



Original research

# Identifying preventable risk factors for hospitalised asthma in young Aboriginal children: a whole-population cohort study

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## ABSTRACT

**Background** Australia has one of the highest rates of asthma worldwide. Indigenous children have a particularly high burden of risk determinants for asthma, yet little is known about the asthma risk profile in this population.

**Aim** To identify and quantify potentially preventable risk factors for hospitalised asthma in Australian Aboriginal children (1–4 years of age).

**Methods** Birth, hospital and emergency data for all Aboriginal children born 2003–2012 in Western Australia were linked (n=32 333). Asthma was identified from hospitalisation codes. ORs and population attributable fractions were calculated for maternal age at birth, remoteness, area-level disadvantage, prematurity, low birth weight, maternal smoking in pregnancy, mode of delivery, maternal trauma and hospitalisations for acute respiratory tract infection (ARTI) in the first year of life.

**Results** There were 705 (2.7%) children hospitalised at least once for asthma. Risk factors associated with asthma included: being hospitalised for an ARTI (OR 4.06, 95% CI 3.44 to 4.78), area-level disadvantage (OR 1.58, 95% CI 1.28 to 1.94), being born at <33 weeks' gestation (OR 3.30, 95% CI 2.52 to 4.32) or birth weight <1500 g (OR 2.35, 95% CI 1.39 to 3.99). The proportion of asthma attributable to an ARTI was 31%, area-level disadvantage 18%, maternal smoking 5%, and low gestational age and birth weight were 3%–7%. We did not observe a higher risk of asthma in those children who were from remote areas.

**Conclusion** Improving care for pregnant Aboriginal women as well as for Aboriginal infants with ARTI may help reduce the burden of asthma in the Indigenous population.

## INTRODUCTION

Asthma is the most common chronic disease in children worldwide, and often persists over the life course. Australia continues to have one of the highest rates of asthma in the world, and nearly 20% of all children have been diagnosed with asthma at some stage in their life by the age of 15 years.<sup>1</sup> Although management of asthma has improved in recent decades and case fatality rates have declined significantly, asthma continues to cause substantial morbidity in children<sup>2,3</sup> and leads to more hospitalisations and general practice (GP) visits than any

## Key messages

### What is the key question?

- What are the potentially preventable risk factors for hospitalised asthma in Australian Aboriginal children?

### What is the bottom line?

- Australian Aboriginals have one of the highest prevalence of asthma worldwide, yet little has been studied on early prevention despite the fact that the Aboriginal population also has a high burden of potential risk factors such as smoking and disadvantage.

### Why read on?

- To improve asthma rates in vulnerable groups such as Aboriginal children and children living with disadvantage, we need to know which points of intervention will have the biggest potential effect.

other illness.<sup>1</sup> In Western Australia (WA) where the current study is set, asthma accounts for the second highest cause of disability-adjusted life years in children after complications attributable to preterm birth and low birth weight.<sup>2</sup>

Aboriginal and Torres Strait Islander (hereafter respectfully referred to as Aboriginal) children in Australia have a 1.8–2.3 times higher asthma prevalence than non-Indigenous children.<sup>1,3</sup> Furthermore, half of all emergency presentations for asthma in Indigenous children (0–16 years) occur between 0 and 4 years.<sup>4</sup> Asthma that starts early in life may be particularly troublesome, leading to emergency room attendance and hospitalisation. In many cases, asthma that persists into later childhood and adult life has its origins in early childhood.<sup>1</sup>

Prevention of asthma can be guided by studying early life risk factors, particularly those that provide possible preventive and intervention strategies. Trials aimed at preventing asthma through nutrition-based strategies or avoidance of allergens during pregnancy or early life have so far proved unsuccessful.<sup>5</sup> Other strategies aimed at the early life period are needed. Apart from inherited genetic risk, early life factors with strong evidence for causing asthma include prenatal exposure to



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environmental tobacco smoke and very preterm birth.<sup>5</sup> Other emerging risk factors include maternal factors such as stress, weight gain during pregnancy and antibiotic or analgesic use during pregnancy; birth factors such as caesarean section; and early life factors such as severe respiratory syncytial virus (RSV) infection.<sup>5</sup>

One hypothesis for why the prevalence of asthma is particularly high in Aboriginal children is the high rate of exposure to several of these early life risk factors including: preterm birth,<sup>6</sup> low birth weight,<sup>6,7</sup> smoking in pregnancy,<sup>6,7</sup> high infectious respiratory disease load,<sup>8</sup> maternal mental health issues<sup>9</sup> and maternal psychological trauma.<sup>10</sup> A considerable proportion of these factors can be attributed to the negative consequences of colonisation over 200 years, including the social and economic marginalisation of Aboriginal people and experience of racism.<sup>11,12</sup> Despite the range of factors influencing this increased propensity for asthma, there is very little research into identifying the specific risk profile for Indigenous populations both in Australia and overseas. A small number of studies in Canada suggest that risk factors for asthma in First Nations infants include low birth weight, obesity, poor housing, maternal daily smoking and chronic ear infection.<sup>13,14</sup> Indigenous populations of the world such as in Canada, Australia, the Americas and the South Pacific share some similarities in long-term social and economic consequences of colonisation, racism and marginalisation, often with higher health burdens than the non-Indigenous populations.<sup>11,12</sup> Therefore, there is an important need for more respiratory research using large Indigenous populations to highlight possible solutions to redress the balance.

The objective of this study is to identify potential preventive early modifiable risk factors for asthma hospitalisation among Western Australian Aboriginal children under 5 years of age.

## METHODS

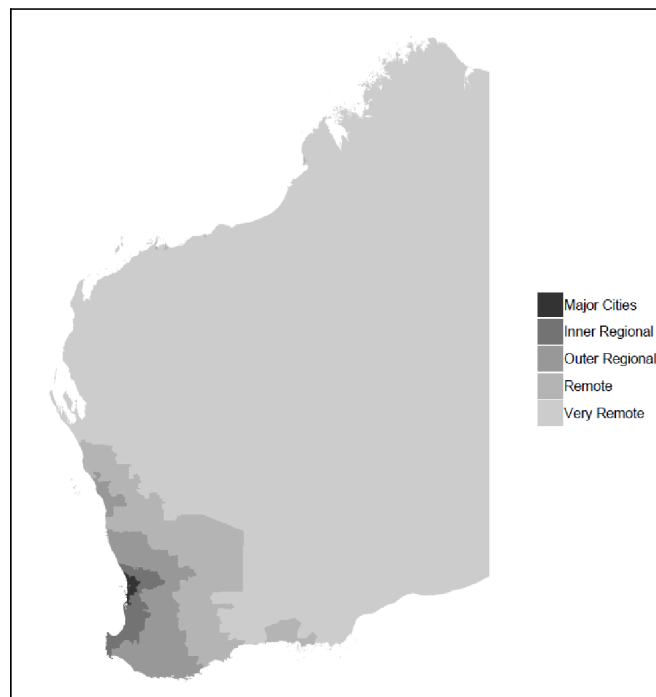
### Study population

The study population includes all Aboriginal children aged 1–4 years old born in WA between 2003 and 2012.<sup>15</sup> A child was included in the cohort if the child or their parent or grandparent was identified as Aboriginal using an algorithm applied to the Aboriginal status indicators within the multiple data sets by the WA Data Linkage Branch (DLB).<sup>16</sup> We excluded children where their full siblings were not identified as Aboriginal.

Linkage of this cohort to other data sets, listed below, was undertaken by WA DLB using probabilistic linkage based on birthdate and other demographic identifiers. The linked data for the broader study known as the ‘Defying the Odds’ Study comprised linkage of 12 administrative and health data sets.<sup>15</sup> For the purposes of the current study the data sets used included: WA Birth Registrations, WA Death Registrations, WA Midwives Notification System (MNS), WA Hospital Morbidity Data Collection (HMDC), WA Emergency Department Data Collection (EDDC), WA Register of Developmental Anomalies (WARDA) and WA Mental Health Information System. Children who were less than 20 weeks’ gestational age (reported in MNS), stillborn (reported in MNS) or who died in the first 5 years of life (reported in WA Death Registrations) were excluded.

### Outcome

*Hospitalisation for asthma*—primary diagnosis—International Classification of Diseases 10th Revision, Australian Modification (ICD-10-AM) code J45 or J46 in the HMDC between ages 1 and 4 years. We only included asthma diagnoses from the primary diagnosis field rather than from the additional diagnosis fields



**Figure 1** Remoteness areas in Western Australia (based on Australia Bureau of Statistics digital boundaries data, <https://www.abs.gov.au/websitedbs/d3310114.nsf/home/digital+boundaries>).

of the HMDC in order to minimise possible selection bias by hospitalisation due to non-asthma primary diagnoses.

### Potential exposures and covariates

From the MNS, data on the following variables were extracted: *plurality*; *parity*; *gestational age in weeks* (<33 weeks=very preterm, 33–36 weeks=preterm, 37–38 weeks=early term, 39–40 weeks=term, >40 weeks=post-term); *birth weight* (<1500 g=very low, 1500–2499 g=low, 2500–4000 g=normal, >4000 g=high); *delivery method* (vaginal, elective caesarean section, emergency caesarean section); *maternal smoking in pregnancy*; *maternal medical conditions in pregnancy* (diabetes type 2, gestational diabetes, hypertension, pre-eclampsia). An infant was classified as *small for gestational age (SGA)* if their birth weight was lower than the first decile for singleton infants of the same gestational age and sex according to national standards.<sup>17</sup>

*Date of birth*, *sex of baby* and *maternal and paternal age at child’s birth* were derived from multiple data sets including the MNS, the birth register, HMDC, EDDC, death register and WARDA. Pre-existing *maternal asthma* was derived from a positive self-report in the MNS or hospitalisation in the HMDC from 1970 up until the child’s birth. *Area-level remoteness of residence at birth* (in order of increasing distance from services: major cities, inner regional, outer regional, remote and very remote) was derived from the Accessibility/Remoteness Index of Area<sup>18</sup> recorded in the MNS, mother’s admission in HMDC and infant’s admission in the HMDC at birth (figure 1). *Disadvantage* in quintiles (Q1=most disadvantaged areas, Q5=least disadvantaged areas) was based on the Australian Bureau of Statistics Index of Relative Socio-economic Disadvantage (IRSD) which is an area-based rather than individual index. IRSD is a summary index of variables that indicate relative disadvantage including income, education, employment, occupation, housing and other miscellaneous indicators.<sup>19</sup> IRSD was assigned based on place of residence at birth. Due to missing data, several geographic

units and data sets were used to assign as IRSD in the following order: (1) MNS, (2) the mother's admission for the birth, (3) the child's hospital record at birth (data sets); (1) Census Collection District, (2) Statistical Local Area, and (3) Local Government Area (geographic units).

*Maternal psychological trauma* during pregnancy was defined as any of: (1) a hospitalisation, emergency department visit or a mental health service visit for alcohol or drug misuse during pregnancy; (2) a hospitalisation, emergency department visit or mental health service visit for a mental health episode in pregnancy and/or 3 months prior to pregnancy; or (3) a hospitalisation for assault/domestic violence in pregnancy and/or 2 years prior to delivery. (ICD-10-AM codes can be found in the online supplemental table S1. The wider time periods prior to pregnancy for (2) and (3) were included because these conditions are generally considered to be ongoing, therefore, likely to be continuing to cause distress during pregnancy even if detected earlier. Women often reduce alcohol and drug intake in pregnancy, therefore we considered that there would be less misclassification if we only included the pregnancy period for this variable.

*Acute respiratory tract infection (ARTI)* in the first year of life was extracted from primary diagnoses recorded in the HMDC for influenza, pneumonia, bronchiolitis and acute lower and upper respiratory tract infections. (See the online supplemental table S1 for ICD-10-AM codes.) Bronchitis, bronchiectasis, asthma and wheeze diagnoses were not included as they are possibly features of the outcome.

### Statistical analysis

The proportion of children admitted to hospital for asthma at least once between the ages of 1 and 5 years was calculated, as well as the median number and range of multiple hospital admissions for asthma. Logistic regression models were used to estimate associations between proposed risk factors and at least one hospitalisation for asthma, expressed as ORs and 95% CIs. *Gestational age*, *birth weight* and *disadvantage* were modelled as categorical variables. A sandwich estimator was used to account for correlation caused by clustering of observations within families. A subject matter-informed directed acyclic graph (DAG) was used to assess covariates as potential confounders (online supplemental figure S1).<sup>20</sup> Based on the DAG, adjusted models that included potential confounders were fitted. The possibility that the effects of risk factors were modified by infant sex was tested by including an interaction term in models. Proportional attributable fractions (PAF) were calculated for those variables that had positive associations with *hospitalised* asthma (based on adjusted models) and which can be considered to be potentially preventable.<sup>21</sup> PAFs indicate the proportion of an outcome that is attributable to a risk factor, such that if that risk factor could be eliminated, the corresponding fraction of the outcome would be prevented. It should be noted that PAFs are not additive, each is independent of the other.

Since asthma in the first year of life may be misclassified as an ARTI (or vice versa), a *sensitivity analysis for the ARTI model* was performed in which we excluded children from the study population who were hospitalised for asthma in the first year of life. Additionally, due to the difficulty of diagnosing asthma in children under 5 years of age, we performed a second sensitivity analysis where we broadened the asthma definition to include bronchiectasis (ICD-10 J47) and wheeze symptoms (ICD-10 R06.2) as the primary diagnoses ('broad asthma').

We have reported and interpreted statistical null hypothesis testing and CIs according to guidelines set by respiratory journals and the American Statistical Association.<sup>20,22</sup> Statistical analyses were conducted using SAS software V.9.4 (SAS Institute).

### RESULTS

The number of Aboriginal children born 2003–2012 in WA was 26 483. After applying the exclusion criteria, the study population included 25 773 Aboriginal children. Of these, 705 (2.7%) children had been hospitalised for asthma at least once between the ages of 1 and 4 years. The median number of asthma hospitalisations for any asthma case was 1, IQR 1–2, and the range was 1–10 hospitalisations.

At birth, 13.3% of children were preterm, 11.8% weighed less than 2500 g and 15.0% were SGA (table 1). During the first year of life, 15.2% of all children had at least one hospitalisation for an ARTI. This proportion was much higher (41.6%) for children who were subsequently hospitalised for asthma. Regarding mothers, 53.1% were under 24 years of age at child's birth, almost half reported smoking during pregnancy, 11.2% reported asthma, 10.3% reported a pregnancy-related condition or diabetes and 9.1% had recently experienced maternal trauma (table 1). Half of the families came from the most disadvantaged quintile, and 61.8% lived in rural areas (half in remote areas and half in regional areas).

Aboriginal children born *preterm* and especially those born *very preterm* were at risk of being hospitalised with asthma (adjusted OR (adjOR) 1.23, 95% CI 0.94 to 1.61, and adjOR 3.30, 95% CI 2.52 to 4.32, respectively) compared with those born at term (table 2). Similarly, *low birth weight* and *very low birth weight* were associated with an increased risk of hospitalisation for asthma (adjOR 1.34, 95% CI 1.00 to 2.79, and adjOR 2.35, 95% CI 1.39 to 3.99, respectively) compared with normal birth weight (table 2). SGA babies had similar risk to other babies of hospitalisation for asthma (adjOR 1.03, 95% CI 0.83 to 1.27) (table 2). A further breakdown by gestational period suggested that SGA babies born very preterm before 33 weeks may have an increased risk for hospitalisation for asthma (adjOR 1.44, 95% CI 0.69 to 2.99, table 3).

Other positive associations with hospitalised asthma included: *maternal asthma* (adjOR 1.58, 95% CI 1.28 to 1.94); living in an area in the *most disadvantaged* quintile compared with an area in the *least disadvantaged* quintile (adjOR 1.52, 95% CI 0.99 to 2.33); *living in outer regional WA compared with urban areas* (adjOR 1.30, 95% CI 1.05 to 1.62); and being hospitalised for an ARTI *in the first year of life* (adjOR 4.06, 95% CI 3.44 to 4.78) (table 2). Being born by *emergency caesarean section* (adjOR 1.18, 95% CI 0.96 to 1.46), *maternal trauma* (adjOR 1.17, 95% CI 0.91 to 1.51) and *maternal smoking in pregnancy* (adjOR 1.12, 95% CI 0.95 to 1.30) were also positively associated with hospitalised asthma, although the estimates are imprecise (table 2). Interaction by sex showed no differences between girls and boys except for parity, where it was suggested for girls but not for boys that having older siblings decreased the odds of being hospitalised for asthma (adjOR 0.77, 95% CI 0.58 to 1.02).

No associations were found with hospitalised asthma for *parity*, *plurality*, *maternal age*, *maternal medical conditions* (other than asthma) or *elective caesarean delivery*.

The proportion of asthma that was attributable to an ARTI hospitalisation in the first year of life was 31.3%, and the proportion attributable to living in an area in the most disadvantaged quintile was 18.4% (table 3). The PAF of hospitalised asthma cases that can be attributed to being born preterm or

**Table 1** Descriptive characteristics, Aboriginal children aged 1–4 years, Western Australia

	All children n=25 773 (%)	Children not hospitalised for asthma n=25 068 (%)	Children hospitalised for asthma n=705 (%)
<b>Sex</b>			
Male	13 042 (50.6)	12 606 (50.2)	436 (61.8)
Female	12 731 (49.4)	12 462 (49.8)	269 (38.2)
<b>Plurality</b>			
Singleton	25 147 (97.6)	24 467 (97.6)	680 (96.5)
Multiples	626 (2.4)	601 (2.4)	25 (3.6)
<b>Maternal age (years)</b>			
≤19	5375 (20.9)	5223 (20.8)	152 (21.6)
20–24	8286 (32.2)	8058 (32.1)	228 (32.3)
25–29	6246 (24.2)	6073 (24.2)	173 (24.5)
≥30	5866 (20.9)	5714 (22.8)	152 (21.6)
<b>Parity</b>			
0	8599 (33.4)	8356 (33.3)	243 (34.5)
1–2	10 963 (42.5)	10 678 (42.6)	285 (40.4)
≥3	6211 (24.1)	6024 (24.1)	177 (25.1)
<b>Gestational age (weeks)</b>			
Very preterm <33	940 (3.7)	867 (3.5)	73 (10.4)
Preterm 33–36	2464 (9.6)	2389 (9.5)	75 (10.6)
Early term 37–38	7981 (31.0)	7775 (31.0)	206 (29.2)
At term 39–40	11 743 (45.6)	11 458 (45.7)	285 (40.4)
Post-term >40	2645 (10.3)	2579 (10.3)	66 (9.4)
<b>Birth weight (g)</b>			
Very low (<1500)	440 (1.7)	397 (1.6)	43 (6.1)
Low (1500–2500)	2603 (10.1)	2500 (10.0)	103 (14.6)
Normal (2500–4000)	20 598 (80.0)	20 088 (80.1)	510 (72.3)
High (>4000)	2132 (8.3)	2083 (8.3)	49 (7.0)
Small for gestational age	3870 (15.0)	3759 (15.0)	111 (15.7)
Maternal smoking in pregnancy	11 477 (44.5)	11 138 (44.4)	339 (48.1)
Maternal asthma	2894 (11.2)	2775 (11.1)	119 (16.9)
Maternal medical conditions	2665 (10.3)	2598 (10.4)	67 (9.5)
<b>Mode of delivery</b>			
Vaginal	20 018 (77.7)	19 482 (77.7)	536 (76.0)
Elective caesarean section	2176 (8.4)	2120 (8.5)	56 (7.9)
Emergency caesarean section	3579 (13.9)	3466 (13.8)	113 (16.0)
Maternal trauma	2336 (9.1)	2262 (9.0)	74 (10.5)
<b>Disadvantage of area of residence</b>			
Q5 (least)	1159 (4.5)	1136 (4.5)	23 (3.3)
Q4	2141 (8.5)	2093 (8.3)	48 (7.0)
Q3	3662 (14.5)	3569 (14.2)	93 (13.5)
Q2	5695 (22.5)	5549 (22.1)	146 (21.2)
Q1 (most)	12 625 (49.9)	12 245 (48.8)	380 (55.1)
Missing	490 (1.9)	475 (1.9)	15 (2.1)
<b>Area-level remoteness of residence at birth</b>			
Major cities	9930 (38.5)	9685 (38.6)	245 (35.5)

Continued

**Table 1** Continued

	All children n=25 773 (%)	Children not hospitalised for asthma n=25 068 (%)	Children hospitalised for asthma n=705 (%)
Inner regional	2452 (9.7)	2385 (9.5)	67 (9.7)
Outer regional	4145 (16.4)	4007 (16.0)	138 (20.0)
Remote	4033 (16.0)	3920 (15.6)	113 (16.4)
Very remote	4723 (18.7)	4596 (18.3)	127 (18.4)
Missing	491 (1.9)	476 (1.9)	15 (2.1)
ARTI <1 year	3926 (15.2)	3633 (14.5)	293 (41.6)

ARTI, acute respiratory tract infection.

very preterm was 2.0% and 7.2%, respectively, and for low birth weight and very low birth weight was 3.7% and 3.5%, respectively. The proportion of asthma that was attributable to maternal smoking was 5.2%, although the 95% CIs included the null (table 4).

The sensitivity analysis excluding children who had asthma in the first year of life (n=75) reduced the effect size slightly of the association between having an ARTI in the first year of life and subsequent hospitalisation for asthma at least once at 1–4 years of age (adjOR 3.79, 95% CI 3.20 to 4.49),  $p < 0.0001$ . The second sensitivity analysis using ‘broad asthma’ definition in adjusted models for all outcomes showed similar effect sizes and PAFs to the main analysis for ARTI (PAF 28.2%), preterm (PAF 7.0% very preterm, 3.3% preterm) and low birthweight births (PAF 2.6% very low birth weight, 2.3% low birth weight, see online supplemental tables S2 and S3). However, the effect sizes and subsequent PAFs for living in an area of disadvantage and smoking in pregnancy were lower than the results for the main analysis (PAF 7.4% and 2.2%, respectively) and 95% CI crossed the null (online supplemental table S3).

## DISCUSSION

This large population-wide study on Aboriginal children aged 1–4 years found that the main attributable risk factors for hospitalised asthma in Aboriginal children were hospitalisation for ARTIs in the first 12 months of life and living in an area of disadvantage. Other important risk factors were being born very preterm or having a low birth weight. There was a small contribution of smoking in pregnancy, and remoteness was not found to be a major contributing factor.

Our study showed that being hospitalised in the first 12 months of life with an ARTI was associated with a four times higher risk of an asthma hospitalisation even after adjusting for preterm birth, low birth weight, disadvantage and remoteness, supporting findings in a number of other populations.<sup>23 24</sup> The combination of this high risk on asthma and a high prevalence of ARTI early in life<sup>8 25</sup> explains why the fraction of hospitalised asthma cases in Aboriginal children that can be attributed to early ARTI is up to 31%. This would suggest that prevention of ARTI could have a significant impact on reducing asthma burden. However, twin research and prophylaxis studies suggest there may not be a causal pathway from early infection to asthma.<sup>26</sup> For example, a recent trial using palivizumab for RSV immunoprophylaxis concluded that prevention of RSV does not reduce asthma risk.<sup>27</sup> Furthermore, it is likely that a proportion of early ARTI diagnoses were misdiagnosed asthma cases (and vice versa).<sup>28</sup> The sensitivity analysis attempted to reduce this bias by excluding cases that had been hospitalised for asthma

**Table 2** Associations between risk factors and asthma in Aboriginal children aged 1–4 years, ORs and 95% CIs

Risk factors	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	(Potential confounders used in adjusted models see (online supplemental file 1))
Maternal age (years)			Disadvantage
≤19	1.07 (0.86 to 1.33) P=0.54	1.08 (0.86 to 1.35) P=0.51	
20–24	1.06 (0.86 to 1.31) P=0.56	1.05 (0.85 to 1.30) P=0.66	
25–29	1.09 (0.87 to 1.38) P=0.45	1.06 (0.83 to 1.36) P=0.65	
≥30	Reference	Reference	
Plurality			Gestational age, birth weight
Singleton	Reference	Reference	
Multiples	1.49 (0.99 to 2.26) P=0.06	0.95 (0.61 to 1.46) P=0.81	
Parity			Maternal age
0	Reference	Reference	
≥1	0.95 (0.81 to 1.11) P=0.53	0.96 (0.80 to 1.17) P=0.71	
Gestational age (weeks)			Maternal age, smoking in pregnancy, maternal asthma, remoteness, plurality
Very preterm <33	3.39 (2.58 to 4.43) P<0.0001	3.31 (2.50 to 4.39) P<0.0001	
Preterm 33–36	1.26 (0.97 to 1.64) P=0.08	1.23 (0.94 to 1.62) P=0.13	
Early term 37–38	1.07 (0.89 to 1.29) P=0.50	1.04 (0.87 to 1.25) P=0.67	
At term 39–40	Reference	Reference	
Post-term >40	1.03 (0.78 to 1.36) P=0.84	1.00 (0.76 to 1.33) P=0.98	
Birth weight (g)			Maternal age, smoking in pregnancy, maternal trauma, maternal asthma, gestational age, remoteness, plurality
Very low (<1500)	4.27 (3.08 to 5.90) P<0.0001	2.37 (1.39 to 4.01) P=0.001	
Low (1500–2499)	1.62 (1.31 to 2.02) P<0.0001	1.34 (1.00 to 1.80) P=0.05	
Normal (2500–4000)	Reference	Reference	
High (>4000)	0.93 (0.69 to 1.25) P=0.61	0.97 (0.72 to 1.32) P=0.86	
Small for gestational age	1.06 (0.86 to 1.30) P=0.58	1.02 (0.82 to 1.26) P=0.87	Maternal age, smoking in pregnancy, maternal trauma, maternal asthma, remoteness
Maternal smoking in pregnancy	1.16 (0.99 to 1.35) P=0.06	1.12 (0.95 to 1.30) P=0.17	Maternal trauma, disadvantage
Maternal asthma	1.53 (1.25 to 1.88) P<0.0001	1.58 (1.28 to 1.94) P<0.0001	Disadvantage, smoking in pregnancy, remoteness
Maternal medical conditions	0.91 (0.70 to 1.17) P=0.46	0.89 (0.68 to 1.15) P=0.37	Disadvantage, parity, maternal age, remoteness
Mode of delivery			Maternal asthma, maternal medical conditions, remoteness
Vaginal	Reference	Reference	
Elective caesarean section	0.96 (0.72 to 1.27) P=0.78	1.00 (0.75 to 1.32) P=0.98	
Emergency caesarean section	1.19 (0.97 to 1.46) P=0.10	1.18 (0.96 to 1.46) P=0.11	
Maternal trauma	1.18 (0.92 to 1.51) P=0.19	1.17 (0.91 to 1.51) P=0.21	Disadvantage

Continued

Table 2 Continued

Risk factors	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	(Potential confounders used in adjusted models see (online supplemental file 1))
Disadvantage			Maternal age
Q5 (least)	Reference	Reference	
Q4	1.13 (0.68 to 1.88) P=0.63	1.13 (0.68 to 1.87) P=0.64	
Q3	1.29 (0.81 to 2.04) P=0.28	1.28 (0.81 to 2.03) P=0.30	
Q2	1.30 (0.83 to 2.02) P=0.25	1.29 (0.83 to 2.02) P=0.26	
Q1 (most)	1.53 (1.00 to 2.34) P=0.05	1.52 (0.99 to 2.33) P=0.05	
Area-level remoteness of residence at birth			Disadvantage
Major cities	Reference	Reference	
Inner regional	1.11 (0.84 to 1.46) P=0.46	1.11 (0.84 to 1.49) P=0.44	
Outer regional	1.36 (1.10 to 1.69) P=0.005	1.30 (1.05 to 1.62) P=0.02	
Remote	1.14 (0.91 to 1.43) P=0.26	1.10 (0.87 to 1.39) P=0.41	
Very remote	1.09 (0.87 to 1.36) P=0.44	0.99 (0.78 to 1.26) P=0.95	
ARTI <1 year	4.19 (3.59 to 4.90) P<0.0001	4.06 (3.44 to 4.78) P<0.0001	Delivery method, disadvantage, birth weight, maternal age, parity, gestational age, remoteness

ARTI, acute respiratory tract infection.

in the first year of life, and continued to show a strong association between early ARTI and subsequent asthma (adjOR 3.79, 95% CI 3.20 to 4.49). Furthermore, given that children with asthma were three times as likely to have an ARTI <1 year than those without asthma, the misdiagnosis rate of ARTI in early life would have to be over 50% to show a null effect between early ARTI and asthma. Another possible explanation for these results is that rather than ARTI being a cause of asthma, both these diseases may indicate lung vulnerability. Therefore, it may be more useful to use severe early respiratory tract infection as a signpost for subsequent asthma to highlight ongoing management for cough and wheezing illnesses.<sup>29</sup>

Our study also found that in the presence of other factors, 18% of hospitalised asthma cases were attributable to living in disadvantaged areas. This finding of an association between disadvantage and asthma is not unique to the Indigenous population and has also been well described in African American populations, ethnic minorities and groups experiencing poverty.<sup>30</sup> Living in an area of disadvantage means fewer resources to seek early and preventive healthcare, adequate nutrition or improved

housing. Overcrowding, increased psychological stress and subsequent alcohol abuse and smoking can all impact on asthma risk.<sup>30</sup> Shifting social determinants is difficult but these findings support the need for resources and empowerment involving a strengths-based approach for long-term positive benefits in Aboriginal health and well-being.<sup>31 32</sup> To quote Sir Michael Marmot speaking on Aboriginal child development, 'Central to action on social determinants of health is empowerment of individuals and communities.'<sup>33</sup> Given that half of the Aboriginal population currently live in the quintile of most disadvantage in WA, a meaningful shift in resources and empowerment in this group should result in a meaningful decrease in asthma burden for this community that continues into adulthood. Further research is needed to establish which aspects of disadvantage (eg, housing, inadequate primary care, low income) are driving this relationship.

**Table 3** Associations for hospitalised asthma in small for gestational age babies stratified by gestational age

Gestational age	Adjusted OR* (95% CI)
Very preterm <33 weeks	1.44 (0.69 to 2.99) p=0.33
Preterm 33–36 weeks	0.98 (0.49 to 1.96) p=0.96
Early term 37–38 weeks	1.12 (0.78 to 1.62) p=0.53
Term 39–40 weeks	1.03 (0.73 to 1.44) p=0.87
Overterm >41 weeks	0.91 (0.42 to 1.95) p=0.80

\*Adjusted for maternal age, smoking in pregnancy, maternal trauma, maternal asthma, geographic location and plurality.

**Table 4** Population attributable fractions for potentially preventable risk factors

Risk factor	Population attributable fraction % (95% CI)*
ARTI <1 year	31.3 (29.5 to 32.9)
Disadvantage (lowest quintile)	18.4 (–0.5 to 30.8)
Very preterm <33 weeks	7.2 (6.2 to 8.0)
Preterm 33–36 weeks	2.0 (–0.7 to 4.0)
Maternal smoking in pregnancy	5.2 (–2.5 to 11.1)
Very low birth weight <1500 g	3.5 (1.7 to 4.6)
Low birth weight 1500–2500 g	3.7 (0.0 to 6.4)
Emergency caesarean section	2.4 (–0.7 to 5.1)

\*Population attributable fractions based on adjusted ORs. ARTI, acute respiratory tract infection.

Our work agrees with others that being born preterm, having a low birth weight or needing to be born by emergency caesarean section are risk factors for developing childhood asthma and for lung vulnerability.<sup>1 5 13 34</sup> Current cultural innovations in Aboriginal prenatal and maternity care to incorporate Indigenous knowledges into practice may help reduce these rates and improve outcomes for Aboriginal mothers and babies.<sup>35</sup>

Although prenatal smoking is well recognised as a modifiable risk factor for childhood asthma,<sup>5</sup> our study suggested only a 5%–6% reduction in asthma if all prenatal smoking was eliminated, and even lower in the sensitivity analysis using the broad asthma definition. Other Indigenous research has had similar findings.<sup>13 36</sup> A possible explanation is that the high rates of smoking in these communities may mean that children have a high rate of exposure to other sources of environmental tobacco smoking in early life, masking the effect of maternal prenatal smoking. Although 44% of the studied population of women reported smoking during pregnancy, Indigenous smoking rates in Australia are declining and reduction of smoking rates remains an important health priority.<sup>37</sup>

Around one-third (35%) of the Aboriginal children in WA live in remote and very remote areas. Although remoteness can be associated with factors associated with asthma risk such as disadvantage,<sup>38</sup> social determinants,<sup>10 38</sup> higher ARTI burden<sup>8</sup> and lower access to health services,<sup>38</sup> our study did not find that hospitalisations for asthma increased with area-level remoteness. This unexpected finding was also seen in a study about parent-reported asthma in Canadian First Nations Children.<sup>14</sup> A possible explanation is that aspects of remote living ‘protect’ against asthma, for example, less day care, more breast feeding and more pet and animal contact, less outdoor air pollution, all of which have been shown to be protective for asthma.<sup>39</sup> Alternatively, perhaps the low hospital diagnosis rate reflects less access to respiratory specialists and paediatricians in the remote areas of Australia and Canada.

The major strength of this study was being able to access an Indigenous population across an entire Australian state over many years, providing a large sample size. Due to the use of administrative linked data, the potential for selection bias due to lower participation by vulnerable groups within WA’s Aboriginal population is minimised, improving the generalisability of our findings. Using a range of different data sources and previously developed algorithms, we were able to maximise the identification of Aboriginal status and minimise missing data for some variables such as geographical location, date of birth and identification of mothers and fathers.<sup>16 40</sup> However, there are also some important limitations from using linked administrative data. The main limitation was that the data were restricted to information that was collected in routine health data sets and were missing some important variables that could provide further insight into preventable asthma risk such as housing conditions, overcrowding, pet ownership, breastfeeding practices, smoking by fathers and other members of the family and cultural aspects. In addition, we were restricted to asthma defined as hospitalisations. We had access to emergency department visit information, but in rural areas asthma comes under a broad code of ‘respiratory disease’ so we were unable to identify asthma cases in these areas. GP data were not available. Therefore, we recognise that a number of mild asthma cases will be misclassified into the comparison group pushing the results towards the null. However, mild asthma in young age is often transient wheeze that does not continue past childhood, whereas we focused on asthma cases that represent persistent asthma which are more likely to be the more severe or uncontrolled asthma cases leading

to hospitalisation. The sensitivity analyses using a broader definition of asthma that included primary diagnoses for wheeze and bronchiectasis attempted to address the difficulty of diagnosing asthma in children under 5 years of age. On the whole, this analysis supports the main analysis particularly regarding ARTI, preterm birth and low birth weight.

In conclusion, this large whole of population study on Aboriginal children in WA has highlighted specific risk factors for asthma which can help inform policy aimed at improving health outcomes and reducing disparities. The study again emphasises the importance of addressing the social determinants of health as key structural issues in Aboriginal health inequalities. In particular, supporting culturally sensitive and appropriate Aboriginal maternal and child care that will help reduce preterm and low birth weights and monitoring and ongoing management of young children who are hospitalised for ARTI.<sup>35 41</sup> Implementation of change to reduce the effects of disadvantage such as high infection rates in the paediatric Indigenous population is likely to have a significant effect in reducing asthma and its ongoing health burden and associated comorbidities.

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#### REFERENCES

- 1 Australian Centre for Asthma Monitoring. *Asthma in Australian children: findings from growing up in Australia, the longitudinal study of Australian children. cat. No. ACM 17*. Canberra: AIHW, 2009.
- 2 Epidemiology Branch, Public Health Division, Western Australian Department of Health. *Burden of disease by age group in Western Australia, 2011*. Perth, Western Australia: Department of Health, 2017.
- 3 Australian Institute of Health and Welfare. *Australian burden of disease study: impact and causes of illness and death in Aboriginal and Torres Strait Islander people 2011. Australian burden of disease study series no6 Catno BOD 7*. Canberra: AIHW, 2016.
- 4 Barnes R, Blyth CC, de Klerk N, et al. Geographical disparities in emergency department presentations for acute respiratory infections and risk factors for presenting: a population-based cohort study of Western Australian children. *BMJ Open* 2019;9:e025360.
- 5 Castro-Rodriguez JA, Forno E, Rodriguez-Martinez CE, et al. Risk and protective factors for childhood asthma: what is the evidence? *J Allergy Clin Immunol Pract* 2016;4:1111–22.
- 6 Australian Institute of Health and Welfare. *Australia's mothers and babies 2018: in brief. Perinatal statistics series no 36 Catno PER 108*. Canberra: AIHW, 2020.
- 7 Diouf I, Gubhaju L, Chamberlain C, et al. Trends in maternal and newborn health characteristics and obstetric interventions among Aboriginal and Torres Strait Islander mothers in Western Australia from 1986 to 2009. *Aust N Z J Obstet Gynaecol* 2016;56:245–51.
- 8 Moore H, Burgner D, Carville K, et al. Diverging trends for lower respiratory infections in non-Aboriginal and Aboriginal children. *J Paediatr Child Health* 2007;43:451–7.
- 9 Lima F, Shepherd C, Wong J, et al. Trends in mental health related contacts among mothers of Aboriginal children in Western Australia (1990–2013): a linked data population-based cohort study of over 40 000 children. *BMJ Open* 2019;9:e027733.
- 10 Berry JG, Harrison JE, Ryan P. Hospital admissions of Indigenous and non-Indigenous Australians due to interpersonal violence, July 1999 to June 2004. *Aust N Z J Public Health* 2009;33:215–22.
- 11 Paradies Y. Colonisation, racism and Indigenous health. *J Popul Res* 2016;33:83–96.
- 12 Griffiths K, Coleman C, Lee V, et al. How colonisation determines social justice and Indigenous health—a review of the literature. *J Popul Res* 2016;33:9–30.
- 13 Chang H-J, Beach J, Senthilselvan A. Prevalence and risk factors of asthma in off-reserve Aboriginal children and adults in Canada. *Can Respir J* 2012;19:e68–74.
- 14 Senthilselvan A, Niruban SJ, King M, et al. Prevalence and risk factors of asthma in first nations children living on reserves in Canada. *Can J Public Health* 2016;106:e483–8.
- 15 McNamara B, Gubhaju L, Jorm L, et al. Exploring factors impacting early childhood health among Aboriginal and Torres Strait Islander families and communities: protocol for a population-based cohort study using data linkage (the 'Defying the Odds' study). *BMJ Open* 2018;8:e021236.
- 16 Christensen D, Davis G, Draper G, et al. Evidence for the use of an algorithm in resolving inconsistent and missing Indigenous status in administrative data collections. *Aust J Soc Issues* 2014;49:423–43.
- 17 Dobbins TA, Sullivan EA, Roberts CL, et al. Australian national birthweight percentiles by sex and gestational age, 1998–2007. *Med J Aust* 2012;197:291–4.
- 18 Australian Bureau of Statistics. *Australian statistical geography standard (ASGS) volume 5- remoteness structure. Cat.no 1270.0.55.005*. Canberra, 2018. Available: <https://www.abs.gov.au/AUSSTATS/abs@.nsf/Lookup/1270.0.55.005Main+Features1July%202016?OpenDocument> [Accessed 16 Jun 2020].
- 19 Australian Bureau of Statistics. *Socio-Economic indexes for areas*. Canberra, 2018. Available: <https://www.abs.gov.au/websitedbs/censushome.nsf/home/seifa> [Accessed 16 Jun 2020].
- 20 Lederer DJ, Bell SC, Branson RD, et al. Control of confounding and reporting of results in causal inference studies. guidance for authors from editors of respiratory, sleep, and critical care journals. *Ann Am Thorac Soc* 2019;16:22–8.
- 21 Greenland S. Concepts and pitfalls in measuring and interpreting attributable fractions, prevented fractions, and causation probabilities. *Ann Epidemiol* 2015;25:155–61.
- 22 Wasserstein RL, Lazar NA. The ASA Statement on p-Values: Context, Process, and Purpose. *Am Stat* 2016;70:129–33.
- 23 Feldman AS, He Y, Moore ML, et al. Toward primary prevention of asthma. Reviewing the evidence for early-life respiratory viral infections as modifiable risk factors to prevent childhood asthma. *Am J Respir Crit Care Med* 2015;191:34–44.
- 24 Moore HC, Hall GL, de Klerk N. Infant respiratory infections and later respiratory hospitalisation in childhood. *Eur Respir J* 2015;46:1334–41.
- 25 O'Grady K-AF, Torzillo PJ, Chang AB. Hospitalisation of Indigenous children in the Northern Territory for lower respiratory illness in the first year of life. *Med J Aust* 2010;192:586–90.
- 26 Thomsen SF, van der Sluis S, Stensballe LG, et al. Exploring the association between severe respiratory syncytial virus infection and asthma: a registry-based twin study. *Am J Respir Crit Care Med* 2009;179:1091–7.
- 27 Scheltema NM, Nibbelke EE, Pouw J, et al. Respiratory syncytial virus prevention and asthma in healthy preterm infants: a randomised controlled trial. *Lancet Respir Med* 2018;6:257–64.
- 28 Bush A, Fleming L. Is asthma overdiagnosed? *Arch Dis Child* 2016;101:688–9.
- 29 Anderson-James S, Marchant JM, Chang AB, et al. Burden and emergency department management of acute cough in children. *J Paediatr Child Health* 2019;55:181–7.
- 30 Williams DR, Sternthal M, Wright RJ. Social determinants: taking the social context of asthma seriously. *Pediatrics* 2009;123(Suppl 3):S174–84.
- 31 Marmot M. Social determinants and the health of Indigenous Australians. *Med J Aust* 2011;194:512–3.
- 32 Askew DA, Brady K, Mukandi B, et al. Closing the gap between rhetoric and practice in strengths-based approaches to Indigenous public health: a qualitative study. *Aust N Z J Public Health* 2020;44:102–5.
- 33 Marmot MG. Empowering communities. *Am J Public Health* 2016;106:230–1.
- 34 Brew BK, Marks GB, CAPS (Childhood Asthma Prevention Study) Investigators. Perinatal factors and respiratory health in children. *Clin Exp Allergy* 2012;42:1621–9.
- 35 Kildea S, Hickey S, Barclay L, et al. Implementing birthing on country services for Aboriginal and Torres Strait Islander families: rise framework. *Women Birth* 2019;32:466–75.
- 36 Moore HC, de Klerk N, Richmond P, et al. A retrospective population-based cohort study identifying target areas for prevention of acute lower respiratory infections in children. *BMC Public Health* 2010;10:757.
- 37 Australian Institute of Health and Welfare. *Alcohol, tobacco and other drugs in Australia. cat. No: PHE221, 2020*. Available: <https://www.aihw.gov.au/reports/alcohol/alcohol-tobacco-other-drugs-australia/contents/introduction> [Accessed 30 Jun 2020].
- 38 Australian Institute of Health and Welfare. *Rural & Remote Health. Cat. no. PHE 255*. Canberra: AIHW, 2019.
- 39 Beasley R, Semprini A, Mitchell EA. Risk factors for asthma: is prevention possible? *Lancet* 2015;386:1075–85.
- 40 Gibberd AJ, Simpson JM, Eades SJ. Use of family relationships improved consistency of identification of Aboriginal people in linked administrative data. *J Clin Epidemiol* 2017;90:144–55.
- 41 Strobel N, Moylan C, Durey A, et al. Understanding an Aboriginal and Torres Strait Islander child's journey through paediatric care in Western Australia. *Aust N Z J Public Health* 2020;44:95–101.