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Early mortality among aboriginal and non-aboriginal women who had a preterm birth in Western Australia: A population-based cohort study

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Abstract

Background: Having a preterm (<37 weeks' gestation) birth may increase a woman's risk of early mortality. Aboriginal and Torres Strait Islander (hereafter Aboriginal) women have higher preterm birth and mortality rates compared with other Australian women.

Objectives: We investigated whether a history of having a preterm birth was associated with early mortality in women and whether these associations differed by Aboriginal status.

Methods: This retrospective cohort study used population-based perinatal records of women who had a singleton birth between 1980 and 2015 in Western Australia linked to Death Registry data until June 2018. The primary and secondary outcomes were all-cause and cause-specific mortality respectively. After stratification by Aboriginal status, rate differences were calculated, and Cox proportional hazard regression was used to estimate adjusted hazard ratios (HR) and 95% confidence intervals (CI) for all-cause and cause-specific mortality.

Results: There were 20,244 Aboriginal mothers (1349 deaths) and 457,357 non-Aboriginal mothers (7646 deaths) with 8.6 million person-years of follow-up. The all-cause mortality rates for Aboriginal mothers who had preterm births and term births were 529.5 and 344.0 (rate difference 185.5, 95% CI 135.5, 238.5) per 100,000 person-years respectively. Among non-Aboriginal mothers, the corresponding figures were 125.5 and 88.6 (rate difference 37.0, 95% CI 29.4, 44.9) per 100,000 person-years. The HR for all-cause mortality for Aboriginal and non-Aboriginal mothers associated with preterm birth were 1.48 (95% CI 1.32, 1.66) and 1.35 (95% CI 1.26, 1.44), respectively, compared with term birth. Compared with mothers who had term births, mothers of preterm births had higher relative risks of mortality from diabetes, cardiovascular, digestive and external causes.

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Conclusions: Both Aboriginal and non-Aboriginal women who had a preterm birth had a moderately increased risk of mortality up to 38 years after the birth, reinforcing the importance of primary prevention and ongoing screening.

KEYWORDS
Aboriginal, birth, data linkage, mortality, preterm, Western Australia, women

1 | BACKGROUND

Preterm birth (<37 weeks) is a universal public health issue, with a global incidence of around 11%.[1] In Australia, the preterm birth rate rose from 6.8% in 1991[2] to 8.6% in 2019,[3] which, at least in more recent years, may be related to an increase in clinician-initiated preterm births.[4] In addition to adverse consequences for the offspring,[5] preterm birth may be associated with long-term health risks for the mother. Having a preterm birth has been associated with maternal early all-cause[6-10] and cause-specific mortality (cardiovascular,[7-11] cancer,[6,7] diabetes,[7] respiratory,[7] non-cardiovascular[10] and alcohol-related[6]) and a doubling of the risk of combined fatal and non-fatal cardiovascular disease (CVD).[12] The biological mechanisms behind these associations between having a preterm birth and early mortality are unknown but could include shared contributary factors or pathophysiology. In response to the increasing evidence, the American Heart Association (AHA) called for the introduction of strategies to reduce later cardiometabolic risk among women with adverse pregnancy outcomes, including preterm birth.[13]

To date, most studies of having a preterm birth and early mortality among women have been conducted in the Scandinavian countries[6,7,9,10,11] where preterm birth rates are low (6%–7%).[14] The AHA has called for more research into the relationship between adverse pregnancy outcomes and CVD in more diverse populations given the paucity of data from ethnic and minority populations,[13] many of whom have higher rates of preterm birth.[1] In Australia, for example, Aboriginal and Torres Strait Islander (hereafter 'Aboriginal') women have both distinctly higher rates of preterm birth (nearly 14%) compared with other Australian women (8%)[15] and higher mortality rates across the lifespan, most notably in the 35–44 years age group with rates 4.5 times higher than other Australian women. While a high proportion of the mortality gap can be explained by CVD, diabetes, respiratory diseases and cancer,[16] Aboriginal women are also more likely to die at an earlier age and from external causes of death (e.g. accidents, assaults and suicides) than non-Aboriginal women.[17] Therefore, any association between having a preterm birth and mortality could add a disproportionate burden to an already vulnerable population.

We investigated whether a history of having a preterm birth is associated with subsequent mortality and whether these associations differed by Aboriginal status. In addition, we investigated cause-specific mortality and whether the association changed by time since the birth, type or number of preterm births.

Synopsis

Study question
The study aimed to investigate whether having a preterm birth was associated with early mortality in Aboriginal and non-Aboriginal women in Western Australia.

What is already known
Having a preterm birth has been associated with maternal all-cause and cause-specific mortality in later life, but there is a paucity of data from minority populations, many of whom who have higher rates of preterm birth.

What this study adds
Having a preterm birth was associated with an increased risk of early mortality, particularly related to diabetes, cardiovascular and digestive conditions, and external causes, compared with those who had a term birth. While the level of relative risk appeared similar among Aboriginal and non-Aboriginal women, the absolute risks of mortality were distinctly higher among Aboriginal women.

2 | MATERIAL AND METHODS

2.1 | Cohort selection

This study followed the REporting of studies Conducted using Observational Routinely collected health Data (RECORD) guidelines[18] (see checklist, Table S1). This was a population-based retrospective cohort study, which included all mothers who had a singleton birth in Western Australia between 1980 and 2015, linked to Death Registry data until June 2018 and stratified by Aboriginal status. For each mother, the index birth was the pregnancy with the shortest gestation irrespective of birth order and was chosen after exclusion of multiple births, pregnancy terminations for foetal anomalies and births with missing data for gestation and maternal age (Figure 1).

2.2 | Data sources

The study data were obtained from population health data sets including those routinely linked by the data linkage team of the Western Australian Department of Health (Midwives Notification

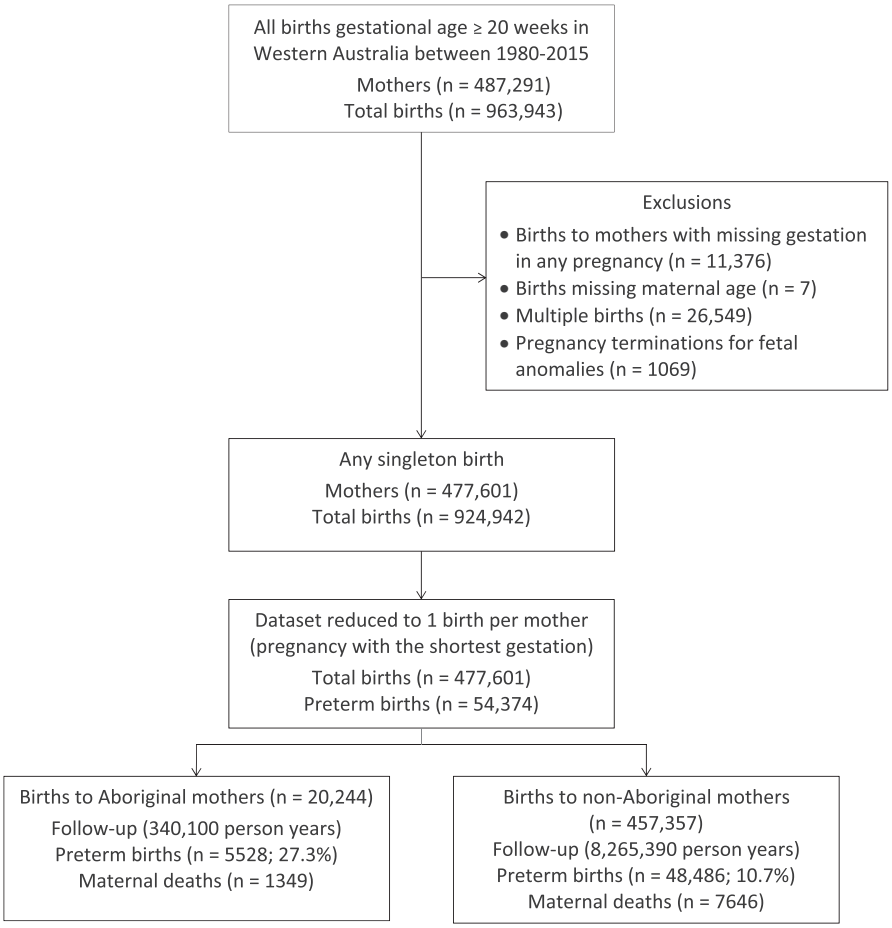

FIGURE 1 Study flow chart for investigation of association between preterm birth and maternal deaths in Western Australia 1980–2015.

System (MNS), Hospital Morbidity Data Collection (HMDC), Birth, Cancer and Death Registers) as well as the Western Australian Register of Developmental Anomalies, Western Australian Electoral Roll and the Derived Aboriginal and Torres Islander Status Flag. After linkage using probabilistic matching techniques[19] by the data linkage team, these data were provided with identifying fields removed. The MNS contained information about all births from 20 weeks' gestation while the HMDC had information about inpatient episodes. The Western Australian Register of Developmental Anomalies contained information about pregnancy terminations for foetal anomalies which allowed their exclusion while the Western Australian Electoral Roll contained information about when registered voters had left the State. Registration is compulsory for all eligible Australian citizens and information about Electoral Roll status was available for 79.2% of Aboriginal and 82.5% of non-Aboriginal mothers. The Derived Aboriginal and Torres Islander Status Flag was a variable created by applying a validated algorithm[20] across a range of administrative data sets to produce a single indicator of Aboriginal status to improve the quality of information about Aboriginal status.

2.2.1 | Aboriginal status

Indigenous status of the mother was identified using the Derived Aboriginal and Torres Islander Status Flag and mothers were classified as Aboriginal or non-Aboriginal.

2.2.2 | Exposures

Prior to 1998, gestation was calculated using the birth and last menstrual period (LMP) dates if LMP was certain, otherwise by clinical signs (fundal height measurement or neonatal assessment).[21] Since 1998, midwives have recorded the basis of the gestational estimate[22] (ultrasound dating (73%), LMP/clinical signs (25%) and unknown for 2%).[22,23] Completed weeks of gestation were categorised as 20–27, 28–31, 32–36 and ≥37 weeks. Preterm births (<37 weeks) were further classified as spontaneous (spontaneous onset of labour or vaginal or caesarean births with pre-labour rupture of membranes) or clinician initiated (induced labour or pre-labour caesarean with intact membranes). The total number of singleton preterm births per mother was categorised as 0, 1, 2 and ≥3.

2.2.3 | Outcomes

Mortality was identified in the Western Australian Death Registry. Causes of Death, coded using the International Classification of Diseases (ICD) were grouped using Australian Institute of Health and Welfare categories[24,25] (Table S2). Cause-specific mortality was examined in groups with more than 30 deaths among mothers with a preterm birth. Mothers were followed from the index birth date until death, the date they left the State as recorded on the Electoral Roll, or until 30 June 2018, whichever came first.

2.2.4 | Covariates

Maternal age at the first and index births were categorised as <20, 20–24, 25–29, 30–34 and ≥35 years. The following were categorised as maternal age at end of follow-up (≤35, 35–44, 45–54 and ≥55 years), parity in the index pregnancy (0, 1, 2 or ≥3) and after the last birth record in MNS (1, 2, 3 or ≥4), and year of the index birth (1980–1989, 1990–1999, 2000–2009 and 2010–2015). Socio-economic status (SES) was categorised using quintiles of a composite, area-based measure of the birth residence[26] based on the Western Australian distribution of the Index of Relative Socio-Economic Disadvantage Small Area 1 values, generated for the Census closest to the birth year. Areas of remoteness of birth residence, based on the five categories of the Accessibility/Remoteness Index of Australia,[27] were collapsed into two groups (Very remote/remote and Perth metropolitan/inner or outer regional). Smoking during pregnancy (since 1998) was categorised as an indicator (yes/no). Appropriateness of fetal growth was categorised as small-, appropriate- or large for gestational age (<10th, 10–90th and >90th centiles, respectively), based on Australian national birthweight centiles for singletons by gestational age and sex.[28]

Pre-birth malignant cancer diagnoses were identified in the Cancer Register. Women were classified as having a mental health-related hospitalisation[29] or other chronic condition (cardiovascular, chronic kidney, asthma/chronic respiratory or autoimmune conditions, thyroid disorders, pre-existing diabetes, human immunodeficiency virus, cystic fibrosis, thalassemia/sickle cell disorders and other diseases of the blood and blood forming organs; see Table S3 for ICD codes) if they had a related diagnosis in a HMDC record between a year prior to conception and birth or were noted in the MNS (pre-existing diabetes, essential hypertension, asthma). The choice of chronic conditions was based on previous Australian[30] and US[31] comorbidity indices. Women were classified as having the following pregnancy complications: gestational diabetes, preeclampsia/gestational hypertension, or placenta praevia/ placental abruption/ other antepartum haemorrhage if noted in the MNS or were listed as a diagnosis in the HMDC during the index pregnancy (see Table S3 for ICD codes). All diagnostic codes were converted into ICD-9-AM and ICD-10-AM and modified to reflect coding changes with the assistance of the Western Australian Clinical Coding Authority.

2.2.5 | Statistical analyses

Unless stated, analyses were stratified by Aboriginal status. Medians and interquartile ranges (IQR) were calculated for key maternal ages and follow-up time. Absolute and relative measures of association between gestation and all-cause and cause-specific mortality were estimated and rate differences calculated. Associations were examined over the maximum possible follow-up period (0–38 years). The Kaplan–Meier method was used to estimate the survival functions while hazard ratios (HR) and 95% confidence intervals (CI) were estimated using Cox proportional hazards regression, with maternal age as the time-scale.[32] Potential confounders were selected based on a priori knowledge and availability of variables in the data set and refined with the development of a Directed Acyclic Graph (Figure S1). The final model included birth year (continuous), maternal age at first birth, parity in index pregnancy, SES, remoteness of residence, gestational diabetes, preeclampsia/gestational hypertension, any antepartum haemorrhage, pre-birth cancer diagnosis, mental health-related hospitalisation and chronic disease. The reference group was term births (37–41 weeks). Further models were run to assess whether the association varied by the type or number of preterm births.

2.2.6 | Missing data

If the mother's first birth record was not in the MNS (births prior to 1980 or not in Western Australia), her age at her first birth was missing (21%) and information about smoking during pregnancy was only collected from 1998, so 43.1% of smoking data were not collected. The MICE (Multivariate Imputation by Chained Equations) imputation method[33] was used with 50 iterations to impute the missing data for maternal age at the first birth as well as missing SES (3.4%) and remoteness of residence (3%) (See Appendix S1 and Table S4 for more details). Because there was a decline in smoking rates among Australian women between 1980 and 1998[34] (the years of missing data), it was not appropriate to impute these data, so smoking was not included as a covariate in the main regression models. After imputation, the final multivariable models included >99% of the cohort.

2.2.7 | Sensitivity analyses

As a woman's risk of having a preterm birth increases with each birth,[35] the analyses were repeated using the first birth in the MNS for each mother (regardless of parity at the time), instead of the shortest gestation. Analyses were repeated excluding mothers missing age at the first birth and smoking during pregnancy in turn. The latter analyses were run with and without smoking as a covariate. Although the sample contained only singleton births, 8572 (1.8%) of these mothers had also had a multiple birth history, so the analyses were repeated excluding them.

Analyses were conducted using SAS version 9.4 (SAS Institute Inc, Cary, NC, USA) and RStudio version 2021.09.0.[36] Cell counts with less than 10 were not tabulated to ensure confidentiality.

2.3 | Ethics approval

Ethics approvals were obtained from the Western Australian Department of Health Human Ethics Research Committee (201610.01) and the Western Australian Aboriginal Health Ethics Committee (797).

3 | RESULTS

The total study size included 487,291 mothers who had a birth between 1980 and 2015. After exclusion of births missing key data (1.1%), multiple births (2.8%) and pregnancy terminations for foetal anomaly (0.1%), the final sample consisted of 477,601 mothers who had a singleton birth (8,605,490 person-years of follow-up), including 20,244 (4.2%) Aboriginal mothers (Figure 1). The maximum follow-up was 38 years with a median (IQR) follow-up of 15 (6, 25) and 17 (7, 27) years among Aboriginal and non-Aboriginal mothers, respectively. There were 1349 deaths (6.7%) among Aboriginal mothers with a median age at death of 43 (IQR 34, 51) years and 7646 deaths (1.7%) among non-Aboriginal mothers, with a median age at death of 49 (IQR 40, 57) years. There were distinct differences in most demographic and other characteristics by Aboriginal status (Table 1). Notably, Aboriginal mothers were younger at their first birth, had a higher final parity, and were more likely to live in a low SES or remote/very remote area, smoke during pregnancy, have a mental health hospitalisation or other chronic condition and have a preterm birth (27.3%) than non-Aboriginal mothers (10.7%). In both population groups, mothers of preterm births were more likely to live in a low SES area, smoke, have a pregnancy complication, mental health hospitalisation or other chronic condition than those with a term birth.

3.1 | All-cause mortality

The Kaplan–Meier survival curves show that Aboriginal mothers died younger than non-Aboriginal mothers (Figure 2). Similarly, mothers who had a preterm died younger than mothers who had only term births, with the difference more pronounced among Aboriginal women. The absolute mortality rates were lowest for term birth and highest in one of the three preterm groups for both Aboriginal and non-Aboriginal mothers—with higher mortality rates among Aboriginal mothers resulting in at least a four-fold excess risk (Table 2).

The adjusted HRs (aHR) for mortality associated with preterm birth compared with term birth were 1.48 (95% CI 1.32, 1.66) for Aboriginal and 1.35 (95% CI 1.26, 1.44) for non-Aboriginal mothers, while the corresponding rate differences were 185.5 (95% CI 135.5, 238.3) and 37.0 (95% CI 29.4, 44.9) per 100,000 person-years, respectively (Table 2). While the absolute rates were higher in mothers following a clinician-initiated than a spontaneous preterm birth, the hazard ratios were too imprecise to detect a difference. (Table 2).

3.2 | Cause-specific mortality

Of the 8995 deaths, 7050 (78.4%) were classified into a cause-specific category. The most common causes of death were cancer (41.2% of total deaths), external causes of death (16.6%), circulatory (11.0%) and digestive (3.0% deaths) systems. Compared to mothers who had a term birth, mothers of preterm birth had higher relative risks of death from most of the causes investigated, with the largest effect sizes recorded for diabetes and diseases of the circulatory system and digestive system. For Aboriginal mothers, there was a more than 10-fold excess risk for diseases of the circulatory and digestive systems, diabetes and external causes (Table 3). Further breakdowns of some of the causes of death (e.g., cancer and external causes) are provided in Table S5.

3.3 | Mortality by number of preterm births

The relative risks of mortality increased by the number of preterm births (Figure 3).

3.4 | Sensitivity analyses

When the analyses were repeated using the first birth in the MNS for each mother, the proportion with a preterm birth decreased from 27.3% to 13.4% and from 10.7% to 7.1% among Aboriginal and non-Aboriginal women respectively. However, the mortality risk results remained similar to the main findings as they did when mothers with unknown age at the first birth or any multiple births were excluded (Table S6). When the analyses were restricted to those with smoking data (births from 1998), the addition of smoking to the model made little difference to the aHR (Table S7).

4 | COMMENT

4.1 | Principal findings

We found that both Aboriginal and non-Aboriginal women who had a history of a singleton preterm birth in Western Australia between 1980 and 2015 had an increased risk of early mortality compared with those who had a term birth. The level of risk decreased with each additional week of gestation and increased with each additional preterm birth. In both populations, mothers who had a preterm birth had an increased risk of death related to diabetes, cardiovascular and digestive conditions and external causes. The absolute mortality risk associated with a preterm birth was distinctly higher among Aboriginal than non-Aboriginal mothers. While the level of relative risk generally appeared to be similar for Aboriginal and non-Aboriginal mothers, this can only be confirmed in studies with larger sample sizes and longer follow-up to give more precise estimates among Aboriginal women.

4.2 | Strengths of the study

This was a population-based study which included linkages to hospital admissions and the cancer register so we could identify potential risk factors present before the birth.

TABLE 1 Demographic and other characteristics of mothers with and without a preterm birth in Western Australia 1980–2015, stratified by Aboriginal status

	Aboriginal mothers			Non-Aboriginal mothers		
	Term (*n* = 14,716)	Preterm (*n* = 5528)	Total (*n* = 20,244)	Term (*n* = 408,511)	Preterm (*n* = 48,846)	Total (*n* = 457,357)
	n (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Maternal age (years) at first birth						
<20	6949 (47.2)	3168 (57.3)	10,117 (50.0)	26,797 (6.6)	5116 (10.5)	31,913 (7.0)
20–24	3728 (25.3)	1145 (20.7)	4873 (24.1)	79,260 (19.4)	10,526 (21.5)	89,786 (19.6)
25–29	1018 (6.9)	262 (4.7)	1280 (6.3)	110,420 (27.0)	12,842 (26.3)	123,262 (27.0)
30–34	356 (2.4)	92 (1.7)	448 (2.2)	74,325 (18.2)	8901 (18.2)	83,226 (18.2)
≥35	122 (0.8)	46 (0.8)	168 (0.8)	28,516 (7.0)	3766 (7.7)	32,282 (7.1)
Missing[a]	2543 (17.3)	815 (14.7)	3358 (16.6)	89,193 (21.8)	7695 (15.8)	96,888 (21.2)
Parity in first pregnancy in MNS						
0	12,173 (82.7)	4713 (85.3)	16,886 (83.4)	319,318 (78.2)	41,151 (84.2)	360,469 (78.8)
1	1070 (6.9)	395 (7.1)	1415 (7.0)	51,430 (12.6)	4369 (8.9)	55,799 (12.2)
2	672 (4.6)	191 (3.5)	863 (4.3)	25,604 (6.3)	2108 (4.3)	27,712 (6.1)
≥3	850 (5.8)	228 (4.1)	1078 (5.3)	12,062 (3.0)	1203 (2.5)	13,265 (2.9)
Maternal age (years) at end of follow-up						
14–34	5982 (40.6)	1719 (31.1)	7701 (38.0)	65,527 (16.0)	6898 (14.1)	72,425 (15.8)
35–44	3551 (24.1)	1613 (29.2)	5164 (25.5)	110,589 (27.1)	13,857 (28.4)	124,446 (27.2)
45–54	3098 (21.1)	1492 (27.0)	4590 (22.7)	112,230 (27.5)	14,591 (29.9)	126,821 (27.7)
≥55	2085 (14.2)	704 (12.7)	2789 (13.8)	120,165 (29.4)	13,500 (27.6)	133,665 (29.2)
Parity after last birth record in MNS						
1	3654 (24.8)	623 (11.3)	4277 (21.1)	99,381 (24.3)	8790 (18.0)	108,171 (23.7)
2	3468 (23.6)	877 (15.9)	4345 (21.5)	173,251 (42.4)	18,385 (37.6)	191,636 (41.9)
3	2862 (19.4)	1057 (19.1)	3919 (19.4)	90,910 (22.3)	12,567 (25.7)	103,477 (22.6)
≥4	4731 (32.1)	2970 (53.7)	7701 (38.0)	44,872 (11.0)	9089 (18.6)	53,961 (11.8)
Index birth						
Gestation (completed weeks)						
20–27		676 (12.2)	676 (3.3)		4007 (8.2)	4007 (0.9)
28–31		665 (12.0)	665 (3.3)		4515 (9.2)	4515 (1.0)
32–36		4187 (75.7)	4187 (20.7)		40,324 (82.6)	40,324 (8.8)
37–38	7555 (51.3)		7555 (37.3)	166,302 (40.7)		166,302 (36.4)
39–41	7026 (47.7)		7026 (34.7)	238,904 (58.5)		238,904 (52.2)
>41	135 (0.9)		135 (0.7)	3305 (0.8)		3305 (0.7)
Birth year group						
1980–1989	3349 (22.8)	1310 (23.7)	4659 (23.0)	103,549 (25.3)	11,414 (23.4)	114,963 (25.1)
1990–1999	3064 (20.8)	1384 (25.0)	4448 (22.0)	96,062 (23.5)	12,507 (25.6)	108,569 (23.7)
2000–2009	4081 (27.7)	1669 (30.2)	5750 (28.4)	106,719 (26.1)	14,028 (28.7)	120,747 (26.4)
2010–2015	4222 (28.7)	1165 (21.1)	5387 (26.6)	102,181 (25.0)	10,897 (22.3)	113,078 (24.7)
Maternal age (years) at index birth						
<20	4601 (31.3)	1593 (28.8)	6194 (30.6)	17,030 (4.2)	2657 (5.4)	19,687 (4.3)
20–24	5128 (34.8)	1817 (32.9)	6945 (34.3)	71,472 (17.5)	8680 (17.8)	80,152 (17.5)
25–29	2922 (19.9)	1121 (20.3)	4043 (20.0)	132,098 (32.3)	14,803 (30.3)	146,901 (32.1)
30–34	1395 (9.5)	632 (11.4)	2027 (10.0)	121,990 (29.9)	13,921 (28.5)	135,911 (29.7)
≥35	670 (4.6)	365 (6.6)	1035 (5.1)	65,921 (16.1)	8785 (18.0)	74,706 (16.3)

TABLE 1 (Continued)

	Aboriginal mothers			Non-Aboriginal mothers		
	Term (n = 14,716)	Preterm (n = 5528)	Total (n = 20,244)	Term (n = 408,511)	Preterm (n = 48,846)	Total (n = 457,357)
	n (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Parity at index birth						
0	7204 (49.0)	1909 (34.5)	9113 (45.0)	208,537 (51.0)	24,514 (50.2)	233,051 (51.0)
1	3518 (23.9)	1366 (24.7)	4884 (24.1)	128,417 (31.4)	13,527 (27.7)	141,944 (31.0)
2	1932 (13.1)	862 (15.6)	2794 (13.8)	49,607 (12.1)	6575 (13.5)	56,182 (12.3)
≥3	2061 (14.0)	1390 (25.1)	7701 (38.0)	21,853 (5.3)	4215 (8.6)	26,068 (5.7)
SES area birth residence quintiles						
1 (Most disadvantaged)	8551 (58.1)	3534 (63.9)	12,085 (59.7)	75,067 (18.4)	10,184 (20.8)	85,251 (18.6)
2	2983 (20.3)	1051 (19.0)	4034 (19.9)	83,376 (20.4)	10,388 (21.3)	93,764 (20.5)
3	1642 (11.2)	518 (9.4)	2160 (10.7)	81,778 (20.0)	9622 (19.7)	91,410 (20.0)
4	840 (5.7)	253(4.6)	1093 (5.4)	80,186 (19.6)	9296 (19.0)	89,482 (19.6)
5 (Least disadvantaged)	330 (2.2)	77 (1.4)	407 (2.0)	73,874 (18.1)	7978 (16.3)	81,852 (17.9)
Missing[b]	370 (2.5)	95 (1.7)	465 (2.3)	14,220 (3.5)	1378 (2.8)	15,598 (3.4)
Remote or very remote birth residence	7069 (48.0)	2692 (48.7)	9761 (48.2)	40,186 (9.8)	4612 (9.4)	44,798 (9.8)
Missing[b]	530 (3.6)	250 (4.5)	780 (3.9)	11,980 (2.9)	1425 (2.9)	13,405 (2.9)
Smoker during pregnancy						
No	5092 (34.6)	1460 (26.4)	6552 (32.4)	203,804 (49.9)	23,161 (47.4)	226,965 (49.6)
Yes	3952 (26.9)	1690 (30.6)	5642 (27.9)	27,175 (6.7)	4573 (9.4)	31,748 (6.9)
Missing [c]	5650 (38.4)	2347 (42.5)	7997 (39.5)	176,952 (43.3)	20,917 (42.8)	197,869 (43.3)
Appropriateness of foetal growth[d]						
Small for gestational age	2234 (15.2)	636 (11.5)	2870 (14.2)	36,169 (8.9)	4773 (9.8)	40,942 (9.0)
Appropriate for gestational age	11,253 (76.5)	3989 (72.2)	15,242 (75.3)	33,3019 (81.5)	36,771 (75.3)	369,790 (80.9)
Large for gestational age	1225 (8.3)	898 (16.2)	2123 (10.5)	39,257 (9.6)	7281 (14.9)	46,538 (10.2)
Pregnancy complications						
Pre-eclampsia/ gestational hypertension	1487 (10.1)	867 (15.7)	2354 (11.6)	36,660 (9.0)	8815 (18.0)	45,475 (9.9)
Gestational diabetes	772 (5.2)	325 (5.9)	1097 (5.4)	1, 774 (4.4)	2715 (5.6)	20,489 (4.5)
Placenta praevia, placental abruption or other ante partum haemorrhage	480 (3.3)	727 (13.2)	1207 (6.0)	17,522 (4.3)	8945 (18.3)	26,467 (5.8)
Existing conditions						
Pre-birth cancer diagnosis	19 (0.1)	10 (0.2)	29 (0.1)	1351 (0.3)	265 (0.5)	1616 (0.4)
Mental health-related hospitalisation[e]	958 (6.5)	582 (10.5)	1540 (7.6)	7577 (1.9)	1969 (4.0)	9546 (2.1)

(Continues)

TABLE 1 (Continued)

	Aboriginal mothers			Non-Aboriginal mothers		
	Term (*n* = 14,716)	Preterm (*n* = 5528)	Total (*n* = 20,244)	Term (*n* = 408,511)	Preterm (*n* = 48,846)	Total (*n* = 457,357)
	n (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Other chronic condition[f]	1593 (10.8)	808 (14.6)	2401 (11.9)	33,400 (8.2)	5820 (11.9)	39,220 (8.6)
Stillbirth	47 (0.3)	428 (7.7)	475 (2.3)	410 (0.1)	3078 (6.3)	3488 (0.8)
Type of censoring						
Left State[g]	228 (1.5)	45 (0.8)	273 (1.3)	6543 (1.6)	1050 (2.1)	10,137 (2.2)
Deceased	838 (5.7)	511 (9.2)	1349 (6.7)	9087 (2.2)	1103 (2.3)	7646 (1.7)
Censored on 30 June 2018	13,651 (92.8)	4972 (89.9)	18,623 (92.0)	392,886 (96.2)	46,694 (95.6)	439,580 (96.1)
Median follow-up year (interquartile range)	14 (7, 26)	16 (9, 26)	15 (7, 26)	17 (8, 28)	17 (9, 28)	17 (8, 28)

Abbreviations: MNS: Midwives Notification System, SES: socio-economic status.

[a]If there was no birth record in the MNS for mother's first birth, the age was classified as unknown (births prior to 1980 or not in Western Australia).

[b]Missing values only given if ≥1% for any of the subgroups.

[c]Data about maternal smoking only collected from 1998.

[d]These were assigned using Australian sex-specific national birthweight for age gestation centiles for singletons.[19]

[e]Any diagnoses in the Hospital Morbidity Data Collection from 1 year prior to conception until the birth hospitalisation (see Table S3).

[f]Chronic conditions were defined as asthma, pre-existing diabetes or hypertension recorded in the Midwives Notification System or any of the following diagnoses in the Hospital Morbidity Data Collection from 1 year prior to conception until the birth hospitalisation: cardiovascular, chronic kidney, asthma/chronic respiratory or autoimmune conditions, thyroid disorders, pre-existing diabetes, human immunodeficiency virus, cystic fibrosis, thalassemia/sickle cell disorders and other diseases of the blood and blood forming organs (see Table S3).

[g]Based on Electoral Roll registrations (Restricted to Australian citizens who had registered for voting ~79% of Aboriginal mothers and 82% of non-Aboriginal mothers).

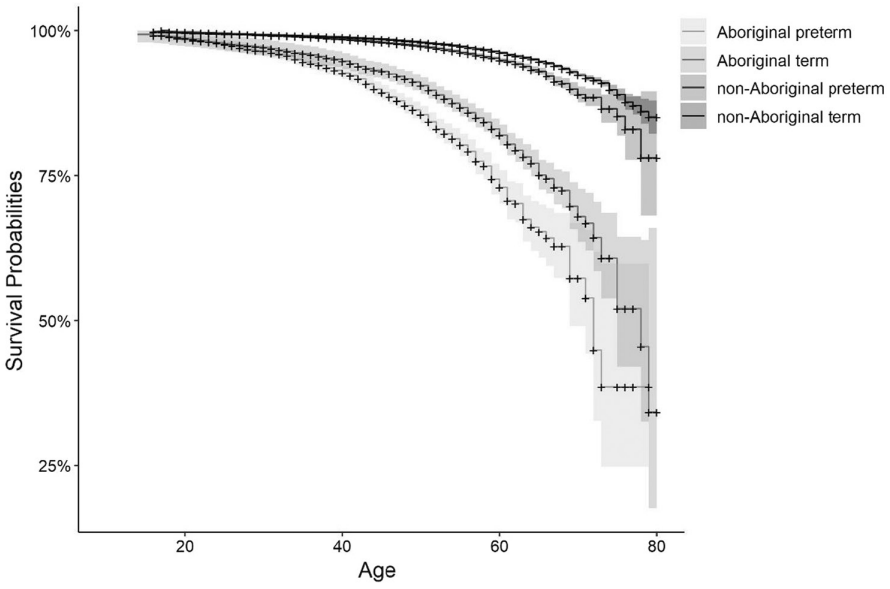

FIGURE 2 Survival probabilities of women stratified by Aboriginal status and birth group (term/preterm).

4.3 | Limitations of the data

While we featured one of the longest follow-up periods for a study of this nature, the median age of the cohort at the end of follow-up was 39 and 47 years for Aboriginal and non-Aboriginal women—well short of the average life expectancy for Aboriginal (76 years) and non-Aboriginal women (83 years)[37] so we could not identify if any excess risk continued later in life. Only information about the main cause of death was available with no data about contributing causes. We also only had information about maternal smoking during pregnancy from 1998. Although smoking made no difference in the sensitivity analyses restricted to a maximum of 20 years

TABLE 2 Association between gestation and maternal all-cause mortality by Aboriginal status Western Australia 1980–2015 (Follow-up time 0–38 years)

Gestation (completed weeks)	Aboriginal mothers (n = 20,244)				Non-Aboriginal mothers (n = 457,357)			
	Person- years	Deaths (Rate[a])	Rate difference (95% CI)	Hazard ratio (95% CI)[b]	Person- years	Deaths (Rate[a])	Rate difference (95% CI)	Hazard ratio (95% CI)[b]
≥37	243, 595	838 (344.0)	0.0 (Reference)	1.00 (Reference)	7,386,735	6543 (88.6)	0.0 (Reference)	1.00 (Reference)
All preterm births								
<37	96, 505	511 (529.5)	185.5 (135.5, 238.3)	1.48 (1.32, 1.66)	878,655	1103 (125.5)	37.0 (29.4, 44.9)	1.35 (1.26, 1.44)
20–27	11, 365	63 (554.3)	210.3 (87.2, 366.2)	1.62 (1.23, 2.12)	74,182	121 (163.1)	74.5 (47.9, 106.3)	1.65 (1.37, 1.98)
28–31	11, 000	76 (690.9)	346.9 (206.3, 521.3)	1.88 (1.47, 2.41)	85,609	118 (137.8)	49.3 (26.4, 76.5)	1.36 (1.13, 1.64)
32–36	74, 140	372 (501.8)	157.7 (103.7, 215.8)	1.41 (1.24, 1.60)	718,864	864 (120.2)	31.6 (23.6, 40.2)	1.31 (1.22, 1.41)
Spontaneous preterm births[c]								
<37	76, 610	373 (486.9)	142.9 (90.2, 199.4)	1.45 (1.27, 1.64)	600,746	709 (118.0)	29.4 (20.8, 38.7)	1.29 (1.20, 1.40)
20–27	9443	50 (529.5)	185.5 (55.6, 354.8)	1.51 (1.12, 2.05)	53,854	83 (154.1)	65.5 (35.7, 102.5)	1.49 (1.19, 1.86)
28–31	8042	46 (572.0)	228.0 (83.1, 419.4)	1.71 (1.26, 2.32)	53,514	66 (123.3)	34.8 (8.3, 68.4)	1.23 (0.96, 1.57)
32–36	59,125	277 (468.5)	124.5 (67.3, 187.0)	1.40 (1.22, 1.61)	493,378	560 (113.5)	24.9 (15.7, 34.9)	1.27 (1.17, 1.39)
Initiated preterm births[c]								
<37	19,804	138 (696.8)	352.8 (243.5, 480.6)	1.62 (1.33, 1.97)	277,274	394 (142.1)	53.5 (40.0, 68.4)	1.47 (1.32, 1.63)
20–27	1844	13 (705.0)	361.0 (67.5, 859.0)	2.15 (1.23, 3.76)	19,734	38 (192.6)	104.0 (51.7, 175.6)	2.11 (1.53, 2.91)
28–31	2945	30 (1018.7)	674.7 (369.5, 1107.1)	2.25 (1.53, 3.32)	32,095	52 (162.0)	73.4 (34.9, 123.9)	1.56 (1.19, 2.06)
32–36	15,015	95 (632.7)	288.7 (171.4, 430.5)	1.45 (1.15, 1.82)	225,445	304 (134.8)	46.3 (31.8, 62.4)	1.39 (1.24, 1.57)

[a]Mortality rate per 100,000 person-years.

[b]Maternal age used as the Cox model time scale and adjusted for birth year, maternal age at first birth, parity at index pregnancy, socio-economic status quintile, remote or very remote birth residence, gestational diabetes, preeclampsia/gestational hypertension, any ante-partum haemorrhage, pre-birth cancer diagnosis, mental health-related hospitalisation or chronic disease from 12 months prior to conception to birth.

[c]Spontaneous preterm births were defined as births with spontaneous onset or labour or vaginal births with pre-labour rupture of membranes. Initiated births were those whose labour was induced or had a pre-labour caesarean section with intact membranes.

TABLE 3 Association between pregnancy length and maternal cause-specific mortality by Aboriginal status Western Australia 1980–2015

		Aboriginal mothers				Non-Aboriginal mothers			
Cause of death	Pregnancy length	Person-years	Deaths (Rate[a])	Rate difference (95% CI)	Hazard ratio (95% CI)[b]	Person- years	Deaths (Rate[a])	Rate difference (95% CI)	Hazard ratio (95% CI)[b]
Cancer									
	Preterm	88,736	43 (48.5)	−9.8 (−26.3, 9.2)	0.87 (0.61, 1.25)	866,926	421 (48.6)	6.1 (1.5, 11.2)	1.18 (1.06, 1.31)
	Term	231,583	135 (58.3)	0.0 (Reference)	1.00 (Reference)	7,321,331	3107 (42.4)	0.0 (Reference)	1.00 (Reference)
External causes									
	Preterm	89,089	109 (122.3)	39.1 (14.7, 66.6)	1.31 (1.02, 1.67)	861,966	183 (21.2)	7.4 (4.4, 10.8)	1.28 (1.08, 1.50)
	Term	230,748	192 (83.2)	0.0 (Reference)	1.00 (Reference)	7,274,710	1005 (13.8)	0.0 (Reference)	1.00 (Reference)
Circulatory system									
	Preterm	89,930	117 (130.1)	64.9 (40.7, 92.5)	1.92 (1.49, 2.47)	861,998	126 (14.6)	6.5 (4, 9.3)	1.66 (1.36, 2.03)
	Term	231,757	151 (65.2)	0.0 (Reference)	1.00 (Reference)	7,273,518	592 (8.1)	0.0 (Reference)	1.00 (Reference)
Diabetes									
	Preterm	88,828	42 (47.3)	29.9 (16.1, 47.1)	2.44 (1.54, 3.87)	860,458	33 (3.8)	2.9 (1.7, 4.4)	3.99 (2.59, 6.15)
	Term	229,701	40 (17.4)	0.0 (Reference)	1.00 (Reference)	7,263,844	70 (1.0)	0.0 (Reference)	1.00 (Reference)
Digestive system									
	Preterm	88,633	37 (41.5)	16.5 (2.9, 33.3)	1.67 (1.09, 2.56)	860,163	28 (3.3)	1.2 (0.2, 2.7)	1.43 (0.94, 2.19)
	Term	229,746	58 (25.2)	0.0 (Reference)	1.00 (Reference)	7,264,994	148 (2.0)	0.0 (Reference)	1.00 (Reference)
Respiratory system									
	Preterm	88,227	18 (20.4)	7.3 (−2.0, 19.8)	1.48 (0.81, 2.71)	860,436	40 (4.6)	1.9(0.6, 3.6)	1.52 (1.06, 2.16)
	Term	229,208	30 (13.1)	0.0 (Reference)	1.00 (Reference)	7,266,135	198 (2.7)	0.0 (Reference)	1.00 (Reference)
Nervous system									
	Preterm	88,122	10 (11.3)	5.2 (−1.4, 15.1)	1.71 (0.73, 4.00)	860,168	23 (2.7)	0.7 (−0.3, 2.1)	1.42 (0.90, 2.25)
	Term	228,988	14 (6.1)	0.0 (Reference)	1.00 (Reference)	7,265,038	143 (2.0)	0.0 (Reference)	1.00 (Reference)

[a]Mortality rate per 100,000 person-years.

[b]Maternal age used as the Cox model time scale and adjusted for birth year, maternal age at first birth, parity at index pregnancy, Socio-economic status quintile, remote or very remote birth residence, gestational diabetes, preeclampsia/gestational hypertension, any ante-partum haemorrhage, pre-birth cancer diagnosis, mental health-related hospitalisation or chronic disease from 12 months prior to conception to birth.

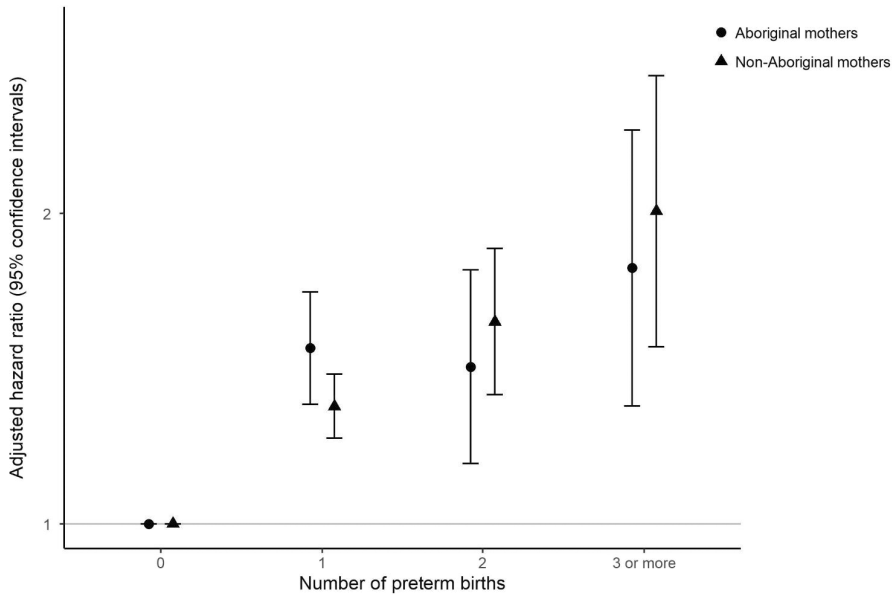

FIGURE 3 Adjusted hazard ratios[a] (95% confidence intervals) for mortality among women by the number of preterm births. [a]Maternal age used as the Cox model time scale and adjusted for birth year, maternal age at first birth, parity at index pregnancy, socio-economic status quintile, remote or very remote birth residence, gestational diabetes, preeclampsia/gestational hypertension, any ante-partum haemorrhage, pre-birth cancer diagnosis, mental health-related hospitalisation, or chronic disease from 12 months prior to conception to birth.

follow-up, this may have been related to the age at the end of follow-up being younger than when smoking-related deaths occur, for example the mean age at death from lung cancer in Australian women is 71 years.[38] We also did not have information about substance misuse which is higher in Aboriginal women[39-41] and contributes to preterm birth (drugs and alcohol)[42] and deaths (alcohol).[43]

4.4 | Interpretation

Only limited epidemiological studies have investigated the relationship between having a preterm birth and subsequent early mortality in mothers,[6,7,8,9,10,11,44,45,46,47] with the majority conducted in Scandinavia,[6,7,9,10,11,47] and none focusing on any minority populations. Despite methodological differences and follow-up duration, four[6,7,8,10] of the five studies which investigated overall mortality,[6-10] also reported a moderately increased risk with aHR estimates ranging from 1.2 (95% CI 1.1, 1.3) in Sweden after up to 25 years of follow-up[6] to 1.7 (95% 1.5, 1.8) in Denmark with up to 30 years of follow-up.[10] Using 39–41 weeks' gestation as the reference, the latest Swedish study by Crump et al.[7] with up to 44 years of follow-up, also found that the risk was highest at very early gestations (22–27 weeks), and with recurrent preterm births. Unlike us, they found that the risk was higher following initiated preterm births than spontaneous ones,[7] which could be due to a larger sample size. However, indications for initiated preterm births (e.g. ischaemic placental disease) can also predispose to spontaneous births.[48]

An umbrella review of literature until 2019[6,7,8,9,10,11,44,45,46] further confirms the relationship between preterm birth and cardiovascular mortality[12] calculating the risk for cardiovascular mortality following a preterm birth to be 1.9 (95% CI 1.8, 2.0) which is similar to estimates from both our study and the more recent study by Crump et al.[7] Like us, Crump et al.[7] reported that diabetes mortality was associated with preterm birth, although our study extends the cause-specific outcomes to digestive disorders and external causes of death.

The biological mechanisms underlying the association between having a preterm birth and early mortality are unknown, but there are several theories and likely to be more than one true mechanism. Firstly, it has been said that pregnancy may unmask a predisposition to disease in a diverse range of systems, particularly cardiometabolic disease but also thrombosis, liver, renal, thyroid and pituitary disorders.[49] Further, shared pathophysiology may contribute both to pregnancy complications including preterm birth and to subsequent causes of mortality, such as, inflammation, which is a key contributor to both spontaneous[50] and initiated[51-53] preterm birth and is also implicated in cardiovascular disease.[54] Whatever the mechanisms, it is likely that social deprivation can accentuate the level of risk as it associated with increased risks of both early death[55] and preterm birth.[56] In particular, a high proportion of poor birth outcomes among Aboriginal women have been attributed to social, economic and environmental factors (poverty, lack of access to appropriate care, smoking, alcohol, substance abuse, violence).[42] Importantly, these inequalities are intrinsically linked to the legacies of colonisation in Australia and the associated distress of ongoing marginalisation, discrimination, dispossession and exclusion experienced by Aboriginal peoples over generations.[57] The literature is now replete with examples highlighting the direct and indirect effects of racial discrimination on social and economic circumstances and myriad health outcomes.[58]

Having a preterm birth can impact a woman's later health. Because of the baby's health needs, these women often have frequent contact with the health system which makes them an easily identifiable target for monitoring and primary prevention, both in the postpartum period and beyond. This fits well with the concept of the postpartum period being treated as the 'fourth trimester' with the woman receiving ongoing care, rather than at a single point of contact.[59] Our findings add to the existing evidence behind the

American Heart Association's call for more primary prevention of cardiovascular disease following adverse pregnancy outcomes,[14] which could be extended to other chronic conditions such as diabetes and those of the digestive system. Policies related to improving the socio-economic circumstances of women, particularly Aboriginal women, and their families, has the potential to reduce the risk of both preterm birth and early mortality among women.

5 | CONCLUSIONS

Both Aboriginal and non-Aboriginal women in Western Australia who had a preterm birth had a moderately increased risk of early mortality up to 38 years. These findings highlight the importance of primary prevention, screening for and management of chronic conditions such as cardiovascular disease and diabetes during and after pregnancy and into middle-age.

AUTHOR CONTRIBUTIONS

HDB, CG, NAS, RM, CCJS and MS conceived and designed the study. CCJS obtained access to the data. HDB managed the data with assistance from AAA. HDB performed the analyses, did the initial data interpretation, and drafted the initial manuscript. All authors made substantial contributions to theanalysis plan and data interpretation and critically revised the manuscript.

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CONFLICT OF INTEREST

None declared.

DATA AVAILABILITY STATEMENT

The data underlying this article were provided by the Data Linkage team of the Western Australian Department of Health and cannot be publicly shared by the authors. Researchers wanting to access these data will need to apply to the Data Linkage team of the Western Australian Department of Health (https://www.datalinkage-wa.org.au/).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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