estimates were not corrected for multiple comparisons.

[a]Analyses involving GDM were restricted to births at>=28 weeks to prevent immortal time bias.

[b]Model 1: Unadjusted model

[c]Model 2 (all outcomes except shoulder dystocia are adjusted for same covariates): adjusting for maternal age, parity group, remoteness (as two categories: remote or non-remote), smoking, marital status and socioeconomic tertiles. For shoulder dystocia, Model 2 is adjusted for maternal age, parity and remoteness.
[d]Model 3: adjusting for variables in Model 2 plus maternal morbidities which include pre-existing hypertension, gestational hypertension, pre-eclampsia/preeclampsia and urinary tract infections. There is no Model 3 for shoulder dystocia because maternal morbidities do not affect the outcome.
[e]Models including shoulder dystocia were restricted to vaginal deliveries.

Table 4: Ratio of relative risks (in Aboriginal relative to non-Aboriginal babies[a]) for the impact of maternal diabetes on adverse neonatal outcomes

	PGDM versus no diabetes			GDM[b] versus no diabetes		
	Model 1[c]	Model 2[d]	Model 3[e]	Model 1[c]	Model 2[d]	Model 3[e]
	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
Perinatal death	1.45 (0.94, 2.25)	1.35 (0.85, 2.14)	1.33 (0.84, 2.10)	1.49 (0.90, 2.46)	1.56 (0.93, 2.61)	1.53 (0.91, 2.56)
Post-neonatal death	0.99 (0.37, 2.65)	1.03 (0.37, 2.88)	1.02 (0.36, 2.86)	1.33 (0.63, 2.78)	1.36 (0.63, 2.94)	1.35 (0.62, 2.90)
LGA	1.35 (1.19, 1.54)	1.26 (1.10, 1.44)	1.25 (1.09, 1.43)	2.22 (2.01, 2.46)	2.01 (1.81, 2.24)	2.00 (1.8, 2.22)
SGA	1.02 (0.78, 1.35)	1.08 (0.81, 1.43)	1.06 (0.8, 1.42)	0.46 (0.39, 0.55)	0.50 (0.42, 0.60)	0.49 (0.41, 0.59)
Preterm	0.68 (0.60, 0.77)	0.64 (0.56, 0.73)	0.60 (0.53, 0.69)	0.72 (0.63, 0.82)	0.71 (0.62, 0.81)	0.67 (0.58, 0.76)
Major congenital anomalies	1.66 (1.29, 2.12)	1.62 (1.25, 2.10)	1.62 (1.24, 2.10)	0.87 (0.69, 1.11)	0.82 (0.63, 1.07)	0.82 (0.63, 1.06)
Macrosomia	1.39 (1.15, 1.68)	1.37 (1.12, 1.66)	1.39 (1.14, 1.69)	2.45 (2.18, 2.75)	2.26 (2.00, 2.55)	2.27 (2.01, 2.56)
Shoulder dystocia[f]	2.17 (1.44, 3.28)	2.19 (1.44, 3.33)	-	2.08 (1.59, 2.74)	2.11 (1.61, 2.77)	-

GDM, gestational diabetes mellitus; LGA, large for gestational age; PGDM, pre-gestational diabetes mellitus; RRR, ratio of relative risks; SGA, small for gestational age

Values across different columns should be interpreted independently as estimates were not corrected for multiple comparisons.

[a]Ratio of relative risks examined whether the estimated relative risks for each outcome in Table 3 differ by Aboriginal status.

[b]Analyses involving GDM were restricted to births at>=28 weeks to prevent immortal time bias.

[c]Model 1: Unadjusted model

[d]Model 2 (all outcomes except shoulder dystocia are adjusted for same covariates): adjusting for maternal age, parity group, remoteness (as two categories: remote or non-remote), smoking, marital status and socioeconomic tertiles. For shoulder dystocia, Model 2 is adjusted for maternal age, parity and remoteness.

[e]Model 3: adjusting for variables in Model 2 plus maternal complications which include pre-existing hypertension, gestational hypertension, pre-eclampsia/preeclampsia and urinary tract infections. There is no Model 3 for shoulder dystocia because maternal morbidities do not affect the outcome.

[f]Models including shoulder dystocia were restricted to vaginal deliveries.

Table 5: Interaction terms[a] between time (decade) and the relative risks of outcomes in Aboriginal versus non-Aboriginal babies born to mothers with diabetes in pregnancy

	Births to mothers with PGDM			Births to mothers with GDM[b]		
	Model 1[c]	Model 2[d]	Model 3[e]	Model 1[c]	Model 2[d]	Model 3[e]
	Interaction term (95% CI)	Interaction term (95% CI)	Interaction term (95% CI)	Interaction term (95% CI)	Interaction term (95% CI)	Interaction term (95% CI)
LGA	1.18 (0.96, 1.46)	1.25 (1.00, 1.55)	1.26 (1.01, 1.56)	1.13 (0.96, 1.35)	1.17 (0.98, 1.41)	1.17 (0.98, 1.40)
SGA				0.68 (0.50, 0.94)	0.66 (0.48, 0.92)	0.66 (0.47, 0.92)
Preterm	1.13 (0.91, 1.40)	1.13 (0.90, 1.41)	1.09 (0.88, 1.35)	1.10 (0.87, 1.40)	1.09 (0.85, 1.40)	1.11 (0.87, 1.42)
Major congenital anomalies	1.16 (0.74, 1.83)	1.22 (0.75, 1.97)	1.20 (0.75, 1.92)			
Macrosomia	1.12 (0.80, 1.58)	1.18 (0.83, 1.67)	1.20 (0.84, 1.70)	1.15 (0.94, 1.42)	1.20 (0.97, 1.49)	1.20 (0.97, 1.49)
Shoulder dystocia[f]	1.10 (0.54, 2.24)	1.10 (0.54, 2.23)	-	0.83 (0.50, 1.38)	[g]	-

GDM, gestational diabetes mellitus; LGA, large for gestational age; PGDM, pre-gestational diabetes mellitus; SGA, small for gestational age

Values across different columns should be interpreted independently as estimates were not corrected for multiple comparisons.

[a]The interaction term described how the disparities between the Aboriginal and non-Aboriginal populations change with time by providing the change in the relative risk of neonatal outcomes (in Aboriginal vs non-Aboriginal babies born to mothers with DIP) per decade. Only the outcomes which showed disparities (differed by Aboriginal status) in Table 4 were investigated.

[b]Analyses involving GDM were restricted to births at>=28 weeks to prevent immortal time bias.

[c]Model 1: Unadjusted model

[d]Model 2 (all outcomes except shoulder dystocia are adjusted for same covariates): adjusting for maternal age, parity group, remoteness (as two categories: remote or non-remote), smoking, marital status and socioeconomic tertiles. For shoulder dystocia, Model 2 is adjusted for maternal age, parity and remoteness.

[e]Model 3: adjusting for variables in Model 2 plus maternal complications which include pre-existing hypertension, gestational hypertension, pre-eclampsia/preeclampsia and urinary tract infections. There is no Model 3 for shoulder dystocia because maternal morbidities do not affect the outcome.

[f]Models including shoulder dystocia are restricted to vaginal deliveries.

[g]Failure of convergence

Table 6: Effect of mediation by birthweight on the association between diabetes in pregnancy and shoulder dystocia in Aboriginal and non-Aboriginal populations in Western Australia

		Aboriginal population			Non-Aboriginal population		
Mediator	Exposure	OR^{NDE} {95% CI)	OR^{NIE} {95% CI)	Proportion mediated[a]	OR^{NDE} {95% CI)	OR^{NIE} {95% CI)	Proportion mediated[a]
Birthweight (grams)	PGDM[b]	3.36 (2.12, 5.33)	1.13 (0.97, 1.33)	16%	2.27 (1.74, 2.96)	0.83 (0.77, 0.89)	-43%
	GDM[c]	2.01 (1.48, 2.72)	1.44 (1.29, 1.62)	47%	1.63 (1.47, 1.80)	0.85 (0.84, 0.87)	-60%
	DIP	2.05 (1.55, 2.70)	1.43 (1.29, 1.58)	45%	1.62 (1.46, 1.80)	0.89 (0.87, 0.91)	-41%

DIP, diabetes in pregnancy; GDM, gestational diabetes mellitus; NDE, natural direct effect; NIE, natural indirect effect; OR, odds ratio; PGDM, pregestational diabetes mellitus

All models were restricted to vaginal deliveries and adjusted for maternal age, parity, smoking during pregnancy, marital status, remoteness, socioeconomic status, pre-existing hypertension, gestational hypertension, eclampsia/preeclampsia and urinary tract infections.

[a]Proportion mediated on a risk difference scale was calculated using methods described by VanderWeele and Vansteelandt (58).

[b]PGDM models excluded GDM pregnancies

[c]GDM models only included births at≥ 28 weeks' gestation and excluded PGDM pregnancies.

Supplementary Material

The impact of diabetes during pregnancy on neonatal outcomes among the Aboriginal population in Western Australia: a whole-population study

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Table of contents

Table S1: International Classification of Disease (Australian modifications) codes for maternal conditions in Hospital Morbidity Data Collection

Maternal condition	International Classification of Disease (ICD) codes (Australian modification)	
	ICD-9-AM code	ICD-10-AM codes
Gestational diabetes	648.8	O24.4, O24.9
Pre-existing diabetes	250	E10-11, E13-14, O24.0-42.3
Pre-eclampsia/eclampsia	642.4-642.7	O11, O14, O15
Pre-existing hypertension	401, 642.0-642.2	I10, O10
Gestational hypertension	642.3, 642.9	O13, O16
Urinary tract infection	646.6	O23

Table S2: Western Australian Datasets from which study variables were ascertained

Variables	MNS	HDMC	WARDA	Death Registrations
Gestational diabetes	✓	✓		
Pre-existing diabetes	✓	✓		
Perinatal death				✓
Post-neonatal death				✓
Gestational age*	✓			
Birth weight**	✓			
Major congenital anomalies			✓	
Shoulder dystocia	✓			
Maternal age	✓			
Remoteness	✓			
Socioeconomic status	✓			
Marital status	✓			
Parity	✓			
smoking during pregnancy	✓			
Pre-eclampsia	✓	✓		
Eclampsia	✓	✓		
Pre-existing hypertension	✓	✓		
Gestational hypertension	✓	✓		
Urinary tract infection	✓	✓		

* Used to define large for gestational age, small for gestational age and preterm birth

** Used to define large for gestational age, small for gestational age and macrosomia

HMDC, Hospital Morbidity Database Collection; LGA, large for gestational age; MNS, Midwives Notification System; SGA, small for gestational age; WARDA, Western Australian Register of Developmental Anomalies

Table S3: Counts and percentages of missing values for study variables

Variable	Numbers missing	Percent Missing
Mother Aboriginal status	0	0.0
Gestational diabetes	1,912	0.4
Pre-existing diabetes	2,056	0.4
Perinatal death	0	0.0
Post-neonatal death	3,373	0.7
LGA	2,248	0.4
SGA	2,248	0.4
Preterm birth	2,163	0.4
Major congenital anomalies	0	0.0
Macrosomia	109	0.0
Shoulder dystocia	0	0.0
Maternal age	106	0.0
Parity group	1,033	0.2
Remoteness	7,969	1.6
Smoking	2,069	0.4
Marital status	1,033	0.2
Socioeconomic status	20,802	4.1
Pre-existing hypertension	2,055	0.4
Gestational hypertension	2,953	0.6
Eclampsia/preeclampsia	1,999	0.4
Urinary tract infection	2,051	0.4

LGA, large for gestational age; SGA, small for gestational age

Table S4: The impact of pregestational diabetes on fetal overgrowth in Indigenous vs. non-Indigenous populations

				Indigenous pregnancies					Non-Indigenous pregnancies					RRR (95% CI)
				No DIP		PGDM		RR (95% CI)	No DIP		PGDM		RR (95% CI)	
Study	Country	Study period	Outcome	Number of pregnancies	Rate of outcome (%)	Number of pregnancies	Rate of outcome (%)		Number of pregnancies	Rate of outcome (%)	Number of pregnancies	Rate of outcome (%)		
Maple-Brown et al. (1)[a]	Australia	2011-2018	LGA	117	10.3	153	37.9	3.70 (2.08, 6.56)	118	15.3	24	25.0	1.64 (0.73, 3.70)	2.26 (0.83, 6.10)
Porter et al. (2)[b]	Australia	2000-2007	HBW (>=4000 gram)	4435	8.3	113	20.4	2.45 (1.68, 3.57)	71195	12.8	541	18.1	1.42 (1.19, 1.70)	1.72 (1.13, 2.62)
Dyck et al. (3)	Canada	1980-2013	HBW (>4000 gram)	65177	17.6	969	29.3	1.67 (1.51, 1.84)	334694	13.1	2232	19.2	1.47 (1.35, 1.60)	1.14 (1.00, 1.29)
Wicklow et al. (4)[c]	Canada	1984-2008	LGA	63160	12.5	1796	38.4	3.07 (2.89, 3.27)	287501	7.4	1992	29.8	4.03 (3.76, 4.32)	0.76 (0.70, 0.84)
Chen et al. (5)	Canada	1996-2010	LGA	14595	21.7	666	49.8	2.29 (2.10, 2.50)	204913	9.0	2395	21.7	2.49 (2.31, 2.70)	0.92 (0.82, 1.03)
Oster et al. (6)[d]	Canada	2000-2009	HBW	26793	16.7	1513	29.3	1.75 (1.61, 1.90)	381092	11.1	17660	12.9	1.16 (1.12, 1.21)	1.51 (1.38, 1.65)

DIP, Diabetes in pregnancy; GDM, Gestational diabetes mellitus; HBW, high birth weight; LGA, Large for gestational age; PGDM, Pregestational diabetes mellitus; RR, Relative risk; RRR, Ratio of Relative Risks

Relative risks and ratios of relative risks were estimated using the methods described by Altman (7) and Altman and Bland (8), respectively.

[a]PGDM included only mothers with type 2 diabetes.

[b]The reference (non-DIP) group included healthy women without pre-existing medical conditions. The non-Indigenous group included only Caucasian women.

[c]PGDM included only mothers with type 2 diabetes.

[d]Study did not differentiate between PGDM and GDM. Data shown in the table thus represents DIP, not PGDM.

Table S5: The impact of gestational diabetes on fetal overgrowth in Indigenous vs. non-Indigenous populations

				Indigenous pregnancies					Non-Indigenous pregnancies					RRR (95% CI)
				No DIP		GDM		RR (95% CI)	No DIP		GDM		RR (95% CI)	
Study	Country	Study period	Outcome	Number of pregnancies	Rate of outcome (%)	Number of pregnancies	Rate of outcome (%)		Number of pregnancies	Rate of outcome (%)	Number of pregnancies	Rate of outcome (%)		
Maple-Brown et al. (1)	Australia	2011-2018	LGA	117	10.3	278	18.3	1.79 (0.99, 3.23)	118	15.3	461	10.4	0.68 (0.41, 1.13)	2.62 (1.21, 5.69)
Porter et al. (2)[a]	Australia	2000-2007	HBW (>=4000 gram)	4435	8.3	418	22.5	2.70 (2.21, 3.31)	71195	12.8	4915	14.5	1.13 (1.06, 1.22)	2.38 (1.92, 2.96)
Dyck et al. (3)	Canada	1980-2013	HBW (>4000 gram)	65177	17.6	3030	34.4	1.95 (1.86, 2.06)	334694	13.1	7484	18.0	1.37 (1.31, 1.44)	1.42 (1.32, 1.53)
Wicklow et al. (4)	Canada	1984-2008	LGA	63160	12.5	1527	36.7	2.93 (2.74, 3.14)	287 501	7.4	2504	19.1	2.58 (2.38, 2.80)	1.14 (1.02, 1.27)
Chen et al. (5)	Canada	1996-2010	LGA	14595	21.7	1829	44.0	2.03 (1.90, 2.17)	204913	9.0	10452	14.7	1.70 (1.62, 1.78)	1.19 (1.10, 1.30)

DIP, Diabetes in pregnancy; GDM, Gestational diabetes mellitus; HBW, high birth weight; LGA, Large for gestational age; PGDM, Pregestational diabetes mellitus; RR, Relative risk; RRR, Ratio of Relative Risks

Relative risks and ratios of relative risks were estimated using the methods described by Altman (7) and Altman and Bland (8), respectively.

[a]The reference (non-DIP) group included healthy women without pre-existing medical conditions. The non-Indigenous group included only Caucasian women.

Table S6: The impact of pregestational diabetes on shoulder dystocia in Indigenous vs. non-Indigenous populations

			Indigenous pregnancies					Non-Indigenous pregnancies					RRR (95% CI)
			No DIP		PGDM		RR (95% CI)	No DIP		PGDM		RR (95% CI)	
Study	Country	Study period	Number of vaginal deliveries	Rate of shoulder dystocia (%)	Number of vaginal deliveries	Rate of shoulder dystocia (%)		Number of vaginal deliveries	Rate of shoulder dystocia (%)	Number of vaginal deliveries	Rate of shoulder dystocia (%)		
Maple-Brown et al. (1)[a]	Australia	2011-2018	85	5.9	42	16.7	2.83 (0.96, 8.40)	84	3.6	13	7.7	2.15 (0.24, 19.18)	1.32 (0.11, 15.12)
Dyck et al. (3)	Canada	1980-2013	56770	1.3	597	5.9	4.64 (3.34, 6.45)	275788	1.5	1328	5.2	3.57 (2.83, 4.50)	1.30 (0.87, 1.95)

DIP, Diabetes in pregnancy; GDM, Gestational diabetes mellitus; PGDM, Pregestational diabetes mellitus; RR, Relative risk; RRR, Ratio of Relative Risks
Relative risks and ratios of relative risks were estimated using the methods described by Altman (7) and Altman and Bland (8), respectively.
[a]PGDM included only mothers with type 2 diabetes.

Table S7: The impact of gestational diabetes on shoulder dystocia in Indigenous vs. non-Indigenous populations

			Indigenous pregnancies					Non-Indigenous pregnancies					RRR (95% CI)
			No DIP		GDM		RR (95% CI)	No DIP		GDM		RR (95% CI)	
Study	Country	Study period	Number of vaginal deliveries	Rate of shoulder dystocia (%)	Number of vaginal deliveries	Rate of shoulder dystocia (%)		Number of vaginal deliveries	Rate of shoulder dystocia (%)	Number of vaginal deliveries	Rate of shoulder dystocia (%)		
Maple-Brown et al. (1)	Australia	2011-2018	85	5.9	141	5.7	0.96 (0.33, 2.85)	84	3.6	267	4.5	1.26 (0.36, 4.35)	0.77 (0.15, 3.98)
Aljohani et al. (9)[a]	Canada	1985-2004	32552	0.9	2148	3.3	3.72 (2.88, 4.81)	232236	1.4	4860	3.7	2.57 (2.22, 2.98)	1.45 (1.08, 1.95)
Dyck et al. (3)	Canada	1980-2013	56770	1.3	2273	4.9	3.90 (3.21, 4.74)	275788	1.5	5508	3.3	2.24 (1.94, 2.60)	1.74 (1.46, 2.07)

DIP, Diabetes in pregnancy; GDM, Gestational diabetes mellitus; PGDM, Pregestational diabetes mellitus; RR, Relative risk; RRR, Ratio of Relative Risks

Relative risks and ratios of relative risks were estimated using the methods described by Altman (7) and Altman and Bland (8), respectively.

[a]The study stratified the cohort into GDM and non-DIP pregnancies, with no mention of PGDM. Pregnancies without diabetes probably included mothers with PGDM.

Table S8: The impact of pregestational diabetes on congenital anomalies in Indigenous vs. non-Indigenous populations

				Indigenous pregnancies					Non-Indigenous pregnancies					RRR (95% CI)
				No DIP		PGDM		RR (95% CI)	No DIP		PGDM		RR (95% CI)	
Study	Country	Study period	Definitions of congenital anomalies	Number of pregnancies	Rate of congenital anomalies (%)	Number of pregnancies	Rate of congenital anomalies (%)		Number of pregnancies	Rate of congenital anomalies (%)	Number of pregnancies	Rate of congenital anomalies (%)		
Maple-Brown et al. (1)[a]	Australia	2011-2018	Major congenital anomalies, years of follow up not stated	117	0	153	4.6	[b]	118	0	24	4.2	[b]	1.10[b] (0.14, 8.54)
Sharpe et al. (10)	Australia	1986-2000	All congenital anomalies in the first 5 years of life	7110	5.1	98	10.2	1.99 (1.10, 3.61)	267469	5.0	848	10.1	2.03 (1.66, 2.48)	0.98 (0.52, 1.84)
Bower et al. (11)[c]	Australia	1980-1984	All congenital anomalies in the first 6 years of life	5383	4.1	25	16.0	3.88 (1.57, 9.61)	105209	4.8	116	11.2	2.31 (1.38, 3.86)	1.68 (0.59, 4.76)
Stanley et al. (12)[d]	Australia	1980-1982	All congenital anomalies in the first 6 years of life	3168	3.4	52	17.3	5.08 (2.72, 9.46)	58872	3.4	173	5.8	1.70 (0.93, 3.11)	2.99 (1.26, 7.11)
Chen et al. (5)	Canada	1996-2010	All congenital anomalies in the first year of life	14595	1.9	666	4.1	2.12 (1.40, 3.22)	204913	1.2	2395	2.9	2.53 (1.99, 3.22)	0.84 (0.52, 1.36)
Oster et al. (6)[d]	Canada	2000-2009	Not defined	26793	1.8	1513	1.4	0.77 (0.50, 1.19)	381092	1.5	17660	1.7	1.13 (1.01, 1.27)	0.68 (0.43, 1.07)

DIP, Diabetes in pregnancy; GDM, Gestational diabetes mellitus; PGDM, Pregestational diabetes mellitus; RR, Relative risk; RRR, Ratio of Relative Risks

Relative risks and ratios of relative risks were estimated using the methods described by Altman (7) and Altman and Bland (8), respectively.

[a]PGDM included only mothers with type 2 diabetes.

[b]Denominator is zero. Since there are no cases of congenital anomalies in Aboriginal and non-Aboriginal mothers without DIP, the reported RRR represented the RR of congenital anomalies in Aboriginal relative non-Aboriginal babies

[c]The study stratified diabetes into insulin-dependent diabetes, non-insulin dependent diabetes and gestational diabetes. We merged insulin-dependent and non-insulin-dependent diabetes as pregestational diabetes

[d]The study did not differentiate between PGDM and GDM. Data shown here thus represents DIP, not PGDM.

Table S9: The impact of gestational diabetes on congenital anomalies in Indigenous vs. non-Indigenous populations

				Indigenous pregnancies					Non-Indigenous pregnancies					RRR (95% CI)
				No DIP		GDM		RR (95% CI)	No DIP		GDM		RR (95% CI)	
Study	Country	Study period	Definitions of congenital anomalies included	Number of pregnancies	Rate of congenital anomalies (%)	Number of pregnancies	Rate of congenital anomalies (%)		Number of pregnancies	Rate of congenital anomalies (%)	Number of pregnancies	Rate of congenital anomalies (%)		
Maple-Brown et al. (1)	Australia	2011-2018	Major congenital anomalies, years of follow up not stated	117	0	278	0.7	[a]	118	0	461	1.3	[a]	0.55[a] (0.11, 2.72)
Sharpe et al. (10)	Australia	1986-2000	All congenital anomalies in the first 5 years of life	7110	5.1	334	8.4	1.63 (1.13, 2.36)	267469	5.0	6401	5.9	1.18 (1.07, 1.30)	1.39 (0.95, 2.03)
Bower et al. (11)	Australia	1980-1984	All congenital anomalies in the first 6 years of life	5383	4.1	73	15.1	3.65 (2.09, 6.39)	105209	4.8	213	5.2	1.07 (0.60, 1.90)	3.43 (1.54, 7.66)
Chen et al. (5)	Canada	1996-2010	All congenital anomalies in the first year of life	14595	1.9	1829	2.4	1.33 (0.94, 1.87)	204913	1.2	10452	1.3	1.13 (0.95, 1.35)	1.18 (0.80, 1.73)

DIP, Diabetes in pregnancy; GDM, Gestational diabetes mellitus; PGDM, Pregestational diabetes mellitus; RR, Relative risk; RRR, Ratio of Relative Risks
Relative risks and ratios of relative risks were estimated using the methods described by Altman (7) and Altman and Bland (8), respectively.
[a]Denominator is zero. Since there are no cases of congenital anomalies in Aboriginal and non-Aboriginal populations without DIP, the reported RRR represented the RR of congenital anomalies in Aboriginal relative non-Aboriginal babies

Table S10: The association between pregestational and gestational diabetes with the subtypes of preterm birth among Aboriginal and non-Aboriginal births in Western Australia

		Term births (%)	Preterm subtypes		
			Spontaneous preterm labour (%)	PROM (%)	Medically indicated (%)
Aboriginal births	No PGDM	86.7	8.9	1.3	3.2
	PGDM	65.2	11.1	2.3	21.4
Non-Aboriginal births	No PGDM	93.4	3.4	0.6	2.6
	PGDM	74.0	6.6	1.6	17.7
Aboriginal births	No GDM	86.7	8.9	1.3	3.2
	GDM	86.4	6.0	1.4	6.2
Non-Aboriginal births	No GDM	93.4	3.4	0.6	2.6
	GDM	90.5	4.3	0.7	4.5

GDM, gestational diabetes mellitus; PGDM, pregestational diabetes mellitus; PROM, premature rupture of membranes

Table S11: The association between pregestational and gestational diabetes with the severity of preterm birth among Aboriginal and non-Aboriginal births in Western Australia

		Gestational age groups for preterm births (severity of preterm)			
		below 28 weeks (%)	28 to 32 weeks (%)	33 to 36 weeks (%)	37 weeks and above (%)
Aboriginal births	No PGDM	1.6	2.0	9.8	86.7
	PGDM	2.7	5.8	26.2	65.2
Non-Aboriginal births	No PGDM	0.7	0.8	5.2	93.4
	PGDM	1.3	2.9	21.7	74.0
Aboriginal births	No GDM	Excluded from analysis	2.1	9.9	88.0
	GDM	Excluded from analysis	2.1	11.0	86.9
Non-Aboriginal births	No GDM	Excluded from analysis	0.8	5.2	94.0
	GDM	Excluded from analysis	1.1	8.4	90.6

GDM, gestational diabetes mellitus; PGDM, pregestational diabetes mellitus

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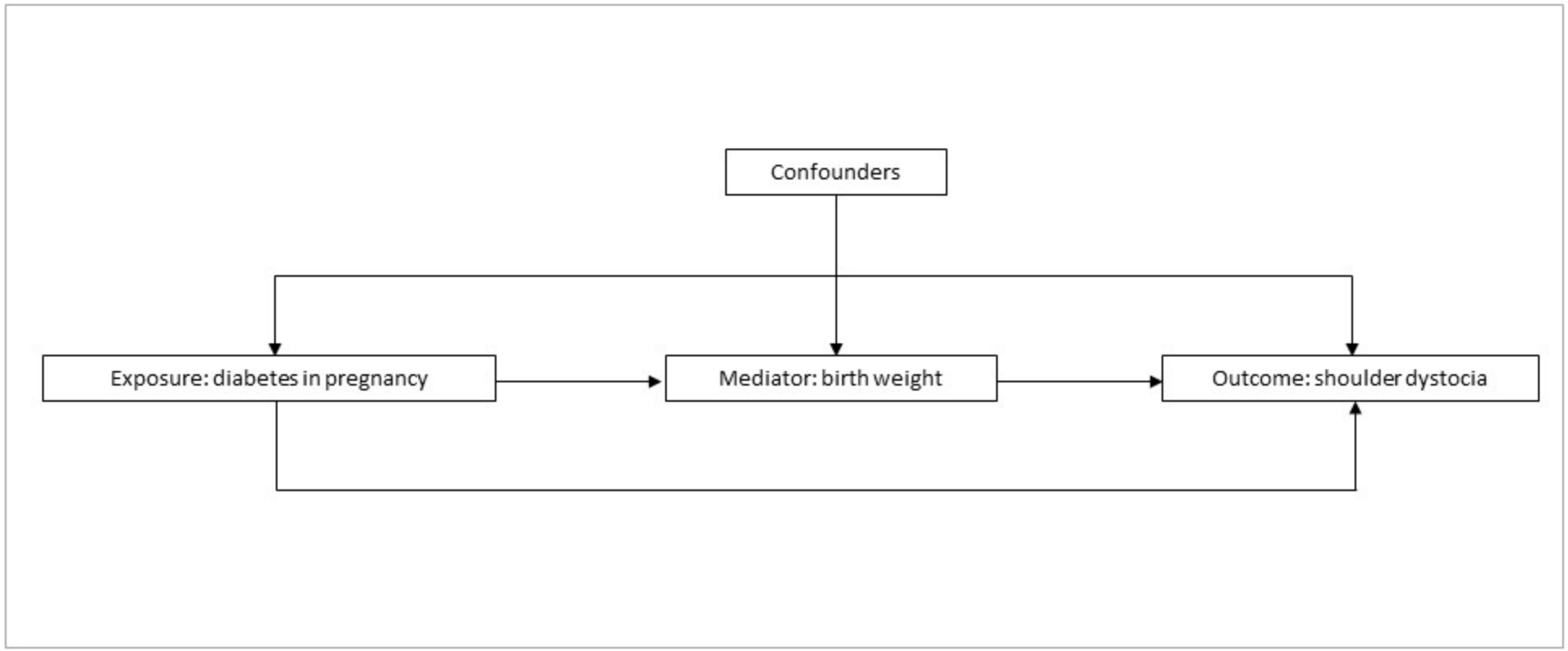

Figure S1: Framework of the association between diabetes in pregnancy and shoulder dystocia with birth weight as a mediator

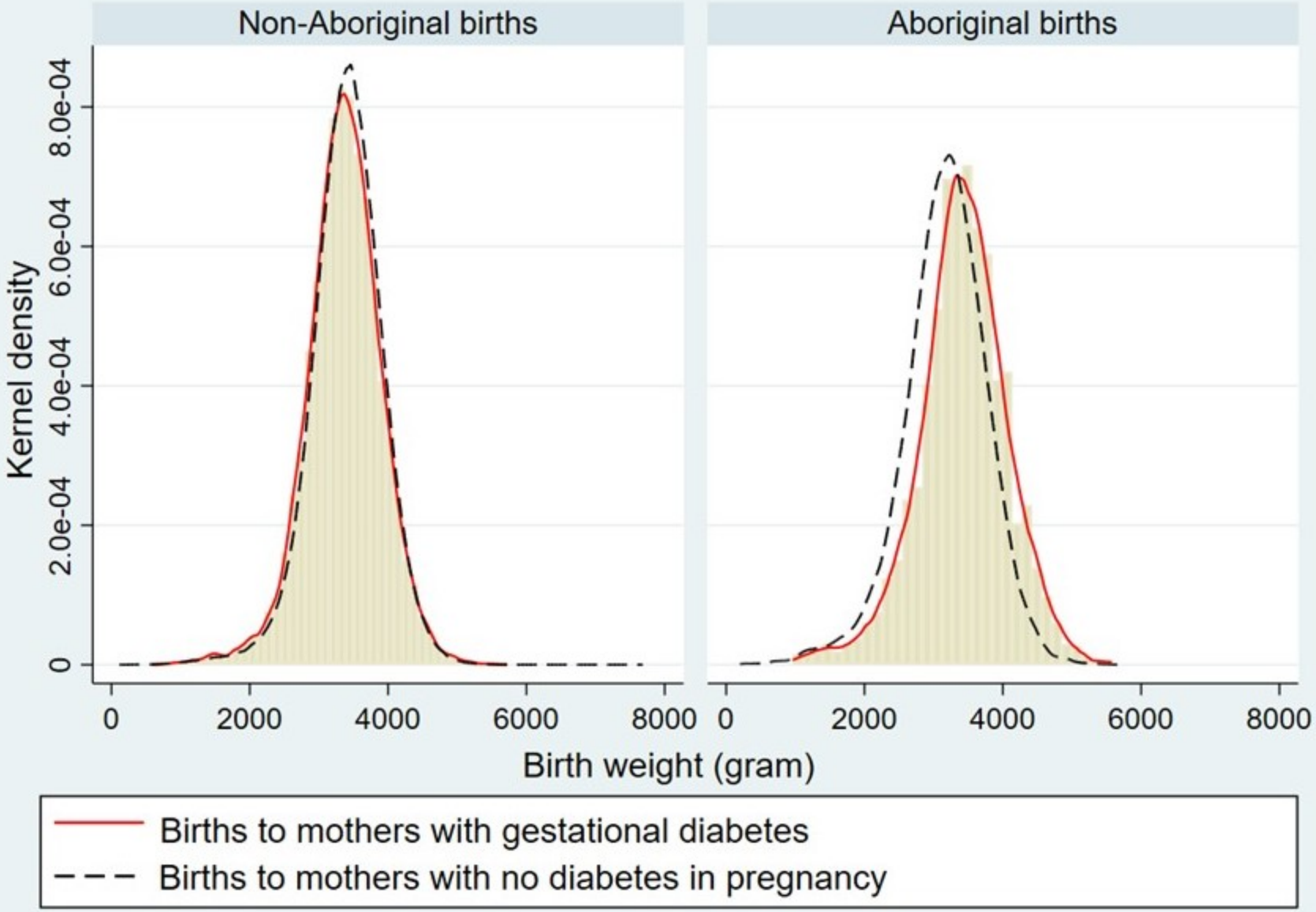

Figure S2: Birth weight distribution of neonates born to mothers with and without gestational diabetes, by Aboriginal status