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The associations between biological and sociodemographic risks for developmental vulnerability in twins at age five: A population data linkage study in Western Australia.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-038846
Article Type:	Original research
Date Submitted by the Author:	26-Mar-2020
Complete List of Authors:	Dhamrait, Gursimran; Telethon Kids Institute, ; The University of Western Australia Faculty of Health and Medical Sciences, School of Population and Global Health Christensen, Daniel; Telethon Kids Institute; The University of Western Australia Pereira, G.F; Telethon Kids Institute; Curtin University, School of Public Health Taylor, Catherine; Telethon Kids Institute; University of Western Australia,
Keywords:	EPIDEMIOLOGY, PAEDIATRICS, PUBLIC HEALTH

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Manuscript

Title: The associations between biological and sociodemographic risks for developmental vulnerability in twins at age five: A population data linkage study in Western Australia.

Gursimran K. Dhamrait,[1,2] Daniel Christensen,[1,3] Gavin Pereira[1,4,5] and Catherine L. Taylor.[1,3]

[1]Telethon Kids Institute, Nedlands, Western Australia, Australia.
[2]School of Population and Global Health, The University of Western Australia, Nedlands, Western Australia, Australia.
[3]Centre for Child Health Research, The University of Western Australia, Nedlands, Western Australia, Australia.
[4]School of Public Health, Curtin University, Perth, Australia.
[5]Centre for Fertility and Health (CeFH), Norwegian Institute of Public Health, Oslo, Norway.

Address correspondence to:
Gursimran K. Dhamrait
Telethon Kids Institute
15 Hospital Avenue, Nedlands, Western Australia, Australia.
Phone: 61+ 8 9489 1183
Fax: 61+ 8 9489 7700
Email: gursimran.dhamrait@telethonkids.org.au

Main Body Word Count: 3,955 words
Abstract Word Count: 293 words

Short Title: Developmental vulnerability in twins at age five

Abbreviations

AEDC: Australian Early Development Census
ARIA: Accessibility and Remoteness Index of Australia
AUSEI06: Australian Socioeconomic Index 2006
DV1: Developmentally Vulnerable on one or more Australian Early Development Census domains
DV2: Developmentally Vulnerable on two or more Australian Early Development Census domains
CI: Confidence Interval

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IRSD: Index of Relative Socioeconomic Disadvantage

MNS: Midwives Notifications System

OR: Odds Ratio

POBW: Proportion of Optimal Birthweight

WA: Western Australia

Keywords (max of 5):

Twins, Australian Early Development Census, Child Development, Record Linkage.

What is already known about this topic

Twin pregnancies are classified as high risk pregnancies and associated with higher rates of pregnancy complications and adverse neonatal, perinatal and developmental outcomes, compared to singleton pregnancies.

What this study adds

Twins are more likely to be classified as developmentally vulnerable in their first year of full-time school than singletons.

Both biological and sociodemographic risk factors are associated with increased odds of developmental vulnerability for twins in their first year of full-time school.

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Abstract

Objective: To investigate the associations between prenatal and perinatal risk factors and developmental vulnerability in twins at age five.

Design: Retrospective cohort study using bivariate and multivariate logistic regression to identify associations between risk factors and developmental vulnerability.

Setting: Western Australia (WA), 2002-2015.

Participants: 828 twin pairs born in WA with an Australian Early Development Census (AEDC) record from 2009, 2012 or 2015.

Main Outcome Measures: The AEDC is a national measure of child development across five domains. Children with scores <10th percentile were classified as developmentally vulnerable (DV1 for one or more domains, DV2 for two or more domains).

Results: In this population, 431 (26.0%) twins were classified as DV1 and 223 (14.1%) as DV2. In the multivariable model, risk factors for DV1 were; maternal age (<20 years; OR 8.69, 95% CI 1.52 to 49.69), language other than English spoken at home by the child (OR 5.25, 95% CI 1.77 to 15.56), male child (OR 5.25, 95% CI: 2.99 to 9.24), age younger than the reference category for the study sample (≥5 years one month to <5 years 10 months) at time of AEDC completion (at time of AEDC completion (OR 3.10, 95% CI: 1.44 to 6.69), and having a proportion of optimal birthweight (POBW) less than the 15th centile (OR 2.04, 95% CI 1.05 to 3.97). Risk factors for DV2 were; male child (OR 7.98, 95% CI: 3.49 to 6.67), age younger than the reference category (OR 4.89, 95% CI: 1.77 to 13.48), an unmarried maternal marital status (OR 4.43, 95% CI: 1.08 to 18.25), and having a POBW <15th of the study sample (OR 3.30, 95% CI: 1.33 to 8.21).

Conclusion: Both biological and sociodemographic risk factors are associated with developmental vulnerability in twins at five years of age.

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Article Summary

Strengths and Limitations

Limitations:

- Datasets did not include data on twin zygosity nor complications of pregnancy that are specific to multiple pregnancies (e.g., twin reversed arterial perfusion, twin-twin transfusion syndrome). However, complications of multiple gestations are captured in the 'other complications of pregnancy' variable used in this study.

Strengths:

- This is the first study of this scale (population-level sample of twins; N>1,600) to assess developmental vulnerabilities in an otherwise healthy sample of Australian twins, at the time of their first year of full-time school.
- The use of population-based cohort design; the use of complete twin pairs for analysis; and use of a population-based estimate of optimal fetal growth and twins who did not have developmental disabilities.

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Introduction

The increased use of assisted reproductive technologies and increasing maternal age at conception have attributed to a significant increase in the number of multifetal pregnancies around the world.[1] Multifetal pregnancies are classified as high risk pregnancies and are associated with higher rates of pregnancy complications and adverse neonatal and perinatal outcomes, compared to singleton pregnancies.[2-6] The majority of the literature assessing higher order pregnancies has focused primarily on birth outcomes, including preterm birth,[7] low birth weight,[3] and developmental disabilities such as cerebral palsy.[8] Studies that have assessed longer-term developmental outcomes of twins have focused on developmental outcomes around the age of two years.[9] Such studies have reported that that twins had poorer performance, in comparison to singletons, on a range of domains including; communication, gross and fine motor skills, problem solving, personal-social skills, and language development.[10,11] Furthermore, most studies examining child development outcomes at school starting age have focused on singleton children, from a single family and have compared children across families.[12] There is a paucity of research on the developmental vulnerability of multifetal pregnancies such as twins, around the time that they commence formal education.

Child development outcomes can vary significantly based on numerous factors including the child's personal characteristics, such as personal dispositions and abilities, social constructs and the environments, both intrauterine and extrauterine, in which they develop.[13-16] Twin studies, aiming to assess the association between genes and the environment have supported the notion that both genes and the environment can impact child development.[17-20] Yet, a number of studies have reported no significant differences in child development outcomes based on zygosity.[21-23] Twins are however, more likely to be classified as preterm[24] or low birth weight, and have fetal growth restriction.[25] Studies that have assessed cognitive and school performance outcomes at the age of five have reported that children who are born preterm,[26-33] with a low birth weight,[34-37] are small for gestational age,[38,39] and male[40-43] are more likely to have poorer developmental outcomes. Given the higher rates of pregnancy neonatal and perinatal adversities observed in twins in comparison to

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singletons, twins are particularly at risk for developmental delays in the early childhood period. A study reported that twins scored lower than singletons in both the Verbal and Performance IQ domains of the Wechsler Preschool and Primary Scale of Intelligence, at the ages of four and five years.[22] Likewise, twin studies have also reported sex differences, with girls scoring higher than boys at ages four and five years.[22] Studies have reported that twins are more likely to have poorer neurodevelopmental outcomes compared to singletons, even after controlling for gestational age and birthweight.[44]

Furthermore, sociodemographic factors such as low socioeconomic status and low levels of parental education, have also been identified to adversely impact child development outcomes.[45-47] Results from twin studies assessing the impact of sociodemographic factors on development outcomes in twins have been mixed. A study of a twin sample from the Quebec Newborn Twin Study reported that the environmental factors shared by twins of the same family, were more significantly associated with early language skills and school readiness in twins at the age of five years, in comparison to genetic factors.[21] Whilst another study reported that poorer early cognitive and non-cognitive development of twins, at the ages of; 6, 12 and 18 months, was associated with biological factors including low birth weight, independently of environmental factors, such as socioeconomic status.[3] Studies assessing both biological and sociodemographic factors and their impact on the longer-term child development of children born from multiple pregnancies remain sparse and the results of the existing studies are mixed.

The aim of this study was to examine the association between biological and sociodemographic risk factors and developmental vulnerability in twins in their first year of full-time school.

Methods

Data Sources and Study Population

Data Sources

This study used anonymised unit records from the Department of Health WA. Australian Early Development Census (AEDC) records were obtained for all available years (2009, 2012 and 2015).

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Perinatal and birth related data were obtained for children born in WA from the Midwives Notification System (MNS), which is statutory record of all births (still- or live-born) in WA with either a birthweight >400 grams or a final gestational length of ≥20 weeks. Variables from MNS were cross validated with corresponding records from WA Birth Registrations. WA Register for Developmental Anomalies (WARDA) records were used to identify children who had a diagnosed developmental disability between birth and age five years.

Study Population

The study population included all children born in WA with an AEDC record in either 2009, 2012 or 2015 (N=73,903). Children were excluded from the study if; 1) they were not from a twin birth (N=71,748), 2) they were identified by their teacher as having 'special-needs' based on a diagnosed physical and/or intellectual disability (N=123), 3) they were reported as having any birth defect in the WARDA datasets (N=119), 4) they had an AEDC score that was either incomplete or missing (N=22), or 5) their twin sibling was excluded based on the aforementioned exclusion criteria (N=235; Figure 1). The final study sample consisted of N=1,656 children; N=828 twin pairs. There were 252 opposite sex twin pairs and 576 same sex twin pairs (277 male and 299 female twin pairs).

Outcome Measure

The AEDC is a national census of early childhood development spanning five developmental domains; 1) Physical Health and Wellbeing, 2) Social Competence, 3) Emotional Maturity, 4) Language and Cognitive skills (school-based), and 5) Communication Skills and General Knowledge. The AEDC is conducted every three years, with the first national data collection conducted in 2009. Children with scores <10th percentile in a given domain are classified as 'developmentally vulnerable.' AEDC cut-off scores are based on the first national AEDC data collection in 2009 and apply to all AEDC data collections. Domain scores for children with special needs are not included in the AEDC results. Two outcomes measures were used; developmentally

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vulnerable one or more AEDC domains (DV1) and developmentally vulnerable two or more AEDC domains (DV2).

Risk Variables

Maternal Variables

Maternal age and marital status at child's birth were obtained from the MNS and Birth Registrations. Maternal occupation at birth was obtained from Birth Registrations data and converted to a four-digit standard code using the Australian and New Zealand Standard Classification of Occupations. These codes were then assigned a value ranging from 0-100 using the Australian Socioeconomic Index 2006 (AUSEI06).[48] Low AUSEI06 values are representative of low-status occupations and high values represent high-status occupations. The distribution of values of AUSEI06 were then divided into five groups; [0,20], (20, 40], (40, 60], (60,80] and (80,100]. An AUSEI06 value of zero were assigned to records if occupation was reported as 'unemployed', 'stay at home parent' or 'pensioner.' For records where maternal occupation was not stated, an AUSEI06 value was not assigned and these cases were reported as missing.

Pregnancy and Birth Variables

We included several binary pregnancy and birth variables to indicate either the presence or absence; of fertility treatments, smoking during pregnancy, pre-eclampsia, gestational diabetes, threatened abortion, threatened pre-term labour, antepartum haemorrhage (APH), placenta praevia, placental abruption, fetal distress, cephalopelvic disproportion, prolapsed cord, precipitate delivery, post-partum haemorrhage (PPH), intubation status, early preterm birth (<34 weeks of gestational age), and time to Spontaneous Respiration (TSR); with a TSR of ≥2 minutes forming the 'at risk' group and five-minute Apgar score; with a five-minute Apgar score of <7 forming the 'at risk' group. The proportion of optimal birthweight (POBW) is a measure of fetal growth and is defined as birth weight divided by expected birth weight, in the absence of pathologic risk factors. This measure also accounts for non-pathologic determinants of growth, including gestational age, birth order, sex of the child and maternal height[49] and has been validated against ultrasound measurements.[50] We

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derived a binary proxy for fetal growth restriction as POBW <15th centile, which corresponded to an observed birth weight less than 75.75% of that expected.[9]

We derived a general category for other pregnancy related complications (not elsewhere stated; such as urinary tract infection, pre-labour rupture of membranes) for all records. As records may have multiple pregnancy related complications, all records that had a complication that was not elsewhere stated in this study or had multiple complications of which at least one complication was not elsewhere stated in this study, formed the 'at risk' group for this variable.

Child Variables

Sex and ethnicity of child was obtained from the MNS and Birth Registrations. Age at the time of AEDC completion and language other than English spoken at home were obtained from the AEDC. Age of children at the time of AEDC completion ranged between; ≥3 years 10 months to <6 years 10 months, with a mean of age category of, ≥5 years one month to 5 years 10 months. To balance frequencies, the age of children at the time of AEDC completion was categorised into three groups; 1) ≥3 years 10 months to <5 years and one month, 2) ≥5 years one month to <5 years 10 months (reference category) and 3) ≥5 years 10 months to <6 years 10 months.

The total number of siblings were derived as the number of live births to each mother prior to the year that the cohort child had the AEDC conducted. Siblings from the twin pregnancy and siblings who died within the neonatal period (i.e. mode of separation post-birth from the hospital was death) were excluded in the calculations for total number of siblings.

Sociodemographic Variables

The Index of Relative Socioeconomic Disadvantage (IRSD)[19] was calculated using the residential address at the time of birth. ISRD is derived from Australian Census data and reflects area-level disadvantage through variables such as low household income, low educational attainment and high levels of unemployment. Geographical areas are given a score from 1 (most disadvantaged) to 5 (most advantaged). Due to smaller cohort numbers in the more disadvantaged areas, these five

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variables were collapsed into two groups; most disadvantaged quintile (i.e. ISRD quintile 1) and greater than the most disadvantaged quintile (i.e. ISRD quintiles 2-5).

Statistical Modelling

For each risk variable, the 'least risk' category (e.g. not early preterm birth) was used as the reference category (Table 1). To estimate the risk of a child being classified as DV1 and DV2, a generalised linear mixed model with a logit link function was used with a random intercept for each twin pair. A total of 30 maternal, pregnancy, birth, child and sociodemographic risk variables were considered for the multivariate models. For DV1, DV2, and each of the five AEDC domains, 24 risk variables were included in the multivariate models; six risks variables were excluded from multivariable analysis due to the prevalence being too small (total N<40 for a given category). The variables excluded were; 1) placenta praevia, 2) placental abruption, 3) cephalopelvic disproportion, 4) prolapsed cord, 5) precipitate delivery and 6) a five-minute Apgar score of <7. Odds ratios (OR) and the associated 95% confidence intervals (CIs) were estimated for both unadjusted and adjusted models. All analyses were undertaken using PROC GLIMMIX in SAS version 9.4 for Windows.[51]

Results

Prevalence of developmental vulnerability in twins

A total of 431 (26.0%) twins were classified as DV1 (Table 1). Of the 28 maternal, pregnancy and birth, child and sociodemographic risk variables considered in the multivariate models, five variables had a statistically significant association with an increased risk of a twin being classified as DV1. In order of decreasing magnitude of associated risk, the ORs were; maternal age of 20 years or younger at time of twins' birth (OR 8.69, 95% CI 1.52 to 49.69), child speaks language other than English at home (OR 5.25, 95% CI 1.77 to 15.56), male twins (OR 5.25, 95% CI: 2.99 to 9.24), child age younger than the reference category for the study sample (≥5 years one month to 5 years 7 months) at time of AEDC completion (OR 3.10, 95% CI: 1.44 to 6.69), and POBW <15th percentile (OR 2.04, 95% CI 1.05 to 3.97).

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A total of 223 (14.1%) twins were classified as DV2 (Table 2). Of the 24 maternal, pregnancy and birth, child and sociodemographic risk variables considered in the adjusted models, four variables had a statistically significant association with an increased risk of a twin being classified as DV2. Risk factors for DV2 were, in order of decreasing magnitude; male twins (OR 7.98, 95% CI 3.49 to 8.25), child age younger than the reference category at time of AEDC completion (OR 4.89, 95% CI: 1.77 to 13.48), unmarried maternal marital status (OR 4.43, 95% CI 1.08 to 18.25), and POBW <15th percentile (OR 3.30, 95% CI 1.33 to 8.21).

Associations with domain-specific developmental vulnerability

A total of, 188 (11.4%) children were classified as developmentally vulnerable for the domains of: Physical Health and Wellbeing; 151 (9.1%) for Social Competence; 147 (8.9%) for Emotional Maturity; 195 (11.8%) for Language and Cognitive Skills (school-based); and 200 (12.0%) for Communication Skills and General Knowledge (Supplementary Tables 1-5, respectively). These results were broadly consistent with the findings for the aggregate measures of developmental vulnerability (DV1 and DV2).

Discussion

This study examined the associations between biological and sociodemographic risk factors and developmental vulnerability in twins in their first year of full-time school. To our knowledge, our study is the first of this scale (population-level sample of twins; N>1,600) to report an elevated prevalence of developmental vulnerabilities, in comparison to singletons, in an otherwise healthy sample twins, at the time of their first year of full-time school. We found that the percentage of twins classified as developmentally vulnerable was higher than the percentage of children classified as developmentally vulnerable in the WA general population. In the WA twin population, 26.0% of twins were classified as DV1 and 14.1% as DV2 across the 2009, 2012 and 2015 AEDC cycles. In the general WA population, which includes twins and higher order multiples, 23.0% of children were classified as DV1 and 11.3% of children were classified as DV2, across these AEDC cycles.[52] A large cohort study of 99,530 singleton children from New South Wales reported that 20.8% were

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classified as DV1 across the 2009 and 2012 AEDC cycles.[53] Thus, we found that twins are at an elevated risk of developmental vulnerability relative to a general population of children in the state of Western Australia and in a singleton population in New South Wales. This is consistent with findings from a study of 142 twin pairs from the Louisville Twin Study, that reported twins scored lower than singletons in both the Verbal and Performance IQ domains of the Wechsler Preschool and Primary Scale of Intelligence at both four and five years of age.[22] As our results were obtained from a sample of twins without any diagnosed developmental disabilities, the higher prevalence rates of twins being classified as DV1 and DV2 observed in our study, when compared to the general Australian population, suggests that healthy twins are more likely to be classified as developmental vulnerable on AEDC domains at school starting age when compared to their singleton counterparts.

The biological factors associated with developmental vulnerability in twins were; male sex, fetal growth restriction, and younger chronological age at the time of AEDC completion. These results are in line with singleton studies[40,54] which have reported that male children are more likely to be classified as developmentally vulnerable in their first year of full-time school, in comparison to female children. A study conducted in South Australia of 13,827 children, of which 3.4% where twins, also reported that male twins were more likely to be classified as DV2, when compared to female twins, however this finding was not statistically significant.[55] The Louisville Twin Study also reported sex differences, with females scoring higher than males at ages four and five years, however, scores tended to converge at six years of age.[22]

We also reported that twins younger than the reference category for this sample were more likely to be classified as developmentally vulnerable in their first year of full-time school. A study of 840 Canadian five-year old twins, aiming to assess the genetic and environmental factors influencing school readiness, reported that in the preliminary models age was positively correlated with the spatial recognition, numbers, and the letters components of the Lollipop test.[56] Furthermore, a recent discussion paper identified the need for further research into assess the effects of delaying

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school entry for twins[57] thus, highlighting that further research is required to better elucidate if delaying school entry is beneficial for both short-term and long-term academic outcomes in twins. The sociodemographic risk factors associated with developmental vulnerability in twins included maternal age and unmarried marital status at the time of twins' birth, the child speaking a language other than English, and age at the time of AEDC completion. These results are supported by the South Australian study, that examined a range of variables also included in our study.[55] This study reported that maternal age and marital status were associated with an increased risk of children being classified as DV2 on the AEDC.[55] Furthermore, the South Australian study reported that maternal and paternal occupation, parity and smoking during pregnancy were also associated with an increased risk of children being classified as DV2.[55] In our study we observed an increased but insignificant association between these risk variables and twins being classified as either DV1 or DV2.

An interesting finding from our study was that speaking a language other than English at home was associated with an increased risk for twins being classified as DV1. Previous studies have reported that approximately a fifth of Australian children are bilingual,[58] and the prevalence of twins speaking a language other than English at home in our study were in line with these results. Results from a study of an Australia wide study of 261,147 children, singletons and multiples, from the 2009 AEDC cycle reported that bilingual children proficient in English have been reported to had equal or slightly lower odds of being classed as DV1 when compared to their English-speaking background peers.[58] However, unlike our study, this study[58] did not report differences in developmental vulnerability based on plurality. Additionally, a Canadian study examining the school readiness profiles of 95,537 children in British Columbia[59] reported that bilingualism was associated with positive social, emotional and cognitive development, as measured by the Early Development Index.[43] Differences in results may be attributed to the fact bilingualism may be a risk factor for twins however, it may not be a significant risk factor in a general population sample. Furthermore, differences in the prevalence rates of particular language groups in WA is likely to be

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different to those that are prevalent in British Colombia and the difference in findings between the Canadian study and our results may be attributable to this fact.

Our findings have some accord with a cohort study examining the associations between biological and sociodemographic risk factors on late language emergency in 473 twins pairs at the age of two years.[9] Taylor et al. reported that the risk factors for late language emergence in twins, without developmental disabilities, include fetal growth restriction.[9] Interestingly, our study also identified fetal growth restriction as a risk factor for developmental vulnerability at age five, suggesting that the biological implications of a suboptimal intrauterine environment may be persist beyond infancy and into early childhood in twins who did not have diagnosed developmental disabilities. In contrast to our study, the Taylor et al. twin sample excluded twins with exposure to languages other than English. Their study found that sociodemographic risk factors (low maternal education, socioeconomic area disadvantage) were not associated with late language emergence at age two years. A subsequent study of the twins at ages four years and six years reported that higher maternal education and older maternal age showed positive effects on language and non-verbal phenotypes.[6] Our results suggest that sociodemographic factors including, maternal age and marital status at time of twins' birth, and the child speaking a language other than English at home are also associated with an increased risk of developmental vulnerability at age five.[9] The differences in findings between this study and our study suggest that sociodemographic characteristics may play a more significant role as risk variables at age five years compared to at the age of two years. This notion is supported by a study of a twin sample from the Quebec Newborn Twin Study, which reported that environmental factors, such as socioeconomic status, rather than genetic factors were attributable to the predictive association observed between early language skills and school readiness, as measured by the Lollipop Test, in twins 63-months of age.[21] However, further research is required to better elucidate the impact and interplay of biological and sociodemographic risk variables at different stages of development in twins.

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Studies assessing twin-singleton differences often control for or select for factors such as prematurity, low birth weight, or parental socioeconomic status our study draws attention to adverse effect of risk factors such as POBW and maternal marital status on child development outcomes at age five.[54,60,61] An Australian cohort study of 1,922 children from the Northern Territory using linked administrative data, reported an increased, but non-significant, risk of twins being classified as DV1 on the AEDC, after controlling for a range of biological and sociodemographic variables used in our study including; sex, 5-minute Apgar score <7, area remoteness, ethnicity, child speaks a language other than English at home and maternal age at time of child's birth.[54] Although this study gave consideration to plurality as a risk factor for developmental vulnerability, it did not aim to assess the association between a comprehensive set of biological and sociodemographic risk factors. A Canadian study of 5-year old twins reported that shared environmental factors substantially accounted for cognitive school readiness (as measured by the Lollipop Test) as compared to genetic effects.[56] Likewise other studies have also reported that a range of family factors, which would be assumed to be shared by both twins, such as family income, maternal occupation, and employment status are associated with cognitive school readiness.[62,63] Further studies in this area are required as the extent and nature of the risk factors associated with developmental vulnerability at age five in twins remain not well-established.

Preventative intervention studies have reported that programs designed to improve school readiness and high quality early childhood education and care, are effective for at-risk populations and can have significant long-term results.[64,65] The higher prevalence rates of DV1 and DV2 in twins observed in this study are indicative of the fact that twins form an at-risk group in terms of developmental vulnerability at the time at which children commence full-time school. Therefore, it is pertinent for those working in the early childhood education sector and for parents to be aware of the developmental vulnerabilities present in twins at the age at which children begin full-time school. In Australia, there has been call to provide increased quantity and quality of support service

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and resources are required for twins and their families due to increased vulnerability[57] and the results of our study highlight this need.

Conclusions

Both biological and sociodemographic risk factors are associated with developmental vulnerability at the age of five. In particular, the results draw attention to the notion that prenatal and more significantly perinatal risk factors and sociodemographic environments in which twins are raised can impact developmental levels in early childhood.

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Acknowledgements:

We gratefully acknowledge the WA Data Linkage Branch and the data custodians who provided data for this study and the people of Western Australia for the use of their administrative data. This study does not necessarily reflect their views. This study uses data from the Australian Early Development Census (AEDC). The AEDC is funded by the Australian Government Department of Education and Training. The findings and views reported are those of the authors and should not be attributed to the Department or the Australian Government.

Patient and Public Involvement:

No patients were involved in the development of the research question or the outcome measures, or in the development of the plans for the design or implementation of the study.

Ethics Approval:

Ethics approval for this study was granted by the Western Australian Department of Health Human Research Ethics Committee (2016/51) and the University of Western Australia Human Research Ethics Committee (RA/4/20/4776).

Declaration of interests:

The authors declare that they have no competing interests, no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Funding:

This study was supported by National Health and Medical Research Grants (GNT1173991 and GNT1099655 to GP), the Research Council of Norway through its Centres of Excellence funding scheme (#262700 to GP) and the Australian Research Council Centre of Excellence for Children and Families over the Life Course (CE140100027 to CLT and DC). GKD was supported by the ARC Centre of Excellence for Children and Families over the Life Course Scholarship, the ARC Centre of Excellence for Children and Families over the Life Course Top-Up Scholarship and the Stan and Jean Perron Top-Up Scholarship.

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Author Contributions:

All authors contributed to study inception, design, interpretation of the results and writing of the paper and manuscript revisions. GKD did the literature review, data analysis and wrote the first draft of the paper. All authors contributed to the interpretation of the results and writing of the paper and all authors approved the final manuscript.

Data Sharing:

The linked administrative data are owned by the government departments who approved the linkage and use of the data for this study. Use of the study data is restricted to named researchers. The current Human Research Ethics Committee approvals were obtained for public sharing and presentation of data on group level only, meaning the data used in this study cannot be shared by the authors. Collaborative research may be conducted according to the ethical requirements and relevant privacy legislations. Potential collaborators should contact author GP with their expression of interest. The steps involved in seeking permission for linkage and use of the data used in this study are the same for all researchers.

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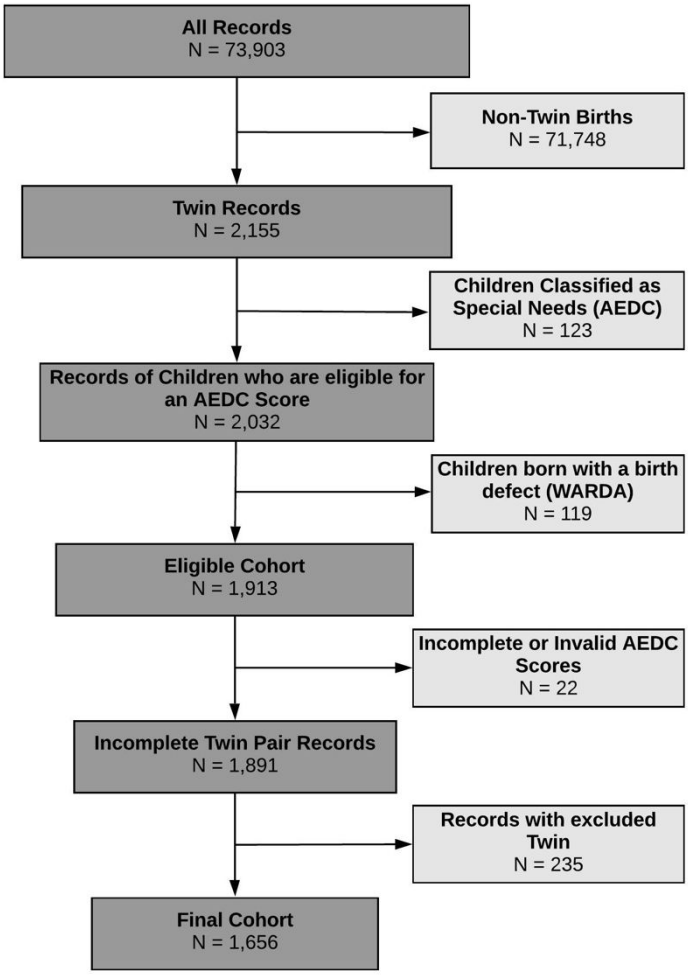
Figures & Tables: Total 1 Figure & 2 Tables

Figure 1. Eligible Cohort and Numbers Included for Analyses.



AEDC = Australian Early Development Census. WARDA= Western Australian Register of Developmental Anomalies.

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583 Table 1. Risk factors for children who are developmentally vulnerable on one or more AEDC
584 domains (DV1).

Characteristic	DV1 (N=431) N (%)	NDV1 (N=1,225) N (%)	Bivariate OR [95% CI]	Multivariable (N=1,352) aOR [95% CI]
Maternal				
Age at Time of Child's Birth				
≤20 years	48 (11.14)	34 (2.78)	**26.92 [6.82-106.31]*****	**8.69 [1.52-49.69]***
21-25 years	69 (16.01)	135 (11.02)	**2.96 [1.15-7.62]**	2.16 [0.75-6.16]
26-30 years	101 (23.43)	333 (27.18)	1.00 [referent]	1.00 [referent]
31-35 years	133 (30.86)	465 (37.96)	0.91 [0.44-1.88]	1.14 [0.49-2.63]
36-40 years	61 (14.15)	229 (18.69)	0.81 [0.34-1.95]	1.22 [0.44-3.39]
>40 years	19 (4.41)	29 (2.37)	4.77 [0.89-25.52]	3.74 [0.51-27.53]
Marital Status				
Married (inc. de facto)	357 (82.83)	1,123 (91.67)	1.00 [referent]	1.00 [referent]
All Other	72 (16.71)	98 (8.00)	**5.99 [2.43-14.75]*****	1.95 [0.65-5.85]
Unavailable	2 (0.46)	4 (0.33)		
Occupational Status Scale at Time of Child's Birth				
0-20	122 (28.31)	187 (15.27)	**7.97 [3.08-20.66]*****	2.41 [0.76-7.64]
>20-40	119 (27.61)	268 (21.88)	**3.74 [1.53-9.14]****	2.52 [0.90-7.11]
>40-60	71 (16.47)	338 (27.59)	0.85 [0.34-2.09]	0.67 [0.24-1.86]
>60-80	35 (8.12)	164 (13.39)	0.90 [0.30-2.64]	0.72 [0.20-2.54]
>80-100	54 (12.53)	236 (19.27)	1.00 [referent]	1.00 [referent]
Unavailable	30 (6.96)	32 (2.61)		
Pregnancy & Birth				
Fertility Treatments				
No	377 (87.47)	1,011 (82.53)	1.00 [referent]	1.00 [referent]
Yes	54 (12.53)	214 (17.47)	0.43 [0.19-0.97]	0.78 [0.29-2.06]
Smoking Status During Pregnancy				
No	339 (78.65)	1,079 (88.08)	1.00 [referent]	1.00 [referent]
Yes	92 (21.35)	146 (11.92)	**4.31 [1.95-9.53]*****	0.91 [0.35-2.37]
Pre-eclampsia				
No	375 (87.01)	1,085 (88.57)	1.00 [referent]	1.00 [referent]
Yes	56 (12.99)	140 (11.43)	1.40 [0.59-3.34]	1.91 [0.71-5.17]
Gestational Diabetes				
No	402 (93.27)	1,152 (94.04)	1.00 [referent]	1.00 [referent]
Yes	29 (6.73)	73 (5.96)	1.30 [0.40-4.22]	1.16 [0.33-4.09]
Threatened Abortion				
No	416 (96.52)	1,156 (94.37)	1.00 [referent]	1.00 [referent]
Yes	15 (3.48)	69 (5.63)	0.36 [0.09-1.45]	0.19 [0.03-1.13]
Other Pregnancy Related Complications				
No	125 (29.00)	451 (36.82)	1.00 [referent]	1.00 [referent]
Yes	306 (71.00)	774 (63.18)	**2.08 [1.12-3.85]***	1.79 [0.84-3.80]
Threatened Preterm Labour				
No	376 (87.24)	1,088 (88.82)	1.00 [referent]	1.00 [referent]
Yes	55 (12.76)	137 (11.18)	1.34 [0.55-3.24]	0.78 [0.29-2.10]
APH				
No	411 (95.36)	1,187 (96.90)	1.00 [referent]	1.00 [referent]
Yes	20 (4.64)	38 (3.10)	2.38 [0.53-10.73]	0.68 [0.12-3.97]
Placenta Praevia				
No	429 (99.54)	1,217 (99.35)		
Yes	2 (0.46)	8 (0.65)		
Placental Abruption [a]				
No	427 (99.07)	1,223 (99.84)		

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Yes	4 (0.93)	2 (0.16)		
Fetal Distress				
No	382 (88.63)	1,136 (92.73)	1.00 [referent]	1.00 [referent]
Yes	49 (11.37)	89 (7.27)	**2.92 [1.13-7.58]***	2.00 [0.68-5.86]
Cephalopelvic Disproportion [a]				
No	431 (100.00)	1,221 (99.67)		
Yes	0 (0.00)	4 (0.33)		
Prolapsed Cord [a]				
No	428 (99.30)	1,215 (99.18)		
Yes	3 (0.70)	10 (0.82)		
Precipitate Delivery [a]				
No	424 (98.38)	1,206 (98.45)		
Yes	7 (1.62)	19 (1.55)		
PPH ≥500mls				
No	281 (65.20)	918 (74.94)	1.00 [referent]	1.00 [referent]
Yes	150 (34.80)	307 (25.06)	**2.59 [1.39-4.82]****	1.48 [0.71-3.07]
TSR ≥2mins				
No	364 (84.45)	1,060 (86.53)	1.00 [referent]	1.00 [referent]
Yes	67 (15.55)	165 (13.47)	1.06 [0.56-1.99]	0.50 [0.22-1.17]
Apgar 5-minutes <7 [a]				
No	425 (98.61)	1,198 (97.80)		
Yes	6 (1.39)	27 (2.20)		
Intubation				
No	353 (81.90)	1,198 (97.80)	1.00 [referent]	1.00 [referent]
Yes	78 (18.10)	27 (2.20)	1.36 [0.75-2.45]	1.41 [0.65-3.08]
Early Preterm Birth				
No	352 (81.67)	1,058 (86.37)	1.00 [referent]	1.00 [referent]
Yes	79 (18.33)	167 (13.63)	2.08 [0.94-4.56]	1.38 [0.56-3.38]
POBW <15th Percentile				
No	305 (70.77)	926 (75.59)	1.00 [referent]	1.00 [referent]
Yes	81 (18.79)	136 (11.10)	**2.09 [1.14-3.84]***	**2.04 [1.05-3.97]***
Unavailable	45 (10.44)	163 (13.31)		
Parity				
0	150 (34.80)	512 (41.80)	1.00 [referent]	1.00 [referent]
1	154 (35.73)	429 (35.02)	1.62 [0.83-3.16]	1.93 [0.74-5.02]
≥2	127 (29.47)	284 (23.18)	**2.50 [1.20-5.22]***	1.60 [0.43-5.98]
Child				
Sex				
Female	176 (40.84)	674 (55.02)	1.00 [referent]	1.00 [referent]
Male	255 (59.16)	551 (44.98)	**4.44 [2.68-7.36]*****	**5.25 [2.99-9.24]*****
Ethnicity				
Other	385 (89.33)	1,187 (96.90)	1.00 [referent]	1.00 [referent]
Indigenous Australian	46 (10.67)	38 (3.10)	**16.98 [4.85-59.46]*****	2.80 [0.53-14.80]
Child Speaks Language Other Than English at Home				
No	367 (85.15)	1,149 (93.80)	1.00 [referent]	1.00 [referent]
Yes	64 (14.85)	76 (6.20)	**6.28 [2.48-15.90]*****	**5.25 [1.77-15.56]****
Age Category at Time of AEDC Completion [b]				
1	109 (25.29)	212 (17.31)	**2.93 [1.45-5.90]****	**3.10 [1.44-6.69]****
2	288 (66.82)	911 (74.37)	1.00 [referent]	1.00 [referent]
3	34 (7.89)	102 (8.33)	1.18 [0.43-3.27]	0.94 [0.29-3.06]
Total Number of Siblings				
1	119 (27.61)	389 (31.76)	1.00 [referent]	1.00 [referent]
2	160 (37.12)	494 (40.33)	1.15 [0.58-2.30]	0.59 [0.22-1.58]
3	74 (17.17)	240 (19.59)	1.04 [0.45-2.41]	0.41 [0.12-1.45]

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>3	78 (18.10)	102 (8.33)	**7.28 [2.73-19.45]*****	2.61 [0.58-11.79]
Sociodemographic				
Index of Relative Socioeconomic Disadvantage				
Lowest Quintile	327 (75.87)	1,046 (85.39)	**3.55 [1.62-7.78]****	1.36 [0.55-3.37]
> Lowest Quintile	87 (20.19)	150 (12.24)	1.00 [referent]	1.00 [referent]
Unavailable	17 (3.94)	29 (2.37)		

*p<0.05, **p<0.01, ***p<0.001

[a] Excluded from multivariable analysis due to small N.

[b] Age categories classified as; ≥3 years 10 months to <5 years and one month, 2) ≥5 years and one month to <5 years and 10 months (reference category), 3) ≥5 years and 10 months to <6 years 10 months.

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Table 2. Risk factors for children who are developmentally vulnerable on two or more AEDC domains (DV2).

Characteristic	DV2 (N=223) N (%)	NDV2 (N=1,433) N (%)	Bivariate OR [95% CI]	Multivariable (N=1,352) aOR [95% CI]
Maternal				
Age at Time of Child's Birth				
≤20 years	31 (13.90)	51 (3.56)	**21.86 [4.97-96.20]*****	3.94 [0.48-32.25]
21-25 years	38 (17.04)	166 (11.58)	2.73 [0.89-8.31]	1.17 [0.31-4.35]
26-30 years	52 (23.32)	382 (26.66)	1.00 [referent]	1.00 [referent]
31-35 years	69 (30.94)	529 (36.92)	0.85 [0.35-2.06]	1.24 [0.40-3.90]
36-40 years	24 (10.76)	266 (18.56)	0.46 [0.15-1.42]	0.60 [0.14-2.55]
>40 years	9 (4.04)	39 (2.72)	2.35 [0.32-17.31]	0.76 [0.04-13.56]
Marital Status				
Married (inc. de facto)	172 (77.13)	1,308 (91.28)	1.00 [referent]	1.00 [referent]
All Other	49 (21.97)	121 (8.44)	**9.91 [3.54-27.77]*****	**4.43 [1.08-18.21]***
Unavailable	2 (0.90)	4 (0.28)		
Occupational Status Scale at Time of Child's Birth				
0-20	78 (34.98)	231 (16.12)	**10.45 [3.23-33.77]*****	3.26 [0.70-15.31]
>20-40	56 (25.11)	331 (23.10)	2.77 [0.91-8.44]	1.54 [0.37-6.40]
>40-60	31 (13.90)	378 (26.38)	0.66 [0.20-2.10]	0.45 [0.10-1.97]
>60-80	15 (6.73)	184 (12.84)	0.64 [0.16-2.64]	0.30 [0.04-2.02]
>80-100	28 (12.56)	262 (18.28)	1.00 [referent]	1.00 [referent]
Unavailable	15 (6.73)	47 (3.28)		
Pregnancy & Birth				
Fertility Treatments				
No	200 (89.69)	1,188 (82.90)	1.00 [referent]	1.00 [referent]
Yes	23 (10.31)	245 (17.10)	0.35 [0.13-0.97]	0.67 [0.16-2.75]
Smoking Status During Pregnancy				
No	166 (74.44)	1,252 (87.37)	1.00 [referent]	1.00 [referent]
Yes	57 (25.56)	181 (12.63)	**5.83 [2.32-14.65]*****	1.28 [0.37-4.43]
Pre-eclampsia				
No	195 (87.44)	1,265 (88.28)	1.00 [referent]	1.00 [referent]
Yes	28 (12.56)	168 (11.72)	1.25 [0.41-3.86]	2.70 [0.71-10.27]
Gestational Diabetes				
No	208 (93.27)	1,346 (93.93)	1.00 [referent]	1.00 [referent]
Yes	15 (6.73)	87 (6.07)	1.44 [0.32-6.42]	2.55 [0.51-12.76]
Threatened Abortion				
No	214 (95.96)	1,358 (94.77)	1.00 [referent]	1.00 [referent]
Yes	9 (4.04)	75 (5.23)	0.54 [0.10-2.94]	0.19 [0.02-2.57]
Other Pregnancy Related Complications				
No	57 (25.56)	519 (36.22)	1.00 [referent]	1.00 [referent]
Yes	166 (74.44)	914 (63.78)	**2.64 [1.22-5.69]***	1.70 [0.59-4.85]
Threatened Preterm Labour				
No	191 (85.65)	1,273 (88.83)	1.00 [referent]	1.00 [referent]
Yes	32 (14.35)	160 (11.17)	2.04 [0.66-6.29]	0.77 [0.21-2.81]
APH				
No	209 (93.72)	1,389 (96.93)	1.00 [referent]	1.00 [referent]
Yes	14 (6.28)	44 (3.07)	5.96 [0.95-37.40]	1.42 [0.17-12.22]
Placenta Praevia [a]				
No	223 (100.00)	1,423 (99.30)		
Yes	0 (0.00)	10 (0.70)		
Placental Abruption [a]				
No	221 (99.10)	1,429 (99.72)		

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Yes	2 (0.90)	4 (0.28)		
Fetal Distress				
No	195 (87.44)	1,323 (92.32)	1.00 [referent]	1.00 [referent]
Yes	28 (12.56)	110 (7.68)	3.03 [0.90-10.23]	1.56 [0.38-6.37]
Cephalopelvic Disproportion [a]				
No	223 (100.00)	1,429 (99.72)		
Yes	0 (0.00)	4 (0.28)		
Prolapsed Cord [a]				
No	220 (98.65)	1,423 (99.30)		
Yes	3 (1.35)	10 (0.70)		
Precipitate Delivery [a]				
No	219 (98.21)	1,411 (98.46)		
Yes	4 (1.79)	22 (1.54)		
PPH ≥500mls				
No	141 (63.23)	1,058 (73.83)	1.00 [referent]	1.00 [referent]
Yes	82 (36.77)	375 (26.17)	**3.43 [1.49-7.94]****	1.48 [0.56-3.94]
TSR ≥2mins				
No	183 (82.06)	1,241 (86.60)	1.00 [referent]	1.00 [referent]
Yes	40 (17.94)	192 (13.40)	1.78 [0.81-3.89]	0.89 [0.30-2.65]
Apgar 5-minutes <7 [a]				
No	219 (98.21)	1,404 (97.98)		
Yes	4 (1.79)	29 (2.02)		
Intubation				
No	178 (79.82)	1,404 (97.98)	1.00 [referent]	1.00 [referent]
Yes	45 (20.18)	29 (2.02)	1.91 [0.90-4.05]	1.50 [0.53-4.24]
Early Preterm Birth				
No	172 (77.13)	1,238 (86.39)	1.00 [referent]	1.00 [referent]
Yes	51 (22.87)	195 (13.61)	**4.18 [1.50-11.67]****	2.22 [0.69-7.19]
POBW <15th Percentile				
No	162 (72.65)	1,069 (74.60)	1.00 [referent]	1.00 [referent]
Yes	42 (18.83)	175 (12.21)	**2.72 [1.25-5.93]***	**3.30 [1.33-8.21]***
Unavailable	19 (8.52)	189 (13.19)		
Parity				
0	79 (35.43)	583 (40.68)	1.00 [referent]	1.00 [referent]
1	73 (32.74)	510 (35.59)	1.18 [0.51-2.76]	1.00 [0.27-3.71]
≥2	71 (31.84)	340 (23.73)	**2.66 [1.04-6.83]***	2.89 [0.48-17.44]
Child				
Sex				
Female	83 (37.22)	767 (53.52)	1.00 [referent]	1.00 [referent]
Male	140 (62.78)	666 (46.48)	**5.42 [2.79-10.55]*****	**7.98 [3.49-18.25]*****
Ethnicity				
Other	197 (88.34)	1,375 (95.95)	1.00 [referent]	1.00 [referent]
Indigenous Australian	26 (11.66)	58 (4.05)	**11.00 [2.78-43.60]*****	2.76 [0.37-20.58]
Child Speaks Language Other Than English at Home				
No	192 (86.10)	1,324 (92.39)	1.00 [referent]	1.00 [referent]
Yes	31 (13.90)	109 (7.61)	3.19 [0.96-10.63]	3.94 [0.97-16.08]
Age Category at Time of AEDC Completion				
1	66 (29.6)	255 (17.79)	**4.11 [1.80-9.39]*****	**4.89 [1.77-13.48]****
2	142 (63.68)	1057 (73.76)	1.00 [referent]	1.00 [referent]
3	15 (6.73)	121 (8.44)	0.95 [0.26-3.46]	0.33 [0.06-1.97]
Total Number of Siblings				
1	58 (26.01)	450 (31.40)	1.00 [referent]	1.00 [referent]
2	84 (37.67)	570 (39.78)	1.35 [0.57-3.19]	1.12 [0.29-4.26]
3	38 (17.04)	276 (19.26)	1.14 [0.40-3.24]	0.41 [0.07-2.38]

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>3	43 (19.28)	137 (9.56)	**7.14 [2.24-22.72]*****	2.25 [0.30-17.06]
Sociodemographic				
Index of Relative Socioeconomic Disadvantage				
Lowest Quintile	175 (78.48)	1,198 (83.60)	2.14 [0.76-6.02]	0.57 [0.17-1.90]
> Lowest Quintile	39 (17.49)	198 (13.82)	1.00 [referent]	1.00 [referent]
Unavailable	9 (4.04)	37 (2.58)		

*p<0.05, **p<0.01, ***p<0.001

[a] Excluded from multivariable analysis due to small N.

[b] Age categories classified as; ≥3 years 10 months to <5 years and one month, 2) ≥5 years and one month to <5 years and 10 months (reference category), 3) ≥5 years and 10 months to <6 years 10 months.

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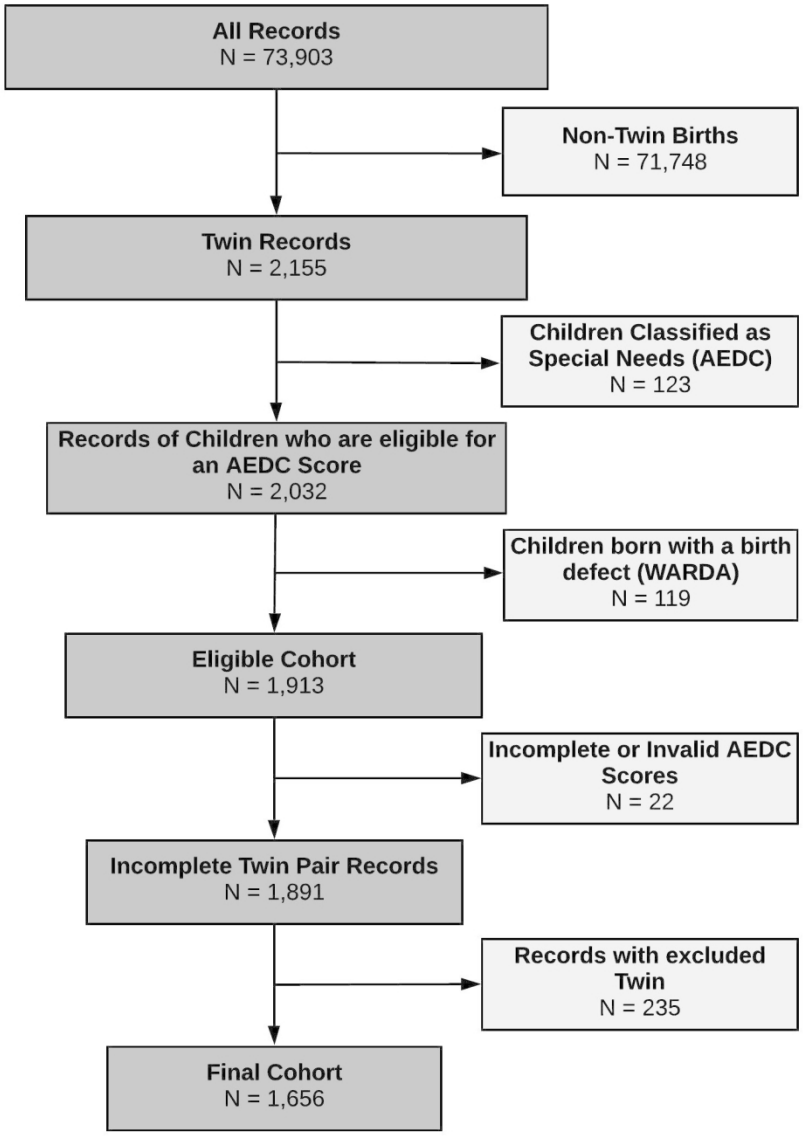

Figure 1. Eligible Cohort and Numbers Included for Analyses.
AEDC = Australian Early Development Census. WARDA= Western Australian Register of Developmental Anomalies.

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Supplementary Tables and Figures (Total: 5 tables, 0 figures)

Table 1. Risk Factors for Developmental Vulnerability on the Physical Health & Wellbeing Domain.

Characteristic	DV (N=188) N (%)	NDV (N=1,468) N (%)	Bivariate OR [95% CI]	Multivariable (N=1,352) aOR [95% CI]
Maternal				
Age at Time of Child's Birth				
≤20 years	24 (12.77)	58 (3.95)	**11.73 [2.52-54.66]*****	3.87 [0.56-26.94]
21-25 years	26 (13.83)	178 (12.13)	1.33 [0.40-4.46]	1.17 [0.31-4.35]
26-30 years	48 (25.53)	386 (26.29)	1.00 [referent]	1.00 [referent]
31-35 years	61 (32.45)	537 (36.58)	0.88 [0.35-2.20]	1.10 [0.39-3.09]
36-40 years	22 (11.70)	268 (18.26)	0.47 [0.15-1.52]	0.42 [0.11-1.66]
>40 years	7 (3.72)	41 (2.79)	1.59 [0.19-13.59]	0.62 [0.04-9.67]
Marital Status				
Married (inc. de facto)	152 (80.85)	1,328 (90.46)	1.00 [referent]	1.00 [referent]
All Other	36 (19.15)	134 (9.13)	**5.54 [1.87-16.35]****	2.21 [0.60-8.13]
Unavailable	0 (0.00)	6 (0.41)		
Occupational Status Scale at Time of Child's Birth				
0-20	52 (27.66)	257 (17.51)	**3.72 [1.18-11.71]***	0.53 [0.12-2.25]
>20-40	48 (25.53)	339 (23.09)	2.10 [0.69-6.34]	0.91 [0.26-3.26]
>40-60	33 (17.55)	376 (25.61)	0.81 [0.26-2.55]	0.43 [0.12-1.57]
>60-80	13 (6.91)	186 (12.67)	0.66 [0.16-2.65]	0.28 [0.05-1.50]
>80-100	25 (13.30)	265 (18.05)	1.00 [referent]	1.00 [referent]
Unavailable	17 (9.04)	45 (3.07)		
Pregnancy & Birth				
Fertility Treatments				
No	163 (86.70)	1,225 (83.45)	1.00 [referent]	1.00 [referent]
Yes	25 (13.30)	243 (16.55)	0.61 [0.21-1.75]	1.15 [0.33-3.93]
Smoking Status During Pregnancy				
No	134 (71.28)	1,284 (87.47)	1.00 [referent]	1.00 [referent]
Yes	54 (28.72)	184 (12.53)	**7.19 [2.76-18.70]*****	2.66 [0.87-8.14]
Pre-eclampsia				
No	163 (86.70)	1,297 (88.35)	1.00 [referent]	1.00 [referent]
Yes	25 (13.30)	171 (11.65)	1.56 [0.46-5.24]	3.11 [0.94-10.34]
Gestational Diabetes				
No	173 (92.02)	1,381 (94.07)	1.00 [referent]	1.00 [referent]
Yes	15 (7.98)	87 (5.93)	1.87 [0.36-9.87]	2.50 [0.56-11.24]
Threatened Abortion				
No	182 (96.81)	1,390 (94.69)	1.00 [referent]	1.00 [referent]
Yes	6 (3.19)	78 (5.31)	0.45 [0.07-2.71]	0.37 [0.04-3.34]
Other Pregnancy Related Complications				
No	51 (27.13)	525 (35.76)	1.00 [referent]	1.00 [referent]
Yes	137 (72.87)	943 (64.24)	1.96 [0.87-4.42]	1.76 [0.67-4.64]
Threatened Preterm Labour				
No	161 (85.64)	1,303 (88.76)	1.00 [referent]	1.00 [referent]
Yes	27 (14.36)	165 (11.24)	1.68 [0.49-5.81]	0.82 [0.25-2.76]
APH				
No	178 (94.68)	1,420 (96.73)	1.00 [referent]	1.00 [referent]
Yes	10 (5.32)	48 (3.27)	3.27 [0.37-28.63]	0.72 [0.09-5.98]
Placenta Praevia [a]				
No	187 (99.47)	1,459 (99.39)		
Yes	1 (0.53)	9 (0.61)		
Placental Abruption [a]				
No	185 (98.40)	1,465 (99.8)		
Yes	3 (1.60)	3 (0.20)		
Fetal Distress				

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No	162 (86.17)	1,356 (92.37)	1.00 [referent]	1.00 [referent]
Yes	26 (13.83)	112 (7.63)	**4.89 [1.20-19.90]***	2.52 [0.70-9.05]
Cephalopelvic Disproportion [a]				
No	188 (100.00)	1,464 (99.73)		
Yes	0 (0.00)	4 (0.27)		
Prolapsed Cord [a]				
No	188 (100.00)	1,455 (99.11)		
Yes	0 (0.00)	13 (0.89)		
Precipitate Delivery [a]				
No	186 (98.94)	1,444 (98.37)		
Yes	2 (1.06)	24 (1.63)		
PPH ≥500mls				
No	124 (65.96)	1,075 (73.23)	1.00 [referent]	1.00 [referent]
Yes	64 (34.04)	393 (26.77)	2.16 [0.90-5.18]	0.86 [0.34-2.13]
TSR ≥2mins				
No	152 (80.85)	1,272 (86.65)	1.00 [referent]	1.00 [referent]
Yes	36 (19.15)	196 (13.35)	1.48 [0.64-3.44]	0.53 [0.19-1.49]
Apgar 5-minutes <7 [a]				
No	182 (96.81)	1,441 (98.16)		
Yes	6 (3.19)	27 (1.84)		
Intubation				
No	147 (78.19)	1,242 (84.60)	1.00 [referent]	1.00 [referent]
Yes	41 (21.81)	226 (15.40)	**2.33 [1.03-5.28]***	1.85 [0.72-4.77]
Early Preterm Birth				
No	146 (77.66)	1,264 (86.1)	1.00 [referent]	1.00 [referent]
Yes	42 (22.34)	204 (13.9)	**3.76 [1.21-11.68]***	2.21 [0.77-6.29]
POBW <15th Percentile				
No	125 (66.49)	1,106 (75.34)	1.00 [referent]	1.00 [referent]
Yes	42 (22.34)	175 (11.92)	**3.44 [1.53-7.74]****	**2.71 [1.21-6.10]***
Unavailable	21 (11.17)	187 (12.74)		
Parity				
0	67 (35.64)	595 (40.53)	1.00 [referent]	1.00 [referent]
1	65 (34.57)	518 (35.29)	1.18 [0.48-2.86]	1.28 [0.40-4.13]
≥2	56 (29.79)	355 (24.18)	1.81 [0.67-4.91]	1.52 [0.28-8.29]
Child				
Sex				
Female	82 (43.62)	768 (52.32)	1.00 [referent]	1.00 [referent]
Male	106 (56.38)	700 (47.68)	**2.50 [1.36-4.61]****	**3.33 [1.65-6.71]*****
Ethnicity				
Other	167 (88.83)	1,405 (95.71)	1.00 [referent]	1.00 [referent]
Indigenous Australian	21 (11.17)	63 (4.29)	**12.56 [2.12-74.52]****	0.87 [0.13-5.91]
Child Speaks Language Other Than English at Home				
No	159 (84.57)	1,357 (92.44)	1.00 [referent]	1.00 [referent]
Yes	29 (15.43)	111 (7.56)	**4.62 [1.24-17.26]***	**4.04 [1.13-14.47]***
Age Category at Time of AEDC Completion				
1	50 (26.6)	271 (18.46)	**2.76 [1.02-7.46]***	2.06 [0.82-5.17]
2	129 (68.62)	1,070 (72.89)	1.00 [referent]	1.00 [referent]
3	9 (4.79)	127 (8.65)	0.44 [0.10-1.93]	0.19 [0.03-1.24]
Total Number of Siblings				
1	51 (27.13)	457 (31.13)	1.00 [referent]	1.00 [referent]
2	69 (36.70)	585 (39.85)	1.10 [0.46-2.63]	0.82 [0.25-2.69]
3	24 (12.77)	290 (19.75)	0.51 [0.16-1.57]	0.34 [0.07-1.77]
>3	44 (23.40)	136 (9.26)	**8.32 [2.57-26.96]*****	5.52 [0.83-36.72]
Sociodemographic				
Index of Relative Socioeconomic Disadvantage				
Lowest Quintile	138 (73.40)	1,235 (84.13)	**3.78 [1.17-12.22]***	1.68 [0.57-4.94]

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> Lowest Quintile	40 (21.28)	197 (13.42)	1.00 [referent]	1.00 [referent]
Unavailable	10 (5.32)	36 (2.45)		

*p<0.05, **p<0.01, ***p<0.001

[a] Excluded from multivariable analysis due to small N.

[b] Age categories classified as; ≥3 years 10 months to <5 years and one month, 2) ≥5 years and one month to <5 years and 10 months (reference category), 3) ≥5 years and 10 months to <6 years 10 months.

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Table 2. Risk Factors for Developmental Vulnerability on the Social Competence Domain.

Characteristic	DV (N=151) N (%)	NDV (N=1,505) N (%)	Bivariate OR [95% CI]	Multivariable (N=1,352) aOR [95% CI]
Maternal				
Age at Time of Child's Birth				
≤20 years	21 (13.91)	61 (4.05)	**11.00 [2.29-52.75]*****	1.84 [0.23-14.81]
21-25 years	23 (15.23)	181 (12.03)	1.63 [0.48-5.54]	1.15 [0.28-4.76]
26-30 years	37 (24.50)	397 (26.38)	1.00 [referent]	1.00 [referent]
31-35 years	43 (28.48)	555 (36.88)	0.65 [0.25-1.71]	0.81 [0.26-2.52]
36-40 years	20 (13.25)	270 (17.94)	0.63 [0.20-2.05]	0.79 [0.19-3.24]
>40 years	7 (4.64)	41 (2.72)	2.45 [0.30-20.20]	0.35 [0.02-7.22]
Marital Status				
Married (inc. de facto)	113 (74.83)	1,367 (90.83)	1.00 [referent]	1.00 [referent]
All Other	36 (23.84)	134 (8.90)	**9.65 [3.20-29.05]*****	**9.31 [2.34-37.13]****
Unavailable	2 (1.32)	4 (0.27)		
Occupational Status Scale at Time of Child's Birth				
0-20	50 (33.11)	259 (17.21)	**3.32 [1.08-10.18]***	0.86 [0.20-3.76]
>20-40	38 (25.17)	349 (23.19)	1.21 [0.41-3.64]	0.52 [0.13-2.04]
>40-60	18 (11.92)	391 (25.98)	0.30 [0.09-1.01]	0.17 [0.04-0.75]
>60-80	11 (7.28)	188 (12.49)	0.38 [0.09-1.65]	0.26 [0.04-1.60]
>80-100	27 (17.88)	263 (17.48)	1.00 [referent]	1.00 [referent]
Unavailable	7 (4.64)	55 (3.65)		
Pregnancy & Birth				
Fertility Treatments				
No	132 (87.42)	1,256 (83.46)	1.00 [referent]	1.00 [referent]
Yes	19 (12.58)	249 (16.54)	0.54 [0.18-1.60]	1.32 [0.35-5.00]
Smoking Status During Pregnancy				
No	116 (76.82)	1,302 (86.51)	1.00 [referent]	1.00 [referent]
Yes	35 (23.18)	203 (13.49)	**3.70 [1.06-12.91]***	1.31 [0.38-4.57]
Pre-eclampsia				
No	134 (88.74)	1,326 (88.11)	1.00 [referent]	1.00 [referent]
Yes	17 (11.26)	179 (11.89)	0.98 [0.31-3.14]	2.03 [0.54-7.58]
Gestational Diabetes				
No	140 (92.72)	1,414 (93.95)	1.00 [referent]	1.00 [referent]
Yes	11 (7.28)	91 (6.05)	1.46 [0.32-6.60]	2.41 [0.48-12.17]
Threatened Abortion				
No	144 (95.36)	1,428 (94.88)	1.00 [referent]	1.00 [referent]
Yes	7 (4.64)	77 (5.12)	0.66 [0.11-4.10]	0.11 [0.01-2.11]
Other Pregnancy Related Complications				
No	38 (25.17)	538 (35.75)	1.00 [referent]	1.00 [referent]
Yes	113 (74.83)	967 (64.25)	2.15 [0.89-5.19]	2.05 [0.71-5.92]
Threatened Preterm Labour				
No	131 (86.75)	1,333 (88.57)	1.00 [referent]	1.00 [referent]
Yes	20 (13.25)	172 (11.43)	1.32 [0.42-4.17]	0.70 [0.19-2.61]
APH				
No	142 (94.04)	1,456 (96.74)	1.00 [referent]	1.00 [referent]
Yes	9 (5.96)	49 (3.26)	3.74 [0.62-22.66]	2.17 [0.28-16.92]
Placenta Praevia [a]				
No	151 (100.00)	1,495 (99.34)		
Yes	0 (0.00)	10 (0.66)		
Placental Abruption [a]				
No	149 (98.68)	1,501 (99.73)		
Yes	2 (1.32)	4 (0.27)		
Fetal Distress				
No	132 (87.42)	1,386 (92.09)	1.00 [referent]	1.00 [referent]

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Yes	19 (12.58)	119 (7.91)	2.77 [0.81-9.50]	1.36 [0.33-5.69]
Cephalopelvic Disproportion [a]				
No	151 (100.00)	1,501 (99.73)		
Yes	0 (0.00)	4 (0.27)		
Prolapsed Cord [a]				
No	148 (98.01)	1,495 (99.34)		
Yes	3 (1.99)	10 (0.66)		
Precipitate Delivery [a]				
No	149 (98.68)	1,476 (98.07)		
Yes	2 (1.32)	29 (1.93)		
PPH ≥500mls				
No	96 (63.58)	1,103 (73.29)	1.00 [referent]	1.00 [referent]
Yes	55 (36.42)	402 (26.71)	**2.61 [1.14-5.97]***	1.34 [0.51-3.53]
TSR ≥2mins				
No	119 (78.81)	1,305 (86.71)	1.00 [referent]	1.00 [referent]
Yes	32 (21.19)	200 (13.29)	1.76 [0.80-3.89]	0.77 [0.26-2.34]
Apgar 5-minutes <7 [a]				
No	147 (97.35)	1,476 (98.07)		
Yes	4 (2.65)	29 (1.93)		
Intubation				
No	112 (74.17)	1,277 (84.85)	1.00 [referent]	1.00 [referent]
Yes	39 (25.83)	228 (15.15)	2.31 [1.00-5.33]	2.49 [0.87-7.15]
Early Preterm Birth				
No	123 (81.46)	1,287 (85.51)	1.00 [referent]	1.00 [referent]
Yes	28 (18.54)	218 (14.49)	1.64 [0.59-4.57]	0.77 [0.23-2.57]
POBW <15th Percentile				
No	114 (75.5)	1,117 (74.22)	1.00 [referent]	1.00 [referent]
Yes	23 (15.23)	194 (12.89)	1.51 [0.65-3.54]	1.65 [0.63-4.31]
Unavailable	14 (9.27)	194 (12.89)		
Parity				
0	58 (38.41)	604 (40.13)	1.00 [referent]	1.00 [referent]
1	49 (32.45)	534 (35.48)	1.06 [0.44-2.56]	0.83 [0.23-3.00]
≥2	44 (29.14)	367 (24.39)	1.73 [0.67-4.50]	1.84 [0.31-10.88]
Child				
Sex				
Female	51 (33.77)	799 (53.09)	1.00 [referent]	1.00 [referent]
Male	100 (66.23)	706 (46.91)	**5.21 [2.58-10.52]*****	**5.42 [2.42-12.14]*****
Ethnicity				
Other	137 (90.73)	1,435 (95.35)	1.00 [referent]	1.00 [referent]
Indigenous Australian	14 (9.27)	70 (4.65)	3.96 [0.86-18.29]	2.74 [0.40-18.97]
Child Speaks Language Other Than English at Home				
No	139 (92.05)	1,377 (91.50)	1.00 [referent]	1.00 [referent]
Yes	12 (7.95)	128 (8.50)	0.67 [0.17-2.62]	1.02 [0.22-4.71]
Age Category at Time of AEDC Completion [b]				
1	40 (26.49)	281 (18.67)	2.42 [0.98-5.94]	**2.83 [1.04-7.66]***
2	98 (64.9)	1,101 (73.16)	1.00 [referent]	1.00 [referent]
3	13 (8.61)	123 (8.17)	1.73 [0.46-6.48]	0.59 [0.11-3.13]
Total Number of Siblings				
1	41 (27.15)	467 (31.03)	1.00 [referent]	1.00 [referent]
2	57 (37.75)	597 (39.67)	1.27 [0.50-3.23]	1.78 [0.46-6.81]
3	27 (17.88)	287 (19.07)	1.27 [0.41-3.91]	0.83 [0.14-4.80]
>3	26 (17.22)	154 (10.23)	**4.06 [1.14-14.39]***	2.35 [0.30-18.43]
Sociodemographic				
Index of Relative Socioeconomic Disadvantage				
Lowest Quintile	118 (78.15)	1,255 (83.39)	1.67 [0.59-4.74]	0.67 [0.20-2.31]
> Lowest Quintile	26 (17.22)	211 (14.02)	1.00 [referent]	1.00 [referent]

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Unavailable	7 (4.64)	39 (2.59)		

*p<0.05, **p<0.01, ***p<0.001

[a] Excluded from multivariable analysis due to small N.

[b] Age categories classified as; ≥3 years 10 months to <5 years and one month, 2) ≥5 years and one month to <5 years and 10 months (reference category), 3) ≥5 years and 10 months to <6 years 10 months.

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Table 3. Risk Factors for Developmental Vulnerability on the Emotional Maturity Domain.

Characteristic	DV (N=147) N (%)	NDV (N=1,509) N (%)	Bivariate OR [95% CI]	Multivariable (N=1,352) aOR [95% CI]
Maternal				
Age at Time of Child's Birth				
≤20 years	22 (14.97)	60 (3.98)	**7.09 [2.58-19.51]*****	2.65 [0.67-10.48]
21-25 years	19 (12.93)	185 (12.26)	1.18 [0.50-2.78]	0.98 [0.36-2.70]
26-30 years	34 (23.13)	400 (26.51)	1.00 [referent]	1.00 [referent]
31-35 years	44 (29.93)	554 (36.71)	0.89 [0.46-1.71]	0.95 [0.43-2.11]
36-40 years	23 (15.65)	267 (17.69)	1.02 [0.47-2.23]	0.92 [0.35-2.43]
>40 years	5 (3.40)	43 (2.85)	1.32 [0.29-5.90]	0.42 [0.05-3.69]
Marital Status				
Married (inc. de facto)	111 (75.51)	1,369 (90.72)	1.00 [referent]	1.00 [referent]
All Other	34 (23.13)	136 (9.01)	**4.58 [2.26-9.27]*****	**3.25 [1.28-8.27]***
Unavailable	2 (1.36)	4 (0.27)		
Occupational Status Scale at Time of Child's Birth				
0-20	45 (30.61)	264 (17.50)	1.80 [0.85-3.82]	0.97 [0.36-2.64]
>20-40	34 (23.13)	353 (23.39)	0.88 [0.41-1.87]	0.60 [0.24-1.53]
>40-60	22 (14.97)	387 (25.65)	0.45 [0.20-1.02]	0.34 [0.13-0.90]
>60-80	11 (7.48)	188 (12.46)	0.49 [0.18-1.30]	0.23 [0.06-0.90]
>80-100	28 (19.05)	262 (17.36)	1.00 [referent]	1.00 [referent]
Unavailable	7 (4.76)	55 (3.64)		
Pregnancy & Birth				
Fertility Treatments				
No	126 (85.71)	1,262 (83.63)	1.00 [referent]	1.00 [referent]
Yes	21 (14.29)	247 (16.37)	0.81 [0.40-1.66]	1.10 [0.44-2.73]
Smoking Status During Pregnancy				
No	118 (80.27)	1,300 (86.15)	1.00 [referent]	1.00 [referent]
Yes	29 (19.73)	209 (13.85)	1.70 [0.86-3.36]	0.85 [0.34-2.11]
Pre-eclampsia				
No	129 (87.76)	1,331 (88.20)	1.00 [referent]	1.00 [referent]
Yes	18 (12.24)	178 (11.80)	1.09 [0.50-2.40]	1.96 [0.79-4.86]
Gestational Diabetes				
No	138 (93.88)	1,416 (93.84)	1.00 [referent]	1.00 [referent]
Yes	9 (6.12)	93 (6.16)	1.02 [0.35-2.97]	1.35 [0.43-4.28]
Threatened Abortion				
No	140 (95.24)	1,432 (94.90)	1.00 [referent]	1.00 [referent]
Yes	7 (4.76)	77 (5.10)	0.91 [0.28-3.03]	0.08 [0.01-1.03]
Other Pregnancy Related Complications				
No	35 (23.81)	541 (35.85)	1.00 [referent]	1.00 [referent]
Yes	112 (76.19)	968 (64.15)	**2.13 [1.20-3.80]***	1.87 [0.89-3.92]
Threatened Preterm Labour				
No	125 (85.03)	1,339 (88.73)	1.00 [referent]	1.00 [referent]
Yes	22 (14.97)	170 (11.27)	1.52 [0.72-3.25]	1.14 [0.48-2.69]
APH				
No	139 (94.56)	1,459 (96.69)	1.00 [referent]	1.00 [referent]
Yes	8 (5.44)	50 (3.31)	2.13 [0.62-7.31]	0.64 [0.13-3.20]
Placenta Praevia [a]				
No	146 (99.32)	1,500 (99.40)		
Yes	1 (0.68)	9 (0.60)		
Placental Abruption [a]				
No	145 (98.64)	1,505 (99.73)		
Yes	2 (1.36)	4 (0.27)		
Fetal Distress				
No	128 (87.07)	1,390 (92.11)	1.00 [referent]	1.00 [referent]

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Yes	19 (12.93)	119 (7.89)	1.95 [0.86-4.44]	1.02 [0.38-2.74]
Cephalopelvic Disproportion [a]				
No	147 (100.00)	1,505 (99.73)		
Yes	0 (0.00)	4 (0.27)		
Prolapsed Cord [a]				
No	145 (98.64)	1,498 (99.27)		
Yes	2 (1.36)	11 (0.73)		
Precipitate Delivery [a]				
No	146 (99.32)	1,484 (98.34)		
Yes	1 (0.68)	25 (1.66)		
PPH ≥500mls				
No	95 (64.63)	1,104 (73.16)	1.00 [referent]	1.00 [referent]
Yes	52 (35.37)	405 (26.84)	**1.75 [1.01-3.05]***	1.00 [0.51-1.97]
TSR ≥2mins				
No	119 (80.95)	1,305 (86.48)	1.00 [referent]	1.00 [referent]
Yes	28 (19.05)	204 (13.52)	1.69 [0.91-3.15]	1.12 [0.46-2.70]
Apgar 5-minutes <7 [a]				
No	143 (97.28)	1,480 (98.08)		
Yes	4 (2.72)	29 (1.92)		
Intubation				
No	114 (77.55)	1,275 (84.49)	1.00 [referent]	1.00 [referent]
Yes	33 (22.45)	234 (15.51)	1.78 [0.98-3.21]	1.44 [0.62-3.35]
Early Preterm Birth				
No	119 (80.95)	1,291 (85.55)	1.00 [referent]	1.00 [referent]
Yes	28 (19.05)	218 (14.45)	1.51 [0.76-3.00]	1.01 [0.45-2.27]
POBW <15th Percentile				
No	106 (72.11)	1,125 (74.55)	1.00 [referent]	1.00 [referent]
Yes	24 (16.33)	193 (12.79)	1.48 [0.76-2.87]	1.64 [0.79-3.41]
Unavailable	17 (11.56)	191 (12.66)		
Parity				
0	61 (41.5)	601 (39.83)	1.00 [referent]	1.00 [referent]
1	52 (35.37)	531 (35.19)	0.99 [0.55-1.78]	0.92 [0.39-2.20]
≥2	34 (23.13)	377 (24.98)	0.89 [0.46-1.72]	0.89 [0.25-3.14]
Child				
Sex				
Female	32 (21.77)	818 (54.21)	1.00 [referent]	1.00 [referent]
Male	115 (78.23)	691 (45.79)	**10.13 [4.94-20.79]*****	**9.63 [4.53-20.45]*****
Ethnicity				
Other	131 (89.12)	1,441 (95.49)	1.00 [referent]	1.00 [referent]
Indigenous Australian	16 (10.88)	68 (4.51)	**3.62 [1.36-9.62]***	**5.91 [1.55-22.54]****
Child Speaks Language Other Than English at Home				
No	135 (91.84)	1,381 (91.52)	1.00 [referent]	1.00 [referent]
Yes	12 (8.16)	128 (8.48)	1.00 [0.40-2.49]	0.86 [0.29-2.56]
Age Category at Time of AEDC Completion [b]				
1	37 (25.17)	284 (18.82)	1.57 [0.85-2.90]	1.39 [0.69-2.81]
2	102 (69.39)	1,097 (72.7)	1.00 [referent]	1.00 [referent]
3	8 (5.44)	128 (8.48)	0.62 [0.22-1.77]	0.34 [0.09-1.24]
Total Number of Siblings				
1	45 (30.61)	463 (30.68)	1.00 [referent]	1.00 [referent]
2	59 (40.14)	595 (39.43)	1.05 [0.57-1.95]	1.38 [0.56-3.41]
3	22 (14.97)	292 (19.35)	0.71 [0.32-1.57]	0.83 [0.24-2.80]
>3	21 (14.29)	159 (10.54)	1.62 [0.69-3.80]	1.72 [0.41-7.26]
Sociodemographic				
Index of Relative Socioeconomic Disadvantage				
Lowest Quintile	118 (80.27)	1,255 (83.17)	1.08 [0.54-2.17]	0.56 [0.23-1.36]
> Lowest Quintile	22 (14.97)	215 (14.25)	1.00 [referent]	1.00 [referent]

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Unavailable	7 (4.76)	39 (2.58)		

*p<0.05, **p<0.01, ***p<0.001

[a] Excluded from multivariable analysis due to small N.

[b] Age categories classified as; ≥3 years 10 months to <5 years and one month, 2) ≥5 years and one month to <5 years and 10 months (reference category), 3) ≥5 years and 10 months to <6 years 10 months.

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Table 4. Risk Factors for Developmental Vulnerability on the Language & Cognitive Skills (school-based) Domain.

Characteristic	DV (N=195) N (%)	NDV (N=1,461) N (%)	Bivariate OR [95% CI]	Multivariable (N=1,352) aOR [95% CI]
Maternal				
Age at Time of Child's Birth				
≤20 years	34 (17.44)	48 (3.29)	**77.73 [13.95-433.08]*****	**50.23 [5.53-456.36]*****
21-25 years	41 (21.03)	163 (11.16)	**7.00 [1.97-24.87]*****	**5.29 [1.25-22.34]***
26-30 years	38 (19.49)	396 (27.10)	1.00 [referent]	1.00 [referent]
31-35 years	53 (27.18)	545 (37.30)	1.07 [0.39-2.96]	1.32 [0.40-4.32]
36-40 years	20 (10.26)	270 (18.48)	0.65 [0.19-2.30]	0.98 [0.23-4.28]
>40 years	9 (4.62)	39 (2.67)	5.98 [0.72-49.99]	6.45 [0.53-79.03]
Marital Status				
Married (inc. de facto)	145 (74.36)	1,335 (91.38)	1.00 [referent]	1.00 [referent]
All Other	50 (25.64)	120 (8.21)	**18.44 [5.70-59.63]*****	**4.65 [1.13-19.18]***
Unavailable	0 (0.00)	6 (0.41)		
Occupational Status Scale at Time of Child's Birth				
0-20	70 (35.90)	239 (16.36)	**10.48 [2.85-38.53]*****	2.48 [0.55-11.3]
>20-40	48 (24.62)	339 (23.20)	2.30 [0.67-7.93]	1.26 [0.31-5.17]
>40-60	24 (12.31)	385 (26.35)	0.43 [0.11-1.60]	0.41 [0.09-1.79]
>60-80	7 (3.59)	192 (13.14)	0.19 [0.03-1.17]	0.20 [0.02-1.69]
>80-100	26 (13.33)	264 (18.07)	1.00 [referent]	1.00 [referent]
Unavailable	20 (10.26)	42 (2.87)		
Pregnancy & Birth				
Fertility Treatments				
No	180 (92.31)	1,208 (82.68)	1.00 [referent]	1.00 [referent]
Yes	15 (7.69)	253 (17.32)	0.16 [0.04-0.55]	0.40 [0.08-1.89]
Smoking Status During Pregnancy				
No	145 (74.36)	1,273 (87.13)	1.00 [referent]	1.00 [referent]
Yes	50 (25.64)	188 (12.87)	**6.35 [2.24-18.01]*****	0.30 [0.08-1.18]
Pre-eclampsia				
No	176 (90.26)	1,284 (87.89)	1.00 [referent]	1.00 [referent]
Yes	19 (9.74)	177 (12.11)	0.61 [0.18-2.10]	1.15 [0.27-4.79]
Gestational Diabetes				
No	184 (94.36)	1,370 (93.77)	1.00 [referent]	1.00 [referent]
Yes	11 (5.64)	91 (6.23)	0.84 [0.16-4.44]	0.75 [0.13-4.46]
Threatened Abortion				
No	189 (96.92)	1,383 (94.66)	1.00 [referent]	1.00 [referent]
Yes	6 (3.08)	78 (5.34)	0.36 [0.05-2.41]	0.17 [0.01-3.21]
Other Pregnancy Related Complications				
No	53 (27.18)	523 (35.80)	1.00 [referent]	1.00 [referent]
Yes	142 (72.82)	938 (64.20)	1.96 [0.84-4.54]	1.37 [0.48-3.91]
Threatened Preterm Labour				
No	162 (83.08)	1,302 (89.12)	1.00 [referent]	1.00 [referent]
Yes	33 (16.92)	159 (10.88)	3.21 [0.80-12.92]	1.43 [0.39-5.32]
APH				
No	183 (93.85)	1,415 (96.85)	1.00 [referent]	1.00 [referent]
Yes	12 (6.15)	46 (3.15)	6.80 [0.62-74.13]	5.55 [0.71-43.47]
Placenta Praevia				
No	195 (100.00)	1,451 (99.32)		
Yes	0 (0.00)	10 (0.68)		
Placental Abruption				
No	195 (100.00)	1,455 (99.59)		
Yes	0 (0.00)	6 (0.41)		
Fetal Distress				

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No	173 (88.72)	1,345 (92.06)	1.00 [referent]	1.00 [referent]
Yes	22 (11.28)	116 (7.94)	2.04 [0.45-9.17]	0.63 [0.13-3.10]
Cephalopelvic Disproportion [a]				
No	195 (100.00)	1,457 (99.73)		
Yes	0 (0.00)	4 (0.27)		
Prolapsed Cord [a]				
No	192 (98.46)	1,451 (99.32)		
Yes	3 (1.54)	10 (0.68)		
Precipitate Delivery [a]				
No	190 (97.44)	1,440 (98.56)		
Yes	5 (2.56)	21 (1.44)		
PPH ≥500mls				
No	123 (63.08)	1076 (73.65)	1.00 [referent]	1.00 [referent]
Yes	72 (36.92)	385 (26.35)	**3.13 [1.22-8.05]***	1.72 [0.64-4.64]
TSR ≥2mins				
No	163 (83.59)	1,261 (86.31)	1.00 [referent]	1.00 [referent]
Yes	32 (16.41)	200 (13.69)	0.95 [0.39-2.30]	0.60 [0.20-1.84]
Apgar 5-minutes <7 [a]				
No	193 (98.97)	1,430 (97.88)		
Yes	2 (1.03)	31 (2.12)		
Intubation				
No	159 (81.54)	1,230 (84.19)	1.00 [referent]	1.00 [referent]
Yes	36 (18.46)	231 (15.81)	1.13 [0.49-2.58]	1.46 [0.51-4.13]
Early Preterm Birth				
No	155 (79.49)	1,255 (85.90)	1.00 [referent]	1.00 [referent]
Yes	40 (20.51)	206 (14.10)	2.57 [0.75-8.80]	0.75 [0.21-2.68]
POBW <15th Percentile				
No	142 (72.82)	1,089 (74.54)	1.00 [referent]	1.00 [referent]
Yes	36 (18.46)	181 (12.39)	1.62 [0.72-3.66]	1.74 [0.71-4.26]
Unavailable	17 (8.72)	191 (13.07)		
Parity				
0	51 (26.15)	611 (41.82)	1.00 [referent]	1.00 [referent]
1	81 (41.54)	502 (34.36)	**4.67 [1.71-12.70]****	**6.24 [1.46-26.73]***
≥2	63 (32.31)	348 (23.82)	**6.18 [2.09-18.27]****	6.25 [0.96-40.69]
Child				
Sex				
Female	85 (43.59)	765 (52.36)	1.00 [referent]	1.00 [referent]
Male	110 (56.41)	696 (47.64)	**3.03 [1.60-5.71]*****	**3.57 [1.70-7.49]*****
Ethnicity				
Other	165 (84.62)	1,407 (96.30)	1.00 [referent]	1.00 [referent]
Indigenous Australian	30 (15.38)	54 (3.70)	**34.27 [7.49-156.82]*****	2.08 [0.30-14.36]
Child Speaks Language Other Than English at Home				
No	167 (85.64)	1,349 (92.33)	1.00 [referent]	1.00 [referent]
Yes	28 (14.36)	112 (7.67)	3.82 [0.89-16.47]	1.59 [0.37-6.87]
Age Category at Time of AEDC Completion [b]				
1	48 (24.62)	273 (18.69)	2.09 [0.74-5.89]	1.98 [0.71-5.53]
2	128 (65.64)	1,071 (73.31)	1.00 [referent]	1.00 [referent]
3	19 (9.74)	117 (8.01)	2.56 [0.56-11.82]	1.21 [0.25-5.84]
Total Number of Siblings				
1	41 (21.03)	467 (31.96)	1.00 [referent]	1.00 [referent]
2	79 (40.51)	575 (39.36)	**2.82 [1.01-7.88]***	0.40 [0.09-1.73]
3	35 (17.95)	279 (19.10)	2.40 [0.71-8.13]	0.18 [0.03-1.11]
>3	40 (20.51)	140 (9.58)	**17.34 [4.37-68.74]*****	1.83 [0.25-13.51]
Sociodemographic				
Index of Relative Socioeconomic Disadvantage				
Lowest Quintile	141 (72.31)	1,232 (84.33)	**6.87 [1.80-26.28]****	1.25 [0.39-4.03]

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> Lowest Quintile	46 (23.59)	191 (13.07)	1.00 [referent]	1.00 [referent]
Unavailable	8 (4.10)	38 (2.60)		

*p<0.05, **p<0.01, ***p<0.001

[a] Excluded from multivariable analysis due to small N.

[b] Age categories classified as; ≥3 years 10 months to <5 years and one month, 2) ≥5 years and one month to <5 years and 10 months (reference category), 3) ≥5 years and 10 months to <6 years 10 months.

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Table 5. Risk Factors for Developmental Vulnerability on the Communication Skills & General Knowledge Domain.

Characteristic	DV (N=200) N (%)	NDV (N=1,456) N (%)	Bivariate OR [95% CI]	Multivariable (N=1,352) aOR [95% CI]
Maternal				
Age at Time of Child's Birth				
≤20 years	30 (15.00)	52 (3.57)	**41.57 [7.10-243.32]*****	3.51 [0.36-34.23]
21-25 years	34 (17.00)	170 (11.68)	3.32 [0.87-12.70]	3.65 [0.83-16.03]
26-30 years	46 (23.00)	388 (26.65)	1.00 [referent]	1.00 [referent]
31-35 years	60 (30.00)	538 (36.95)	0.81 [0.28-2.38]	1.77 [0.51-6.05]
36-40 years	22 (11.00)	268 (18.41)	0.49 [0.13-1.84]	1.54 [0.34-7.09]
>40 years	8 (4.00)	40 (2.75)	2.98 [0.29-31.20]	6.24 [0.39-100.11]
Marital Status				
Married (inc. de facto)	160 (80.00)	1,320 (90.66)	1.00 [referent]	1.00 [referent]
All Other	40 (20.00)	130 (8.93)	**14.40 [2.74-75.72]*****	2.24 [0.50-9.97]
Unavailable	0 (0.00)	6 (0.41)		
Occupational Status Scale at Time of Child's Birth				
0-20	68 (34.00)	241 (16.55)	**24.18 [5.14-113.78]*****	5.54 [1.00-30.80]
>20-40	65 (32.50)	322 (22.12)	**11.01 [2.55-47.62]****	**6.60 [1.33-32.64]***
>40-60	21 (10.50)	388 (26.65)	0.68 [0.16-2.99]	0.63 [0.12-3.34]
>60-80	12 (6.00)	187 (12.84)	0.83 [0.14-4.79]	1.00 [0.13-7.32]
>80-100	19 (9.50)	271 (18.61)	1.00 [referent]	1.00 [referent]
Unavailable	15 (7.50)	47 (3.23)		
Pregnancy & Birth				
Fertility Treatments				
No	188 (94.00)	1,200 (82.42)	1.00 [referent]	1.00 [referent]
Yes	12 (6.00)	256 (17.58)	0.10 [0.02-0.39]	0.29 [0.06-1.48]
Smoking Status During Pregnancy				
No	148 (74.00)	1,270 (87.23)	1.00 [referent]	1.00 [referent]
Yes	52 (26.00)	186 (12.77)	**7.79 [2.61-23.28]*****	1.49 [0.41-5.32]
Pre-eclampsia				
No	175 (87.50)	1,285 (88.26)	1.00 [referent]	1.00 [referent]
Yes	25 (12.50)	171 (11.74)	1.07 [0.29-3.90]	1.11 [0.26-4.88]
Gestational Diabetes				
No	187 (93.50)	1,367 (93.89)	1.00 [referent]	1.00 [referent]
Yes	13 (6.50)	89 (6.11)	1.16 [0.20-6.72]	1.23 [0.20-7.42]
Threatened Abortion				
No	192 (96.00)	1,380 (94.78)	1.00 [referent]	1.00 [referent]
Yes	8 (4.00)	76 (5.22)	0.55 [0.09-3.48]	0.27 [0.02-4.28]
Other Pregnancy Related Complications				
No	51 (25.50)	525 (36.06)	1.00 [referent]	1.00 [referent]
Yes	149 (74.50)	931 (63.94)	**2.53 [1.07-6.00]***	1.50 [0.49-4.57]
Threatened Preterm Labour				
No	178 (89.00)	1,286 (88.32)	1.00 [referent]	1.00 [referent]
Yes	22 (11.00)	170 (11.68)	1.00 [0.27-3.61]	0.54 [0.13-2.27]
APH				
No	188 (94.00)	1,410 (96.84)	1.00 [referent]	1.00 [referent]
Yes	12 (6.00)	46 (3.16)	9.09 [0.70-117.63]	1.17 [0.12-11.45]
Placenta Praevia [a]				
No	200 (100.00)	1,446 (99.31)		
Yes	0 (0.00)	10 (0.69)		
Placental Abruption [a]				
No	199 (99.50)	1,451 (99.66)		
Yes	1 (0.50)	5 (0.34)		
Fetal Distress				

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No	172 (86.00)	1,346 (92.45)	1.00 [referent]	1.00 [referent]
Yes	28 (14.00)	110 (7.55)	4.73 [1.00-22.38]	2.73 [0.64-11.65]
Cephalopelvic Disproportion [a]				
No	200 (100.00)	1,452 (99.73)		
Yes	0 (0.00)	4 (0.27)		
Prolapsed Cord [a]				
No	200 (100)	1,443 (99.11)		
Yes	0 (0.00)	13 (0.89)		
Precipitate Delivery [a]				
No	195 (97.50)	1,435 (98.56)		
Yes	5 (2.50)	21 (1.44)		
PPH ≥500mls				
No	122 (61.00)	1,077 (73.97)	1.00 [referent]	1.00 [referent]
Yes	78 (39.00)	379 (26.03)	**3.72 [1.41-9.86]****	2.22 [0.79-6.23]
TSR ≥2mins				
No	163 (81.50)	1,261 (86.61)	1.00 [referent]	1.00 [referent]
Yes	37 (18.50)	195 (13.39)	**2.80 [1.08-7.22]***	1.45 [0.47-4.45]
Apgar 5-minutes <7 [a]				
No	198 (99.00)	1,425 (97.87)		
Yes	2 (1.00)	31 (2.13)		
Intubation				
No	162 (81.00)	1,227 (84.27)	1.00 [referent]	1.00 [referent]
Yes	38 (19.00)	229 (15.73)	1.91 [0.80-4.56]	1.27 [0.44-3.71]
Early Preterm Birth				
No	157 (78.50)	1,253 (86.06)	1.00 [referent]	1.00 [referent]
Yes	43 (21.50)	203 (13.94)	3.73 [0.99-14.09]	1.95 [0.57-6.75]
POBW <15th Percentile				
No	146 (73.00)	1,085 (74.52)	1.00 [referent]	1.00 [referent]
Yes	36 (18.00)	181 (12.43)	1.83 [0.78-4.33]	1.74 [0.71-4.29]
Unavailable	18 (9.00)	190 (13.05)		
Parity				
0	65 (32.50)	597 (41.00)	1.00 [referent]	1.00 [referent]
1	68 (34.00)	515 (35.37)	1.51 [0.59-3.86]	1.26 [0.30-5.35]
≥2	67 (33.50)	344 (23.63)	**4.54 [1.47-14.09]****	1.48 [0.23-9.64]
Child				
Sex				
Female	87 (43.50)	763 (52.40)	1.00 [referent]	1.00 [referent]
Male	113 (56.50)	693 (47.60)	**3.00 [1.56-5.79]****	**3.25 [1.50-7.03]****
Ethnicity				
Other	179 (89.50)	1,393 (95.67)	1.00 [referent]	1.00 [referent]
Indigenous Australian	21 (10.50)	63 (4.33)	**21.66 [2.34-200.50]****	1.06 [0.13-8.59]
Child Speaks Language Other Than English at Home				
No	161 (80.50)	1,355 (93.06)	1.00 [referent]	1.00 [referent]
Yes	39 (19.50)	101 (6.94)	**11.16 [3.30-37.77]*****	**15.16 [3.57-64.30]*****
Age Category at Time of AEDC Completion [b]				
1	57 (28.5)	264 (18.13)	**5.60 [1.73-18.09]****	**5.11 [1.71-15.30]****
2	125 (62.5)	1074 (73.76)	1.00 [referent]	1.00 [referent]
3	18 (9)	118 (8.1)	1.91 [0.44-8.30]	1.63 [0.31-8.57]
Total Number of Siblings				
1	49 (24.50)	459 (31.52)	1.00 [referent]	1.00 [referent]
2	77 (38.50)	577 (39.63)	1.54 [0.58-4.13]	0.89 [0.20-3.94]
3	37 (18.50)	277 (19.02)	1.64 [0.49-5.44]	1.07 [0.17-6.68]
>3	37 (18.50)	143 (9.82)	**15.85 [2.91-86.42]****	4.07 [0.48-34.74]
Sociodemographic				
Index of Relative Socioeconomic Disadvantage				
Lowest Quintile	153 (76.50)	1,220 (83.79)	**4.24 [1.12-16.03]***	0.69 [0.20-2.44]

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> Lowest Quintile	42 (21.00)	195 (13.39)	1.00 [referent]	1.00 [referent]
Unavailable	5 (2.50)	41 (2.82)		

*p<0.05, **p<0.01, ***p<0.001

[a] Excluded from multivariable analysis due to small N.

[b] Age categories classified as; ≥3 years 10 months to <5 years and one month, 2) ≥5 years and one month to <5 years and 10 months (reference category), 3) ≥5 years and 10 months to <6 years 10 months.

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-10
Bias	9	Describe any efforts to address potential sources of bias	7-10
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10
		(*b*) Describe any methods used to examine subgroups and interactions	10
		(*c*) Explain how missing data were addressed	10
		(*d*) If applicable, explain how loss to follow-up was addressed	10
		(*e*) Describe any sensitivity analyses	10
Results			

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Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10-11
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10-11
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-11
		(*b*) Report category boundaries when continuous variables were categorized	10-11
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	4
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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BMJ Open

The associations between biological and sociodemographic risks for developmental vulnerability in twins at age five: A population data linkage study in Western Australia.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-038846.R1
Article Type:	Original research
Date Submitted by the Author:	02-Jul-2020
Complete List of Authors:	Dhamrait, Gursimran; Telethon Kids Institute, ; The University of Western Australia Faculty of Health and Medical Sciences, School of Population and Global Health Christensen, Daniel; Telethon Kids Institute; The University of Western Australia Pereira, G.F; Telethon Kids Institute; Curtin University, School of Public Health Taylor, Catherine; Telethon Kids Institute; University of Western Australia,
Primary Subject Heading:	Paediatrics
Secondary Subject Heading:	Public health, Epidemiology
Keywords:	EPIDEMIOLOGY, PAEDIATRICS, PUBLIC HEALTH

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Manuscript

Title: The associations between biological and sociodemographic risks for developmental vulnerability in twins at age five: A population data linkage study in Western Australia.

Gursimran K. Dhamrait,[1,2] Daniel Christensen,[1,3] Gavin Pereira[1,4,5] and Catherine L. Taylor.[1,3]

[1]Telethon Kids Institute, Nedlands, Western Australia, Australia.

[2]School of Population and Global Health, The University of Western Australia, Nedlands, Western Australia, Australia.

[3]Centre for Child Health Research, The University of Western Australia, Nedlands, Western Australia, Australia.

[4]School of Public Health, Curtin University, Perth, Australia.

[5]Centre for Fertility and Health (CeFH), Norwegian Institute of Public Health, Oslo, Norway.

Address correspondence to:

Gursimran K. Dhamrait

Telethon Kids Institute

15 Hospital Avenue, Nedlands, Western Australia, Australia.

Phone: 61+ 8 9489 1183

Fax: 61+ 8 9489 7700

Email: gursimran.dhamrait@telethonkids.org.au

Main Body Word Count: 4,181 words

Abstract Word Count: 300 words

Short Title: Developmental vulnerability in twins at age five

Abbreviations

AEDC: Australian Early Development Census

ARIA: Accessibility and Remoteness Index of Australia

AUSEI06: Australian Socioeconomic Index 2006

DV1: Developmentally Vulnerable on one or more Australian Early Development Census domains

DV2: Developmentally Vulnerable on two or more Australian Early Development Census domains

CI: Confidence Interval

IRSD: Index of Relative Socioeconomic Disadvantage

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MNS: Midwives Notifications System

OR: Odds Ratio

POBW: Proportion of Optimal Birthweight

WA: Western Australia

Keywords (max of 5):

Twins, Australian Early Development Census, Child Development, Record Linkage.

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Abstract

Objective: To investigate the prevalence of, and associations between, prenatal and perinatal risk factors and developmental vulnerability in twins at age five.

Design: Retrospective cohort study using bivariate and multivariable logistic regression.

Setting: Western Australia (WA), 2002-2015.

Participants: 828 twin pairs born in WA with an Australian Early Development Census (AEDC) record from 2009, 2012 or 2015.

Main Outcome Measures: The AEDC is a national measure of child development across five domains. Children with scores <10th percentile were classified as developmentally vulnerable on, one or more domains (DV1), or two or more domains (DV2).

Results: In this population, 26.0% twins were classified as DV1 and 14.1% as DV2. In the multivariable model, risk factors for DV1 were; maternal age <25 years (OR 7.06, 95% CI 2.29-21.76), child speaking a language other than English at home (OR 6.45, 95% CI 2.17-19.17), male child (OR 5.08, 95% CI: 2.89-8.92), age younger than the reference category for the study sample (≥5 years one month to <5 years 10 months) at time of AEDC completion (OR 3.34, 95% CI: 1.55-7.22), and having a proportion of optimal birthweight (POBW) <15th percentile of the study sample (OR 2.06, 95% CI 1.07-3.98). Risk factors for DV2 were; male child (OR 7.87, 95% CI: 3.45-17.97), maternal age <25 years (OR 5.60, 95% CI: 1.30-24.10), age younger than the reference category (OR 5.36, 95% CI: 1.94-14.82), child speaking a language other than English at home (OR 4.65, 95% CI: 1.14-19.03), mother's marital status as not married at the time of twins' birth (OR 4.59, 95% CI: 1.13-18.55), maternal occupation status in the lowest quintile (OR 3.30, 95% CI: 1.11-9.81) and having a POBW <15th (OR 3.11, 95% CI: 1.26-7.64).

Conclusion: Both biological and sociodemographic risk factors are associated with developmental vulnerability in twins at five years of age.

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Article Summary

Strengths and Limitations

- The study is based on a large population-level sample of 1,656 twins.
- This is the first twin study to assess developmental vulnerabilities in an otherwise healthy sample of Australian twins, at the time of their first year of full-time school.
- Bivariate and multivariable logistic regression analysis with the calculation of adjusted odds ratios was performed to explore the associations between a large range of prenatal and perinatal risk factors.
- Twin pairs for which data was complete were used for the analysis.
- The datasets used in this study did not report on twin zygosity nor on complications of pregnancy that are specific to multiple pregnancies (e.g., twin reversed arterial perfusion, twin-twin transfusion syndrome).

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Introduction

The increased use of assisted reproductive technologies and increasing maternal age at conception have attributed to a significant increase in the number of multifetal pregnancies around the world.[1] Multifetal pregnancies are classified as high risk pregnancies and are associated with higher rates of pregnancy complications and adverse neonatal and perinatal outcomes, compared to singleton pregnancies.[2-6] The majority of the literature assessing higher order pregnancies has focused primarily on birth outcomes, including preterm birth,[7] low birth weight,[3] and developmental disabilities such as cerebral palsy.[8] Studies that have assessed longer-term developmental outcomes of twins have focused on developmental outcomes around the age of two years.[9] Such studies have reported that twins had poorer performance, in comparison to singletons, on a range of domains including; communication, gross and fine motor skills, problem solving, personal-social skills, and language development.[10,11] Furthermore, most studies examining child development outcomes at school starting age have focused on singleton children, from a single family and have compared children across families.[12] There is a paucity of research on the developmental vulnerability of multifetal pregnancies such as twins, around the time that they commence formal education.

Child development outcomes can vary significantly based on numerous factors including the child's personal characteristics, such as personal dispositions and abilities, social constructs and the environments, both intrauterine and extrauterine, in which they develop.[13-16] Studies that have assessed cognitive and school performance outcomes at the age of five have reported that children who are born preterm,[17-24] with a low birth weight,[25-28] are small for gestational age,[29,30] and male[31-34] are more likely to have poorer developmental outcomes. In comparison to singletons, twins are more likely to be classified as preterm[35] or low birth weight, and have fetal growth restriction.[36] Studies have reported that twins are more likely to have poorer neurodevelopmental outcomes compared to singletons, even after controlling for gestational age and birthweight.[37] A study reported that twins scored lower than singletons in both the Verbal and Performance IQ domains of the Wechsler Preschool and Primary Scale of Intelligence, at the ages of four and five years.[38] Likewise, twin studies have also reported sex differences, with girls scoring higher than boys at ages four and five

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years.[38] The cumulative nature of school-based learning means that developmental gaps at school entry, are difficult to close over time.[39] Children who begin school with poor school readiness often struggle to catch up with their peers and tend to fall further behind as they progress through the subsequent years of schooling.[39] As the educational achievement trajectories are largely established by 7 years of age (year 3) children with poor school readiness are more likely to have lower later-life educational achievement.[40] Given the higher rates of pregnancy, neonatal and perinatal adversities observed in twins in comparison to singletons, twins are particularly at risk for developmental delays in the early childhood period.

Twin studies, assessing the contribution of genes and the environment, have supported the hypothesis that both factors impact child development.[41-44] Yet, a number of studies have reported no significant differences in child development outcomes based on zygosity.[38,45,46] Sociodemographic factors such as low socioeconomic status and low levels of parental education, have also been identified to adversely impact child development outcomes.[47-49] A study conducted in younger twins (assessed at age 6, 12 and 18 months) reported that biological factors including low birth weight, were associated with poorer early cognitive and non-cognitive, independently of environmental factors, such as socioeconomic status.[3] Alternatively, a study reported that the environmental factors shared by twins of the same family, were more significantly associated with early language skills and school readiness in twins at the age of five years, in comparison to genetic factors.[45] Overall, studies assessing both biological and sociodemographic factors and their impact on the longer-term child development of children born from multiple pregnancies remain sparse and the results of the existing studies are mixed.

The aim of this study was to examine the prevalence of, and the association between, biological and sociodemographic risk factors and developmental vulnerability in twins in their first year of full-time school.

Methods

Data Sources and Study Population

Data Sources

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This study used anonymised individual-level data from the Midwives Notification System (MNS), which is statutory record of all births (still- or live-born) in WA with either a birthweight >400 grams and/or a final gestational length of ≥20 weeks. Variables from MNS were cross validated with corresponding records from WA Birth Registrations. Australian Early Development Census (AEDC) records were obtained for all available years (2009, 2012 and 2015) for all children with WA birth and perinatal records. WA Register for Developmental Anomalies (WARDA) records were used to identify children who had a diagnosed developmental disability between birth and age five years. Statistical linkage of all records, by matching identifiers (e.g. name, address, date of birth etc.) common to sets of records,[50] was provided by the WA Data Linkage Branch from the Department of Health WA.

Patient and Public Involvement

No patients were involved in the development of the research question or the outcome measures, or in the development of the plans for the design or implementation of the study.

Study Population

The study population included all children born in WA with an AEDC record in either 2009, 2012 or 2015 (N=73,903). Children were excluded from the study if; 1) they were not from a twin birth (N=71,748), 2) they were identified by their teacher as having 'special-needs' based on a diagnosed physical and/or intellectual disability (N=123), 3) they were reported as having any birth defect in the WARDA datasets (N=119), 4) they had an AEDC score that was either incomplete or missing (N=22), or 5) their twin sibling was excluded based on the aforementioned exclusion criteria (N=235; Figure 1). The final study sample consisted of N=1,656 children; N=828 twin pairs. There were 252 opposite sex twin pairs and 576 same sex twin pairs (277 male and 299 female twin pairs).

Outcome Measure

The AEDC is a national census of early childhood development spanning five developmental domains; 1) Physical Health and Wellbeing, 2) Social Competence, 3) Emotional Maturity, 4) Language and Cognitive skills (school-based), and 5) Communication Skills and General Knowledge. The AEDC is conducted every three years, with the first national data collection conducted in 2009.

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Children with scores <10th percentile in a given domain are classified as 'developmentally vulnerable.' AEDC cut-off scores are based on the first national AEDC data collection in 2009 and apply to all AEDC data collections. Domain scores for children with special needs are not included in the AEDC results. Two outcomes measures were used; developmentally vulnerable on one or more AEDC domains (DV1) and developmentally vulnerable on two or more AEDC domains (DV2).

Risk Variables

Maternal Variables

Maternal age and marital status at child's birth were obtained from the MNS and Birth Registrations. Maternal occupation at birth was obtained from Birth Registrations data and converted to a four-digit standard code using the Australian and New Zealand Standard Classification of Occupations. These codes were then assigned a value ranging from 0-100 using the Australian Socioeconomic Index 2006 (AUSEI06).[51] Low AUSEI06 values are representative of low-status occupations and high values represent high-status occupations. This variable was collapsed into two categories; most disadvantaged quintile (i.e. AUSEI06 [0-20]) and greater than the most disadvantaged quintile (i.e. AUSEI06 >20). An AUSEI06 value of zero was assigned to records if occupation was reported as 'unemployed', 'stay at home parent' or 'pensioner.' For records where maternal occupation was not stated, an AUSEI06 value was not assigned and these cases were reported as missing.

Pregnancy and Birth Variables

We included several binary pregnancy and birth variables to indicate either the presence or absence; of fertility treatments, smoking during pregnancy, pre-eclampsia, gestational diabetes, threatened abortion, threatened preterm labour, antepartum haemorrhage (APH), placenta praevia, placental abruption, fetal distress, cephalopelvic disproportion, prolapsed cord, precipitate delivery, post-partum haemorrhage (PPH), intubation status, early preterm birth (<34 weeks of gestational age), and time to Spontaneous Respiration (TSR); with a TSR of ≥2 minutes forming the 'at risk' group and five-minute Apgar score; with a five-minute Apgar score of <7 forming the 'at risk' group.

The proportion of optimal birthweight (POBW) is a measure of fetal growth and is defined as birth weight divided by expected birth weight, in the absence of pathologic risk factors. This measure also

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accounts for non-pathologic determinants of growth, including gestational age, birth order, sex of the child and maternal height[52] and has been validated against ultrasound measurements.[53] We derived a binary proxy for fetal growth restriction as POBW <15th percentile, which corresponded to an observed birth weight less than 75.75% of that expected.[9]

We derived a general category for other pregnancy related complications (not elsewhere stated; such as urinary tract infection, pre-labour rupture of membranes) for all records. As records may have multiple pregnancy related complications, all records that had a complication that was not elsewhere stated in this study or had multiple complications of which at least one complication was not elsewhere stated in this study, formed the 'at risk' group for this variable.

Child Variables

Sex and ethnicity of child was obtained from the MNS and Birth Registrations. Age at the time of AEDC completion and language other than English spoken at home by the child were obtained from the AEDC. Age of children at the time of AEDC completion ranged between; ≥3 years 10 months to <6 years 10 months, with a mean of age category of, ≥5 years one month to 5 years 10 months. To balance frequencies, the age of children at the time of AEDC completion was categorised into three groups; 1) ≥3 years 10 months to <5 years and one month, 2) ≥5 years one month to <5 years 10 months (reference category) and 3) ≥5 years 10 months to <6 years 10 months.

The total number of siblings were derived as the number of live births to each mother prior to the year that the cohort child had the AEDC conducted. Siblings who died within the neonatal period (i.e. mode of separation post-birth from the hospital was death) were excluded in the calculations for total number of siblings.

Sociodemographic Variables

The Index of Relative Socioeconomic Disadvantage (IRSD)[19] was calculated using the residential address at the time of birth. ISRD is derived from Australian Census data and reflects area-level disadvantage through variables such as low household income, low educational attainment and high levels of unemployment. This variable was collapsed into two groups; most disadvantaged quintile (i.e. ISRD quintile 1) and greater than the most disadvantaged quintile (i.e. ISRD quintiles 2-5).

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Statistical Modelling

For each risk variable, the 'least risk' category (e.g. not early preterm birth) was used as the reference category (Table 1). To estimate the risk of a child being classified as DV1 and DV2, a generalised linear mixed model with a logit link function was used with a random intercept for each twin pair. A total of 30 maternal, pregnancy, birth, child and sociodemographic risk variables were considered for the multivariable models. For DV1, DV2, and each of the five AEDC domains, 24 risk variables were included in the multivariable models; six risks variables were excluded from multivariable analysis due to the prevalence being too small (total N<50 for a given category of a given variable). The variables excluded were; 1) placenta praevia, 2) placental abruption, 3) cephalopelvic disproportion, 4) prolapsed cord, 5) precipitate delivery and 6) a five-minute Apgar score of <7. All variables were added simultaneously to the models. Odds ratios (OR) and the associated 95% confidence intervals (CIs) were estimated for both unadjusted and adjusted models. All analyses were undertaken using PROC GLIMMIX in SAS version 9.4 for Windows.[54]

Results

Prevalence of developmental vulnerability in twins

A total of 431 (26.0%) twins were classified as DV1 (Table 1). A total of 151 (18.2%) twin pairs had one twin identified as DV1 and 140 (16.9%) twin pairs had both twins were identified as DV1. Of the 24 maternal, pregnancy and birth, child and sociodemographic risk variables considered in the multivariable models, five variables had a statistically significant association with an increased risk of a twin being classified as DV1. In order of decreasing magnitude of associated risk, the ORs were; maternal age of <25 younger at time of twins' birth (OR 7.06, 95% CI 2.29 to 21.76), child speaks language other than English at home (OR 6.45, 95% CI 2.17 to 19.17), male twins (OR 5.08, 95% CI 2.89 to 8.92), child's age younger than the reference category for the study sample (≥5 years one month to 5 years 7 months) at time of AEDC completion (OR 3.34, 95% CI: 1.55 to 7.22), and POBW <15th percentile (OR 2.06, 95% CI 1.07 to 3.98).

A total of 223 (14.1%) twins were classified as DV2 (Table 2). In 95 (11.5%) twin pairs, one twin was identified as DV2 and in 64 twin pairs (7.9%), both twins were identified as DV2. Of the 24 maternal,

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pregnancy and birth, child and sociodemographic risk variables considered in the adjusted models, seven variables had a statistically significant association with an increased risk of a twin being classified as DV2. Risk factors for DV2 were, in order of decreasing magnitude; male twins (OR 7.87, 95% CI: 3.45 to 17.97), maternal age of <25 younger at time of twins' birth (OR 5.60, 95% CI: 1.30 to 24.10), child's age younger than the reference category at time of AEDC completion (OR 5.36, 95% CI: 1.94 to 14.82), child speaking a language other than English at home (OR 4.65, 95% CI: 1.14 to 19.03), mother's marital status as not married at the time of twins' birth (OR 4.59, 95% CI: 1.13 to 18.55), maternal occupation status in the lowest quintile (OR 3.30, 95% CI: 1.11 to 9.81) and POBW <15th percentile (OR 3.11, 95% CI: 1.26 to 7.64).

Associations with domain-specific developmental vulnerability

A total of, 188 (11.4%) children were classified as developmentally vulnerable for the domains of: Physical Health and Wellbeing; 151 (9.1%) for Social Competence; 147 (8.9%) for Emotional Maturity; 195 (11.8%) for Language and Cognitive Skills (school-based); and 200 (12.0%) for Communication Skills and General Knowledge (Supplementary Tables 1-5, respectively). These results were broadly consistent with the findings for the aggregate measures of developmental vulnerability (DV1 and DV2). All variables that were statistically significant in the aggregated measures of developmental vulnerability were statistically significant for the domains.

Discussion

This study examined the associations between biological and sociodemographic risk factors and developmental vulnerability in twins in their first year of full-time school. To our knowledge, our study is the first of this scale (population-level sample of twins; N>1,600) to report on the prevalence of developmental vulnerabilities, in an otherwise healthy sample twins, at the time of their first year of full-time school. As studies have reported that twins are more likely to have poorer performance, in comparison to singletons, at the age of two[10,11] it was pertinent to assess if the prevalence rates of developmental vulnerabilities is higher in twins at age five. We reported that in the WA population, 26.0% of twins were classified as DV1 and 14.1% as DV2 across the 2009, 2012 and 2015 AEDC cycles. In the general WA population, which includes twins and higher order multiples, 23.0% of

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children were classified as DV1 and 11.3% of children were classified as DV2, across these AEDC cycles.[55] A large cohort study of 99,530 singleton children from New South Wales reported that 20.8% were classified as DV1 across the 2009 and 2012 AEDC cycles.[56] Thus, we found that twins are at an elevated risk of developmental vulnerability relative to a general population of children in the state of Western Australia and in a singleton population in New South Wales. This is consistent with findings from a study of 142 twin pairs from the Louisville Twin Study, that reported twins scored lower than singletons in both the Verbal and Performance IQ domains of the Wechsler Preschool and Primary Scale of Intelligence at both four and five years of age.[38] As our results were obtained from a sample of twins without any diagnosed developmental disabilities, the higher prevalence rates of twins being classified as DV1 and DV2 observed in our study, when compared to the general Australian population, suggests that healthy twins are more likely to be classified as developmental vulnerable on AEDC domains at school starting age when compared to their singleton counterparts.

The biological factors associated with developmental vulnerability in twins were; male sex, fetal growth restriction, and younger chronological age at the time of AEDC completion. These results are in line with singleton studies[31,57] which have reported that male children are more likely to be classified as developmentally vulnerable in their first year of full-time school, in comparison to female children. A study conducted in South Australia of 13,827 children, of which 3.4% where twins, also reported that male twins were more likely to be classified as DV2, when compared to female twins, however this finding was not statistically significant.[58] The Louisville Twin Study also reported sex differences, with females scoring higher on Full Scale, Verbal, and Performance IQ, than males at ages four and five years, however, scores tended to converge at six years of age.[38]

We also reported that twins younger than the reference category for this sample were more likely to be classified as developmentally vulnerable in their first year of full-time school. A study of 840 Canadian five-year old twins, aiming to assess the genetic and environmental factors influencing school readiness, reported that in the preliminary models age was positively correlated with the spatial recognition, numbers, and the letters components of the Lollipop test.[59] Furthermore, a recent

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discussion paper identified the need for further research to assess the effects of delaying school entry for twins[60] thus, highlighting that further research is required to better understand if delaying school entry is beneficial for both short-term and long-term academic outcomes in twins.

The sociodemographic risk factors associated with developmental vulnerability in twins included; maternal age and occupational status, and a not married maternal marital status, at the time of twins' birth, and the child speaking a language other than English at home. These results are supported by the South Australian study, that examined a range of variables also included in our study.[58] This study reported that maternal age, marital status and maternal occupation were associated with an increased risk of children being classified as DV2 on the AEDC.[58] The South Australian study also reported that parity and smoking during pregnancy were also associated with an increased risk of children being classified as DV2.[58] In our study we observed an increased but insignificant association between these risk variables and twins being classified as either DV1 or DV2.

An interesting finding from our study was that speaking a language other than English at home was associated with an increased risk for twins being classified as DV1 and DV2. Previous studies have reported that approximately a fifth of Australian children are bilingual,[61] and the prevalence of twins speaking a language other than English at home in our study were in line with these results. Results from a study of an Australia wide study of 261,147 children, singletons and multiples, from the 2009 AEDC cycle reported that bilingual children proficient in English have been reported to have equal or slightly lower odds of being classed as DV1 when compared to their English-speaking background peers.[61] However, unlike our study, this study[61] did not report differences in developmental vulnerability based on plurality. Additionally, a Canadian study examining the school readiness profiles of 95,537 children in British Columbia[62] reported that bilingualism was associated with positive social, emotional and cognitive development, as measured by the Early Development Index.[34] Differences in results may be attributed to the fact bilingualism may be a risk factor for twins however, it may not be a significant risk factor in a general population sample. The language groups most commonly spoken in WA after English (Mandarin, Italian and Vietnamese)[63] are different to

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those most prevalent in British Colombia (Punjabi, Chinese and German).[64] Thus, the difference in findings between the Canadian study and our results may be attributable to this fact.

Our findings have some accord with a cohort study examining the associations between biological and sociodemographic risk factors on late language emergence in 473 twins pairs at the age of two years.[9] Taylor et al. reported that the risk factors for late language emergence in twins, without developmental disabilities, include fetal growth restriction.[9] Interestingly, our study also identified fetal growth restriction as a risk factor for developmental vulnerability at age five, suggesting that the biological implications of a suboptimal intrauterine environment may be persist beyond infancy and into early childhood in twins who did not have diagnosed developmental disabilities. In contrast to our study, the Taylor et al. twin sample excluded twins with exposure to languages other than English. Their study found that sociodemographic risk factors (low maternal education, socioeconomic area disadvantage) were not associated with late language emergence at age two years. Our results suggest that sociodemographic factors including, maternal; age, marital status and occupational status, at time of twins' birth, and the child speaking a language other than English at home are also associated with an increased risk of developmental vulnerability at age five.[9] The differences in findings between this study and our study suggest that sociodemographic characteristics may play a more significant role as risk variables at age five years compared to at the age of two years. This hypothesis is supported by a subsequent study of twins aged four years and six years, which reported that higher maternal education and older maternal age showed positive effects on language and non-verbal phenotypes.[6] Furthermore, a study of a twin sample from the Quebec Newborn Twin Study, reported that environmental factors, such as socioeconomic status, rather than genetic factors were attributable to the predictive association observed between early language skills and school readiness, as measured by the Lollipop Test, in twins 63-months of age.[45] In our study, zygosity of twins could not be established as WA administrative data does not contain information on zygosity. Furthermore, we did not aim to assess the impact of within twin-pair discordance in regards to developmental vulnerabilities at age five. Thus, further research is required to better elucidate the impact and

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interplay of biological and sociodemographic risk variables at different stages of development in twins.

Studies assessing twin-singleton differences often control for or select for factors such as prematurity, low birth weight, or parental socioeconomic status.[57,65,66] Our study however, draws attention to adverse effects of other risk factors, including POBW and maternal marital status, on child development outcomes at age five. An Australian cohort study of 1,922 children from the Northern Territory using linked administrative data, reported an increased, but non-significant, risk of twins being classified as DV1 on the AEDC, after controlling for a range of biological and sociodemographic variables used in our study including; sex, 5-minute Apgar score <7, area remoteness, ethnicity, child speaks a language other than English at home and maternal age at time of child's birth.[57] Although this study gave consideration to plurality as a risk factor for developmental vulnerability, it did not aim to assess the association between a comprehensive set of biological and sociodemographic risk factors. A Canadian study of 5-year old twins reported that shared environmental factors substantially accounted for cognitive school readiness (as measured by the Lollipop Test) as compared to genetic effects.[59] Likewise other studies have also reported that a range of family factors, which would be assumed to be shared by both twins, such as family income, maternal occupation, and employment status are associated with cognitive school readiness.[67,68] Further studies in this area are required, as the extent and nature of the risk factors associated with developmental vulnerability at age five in twins, remain not well-established.

Preventative intervention studies have reported that programs designed to improve school readiness and high quality early childhood education and care, are effective for at-risk populations and can have significant long-term results.[69,70] The higher prevalence rates of DV1 and DV2 in twins observed in this study are indicative of the fact that twins form an at-risk group in terms of developmental vulnerability at the time at which children commence full-time school. Therefore, it is pertinent for those working in the early childhood education sector and for parents to be aware of the developmental vulnerabilities present in twins at the age at which children begin full-time school. In Australia, there has been call to provide increased quantity and quality of support service and

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resources are required for twins and their families due to increased vulnerability[60] and the results of our study highlight this need.

Conclusions

Both biological and sociodemographic risk factors are associated with developmental vulnerability at the age of five in twins. The findings of our study suggest that twins are more likely to be classified as developmentally vulnerable at school starting age when compared to their singleton counterparts. In particular, the results draw attention to the hypothesis that prenatal and more significantly perinatal risk factors and sociodemographic environments in which twins are raised can impact developmental vulnerability in early childhood.

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Acknowledgements:

We gratefully acknowledge the WA Data Linkage Branch and the data custodians who provided data for this study and the people of Western Australia for the use of their administrative data. This study does not necessarily reflect their views. This study uses data from the Australian Early Development Census (AEDC). The AEDC is funded by the Australian Government Department of Education and Training. The findings and views reported are those of the authors and should not be attributed to the Department or the Australian Government.

Ethics Approval:

Ethics approval for this study was granted by the Western Australian Department of Health Human Research Ethics Committee (2016/51) and the University of Western Australia Human Research Ethics Committee (RA/4/20/4776).

Declaration of interests:

The authors declare that they have no competing interests, no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Funding:

This study was supported by National Health and Medical Research Grants (GNT1173991 and GNT1099655 to GP), the Research Council of Norway through its Centres of Excellence funding scheme (#262700 to GP) and the Australian Research Council Centre of Excellence for Children and Families over the Life Course (CE140100027 to CLT and DC). GKD was supported by the ARC Centre of Excellence for Children and Families over the Life Course Scholarship, the ARC Centre of Excellence for Children and Families over the Life Course Top-Up Scholarship and the Stan and Jean Perron Top-Up Scholarship.

Author Contributions:

GKD: led study conceptualisation and design, conducted the literature review, performed data manipulation, analysis and interpretation of findings, drafted the initial manuscript and reviewed and revised the manuscript critically for important intellectual content.

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DC, GP and CLT: contributed to the study inception, the development of the design, interpretation of the results, manuscript revisions, the interpretation of the results and revised the manuscript critically for important intellectual content.

GKD, DC, GP and CLT: approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Data Sharing:

The linked administrative data are owned by the government departments who approved the linkage and use of the data for this study. Use of the study data is restricted to named researchers. The current Human Research Ethics Committee approvals were obtained for public sharing and presentation of data on group level only, meaning the data used in this study cannot be shared by the authors. Collaborative research may be conducted according to the ethical requirements and relevant privacy legislations. Potential collaborators should contact author GP with their expression of interest. The steps involved in seeking permission for linkage and use of the data used in this study are the same for all researchers.

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Figures & Tables: (Total 1 Figure & 2 Tables)

Figure 1. Eligible Cohort and Numbers Included for Analyses.
AEDC = Australian Early Development Census. WARDA= Western Australian Register of Developmental Anomalies.

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Table 1. Risk factors for children who are developmentally vulnerable on one or more AEDC domains (DV1).

Characteristic	DV1 (N=431) N (%)	NDV1 (N=1,225) N (%)	Bivariate OR [95% CI]	p-value	Multivariable (N=1,352) aOR [95% CI]	p-value
Maternal						
Age at Time of Child's Birth (years)						
<25	105 (24.36)	117 (9.55)	**9.66 [3.68-25.32]**	**<0.0001**	**7.06 [2.29-21.76]**	**0.0007**
25-29	90 (20.88)	294 (24.00)	1.00 [referent]		1.00 [referent]	
30-34	130 (30.16)	476 (38.86)	0.81 [0.38-1.72]	0.5763	0.89 [0.38-2.07]	0.7796
≥35	106 (24.59)	338 (27.59)	1.06 [0.48-2.36]	0.8856	1.19 [0.47-2.99]	0.7149
Marital Status						
Married (inc. de facto)	357 (82.83)	1,123 (91.67)	1.00 [referent]		1.00 [referent]	
All Other	72 (16.71)	98 (8.00)	**5.99 [2.43-14.75]**	**0.0001**	2.26 [0.76-6.71]	0.1401
Unavailable	2 (0.46)	4 (0.33)				
Occupational Status Scale at Time of Child's Birth						
0-20	122 (28.31)	187 (15.27)	**5.58 [2.71-11.46]**	**<0.0001**	1.83 [0.79-4.26]	0.1586
>20-100	279 (64.73)	1,006 (82.12)	1.00 [referent]		1.00 [referent]	
Unavailable	30 (6.96)	32 (2.61)				
Pregnancy & Birth						
Fertility Treatments						
No	377 (87.47)	1,011 (82.53)	1.00 [referent]		1.00 [referent]	
Yes	54 (12.53)	214 (17.47)	0.43 [0.19-0.97]	0.0417	0.84 [0.32-2.23]	0.7291
Smoking Status During Pregnancy						
No	339 (78.65)	1,079 (88.08)	1.00 [referent]		1.00 [referent]	
Yes	92 (21.35)	146 (11.92)	**4.31 [1.95-9.53]**	**0.0003**	0.87 [0.34-2.27]	0.7785
Pre-eclampsia						
No	375 (87.01)	1,085 (88.57)	1.00 [referent]		1.00 [referent]	
Yes	56 (12.99)	140 (11.43)	1.40 [0.59-3.34]	0.4443	1.82 [0.68-4.88]	0.2373
Gestational Diabetes						
No	402 (93.27)	1,152 (94.04)	1.00 [referent]		1.00 [referent]	
Yes	29 (6.73)	73 (5.96)	1.30 [0.40-4.22]	0.6571	1.15 [0.33-4.09]	0.8263
Threatened Abortion						
No	416 (96.52)	1,156 (94.37)	1.00 [referent]		1.00 [referent]	
Yes	15 (3.48)	69 (5.63)	0.36 [0.09-1.45]	0.1514	0.23 [0.04-1.35]	0.1031
Other Pregnancy Related Complications						
No	125 (29.00)	451 (36.82)	1.00 [referent]		1.00 [referent]	
Yes	306 (71.00)	774 (63.18)	**2.08 [1.12-3.85]**	**0.0198**	1.79 [0.85-3.79]	0.1285
Threatened Preterm Labour						
No	376 (87.24)	1,088 (88.82)	1.00 [referent]		1.00 [referent]	
Yes	55 (12.76)	137 (11.18)	1.34 [0.55-3.24]	0.5189	0.68 [0.25-1.83]	0.4461
APH						
No	411 (95.36)	1,187 (96.90)	1.00 [referent]		1.00 [referent]	
Yes	20 (4.64)	38 (3.10)	2.38 [0.53-10.73]	0.2603	0.67 [0.12-3.85]	0.6502
Placenta Praevia [a]						
No	429 (99.54)	1,217 (99.35)				
Yes	2 (0.46)	8 (0.65)				
Placental Abruption [a]						
No	427 (99.07)	1,223 (99.84)				
Yes	4 (0.93)	2 (0.16)				
Fetal Distress						
No	382 (88.63)	1,136 (92.73)	1.00 [referent]		1.00 [referent]	
Yes	49 (11.37)	89 (7.27)	**2.92 [1.13-7.58]**	**0.0277**	1.76 [0.60-5.13]	0.3013
Cephalopelvic Disproportion [a]						
No	431 (100.00)	1,221 (99.67)				
Yes	0 (0.00)	4 (0.33)				
Prolapsed Cord [a]						

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No	428 (99.30)	1,215 (99.18)				
Yes	3 (0.70)	10 (0.82)				
Precipitate Delivery [a]						
No	424 (98.38)	1,206 (98.45)				
Yes	7 (1.62)	19 (1.55)				
PPH ≥500mls						
No	281 (65.20)	918 (74.94)	1.00 [referent]		1.00 [referent]	
Yes	150 (34.80)	307 (25.06)	**2.59 [1.39-4.82]**	**0.0029**	1.52 [0.73-3.16]	0.2603
TSR ≥2mins						
No	364 (84.45)	1,060 (86.53)	1.00 [referent]		1.00 [referent]	
Yes	67 (15.55)	165 (13.47)	1.06 [0.56-1.99]	0.8628	0.52 [0.22-1.21]	0.1277
Apgar 5-minutes <7 [a]						
No	425 (98.61)	1,198 (97.80)				
Yes	6 (1.39)	27 (2.20)				
Intubation						
No	353 (81.90)	1,036 (84.57)	1.00 [referent]		1.00 [referent]	
Yes	78 (18.10)	189 (15.43)	1.36 [0.75-2.45]	0.3129	1.54 [0.71-3.37]	0.2770
Early Preterm Birth						
No	352 (81.67)	1,058 (86.37)	1.00 [referent]		1.00 [referent]	
Yes	79 (18.33)	167 (13.63)	2.08 [0.94-4.56]	0.0691	1.29 [0.53-3.15]	0.5788
POBW <15th Percentile						
No	305 (70.77)	926 (75.59)	1.00 [referent]		1.00 [referent]	
Yes	81 (18.79)	136 (11.10)	**2.09 [1.14-3.84]**	**0.0174**	**2.06 [1.07-3.98]**	**0.0309**
Unavailable	45 (10.44)	163 (13.31)				
Parity						
0	150 (34.80)	512 (41.80)	1.00 [referent]		1.00 [referent]	
1	154 (35.73)	429 (35.02)	1.62 [0.83-3.16]	0.1579	1.96 [0.77-5.00]	0.1594
≥2	127 (29.47)	284 (23.18)	**2.50 [1.20-5.22]**	**0.0145**	2.03 [0.55-7.48]	0.2881
Child						
Sex						
Female	176 (40.84)	674 (55.02)	1.00 [referent]		1.00 [referent]	
Male	255 (59.16)	551 (44.98)	**4.44 [2.68-7.36]**	**<0.0001**	**5.08 [2.89-8.92]**	**<0.0001**
Ethnicity						
Other	385 (89.33)	1,187 (96.90)	1.00 [referent]		1.00 [referent]	
Indigenous Australian	46 (10.67)	38 (3.10)	**16.98 [4.85-59.46]**	**<0.0001**	2.46 [0.46-13.03]	0.2909
Child Speaks Language Other Than English at Home						
No	367 (85.15)	1,149 (93.80)	1.00 [referent]		1.00 [referent]	
Yes	64 (14.85)	76 (6.20)	**6.28 [2.48-15.90]**	**0.0001**	**6.45 [2.17-19.17]**	**0.0008**
Age Category at Time of AEDC Completion [b]						
1	109 (25.29)	212 (17.31)	**2.93 [1.45-5.90]**	**0.0028**	**3.34 [1.55-7.22]**	**0.0022**
2	288 (66.82)	911 (74.37)	1.00 [referent]		1.00 [referent]	
3	34 (7.89)	102 (8.33)	1.18 [0.43-3.27]	0.7460	0.77 [0.23-2.54]	0.6660
Total Number of Siblings						
1	119 (27.61)	389 (31.76)	1.00 [referent]		1.00 [referent]	
2	160 (37.12)	494 (40.33)	1.15 [0.58-2.30]	0.6845	0.70 [0.27-1.83]	0.4610
3	74 (17.17)	240 (19.59)	1.04 [0.45-2.41]	0.9264	0.44 [0.13-1.55]	0.1996
>3	78 (18.10)	102 (8.33)	**7.28 [2.73-19.45]**	**<0.0001**	2.71 [0.60-12.22]	0.1939
Sociodemographic						
Index of Relative Socioeconomic Disadvantage						
Lowest Quintile	327 (75.87)	1,046 (85.39)	**3.55 [1.62-7.78]**	**0.0016**	1.63 [0.66-4.02]	0.2871
> Lowest Quintile	87 (20.19)	150 (12.24)	1.00 [referent]		1.00 [referent]	
Unavailable	17 (3.94)	29 (2.37)				

[a] Excluded from multivariable analysis due to small N.

[b] Age categories classified as; ≥3 years 10 months to <5 years and one month, 2) ≥5 years and one month to <5 years and 10 months (reference category), 3) ≥5 years and 10 months to <6 years 10 months.

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Table 2. Risk factors for children who are developmentally vulnerable on two or more AEDC domains (DV2).

Characteristic	DV2 (N=223) N (%)	NDV2 (N=1,433) N (%)	Bivariate OR [95% CI]	p-value	Multivariable (N=1,352) aOR [95% CI]	p-value
Maternal						
Age at Time of Child's Birth (years)						
<25	63 (28.25)	159 (11.10)	**7.81 [2.60-23.45]**	**0.0003**	**5.60 [1.30-24.10]**	**0.0208**
25-29	48 (21.52)	336 (23.45)	1.00 [referent]		1.00 [referent]	
30-34	64 (28.70)	542 (37.82)	0.65 [0.26-1.63]	0.3563	0.92 [0.29-2.91]	0.8854
≥35	48 (21.52)	396 (27.63)	0.67 [0.25-1.81]	0.4335	0.77 [0.22-2.76]	0.6892
Marital Status						
Married (inc. de facto)	172 (77.13)	1,308 (91.28)	1.00 [referent]			
All Other	49 (21.97)	121 (8.44)	**9.91 [3.54-27.77]**	**<0.0001**	**4.59 [1.13-18.55]**	**0.0327**
Unavailable	2 (0.90)	4 (0.28)				
Occupational Status Scale at Time of Child's Birth						
0-20	78 (34.98)	231 (16.12)	**8.82 [3.72-20.89]**	**<0.0001**	**3.30 [1.11-9.81]**	**0.0322**
>20-100	130 (58.30)	1,155 (80.60)	1.00 [referent]		1.00 [referent]	
Unavailable	15 (6.73)	47 (3.28)				
Pregnancy & Birth						
Fertility Treatments						
No	200 (89.69)	1,188 (82.90)	1.00 [referent]		1.00 [referent]	
Yes	23 (10.31)	245 (17.10)	0.35 [0.13-0.97]	0.0424	0.67 [0.17-2.69]	0.5673
Smoking Status During Pregnancy						
No	166 (74.44)	1,252 (87.37)	1.00 [referent]		1.00 [referent]	
Yes	57 (25.56)	181 (12.63)	**5.83 [2.32-14.65]**	**0.0002**	1.27 [0.38-4.30]	0.7000
Pre-eclampsia						
No	195 (87.44)	1,265 (88.28)	1.00 [referent]		1.00 [referent]	
Yes	28 (12.56)	168 (11.72)	1.25 [0.41-3.86]	0.6930	2.45 [0.65-9.17]	0.1844
Gestational Diabetes						
No	208 (93.27)	1,346 (93.93)	1.00 [referent]		1.00 [referent]	
Yes	15 (6.73)	87 (6.07)	1.44 [0.32-6.42]	0.6353	2.29 [0.46-11.44]	0.3124
Threatened Abortion						
No	214 (95.96)	1,358 (94.77)	1.00 [referent]		1.00 [referent]	
Yes	9 (4.04)	75 (5.23)	0.54 [0.10-2.94]	0.4784	0.24 [0.02-3.08]	0.2735
Other Pregnancy Related Complications						
No	57 (25.56)	519 (36.22)	1.00 [referent]		1.00 [referent]	
Yes	166 (74.44)	914 (63.78)	**2.64 [1.22-5.69]**	**0.0136**	1.64 [0.58-4.61]	0.3510
Threatened Preterm Labour						
No	191 (85.65)	1,273 (88.83)	1.00 [referent]		1.00 [referent]	
Yes	32 (14.35)	160 (11.17)	2.04 [0.66-6.29]	0.2163	0.72 [0.20-2.61]	0.6131
APH						
No	209 (93.72)	1,389 (96.93)	1.00 [referent]		1.00 [referent]	
Yes	14 (6.28)	44 (3.07)	5.96 [0.95-37.40]	0.0568	1.56 [0.59-4.15]	0.3677
Placenta Praevia [a]						
No	223 (100.00)	1,423 (99.30)				
Yes	0 (0.00)	10 (0.70)				
Placental Abruption [a]						
No	221 (99.10)	1,429 (99.72)				
Yes	2 (0.90)	4 (0.28)				
Fetal Distress						
No	195 (87.44)	1,323 (92.32)	1.00 [referent]		1.00 [referent]	
Yes	28 (12.56)	110 (7.68)	3.03 [0.90-10.23]	0.0735	1.56 [0.59-4.15]	0.3677
Cephalopelvic Disproportion [a]						
No	223 (100.00)	1,429 (99.72)				
Yes	0 (0.00)	4 (0.28)				
Prolapsed Cord [a]						

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No	220 (98.65)	1,423 (99.30)				
Yes	3 (1.35)	10 (0.70)				
Precipitate Delivery [a]						
No	219 (98.21)	1,411 (98.46)				
Yes	4 (1.79)	22 (1.54)				
PPH ≥500mls						
No	141 (63.23)	1,058 (73.83)	1.00 [referent]		1.00 [referent]	
Yes	82 (36.77)	375 (26.17)	**3.43 [1.49-7.94]**	**0.0040**	1.38 [0.16-11.79]	0.7661
TSR ≥2mins						
No	183 (82.06)	1,241 (86.60)	1.00 [referent]		1.00 [referent]	
Yes	40 (17.94)	192 (13.40)	1.78 [0.81-3.89]	0.1486	0.91 [0.30-2.72]	0.8631
Apgar 5-minutes <7 [a]						
No	219 (98.21)	1,404 (97.98)				
Yes	4 (1.79)	29 (2.02)				
Intubation						
No	178 (79.82)	1,211 (84.51)	1.00 [referent]		1.00 [referent]	
Yes	45 (20.18)	222 (15.49)	1.91 [0.90-4.05]	0.0931	1.53 [0.54-4.35]	0.4290
Early Preterm Birth						
No	172 (77.13)	1,238 (86.39)	1.00 [referent]		1.00 [referent]	
Yes	51 (22.87)	195 (13.61)	**4.18 [1.50-11.67]**	**0.0064**	2.06 [0.64-6.58]	0.2243
POBW <15th Percentile						
No	162 (72.65)	1,069 (74.60)	1.00 [referent]		1.00 [referent]	
Yes	42 (18.83)	175 (12.21)	**2.72 [1.25-5.93]**	**0.0119**	**3.11 [1.26-7.64]**	**0.0136**
Unavailable	19 (8.52)	189 (13.19)				
Parity						
0	79 (35.43)	583 (40.68)	1.00 [referent]		1.00 [referent]	
1	73 (32.74)	510 (35.59)	1.18 [0.51-2.76]	0.7002	1.12 [0.31-4.04]	0.8612
≥2	71 (31.84)	340 (23.73)	**2.66 [1.04-6.83]**	**0.0420**	3.61 [0.61-21.22]	0.1551
Child						
Sex						
Female	83 (37.22)	767 (53.52)	1.00 [referent]		1.00 [referent]	
Male	140 (62.78)	666 (46.48)	**5.42 [2.79-10.55]**	**<0.0001**	**7.87 [3.45-17.97]**	**<0.0001**
Ethnicity						
Other	197 (88.34)	1,375 (95.95)	1.00 [referent]		1.00 [referent]	
Indigenous Australian	26 (11.66)	58 (4.05)	**11.00 [2.78-43.60]**	**0.0007**	2.32 [0.32-16.84]	0.4037
Child Speaks Language Other Than English at Home						
No	192 (86.10)	1,324 (92.39)	1.00 [referent]		1.00 [referent]	
Yes	31 (13.90)	109 (7.61)	3.19 [0.96-10.63]	0.0589	**4.65 [1.14-19.03]**	**0.0330**
Age Category at Time of AEDC Completion						
1	66 (29.60)	255 (17.79)	**4.11 [1.80-9.39]**	**0.0008**	**5.36 [1.94-14.82]**	**0.0013**
2	142 (63.68)	1,057 (73.76)	1.00 [referent]		1.00 [referent]	
3	15 (6.73)	121 (8.44)	0.95 [0.26-3.46]	0.9416	0.28 [0.05-1.70]	0.1672
Total Number of Siblings						
1	58 (26.01)	450 (31.40)	1.00 [referent]		1.00 [referent]	
2	84 (37.67)	570 (39.78)	1.35 [0.57-3.19]	0.4887	1.26 [0.34-4.71]	0.7326
3	38 (17.04)	276 (19.26)	1.14 [0.40-3.24]	0.8098	0.47 [0.08-2.70]	0.3953
>3	43 (19.28)	137 (9.56)	**7.14 [2.24-22.72]**	**0.0009**	2.52 [0.34-18.73]	0.3659
Sociodemographic						
Index of Relative Socioeconomic Disadvantage						
Lowest Quintile	175 (78.48)	1,198 (83.60)	2.14 [0.76-6.02]	0.1510	0.68 [0.21-2.25]	0.5294
> Lowest Quintile	39 (17.49)	198 (13.82)	1.00 [referent]		1.00 [referent]	
Unavailable	9 (4.04)	37 (2.58)				

[a] Excluded from multivariable analysis due to small N.

[b] Age categories classified as; ≥3 years 10 months to <5 years and one month, 2) ≥5 years and one month to <5 years and 10 months (reference category), 3) ≥5 years and 10 months to <6 years 10 months.

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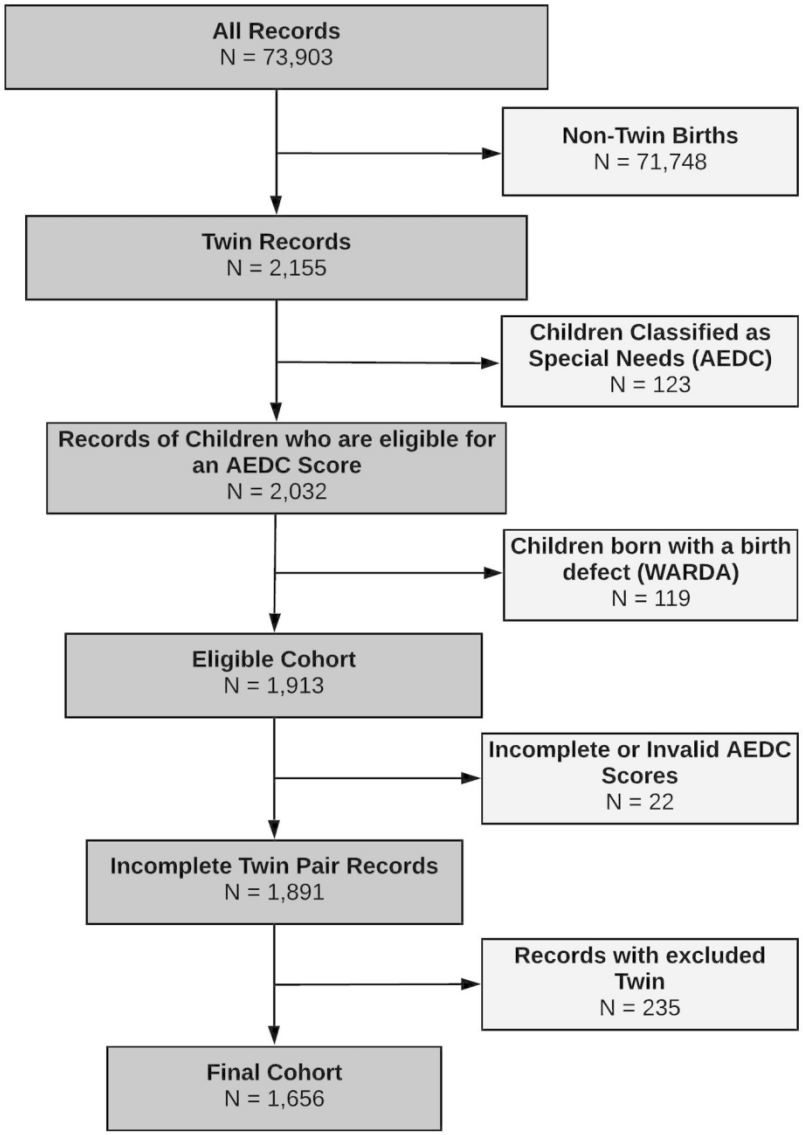

Figure 1. Eligible Cohort and Numbers Included for Analyses.AEDC = Australian Early Development Census. WARDA= Western Australian Register of Developmental Anomalies.

132x182mm (300 x 300 DPI)

Supplementary Tables and Figures (Total: 5 tables, 0 figures)

Table 1. Risk Factors for Developmental Vulnerability on the Physical Health & Wellbeing Domain.

Characteristic	DV (N=188) N (%)	NDV (N=1,468) N (%)	Bivariate OR [95% CI]	p-value	Multivariable (N=1,352) aOR [95% CI]	p-value
Maternal						
Age at Time of Child's Birth (years)						
<25	46 (24.47)	176 (11.99)	**5.36 [1.64-17.48]**	**0.0018**	3.59 [0.93-13.90]	0.0646
25-29	39 (20.74)	345 (23.50)	1.00 [referent]		1.00 [referent]	
30-34	62 (32.98)	544 (37.06)	1.08 [0.41-2.87]	0.6456	1.13 [0.39-3.25]	0.8209
≥35	41 (21.81)	403 (27.45)	0.83 [0.29-2.38]	0.7761	0.97 [0.30-3.13]	0.9589
Marital Status						
Married (inc. de facto)	152 (80.85)	1,328 (90.46)	1.00 [referent]		1.00 [referent]	
All Other	36 (19.15)	134 (9.13)	**5.54 [1.87-16.35]**	**0.0020**	2.39 [0.66-8.70]	0.1847
Unavailable	0 (0.00)	6 (0.41)				
Occupational Status Scale at Time of Child's Birth						
0-20	52 (27.66)	257 (17.51)	**3.29 [1.40-7.75]**	**0.0250**	0.79 [0.28-2.27]	0.6631
>20-100	119 (63.30)	1,166 (79.43)	1.00 [referent]		1.00 [referent]	
Unavailable	17 (9.04)	45 (3.07)				
Pregnancy & Birth						
Fertility Treatments						
No	163 (86.70)	1,225 (83.45)	1.00 [referent]		1.00 [referent]	
Yes	25 (13.30)	243 (16.55)	0.61 [0.21-1.75]	0.3594	1.07 [0.32-3.62]	0.9141
Smoking Status During Pregnancy						
No	134 (71.28)	1,284 (87.47)	1.00 [referent]		1.00 [referent]	
Yes	54 (28.72)	184 (12.53)	**7.19 [2.76-18.70]**	**<0.0001**	2.49 [0.83-7.51]	0.1047
Pre-eclampsia						
No	163 (86.70)	1,297 (88.35)	1.00 [referent]		1.00 [referent]	
Yes	25 (13.30)	171 (11.65)	1.56 [0.46-5.24]	0.4752	2.99 [0.90-9.91]	0.0736
Gestational Diabetes						
No	173 (92.02)	1,381 (94.07)	1.00 [referent]		1.00 [referent]	
Yes	15 (7.98)	87 (5.93)	1.87 [0.36-9.87]	0.4596	2.26 [0.50-10.20]	0.2903
Threatened Abortion						
No	182 (96.81)	1,390 (94.69)	1.00 [referent]		1.00 [referent]	
Yes	6 (3.19)	78 (5.31)	0.45 [0.07-2.71]	0.3787	0.43 [0.05-3.77]	0.4425
Other Pregnancy Related Complications						
No	51 (27.13)	525 (35.76)	1.00 [referent]		1.00 [referent]	
Yes	137 (72.87)	943 (64.24)	1.96 [0.87-4.42]	0.1025	1.69 [0.65-4.42]	0.2835
Threatened Preterm Labour						
No	161 (85.64)	1,303 (88.76)	1.00 [referent]		1.00 [referent]	
Yes	27 (14.36)	165 (11.24)	1.68 [0.49-5.81]	0.4108	0.86 [0.26-2.82]	0.7969
APH						
No	178 (94.68)	1,420 (96.73)	1.00 [referent]		1.00 [referent]	
Yes	10 (5.32)	48 (3.27)	3.27 [0.37-28.63]	0.2850	0.73 [0.09-5.96]	0.7661
Placenta Praevia [a]						
No	187 (99.47)	1,459 (99.39)				
Yes	1 (0.53)	9 (0.61)				
Placental Abruption [a]						
No	185 (98.40)	1,465 (99.8)				
Yes	3 (1.60)	3 (0.20)				
Fetal Distress						
No	162 (86.17)	1,356 (92.37)	1.00 [referent]		1.00 [referent]	
Yes	26 (13.83)	112 (7.63)	**4.89 [1.20-19.90]**	**0.0267**	2.57 [0.72-9.19]	0.1450
Cephalopelvic Disproportion [a]						
No	188 (100.00)	1,464 (99.73)				
Yes	0 (0.00)	4 (0.27)				
Prolapsed Cord [a]						
No	188 (100.00)	1,455 (99.11)				

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Yes	0 (0.00)	13 (0.89)				
Precipitate Delivery [a]						
No	186 (98.94)	1,444 (98.37)				
Yes	2 (1.06)	24 (1.63)				
PPH ≥500mls						
No	124 (65.96)	1,075 (73.23)	1.00 [referent]		1.00 [referent]	
Yes	64 (34.04)	393 (26.77)	2.16 [0.90-5.18]	0.0839	0.90 [0.36-2.25]	0.8256
TSR ≥2mins						
No	152 (80.85)	1,272 (86.65)	1.00 [referent]		1.00 [referent]	
Yes	36 (19.15)	196 (13.35)	1.48 [0.64-3.44]	0.3631	0.55 [0.19-1.55]	0.2581
Apgar 5-minutes <7 [a]						
No	182 (96.81)	1,441 (98.16)				
Yes	6 (3.19)	27 (1.84)				
Intubation						
No	147 (78.19)	1,242 (84.60)	1.00 [referent]		1.00 [referent]	
Yes	41 (21.81)	226 (15.40)	**2.33 [1.03-5.28]**	**0.0427**	1.96 [0.75-5.10]	0.1670
Early Preterm Birth						
No	146 (77.66)	1,264 (86.1)	1.00 [referent]		1.00 [referent]	
Yes	42 (22.34)	204 (13.9)	**3.76 [1.21-11.68]**	**0.0223**	2.15 [0.76-6.11]	0.1511
POBW <15th Percentile						
No	125 (66.49)	1,106 (75.34)	1.00 [referent]		1.00 [referent]	
Yes	42 (22.34)	175 (11.92)	**3.44 [1.53-7.74]**	**0.0029**	**2.58 [1.15-5.77]**	**0.0216**
Unavailable	21 (11.17)	187 (12.74)				
Parity						
0	67 (35.64)	595 (40.53)	1.00 [referent]		1.00 [referent]	
1	65 (34.57)	518 (35.29)	1.18 [0.48-2.86]	0.7211	1.29 [0.41-4.08]	0.6653
≥2	56 (29.79)	355 (24.18)	1.81 [0.67-4.91]	0.2443	1.53 [0.29-8.17]	0.6173
Child						
Sex						
Female	82 (43.62)	768 (52.32)	1.00 [referent]		1.00 [referent]	
Male	106 (56.38)	700 (47.68)	**2.50 [1.36-4.61]**	**0.0034**	**3.31 [1.64-6.69]**	**0.0009**
Ethnicity						
Other	167 (88.83)	1,405 (95.71)	1.00 [referent]		1.00 [referent]	
Indigenous Australian	21 (11.17)	63 (4.29)	**12.56 [2.12-74.52]**	**0.0054**	0.80 [0.12-5.40]	0.8160
Child Speaks Language Other Than English at Home						
No	159 (84.57)	1,357 (92.44)	1.00 [referent]		1.00 [referent]	
Yes	29 (15.43)	111 (7.56)	**4.62 [1.24-17.26]**	**0.0230**	**4.84 [1.34-17.48]**	**0.0162**
Age Category at Time of AEDC Completion						
1	50 (26.60)	271 (18.46)	**2.76 [1.02-7.46]**	**0.0008**	2.22 [0.88-5.60]	0.0917
2	129 (68.62)	1,070 (72.89)	1.00 [referent]		1.00 [referent]	
3	9 (4.79)	127 (8.65)	0.44 [0.10-1.93]	0.9416	0.19 [0.03-1.18]	0.0739
Total Number of Siblings						
1	51 (27.13)	457 (31.13)	1.00 [referent]		1.00 [referent]	
2	69 (36.70)	585 (39.85)	1.10 [0.46-2.63]	0.8273	0.98 [0.30-3.15]	0.9697
3	24 (12.77)	290 (19.75)	0.51 [0.16-1.57]	0.2387	0.41 [0.08-2.10]	0.2836
>3	44 (23.40)	136 (9.26)	**8.32 [2.57-26.96]**	**0.0004**	6.47 [0.98-42.75]	0.0525
Sociodemographic						
Index of Relative Socioeconomic Disadvantage						
Lowest Quintile	138 (73.40)	1,235 (84.13)	**3.78 [1.17-12.22]**	**0.0261**	1.85 [0.63-5.44]	0.2639
> Lowest Quintile	40 (21.28)	197 (13.42)	1.00 [referent]		1.00 [referent]	
Unavailable	10 (5.32)	36 (2.45)				

[a] Excluded from multivariable analysis due to small N.

[b] Age categories classified as; ≥3 years 10 months to <5 years and one month, 2) ≥5 years and one month to <5 years and 10 months (reference category), 3) ≥5 years and 10 months to <6 years 10 months.

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Table 2. Risk Factors for Developmental Vulnerability on the Social Competence Domain.

Characteristic	DV (N=151) N (%)	NDV (N=1,505) N (%)	Bivariate OR [95% CI]	p-value	Multivariable (N=1,352) aOR [95% CI]	p-value
Maternal						
Age at Time of Child's Birth (years)						
<25	43 (28.48)	179 (11.89)	**6.32 [1.91-20.95]**	**0.0026**	3.13 [0.74-13.30]	0.1219
25-29	31 (20.53)	353 (23.46)	1.00 [referent]		1.00 [referent]	
30-34	44 (29.14)	562 (37.34)	0.78 [0.29-2.15]	0.6340	1.36 [0.43-4.36]	0.6038
≥35	33 (21.85)	411 (27.31)	0.81 [0.27-2.37]	0.6955	0.99 [0.27-3.59]	0.9822
Marital Status						
Married (inc. de facto)	113 (74.83)	1,367 (90.83)	1.00 [referent]		1.00 [referent]	
All Other	36 (23.84)	134 (8.90)	**9.65 [3.20-29.05]**	**<0.0001**	**10.16 [2.56-40.41]**	**0.0010**
Unavailable	2 (1.32)	4 (0.27)				
Occupational Status Scale at Time of Child's Birth						
0-20	50 (33.11)	259 (17.21)	**5.05 [2.07-12.29]**	**0.0004**	1.93 [0.64-5.79]	0.2414
>20-100	94 (62.25)	1,191 (79.14)	1.00 [referent]		1.00 [referent]	
Unavailable	7 (4.64)	55 (3.65)				
Pregnancy & Birth						
Fertility Treatments						
No	132 (87.42)	1,256 (83.46)	1.00 [referent]		1.00 [referent]	
Yes	19 (12.58)	249 (16.54)	0.54 [0.18-1.60]	0.2688	1.38 [0.37-5.17]	0.6347
Smoking Status During Pregnancy						
No	116 (76.82)	1,302 (86.51)	1.00 [referent]		1.00 [referent]	
Yes	35 (23.18)	203 (13.49)	**3.70 [1.06-12.91]**	**0.0406**	1.22 [0.35-4.20]	0.7525
Pre-eclampsia						
No	134 (88.74)	1,326 (88.11)	1.00 [referent]		1.00 [referent]	
Yes	17 (11.26)	179 (11.89)	0.98 [0.31-3.14]	0.9754	1.84 [0.49-6.84]	0.3645
Gestational Diabetes						
No	140 (92.72)	1,414 (93.95)	1.00 [referent]		1.00 [referent]	
Yes	11 (7.28)	91 (6.05)	1.46 [0.32-6.60]	0.6268	2.11 [0.41-10.74]	0.3692
Threatened Abortion						
No	144 (95.36)	1,428 (94.88)	1.00 [referent]		1.00 [referent]	
Yes	7 (4.64)	77 (5.12)	0.66 [0.11-4.10]	0.6579	0.13 [0.01-2.43]	0.1714
Other Pregnancy Related Complications						
No	38 (25.17)	538 (35.75)	1.00 [referent]		1.00 [referent]	
Yes	113 (74.83)	967 (64.25)	2.15 [0.89-5.19]	0.0884	2.00 [0.70-5.74]	0.1960
Threatened Preterm Labour						
No	131 (86.75)	1,333 (88.57)	1.00 [referent]		1.00 [referent]	
Yes	20 (13.25)	172 (11.43)	1.32 [0.42-4.17]	0.6403	0.69 [0.19-2.59]	0.5839
APH						
No	142 (94.04)	1,456 (96.74)	1.00 [referent]		1.00 [referent]	
Yes	9 (5.96)	49 (3.26)	3.74 [0.62-22.66]	0.1507	2.12 [0.27-16.50]	0.4734
Placenta Praevia [a]						
No	151 (100.00)	1,495 (99.34)				
Yes	0 (0.00)	10 (0.66)				
Placental Abruption [a]						
No	149 (98.68)	1,501 (99.73)				
Yes	2 (1.32)	4 (0.27)				
Fetal Distress						
No	132 (87.42)	1,386 (92.09)	1.00 [referent]		1.00 [referent]	
Yes	19 (12.58)	119 (7.91)	2.77 [0.81-9.50]	0.1045	1.39 [0.33-5.82]	0.6558
Cephalopelvic Disproportion [a]						
No	151 (100.00)	1,501 (99.73)				
Yes	0 (0.00)	4 (0.27)				
Prolapsed Cord [a]						
No	148 (98.01)	1,495 (99.34)				
Yes	3 (1.99)	10 (0.66)				

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Precipitate Delivery [a]						
No	149 (98.68)	1,481 (98.41)				
Yes	2 (1.32)	24 (1.59)				
PPH ≥500mls						
No	96 (63.58)	1,103 (73.29)	1.00 [referent]		1.00 [referent]	
Yes	55 (36.42)	402 (26.71)	**2.61 [1.14-5.97]**	**0.0233**	1.42 [0.54-3.76]	0.4770
TSR ≥2mins						
No	119 (78.81)	1,305 (86.71)	1.00 [referent]		1.00 [referent]	
Yes	32 (21.19)	200 (13.29)	1.76 [0.80-3.89]	0.1607	0.80 [0.26-2.46]	0.6967
Apgar 5-minutes <7 [a]						
No	147 (97.35)	1,476 (98.07)				
Yes	4 (2.65)	29 (1.93)				
Intubation						
No	112 (74.17)	1,277 (84.85)	1.00 [referent]		1.00 [referent]	
Yes	39 (25.83)	228 (15.15)	2.31 [1.00-5.33]	0.0505	2.48 [0.86-7.20]	0.0934
Early Preterm Birth						
No	123 (81.46)	1,287 (85.51)	1.00 [referent]		1.00 [referent]	
Yes	28 (18.54)	218 (14.49)	1.64 [0.59-4.57]	0.3453	0.68 [0.20-2.27]	0.5254
POBW <15th Percentile						
No	114 (75.5)	1,117 (74.22)	1.00 [referent]		1.00 [referent]	
Yes	23 (15.23)	194 (12.89)	1.51 [0.65-3.54]	0.3408	1.65 [0.63-4.30]	0.3039
Unavailable	14 (9.27)	194 (12.89)				
Parity						
0	58 (38.41)	604 (40.13)	1.00 [referent]		1.00 [referent]	
1	49 (32.45)	534 (35.48)	1.06 [0.44-2.56]	0.9059	0.87 [0.25-3.08]	0.8268
≥2	44 (29.14)	367 (24.39)	1.73 [0.67-4.50]	0.2588	2.02 [0.35-11.63]	0.4317
Child						
Sex						
Female	51 (33.77)	799 (53.09)	1.00 [referent]		1.00 [referent]	
Male	100 (66.23)	706 (46.91)	**5.21 [2.58-10.52]**	**<0.0001**	**5.35 [2.38-12.00]**	**<0.0001**
Ethnicity						
Other	137 (90.73)	1,435 (95.35)	1.00 [referent]		1.00 [referent]	
Indigenous Australian	14 (9.27)	70 (4.65)	3.96 [0.86-18.29]	0.0777	2.43 [0.36-16.63]	0.3644
Child Speaks Language Other Than English at Home						
No	139 (92.05)	1,377 (91.50)	1.00 [referent]		1.00 [referent]	
Yes	12 (7.95)	128 (8.50)	0.67 [0.17-2.62]	0.5667	1.13 [0.24-5.18]	0.8797
Age Category at Time of AEDC Completion [b]						
1	40 (26.49)	281 (18.67)	2.42 [0.98-5.94]	0.0547	**2.84 [1.05-7.73]**	**0.0406**
2	98 (64.9)	1,101 (73.16)	1.00 [referent]		1.00 [referent]	
3	13 (8.61)	123 (8.17)	1.73 [0.46-6.48]	0.4174	0.51 [0.09-2.75]	0.4309
Total Number of Siblings						
1	41 (27.15)	467 (31.03)	1.00 [referent]		1.00 [referent]	
2	57 (37.75)	597 (39.67)	1.27 [0.50-3.23]	0.6133	1.97 [0.52-7.49]	0.3223
3	27 (17.88)	287 (19.07)	1.27 [0.41-3.91]	0.6779	0.91 [0.16-5.21]	0.9149
>3	26 (17.22)	154 (10.23)	**4.06 [1.14-14.39]**	**0.0303**	2.53 [0.33-19.66]	0.3737
Sociodemographic						
Index of Relative Socioeconomic Disadvantage						
Lowest Quintile	118 (78.15)	1,255 (83.39)	1.67 [0.59-4.74]	0.3362	0.72 [0.21-2.45]	0.5956
> Lowest Quintile	26 (17.22)	211 (14.02)	1.00 [referent]		1.00 [referent]	
Unavailable	7 (4.64)	39 (2.59)				

[a] Excluded from multivariable analysis due to small N.

[b] Age categories classified as; ≥3 years 10 months to <5 years and one month, 2) ≥5 years and one month to <5 years and 10 months (reference category), 3) ≥5 years and 10 months to <6 years 10 months.

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Table 3. Risk Factors for Developmental Vulnerability on the Emotional Maturity Domain.

Characteristic	DV (N=147) N (%)	NDV (N=1,509) N (%)	Bivariate OR [95% CI]	p-value	Multivariable (N=1,352) aOR [95% CI]	p-value
Maternal						
Age at Time of Child's Birth (years)						
<25	39 (26.53)	183 (12.13)	**3.14 [1.44-6.89]**	**0.0042**	1.89 [0.70-5.05]	0.2063
25-29	31 (21.09)	353 (23.39)	1.00 [referent]		1.00 [referent]	
30-34	38 (25.85)	568 (37.64)	0.70 [0.35-1.40]	0.3113	1.03 [0.46-2.34]	0.9373
≥35	39 (26.53)	405 (26.84)	1.12 [0.55-2.27]	0.7615	1.16 [0.48-2.81]	0.7415
Marital Status						
Married (inc. de facto)	111 (75.51)	1,369 (90.72)	1.00 [referent]		1.00 [referent]	
All Other	34 (23.13)	136 (9.01)	**4.58 [2.26-9.27]**	**<0.0001**	**3.77 [1.48-9.58]**	**0.0055**
Unavailable	2 (1.36)	4 (0.27)				
Occupational Status Scale at Time of Child's Birth						
0-20	45 (30.61)	264 (17.50)	**2.62 [1.46-4.72]**	**0.0014**	1.85 [0.86-3.97]	0.1131
>20-100	95 (64.63)	1,190 (78.86)	1.00 [referent]		1.00 [referent]	
Unavailable	7 (4.76)	55 (3.64)				
Pregnancy & Birth						
Fertility Treatments						
No	126 (85.71)	1,262 (83.63)	1.00 [referent]		1.00 [referent]	
Yes	21 (14.29)	247 (16.37)	0.81 [0.40-1.66]	0.5666	1.03 [0.42-2.53]	0.9569
Smoking Status During Pregnancy						
No	118 (80.27)	1,300 (86.15)	1.00 [referent]		1.00 [referent]	
Yes	29 (19.73)	209 (13.85)	1.70 [0.86-3.36]	0.1304	0.82 [0.33-2.02]	0.6620
Pre-eclampsia						
No	129 (87.76)	1,331 (88.20)	1.00 [referent]		1.00 [referent]	
Yes	18 (12.24)	178 (11.80)	1.09 [0.50-2.40]	0.8272	1.87 [0.75-4.63]	0.1764
Gestational Diabetes						
No	138 (93.88)	1,416 (93.84)	1.00 [referent]		1.00 [referent]	
Yes	9 (6.12)	93 (6.16)	1.02 [0.35-2.97]	0.9752	1.18 [0.37-3.76]	0.7845
Threatened Abortion						
No	140 (95.24)	1,432 (94.90)	1.00 [referent]		1.00 [referent]	
Yes	7 (4.76)	77 (5.10)	0.91 [0.28-3.03]	0.8823	0.09 [0.01-1.06]	0.0553
Other Pregnancy Related Complications						
No	35 (23.81)	541 (35.85)	1.00 [referent]		1.00 [referent]	
Yes	112 (76.19)	968 (64.15)	**2.13 [1.20-3.80]**	**0.0101**	1.80 [0.86-3.78]	0.1208
Threatened Preterm Labour						
No	125 (85.03)	1,339 (88.73)	1.00 [referent]		1.00 [referent]	
Yes	22 (14.97)	170 (11.27)	1.52 [0.72-3.25]	0.2742	1.21 [0.51-2.85]	0.6642
APH						
No	139 (94.56)	1,459 (96.69)	1.00 [referent]		1.00 [referent]	
Yes	8 (5.44)	50 (3.31)	2.13 [0.62-7.31]	0.2304	0.67 [0.13-3.31]	0.6180
Placenta Praevia [a]						
No	146 (99.32)	1,500 (99.40)				
Yes	1 (0.68)	9 (0.60)				
Placental Abruption [a]						
No	145 (98.64)	1,505 (99.73)				
Yes	2 (1.36)	4 (0.27)				
Fetal Distress						
No	128 (87.07)	1,390 (92.11)	1.00 [referent]		1.00 [referent]	
Yes	19 (12.93)	119 (7.89)	1.95 [0.86-4.44]	0.1107	1.09 [0.40-2.93]	0.8689
Cephalopelvic Disproportion [a]						
No	147 (100.00)	1,505 (99.73)				
Yes	0 (0.00)	4 (0.27)				
Prolapsed Cord [a]						
No	145 (98.64)	1,498 (99.27)				
Yes	2 (1.36)	11 (0.73)				

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Precipitate Delivery [a]						
No	146 (99.32)	1,484 (98.34)				
Yes	1 (0.68)	25 (1.66)				
PPH ≥500mls						
No	95 (64.63)	1,104 (73.16)	1.00 [referent]		1.00 [referent]	
Yes	52 (35.37)	405 (26.84)	**1.75 [1.01-3.05]**	**0.0473**	1.03 [0.52-2.03]	0.9320
TSR ≥2mins						
No	119 (80.95)	1,305 (86.48)	1.00 [referent]		1.00 [referent]	
Yes	28 (19.05)	204 (13.52)	1.69 [0.91-3.15]	0.0963	1.12 [0.45-2.74]	0.8123
Apgar 5-minutes <7 [a]						
No	143 (97.28)	1,480 (98.08)				
Yes	4 (2.72)	29 (1.92)				
Intubation						
No	114 (77.55)	1,275 (84.49)	1.00 [referent]		1.00 [referent]	
Yes	33 (22.45)	234 (15.51)	1.78 [0.98-3.21]	0.0572	1.48 [0.63-3.49]	0.3664
Early Preterm Birth						
No	119 (80.95)	1,291 (85.55)	1.00 [referent]		1.00 [referent]	
Yes	28 (19.05)	218 (14.45)	1.51 [0.76-3.00]	0.2372	0.95 [0.42-2.13]	0.8986
POBW <15th Percentile						
No	106 (72.11)	1,125 (74.55)	1.00 [referent]		1.00 [referent]	
Yes	24 (16.33)	193 (12.79)	1.48 [0.76-2.87]	0.2519	1.59 [0.77-3.30]	0.2103
Unavailable	17 (11.56)	191 (12.66)				
Parity						
0	61 (41.5)	601 (39.83)	1.00 [referent]		1.00 [referent]	
1	52 (35.37)	531 (35.19)	0.99 [0.55-1.78]	0.9677	0.86 [0.36-2.03]	0.7233
≥2	34 (23.13)	377 (24.98)	0.89 [0.46-1.72]	0.7269	0.84 [0.24-2.95]	0.7858
Child						
Sex						
Female	32 (21.77)	818 (54.21)	1.00 [referent]		1.00 [referent]	
Male	115 (78.23)	691 (45.79)	**10.13 [4.94-20.79]**	**<0.0001**	**9.37 [4.42-19.87]**	**<0.0001**
Ethnicity						
Other	131 (89.12)	1,441 (95.49)	1.00 [referent]		1.00 [referent]	
Indigenous Australian	16 (10.88)	68 (4.51)	**3.62 [1.36-9.62]**	**0.0101**	**5.61 [1.48-21.31]**	**0.0115**
Child Speaks Language Other Than English at Home						
No	135 (91.84)	1,381 (91.52)	1.00 [referent]		1.00 [referent]	
Yes	12 (8.16)	128 (8.48)	1.00 [0.40-2.49]	0.9937	1.02 [0.34-3.04]	0.9749
Age Category at Time of AEDC Completion [b]						
1	37 (25.17)	284 (18.82)	1.57 [0.85-2.90]	0.1475	1.38 [0.68-2.80]	0.3767
2	102 (69.39)	1,097 (72.7)	1.00 [referent]		1.00 [referent]	
3	8 (5.44)	128 (8.48)	0.62 [0.22-1.77]	0.3720	0.31 [0.08-1.17]	0.0846
Total Number of Siblings						
1	45 (30.61)	463 (30.68)	1.00 [referent]		1.00 [referent]	
2	59 (40.14)	595 (39.43)	1.05 [0.57-1.95]	0.8726	1.72 [0.69-4.25]	0.2413
3	22 (14.97)	292 (19.35)	0.71 [0.32-1.57]	0.4004	0.95 [0.28-3.24]	0.9354
>3	21 (14.29)	159 (10.54)	1.62 [0.69-3.80]	0.2700	1.93 [0.46-8.19]	0.3703
Sociodemographic						
Index of Relative Socioeconomic Disadvantage						
Lowest Quintile	118 (80.27)	1,255 (83.17)	1.08 [0.54-2.17]	0.8345	0.58 [0.24-1.43]	0.2376
> Lowest Quintile	22 (14.97)	215 (14.25)	1.00 [referent]		1.00 [referent]	
Unavailable	7 (4.76)	39 (2.58)				

[a] Excluded from multivariable analysis due to small N.

[b] Age categories classified as; ≥3 years 10 months to <5 years and one month, 2) ≥5 years and one month to <5 years and 10 months (reference category), 3) ≥5 years and 10 months to <6 years 10 months.

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Table 4. Risk Factors for Developmental Vulnerability on the Language & Cognitive Skills (school-based) Domain.

Characteristic	DV (N=195) N (%)	NDV (N=1,461) N (%)	Bivariate OR [95% CI]	p-value	Multivariable (N=1,352) aOR [95% CI]	p-value
Maternal						
Age at Time of Child's Birth (years)						
<25	68 (34.87)	154 (10.54)	**18.41 [5.21-65.05]**	**<0.0001**	**12.90 [2.81-59.16]**	**0.0010**
25-29	38 (19.49)	346 (23.68)	1.00 [referent]		1.00 [referent]	
30-34	52 (26.67)	554 (37.92)	0.72 [0.25-2.02]	0.5279	0.80 [0.24-2.67]	0.7162
≥35	37 (18.97)	407 (27.86)	0.70 [0.23-2.13]	0.5283	0.98 [0.27-3.57]	0.9697
Marital Status						
Married (inc. de facto)	145 (74.36)	1,335 (91.38)	1.00 [referent]		1.00 [referent]	
All Other	50 (25.64)	120 (8.21)	**18.44 [5.70-59.63]**	**<0.0001**	**5.92 [1.43-24.59]**	**0.0144**
Unavailable	0 (0.00)	6 (0.41)				
Occupational Status Scale at Time of Child's Birth						
0-20	70 (35.90)	239 (16.36)	**12.68 [4.58-35.09]**	**<0.0001**	**3.61 [1.19-10.95]**	**0.0235**
>80-100	105 (53.85)	1,180 (80.77)	1.00 [referent]		1.00 [referent]	
Unavailable	20 (10.26)	42 (2.87)				
Pregnancy & Birth						
Fertility Treatments						
No	180 (92.31)	1,208 (82.68)	1.00 [referent]		1.00 [referent]	
Yes	15 (7.69)	253 (17.32)	0.16 [0.04-0.55]	0.0041	0.42 [0.09-1.95]	0.2644
Smoking Status During Pregnancy						
No	145 (74.36)	1,273 (87.13)	1.00 [referent]		1.00 [referent]	
Yes	50 (25.64)	188 (12.87)	**6.35 [2.24-18.01]**	**0.0005**	0.28 [0.07-1.09]	0.0655
Pre-eclampsia						
No	176 (90.26)	1,284 (87.89)	1.00 [referent]		1.00 [referent]	
Yes	19 (9.74)	177 (12.11)	0.61 [0.18-2.10]	0.4336	1.09 [0.26-4.60]	0.9080
Gestational Diabetes						
No	184 (94.36)	1,370 (93.77)	1.00 [referent]		1.00 [referent]	
Yes	11 (5.64)	91 (6.23)	0.84 [0.16-4.44]	0.8360	0.66 [0.11-4.01]	0.6511
Threatened Abortion						
No	189 (96.92)	1,383 (94.66)	1.00 [referent]		1.00 [referent]	
Yes	6 (3.08)	78 (5.34)	0.36 [0.05-2.41]	0.2905	0.20 [0.01-3.32]	0.2578
Other Pregnancy Related Complications						
No	53 (27.18)	523 (35.80)	1.00 [referent]		1.00 [referent]	
Yes	142 (72.82)	938 (64.20)	1.96 [0.84-4.54]	0.1191	1.29 [0.45-3.71]	0.6348
Threatened Preterm Labour						
No	162 (83.08)	1,302 (89.12)	1.00 [referent]		1.00 [referent]	
Yes	33 (16.92)	159 (10.88)	3.21 [0.80-12.92]	0.1002	1.20 [0.32-4.48]	0.7821
APH						
No	183 (93.85)	1,415 (96.85)	1.00 [referent]		1.00 [referent]	
Yes	12 (6.15)	46 (3.15)	6.80 [0.62-74.13]	0.1156	4.92 [0.62-39.01]	0.1315
Placenta Praevia						
No	195 (100.00)	1,451 (99.32)				
Yes	0 (0.00)	10 (0.68)				
Placental Abruption						
No	195 (100.00)	1,455 (99.59)				
Yes	0 (0.00)	6 (0.41)				
Fetal Distress						
No	173 (88.72)	1,345 (92.06)	1.00 [referent]		1.00 [referent]	
Yes	22 (11.28)	116 (7.94)	2.04 [0.45-9.17]	0.3531	0.56 [0.11-2.76]	0.4753
Cephalopelvic Disproportion [a]						
No	195 (100.00)	1,457 (99.73)				
Yes	0 (0.00)	4 (0.27)				
Prolapsed Cord [a]						
No	192 (98.46)	1,451 (99.32)				

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Yes	3 (1.54)	10 (0.68)				
Precipitate Delivery [a]						
No	190 (97.44)	1,440 (98.56)				
Yes	5 (2.56)	21 (1.44)				
PPH ≥500mls						
No	123 (63.08)	1,076 (73.65)	1.00 [referent]		1.00 [referent]	
Yes	72 (36.92)	385 (26.35)	**3.13 [1.22-8.05]**	**0.0177**	1.84 [0.67-5.03]	0.2374
TSR ≥2mins						
No	163 (83.59)	1,261 (86.31)	1.00 [referent]		1.00 [referent]	
Yes	32 (16.41)	200 (13.69)	0.95 [0.39-2.30]	0.9080	0.62 [0.20-1.91]	0.3991
Apgar 5-minutes <7 [a]						
No	193 (98.97)	1,430 (97.88)				
Yes	2 (1.03)	31 (2.12)				
Intubation						
No	159 (81.54)	1,230 (84.19)	1.00 [referent]		1.00 [referent]	
Yes	36 (18.46)	231 (15.81)	1.13 [0.49-2.58]	0.7789	1.68 [0.59-4.81]	0.3326
Early Preterm Birth						
No	155 (79.49)	1,255 (85.90)	1.00 [referent]		1.00 [referent]	
Yes	40 (20.51)	206 (14.10)	2.57 [0.75-8.80]	0.1333	0.79 [0.23-2.80]	0.7200
POBW <15th Percentile						
No	142 (72.82)	1,089 (74.54)	1.00 [referent]		1.00 [referent]	
Yes	36 (18.46)	181 (12.39)	1.62 [0.72-3.66]	0.2464	1.74 [0.71-4.25]	0.2224
Unavailable	17 (8.72)	191 (13.07)				
Parity						
0	51 (26.15)	611 (41.82)	1.00 [referent]		1.00 [referent]	
1	81 (41.54)	502 (34.36)	**4.67 [1.71-12.70]**	**0.0026**	**5.12 [1.25-20.99]**	**0.0232**
≥2	63 (32.31)	348 (23.82)	**6.18 [2.09-18.27]**	**0.0010**	6.37 [1.00-40.66]	0.0504
Child						
Sex						
Female	85 (43.59)	765 (52.36)	1.00 [referent]		1.00 [referent]	
Male	110 (56.41)	696 (47.64)	**3.03 [1.60-5.71]**	**0.0007**	**3.57 [1.66-7.65]**	**0.0011**
Ethnicity						
Other	165 (84.62)	1,407 (96.30)	1.00 [referent]		1.00 [referent]	
Indigenous Australian	30 (15.38)	54 (3.70)	**34.27 [7.49-156.82]**	**<0.0001**	2.22 [0.32-15.52]	0.4199
Child Speaks Language Other Than English at Home						
No	167 (85.64)	1,349 (92.33)	1.00 [referent]		1.00 [referent]	
Yes	28 (14.36)	112 (7.67)	3.82 [0.89-16.47]	0.0724	2.14 [0.49-9.35]	0.3127
Age Category at Time of AEDC Completion [b]						
1	48 (24.62)	273 (18.69)	2.09 [0.74-5.89]	0.1641	2.18 [0.77-6.16]	0.1401
2	128 (65.64)	1,071 (73.31)	1.00 [referent]		1.00 [referent]	
3	19 (9.74)	117 (8.01)	2.56 [0.56-11.82]	0.2273	1.06 [0.22-5.19]	0.9434
Total Number of Siblings						
1	41 (21.03)	467 (31.96)	1.00 [referent]		1.00 [referent]	
2	79 (40.51)	575 (39.36)	**2.82 [1.01-7.88]**	**0.0478**	0.63 [0.15-2.60]	0.5215
3	35 (17.95)	279 (19.10)	2.40 [0.71-8.13]	0.1600	0.23 [0.04-1.40]	0.1104
>3	40 (20.51)	140 (9.58)	**17.34 [4.37-68.74]**	**<0.0001**	2.14 [0.29-15.84]	0.4546
Sociodemographic						
Index of Relative Socioeconomic Disadvantage						
Lowest Quintile	141 (72.31)	1,232 (84.33)	**6.87 [1.80-26.28]**	**0.0049**	1.52 [0.47-4.94]	0.4863
> Lowest Quintile	46 (23.59)	191 (13.07)	1.00 [referent]		1.00 [referent]	
Unavailable	8 (4.10)	38 (2.60)				

[a] Excluded from multivariable analysis due to small N.

[b] Age categories classified as; ≥3 years 10 months to <5 years and one month, 2) ≥5 years and one month to <5 years and 10 months (reference category), 3) ≥5 years and 10 months to <6 years 10 months.

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Table 5. Risk Factors for Developmental Vulnerability on the Communication Skills & General Knowledge Domain.

Characteristic	DV (N=200) N (%)	NDV (N=1,456) N (%)	Bivariate OR [95% CI]	p-value	Multivariable (N=1,352) aOR [95% CI]	p-value
Maternal						
Age at Time of Child's Birth (years)						
<25	59 (29.50)	163 (11.20)	**13.25 [3.50-50.17]**	**0.0002**	**10.96 [2.24-53.75]**	**0.0032**
25-29	40 (20.00)	344 (23.63)	1.00 [referent]		1.00 [referent]	
30-34	59 (29.50)	547 (37.57)	0.74 [0.24-2.28]	0.6016	1.17 [0.33-4.09]	0.8113
≥35	42 (21.00)	402 (27.61)	0.75 [0.23-2.47]	0.6322	1.34 [0.34-5.26]	0.6752
Marital Status						
Married (inc. de facto)	160 (80.00)	1,320 (90.66)	1.00 [referent]		1.00 [referent]	
All Other	40 (20.00)	130 (8.93)	**14.40 [2.74-75.72]**	**0.0017**	2.28 [0.52-10.04]	0.2762
Unavailable	0 (0.00)	6 (0.41)				
Occupational Status Scale at Time of Child's Birth						
0-20	68 (34.00)	241 (16.55)	**11.20 [3.86-32.50]**	**<0.0001**	2.11 [0.67-6.65]	0.2026
>20-100	117 (58.50)	1,168 (80.22)	1.00 [referent]		1.00 [referent]	
Unavailable	15 (7.50)	47 (3.23)				
Pregnancy & Birth						
Fertility Treatments						
No	188 (94.00)	1,200 (82.42)	1.00 [referent]		1.00 [referent]	
Yes	12 (6.00)	256 (17.58)	0.10 [0.02-0.39]	0.0009	0.32 [0.06-1.64]	0.1721
Smoking Status During Pregnancy						
No	148 (74.00)	1,270 (87.23)	1.00 [referent]		1.00 [referent]	
Yes	52 (26.00)	186 (12.77)	**7.79 [2.61-23.28]**	**0.0002**	1.51 [0.42-5.45]	0.5321
Pre-eclampsia						
No	175 (87.50)	1,285 (88.26)	1.00 [referent]		1.00 [referent]	
Yes	25 (12.50)	171 (11.74)	1.07 [0.29-3.90]	0.9240	0.95 [0.21-4.20]	0.9441
Gestational Diabetes						
No	187 (93.50)	1,367 (93.89)	1.00 [referent]		1.00 [referent]	
Yes	13 (6.50)	89 (6.11)	1.16 [0.20-6.72]	0.8696	1.39 [0.23-8.50]	0.7243
Threatened Abortion						
No	192 (96.00)	1,380 (94.78)	1.00 [referent]		1.00 [referent]	
Yes	8 (4.00)	76 (5.22)	0.55 [0.09-3.48]	0.5237	0.37 [0.02-5.73]	0.4767
Other Pregnancy Related Complications						
No	51 (25.50)	525 (36.06)	1.00 [referent]		1.00 [referent]	
Yes	149 (74.50)	931 (63.94)	**2.53 [1.07-6.00]**	**0.0352**	1.61 [0.53-4.90]	0.4040
Threatened Preterm Labour						
No	178 (89.00)	1,286 (88.32)	1.00 [referent]		1.00 [referent]	
Yes	22 (11.00)	170 (11.68)	1.00 [0.27-3.61]	0.9937	0.45 [0.11-1.88]	0.2716
APH						
No	188 (94.00)	1,410 (96.84)	1.00 [referent]		1.00 [referent]	
Yes	12 (6.00)	46 (3.16)	9.09 [0.70-117.63]	0.0910	1.15 [0.12-11.44]	0.9047
Placenta Praevia [a]						
No	200 (100.00)	1,446 (99.31)				
Yes	0 (0.00)	10 (0.69)				
Placental Abruption [a]						
No	199 (99.50)	1,451 (99.66)				
Yes	1 (0.50)	5 (0.34)				
Fetal Distress						
No	172 (86.00)	1,346 (92.45)	1.00 [referent]		1.00 [referent]	
Yes	28 (14.00)	110 (7.55)	4.73 [1.00-22.38]	0.0503	2.21 [0.52-9.41]	0.2853
Cephalopelvic Disproportion [a]						
No	200 (100.00)	1,452 (99.73)				
Yes	0 (0.00)	4 (0.27)				
Prolapsed Cord [a]						
No	200 (100)	1,443 (99.11)				

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Yes	0 (0.00)	13 (0.89)				
Precipitate Delivery [a]						
No	195 (97.50)	1,435 (98.56)				
Yes	5 (2.50)	21 (1.44)				
PPH ≥500mls						
No	122 (61.00)	1,077 (73.97)	1.00 [referent]		1.00 [referent]	
Yes	78 (39.00)	379 (26.03)	**3.72 [1.41-9.86]**	**0.0082**	2.38 [0.84-6.74]	0.1040
TSR ≥2mins						
No	163 (81.50)	1,261 (86.61)	1.00 [referent]		1.00 [referent]	
Yes	37 (18.50)	195 (13.39)	**2.80 [1.08-7.22]**	**0.0335**	1.55 [0.50-4.86]	0.4481
Apgar 5-minutes <7 [a]						
No	198 (99.00)	1,425 (97.87)				
Yes	2 (1.00)	31 (2.13)				
Intubation						
No	162 (81.00)	1,227 (84.27)	1.00 [referent]		1.00 [referent]	
Yes	38 (19.00)	229 (15.73)	1.91 [0.80-4.56]	0.1467	1.32 [0.45-3.90]	0.6143
Early Preterm Birth						
No	157 (78.50)	1,253 (86.06)	1.00 [referent]		1.00 [referent]	
Yes	43 (21.50)	203 (13.94)	3.73 [0.99-14.09]	0.0527	1.68 [0.48-5.82]	0.4133
POBW <15th Percentile						
No	146 (73.00)	1,085 (74.52)	1.00 [referent]		1.00 [referent]	
Yes	36 (18.00)	181 (12.43)	1.83 [0.78-4.33]	0.1657	1.77 [0.72-4.32]	0.2113
Unavailable	18 (9.00)	190 (13.05)				
Parity						
0	65 (32.50)	597 (41.00)	1.00 [referent]		1.00 [referent]	
1	68 (34.00)	515 (35.37)	1.51 [0.59-3.86]	0.3845	1.56 [0.38-6.42]	0.5363
≥2	67 (33.50)	344 (23.63)	**4.54 [1.47-14.09]**	**0.0088**	2.48 [0.38-15.95]	0.3397
Child						
Sex						
Female	87 (43.50)	763 (52.40)	1.00 [referent]		1.00 [referent]	
Male	113 (56.50)	693 (47.60)	**3.00 [1.56-5.79]**	**0.0011**	**3.26 [1.49-7.10]**	**0.0030**
Ethnicity						
Other	179 (89.50)	1,393 (95.67)	1.00 [referent]		1.00 [referent]	
Indigenous Australian	21 (10.50)	63 (4.33)	**21.66 [2.34-200.50]**	**0.0068**	0.81 [0.10-6.68]	0.8416
Child Speaks Language Other Than English at Home						
No	161 (80.50)	1,355 (93.06)	1.00 [referent]		1.00 [referent]	
Yes	39 (19.50)	101 (6.94)	**11.16 [3.30-37.77]**	**0.0001**	**17.83 [4.10-77.61]**	**0.0001**
Age Category at Time of AEDC Completion [b]						
1	57 (28.5)	264 (18.13)	**5.60 [1.73-18.09]**	**0.0041**	**6.01 [1.97-18.31]**	**0.0016**
2	125 (62.5)	1,074 (73.76)	1.00 [referent]		1.00 [referent]	
3	18 (9)	118 (8.1)	1.91 [0.44-8.30]	0.3869	1.30 [0.24-6.95]	0.7618
Total Number of Siblings						
1	49 (24.50)	459 (31.52)	1.00 [referent]		1.00 [referent]	
2	77 (38.50)	577 (39.63)	1.54 [0.58-4.13]	0.3870	0.88 [0.20-3.81]	0.8637
3	37 (18.50)	277 (19.02)	1.64 [0.49-5.44]	0.4189	1.11 [0.18-6.78]	0.9131
>3	37 (18.50)	143 (9.82)	**15.85 [2.91-86.42]**	**0.0014**	4.07 [0.48-34.47]	0.1976
Sociodemographic						
Index of Relative Socioeconomic Disadvantage						
Lowest Quintile	153 (76.50)	1,220 (83.79)	**4.24 [1.12-16.03]**	**0.0332**	0.92 [0.26-3.26]	0.8903
> Lowest Quintile	42 (21.00)	195 (13.39)	1.00 [referent]		1.00 [referent]	
Unavailable	5 (2.50)	41 (2.82)				

[a] Excluded from multivariable analysis due to small N.

[b] Age categories classified as; ≥3 years 10 months to <5 years and one month, 2) ≥5 years and one month to <5 years and 10 months (reference category), 3) ≥5 years and 10 months to <6 years 10 months.

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3 and 7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-10
Bias	9	Describe any efforts to address potential sources of bias	6-10
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10
		(*b*) Describe any methods used to examine subgroups and interactions	10
		(*c*) Explain how missing data were addressed	10
		(*d*) If applicable, explain how loss to follow-up was addressed	10
		(*e*) Describe any sensitivity analyses	10
Results			

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Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7-11
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10-11 and 26-29
		(b) Indicate number of participants with missing data for each variable of interest	26-31
		(c) Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	Report numbers of outcome events or summary measures over time	26-29
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-11 and 26-29
		(*b*) Report category boundaries when continuous variables were categorized	10-11
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	4 and 14
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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The associations between biological and sociodemographic risks for developmental vulnerability in twins at age five: A population data linkage study in Western Australia.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-038846.R2
Article Type:	Original research
Date Submitted by the Author:	15-Sep-2020
Complete List of Authors:	Dhamrait, Gursimran; Telethon Kids Institute, ; The University of Western Australia Faculty of Health and Medical Sciences, School of Population and Global Health Christensen, Daniel; Telethon Kids Institute Pereira, G.F; Telethon Kids Institute; Curtin University, School of Public Health Taylor, Catherine; Telethon Kids Institute; University of Western Australia,
Primary Subject Heading:	Paediatrics
Secondary Subject Heading:	Public health, Epidemiology
Keywords:	EPIDEMIOLOGY, PAEDIATRICS, PUBLIC HEALTH

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Title: The associations between biological and sociodemographic risks for developmental vulnerability in twins at age five: A population data linkage study in Western Australia.

Gursimran K. Dhamrait,[1,2] Daniel Christensen,[1,3] Gavin Pereira[1,4,5] and Catherine L. Taylor.[1,3]

[1]Telethon Kids Institute, Nedlands, Western Australia, Australia.

[2]School of Population and Global Health, The University of Western Australia, Nedlands, Western Australia, Australia.

[3]Centre for Child Health Research, The University of Western Australia, Nedlands, Western Australia, Australia.

[4]School of Public Health, Curtin University, Perth, Australia.

[5]Centre for Fertility and Health (CeFH), Norwegian Institute of Public Health, Oslo, Norway.

Address correspondence to:

Gursimran K. Dhamrait

Telethon Kids Institute

15 Hospital Avenue, Nedlands, Western Australia, Australia.

Phone: 61+ 8 9489 1183

Fax: 61+ 8 9489 7700

Email: gursimran.dhamrait@telethonkids.org.au

Main Body Word Count: 4,287 words

Abstract Word Count: 300 words

Short Title: Developmental vulnerability in twins at age five

Abbreviations

AEDC: Australian Early Development Census

ARIA: Accessibility and Remoteness Index of Australia

AUSEI06: Australian Socioeconomic Index 2006

DV1: Developmentally Vulnerable on one or more Australian Early Development Census domains

DV2: Developmentally Vulnerable on two or more Australian Early Development Census domains

CI: Confidence Interval

IRSD: Index of Relative Socioeconomic Disadvantage

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MNS: Midwives Notifications System

OR: Odds Ratio

POBW: Proportion of Optimal Birth Weight

WA: Western Australia

Keywords (max of 5):

Twins, Australian Early Development Census, Child Development, Record Linkage.

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Abstract

Objective: To investigate the prevalence of, and associations between, prenatal and perinatal risk factors and developmental vulnerability in twins at age five.

Design: Retrospective cohort study using bivariate and multivariable logistic regression.

Setting: Western Australia (WA), 2002-2015.

Participants: 828 twin pairs born in WA with an Australian Early Development Census (AEDC) record from 2009, 2012 or 2015.

Main Outcome Measures: The AEDC is a national measure of child development across five domains. Children with scores <10th percentile were classified as developmentally vulnerable on, one or more domains (DV1), or two or more domains (DV2).

Results: In this population, 26.0% twins were classified as DV1 and 14.1% as DV2. In the multivariable model, risk factors for DV1 were; maternal age <25 years (aOR 7.06, 95% CI 2.29-21.76), child speaking a language other than English at home (aOR 6.45, 95% CI 2.17-19.17), male child (aOR 5.08, 95% CI: 2.89-8.92), age younger than the reference category for the study sample (≥5 years one month to <5 years 10 months) at time of AEDC completion (aOR 3.34, 95% CI: 1.55-7.22), and having a proportion of optimal birthweight (POBW) <15th percentile of the study sample (aOR 2.06, 95% CI 1.07-3.98). Risk factors for DV2 were; male child (aOR 7.87, 95% CI: 3.45-17.97), maternal age <25 years (aOR 5.60, 95% CI: 1.30-24.10), age younger than the reference category (aOR 5.36, 95% CI: 1.94-14.82), child speaking a language other than English at home (aOR 4.65, 95% CI: 1.14-19.03), mother's marital status as not married at the time of twins' birth (aOR 4.59, 95% CI: 1.13-18.55), maternal occupation status in the lowest quintile (aOR 3.30, 95% CI: 1.11-9.81) and a POBW <15th percentile (aOR 3.11, 95% CI: 1.26-7.64).

Conclusion: Both biological and sociodemographic risk factors are associated with developmental vulnerability in twins at five years of age.

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Article Summary

Strengths and Limitations

- The study is based on a large population-level sample of 1,656 twins.
- This is the first twin study to assess developmental vulnerabilities in an otherwise healthy sample of Australian twins, at the time of their first year of full-time school.
- Bivariate and multivariable logistic regression analysis with the calculation of adjusted odds ratios was performed to explore the associations between a large range of prenatal and perinatal risk factors.
- Twin pairs for which data was complete were used for the analysis.
- The datasets used in this study did not report on twin zygosity nor on complications of pregnancy that are specific to multiple pregnancies (e.g., twin reversed arterial perfusion, twin-twin transfusion syndrome).

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Introduction

The increased use of assisted reproductive technologies and increasing maternal age at conception have attributed to a significant increase in the number of multifetal pregnancies around the world.[1] Multifetal pregnancies are classified as high-risk pregnancies and compared to singleton pregnancies, are associated with higher rates of pregnancy complications and adverse neonatal and perinatal outcomes.[2-6] The majority of the literature assessing higher-order pregnancies has focused primarily on birth outcomes, including preterm birth,[7] low birthweight,[3] and developmental disabilities such as cerebral palsy.[8] Studies that have assessed the longer-term developmental outcomes of twins have focused on developmental outcomes around the age of two years.[9] Such studies have reported that twins had poorer performance, in comparison to singletons, on a range of domains including; communication, gross and fine motor skills, problem solving, personal-social skills, and language development.[10,11] Furthermore, most studies examining child development outcomes at school starting age have focused on singleton children, from a single family and have compared children across families.[12] There is a paucity of research on the developmental vulnerability of multifetal pregnancies such as twins, around the time that they commence formal education.

Child development outcomes can vary significantly based on numerous factors including the child's personal characteristics, such as personal dispositions and abilities, social constructs, and the environments, both intrauterine and extrauterine, in which they develop.[13-16] Studies that have assessed cognitive and school performance outcomes at the age of five have reported that children who are born preterm,[17-24] with a low birthweight,[25-28] are small for gestational age,[29,30] and male[31-34] are more likely to have poorer developmental outcomes. In comparison to singletons, twins are more likely to be classified as preterm[35] or low birthweight, and have fetal growth restriction.[36] Studies have also reported that twins are more likely to have poorer neurodevelopmental outcomes compared to singletons, even after controlling for gestational age and birthweight.[37] A study reported that twins scored lower than singletons in both the Verbal and Performance IQ domains of the Wechsler Preschool and Primary Scale of Intelligence, at the ages of four and five years.[38] Likewise, twin studies have also reported sex differences, with girls scoring higher than boys at ages four and five

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years.[38] The cumulative nature of school-based learning means that developmental gaps at school entry, are difficult to close over time.[39] Children who begin school with poor school readiness often struggle to catch up with their peers and tend to fall further behind as they progress through the subsequent years of schooling.[39] As educational achievement trajectories are largely established by 7 years of age (year 3) children with poor school readiness are more likely to have lower later-life educational achievement.[40] Given the higher rates of pregnancy, neonatal and perinatal adversities observed in twins in comparison to singletons, twins are particularly at risk for developmental delays in the early childhood period.

Twin studies, assessing the contribution of genes and the environment, have supported the hypothesis that both factors impact child development.[41-44] Yet, a number of studies have reported no significant differences in child development outcomes based on zygosity.[38,45,46] Sociodemographic factors such as low socioeconomic status and low levels of parental education have also been identified to adversely impact child development outcomes.[47-49] A study conducted in younger twins (assessed at age 6, 12, and 18 months) reported that biological factors including low birthweight were associated with poorer early cognitive and non-cognitive development, independently of environmental factors, such as socioeconomic status.[3] Alternatively, a study reported that the environmental factors shared by twins of the same family were more significantly associated with early language skills and school readiness in twins at the age of five years, in comparison to genetic factors.[45] Overall, studies assessing both biological and sociodemographic factors, and their impact on the longer-term child development of children born from multiple pregnancies, remain sparse and the results of the existing studies are mixed.

The aim of this study was to examine the prevalence of, and the association between, biological and sociodemographic risk factors and developmental vulnerability in twins in their first year of full-time school.

Methods

Data Sources and Study Population

Data Sources

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This study used anonymised individual-level data from the Midwives Notification System (MNS), which is a statutory record of all births (still- or live-born) in WA with either a birthweight >400 grams and/or a final gestational length of ≥20 weeks. Variables from MNS were cross validated with corresponding records from WA Birth Registrations. Australian Early Development Census (AEDC) records were obtained for all available years (2009, 2012, and 2015) for all children with WA birth and perinatal records. Across the 2009, 2012, and 2015 AEDC data collections child participation for the State of WA ranged between 98.7-99.6%.[50] WA Register for Developmental Anomalies (WARDA) records were used to identify children who had a diagnosed developmental disability between birth and age five years. Statistical linkage of all records, by matching identifiers (e.g. name, address, date of birth, etc.) common to sets of records,[51] was provided by the WA Data Linkage Branch from the Department of Health WA.

Patient and Public Involvement

No patients were involved in the development of the research question or the outcome measures, or in the development of the plans for the design or implementation of the study.

Study Population

The study population included all children born in WA with an AEDC record in either 2009, 2012 or 2015 (N=73,903). Children were excluded from the study if; 1) they were not from a twin birth (N=71,748), 2) they were identified by their teacher as having 'special-needs' based on a diagnosed physical and/or intellectual disability (N=123), 3) they were reported as having any birth defect in the WARDA datasets (N=119), 4) they had an AEDC score that was either incomplete or missing (N=22), or 5) their twin sibling was excluded based on the aforementioned exclusion criteria (N=235; Figure 1). The final study sample consisted of N=1,656 children; N=828 twin pairs. There were 252 opposite sex twin pairs and 576 same sex twin pairs (277 male and 299 female twin pairs).

Outcome Measure

The AEDC is a national census of early childhood development spanning five developmental domains; 1) Physical Health and Wellbeing, 2) Social Competence, 3) Emotional Maturity, 4) Language and Cognitive Skills (school-based), and 5) Communication Skills and General Knowledge.

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The AEDC is conducted every three years, with the first national data collection conducted in 2009. Children with scores <10th percentile in a given domain are classified as 'developmentally vulnerable' (DV). For this study children who scored >10th percentile for a given domain were classified as 'not developmentally vulnerable' (NDV). AEDC cut-off scores are based on the first national AEDC data collection in 2009 and apply to all AEDC data collections. Domain scores for children with special needs are not included in the AEDC results. In this study, two summarised outcome measures were used; developmentally vulnerable on one or more AEDC domains (DV1) and developmentally vulnerable on two or more AEDC domains (DV2).

Risk Variables

Maternal Variables

Maternal age and marital status at twins' birth were obtained from the MNS and Birth Registrations. Maternal occupation at birth was obtained from Birth Registrations data and converted to a four-digit standard code using the Australian and New Zealand Standard Classification of Occupations. These codes were then assigned a value ranging from 0-100 using the Australian Socioeconomic Index 2006 (AUSEI06).[52] Low AUSEI06 values are representative of low-status occupations and high values represent high-status occupations. This variable was collapsed into two categories; the most disadvantaged quintile (i.e. AUSEI06 [0-20]) and greater than the most disadvantaged quintile (i.e. AUSEI06 >20). An AUSEI06 value of zero was assigned to records if maternal occupation was reported as 'unemployed,' 'stay at home parent,' or 'pensioner.' For records where maternal occupation was not stated, an AUSEI06 value was not assigned and these cases were reported as missing.

Pregnancy and Birth Variables

We included several binary pregnancy and birth variables to indicate either the presence or absence; of fertility treatments, smoking during pregnancy, pre-eclampsia, gestational diabetes, threatened abortion, threatened preterm labour, antepartum haemorrhage (APH), placenta praevia, placental abruption, fetal distress, cephalopelvic disproportion, prolapsed cord, precipitate delivery, post-partum haemorrhage (PPH), intubation status, early preterm birth (<34 weeks of gestational age), and time to

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Spontaneous Respiration (TSR); with a TSR of ≥2 minutes forming the 'at risk' group, and five-minute Apgar score; with a five-minute Apgar score of <7 forming the 'at risk' group.

The proportion of optimal birthweight (POBW) is a measure of fetal growth and is defined as birthweight divided by expected birthweight in the absence of pathologic risk factors. This measure also accounts for non-pathologic determinants of growth, including gestational age, birth order, sex of the child, and maternal height,[53] and has been validated against ultrasound measurements.[54] We derived a binary proxy for fetal growth restriction as POBW <15th percentile, which corresponded to an observed birthweight less than 75.75% of that expected.[9]

We derived a general category for other pregnancy-related complications (not elsewhere stated; such as urinary tract infection, pre-labour rupture of membranes) for all records. As records may have multiple pregnancy-related complications, all records that had a complication that was not elsewhere stated in this study or had multiple complications of which at least one complication was not elsewhere stated in this study, formed the 'at risk' group for this variable.

Child Variables

Sex and ethnicity of the child were obtained from the MNS and Birth Registrations. Age at the time of AEDC completion and language other than English spoken at home by the child were obtained from the AEDC. Age of children at the time of AEDC completion ranged between; ≥3 years 10 months to <6 years 10 months, with a mean of age category of, ≥5 years one month to 5 years 10 months. To balance frequencies, the age of children at the time of AEDC completion was categorised into three groups; 1) ≥3 years 10 months to <5 years and one month, 2) ≥5 years one month to <5 years 10 months (reference category) and 3) ≥5 years 10 months to <6 years 10 months.

The total number of siblings was derived as the number of live births to each mother prior to the year that the cohort child had the AEDC conducted. Siblings who died within the neonatal period (i.e. mode of separation post-birth from the hospital was death) were excluded in the calculations for the total number of siblings.

Sociodemographic Variables

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The Index of Relative Socioeconomic Disadvantage (IRSD)[19] was calculated using the residential address at the time of birth. ISRD is derived from Australian Census data and reflects area-level disadvantage through variables such as low household income, low educational attainment, and high levels of unemployment. This variable was collapsed into two groups; most disadvantaged quintile (i.e. ISRD quintile 1) and greater than the most disadvantaged quintile (i.e. ISRD quintiles 2-5).

Statistical Modelling

For each risk variable, the 'least risk' category (e.g. not early preterm birth) was used as the reference category (Table 1). To estimate the risk of a child being classified as DV1 and DV2, a generalised linear mixed model with a logit link function was used with a random intercept for each twin pair. A total of 30 maternal, pregnancy, birth, child, and sociodemographic risk variables were considered for the multivariable models. For DV1, DV2, and each of the five AEDC domains, 24 risk variables were included in the multivariable models; six risk variables were excluded from multivariable analysis due to the prevalence being too small (total N<50 for a given category of a given variable). The variables excluded were; 1) placenta praevia, 2) placental abruption, 3) cephalopelvic disproportion, 4) prolapsed cord, 5) precipitate delivery and 6) a five-minute Apgar score of <7. All variables were added simultaneously to the models. Odds ratios (OR) and the associated 95% confidence intervals (CIs) were estimated for both unadjusted and adjusted models. All analyses were undertaken using PROC GLIMMIX in SAS version 9.4 for Windows.[55]

Results

Prevalence of developmental vulnerability in twins

A total of 431 (26.0%) twins were classified as DV1 (Table 1). A total of 151 (18.2%) twin pairs had one twin identified as DV1 and 140 (16.9%) twin pairs had both twins were identified as DV1. Of the 24 maternal, pregnancy and birth, child, and sociodemographic risk variables considered in the multivariable models, five variables had a statistically significant association with an increased risk of a twin being classified as DV1. In order of decreasing magnitude of associated risk, the ORs were; maternal age of <25 younger at time of twins' birth (aOR 7.06, 95% CI 2.29 to 21.76), child speaks a language other than English at home (aOR 6.45, 95% CI 2.17 to 19.17), male twins (aOR 5.08, 95%

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CI 2.89 to 8.92), child's age younger than the reference category for the study sample (≥5 years one month to 5 years 7 months) at the time of AEDC completion (aOR 3.34, 95% CI: 1.55 to 7.22), and POBW <15th percentile (aOR 2.06, 95% CI 1.07 to 3.98). There was a statistically significant association between an increased risk of a twin being classified as DV1 and maternal age at the time of twins' birth (p=0.003), age category at time of ADEC completion (p=0.006), and the total number of sibling (p=0.0248).

A total of 223 (14.1%) twins were classified as DV2 (Table 2). In 95 (11.5%) twin pairs, one twin was identified as DV2 and in 64 twin pairs (7.9%), both twins were identified as DV2. Of the 24 maternal, pregnancy and birth, child, and sociodemographic risk variables considered in the adjusted models, seven variables had a statistically significant association with an increased risk of a twin being classified as DV2. Risk factors for DV2 were, in order of decreasing magnitude; male twins (aOR 7.87, 95% CI: 3.45 to 17.97), maternal age of <25 younger at time of twins' birth (aOR 5.60, 95% CI: 1.30 to 24.10), child's age younger than the reference category at time of AEDC completion (aOR 5.36, 95% CI: 1.94 to 14.82), child speaking a language other than English at home (aOR 4.65, 95% CI: 1.14 to 19.03), mother's marital status as not married at the time of twins' birth (aOR 4.59, 95% CI: 1.13 to 18.55), maternal occupation status in the lowest quintile (aOR 3.30, 95% CI: 1.11 to 9.81) and POBW <15th percentile (aOR 3.11, 95% CI: 1.26 to 7.64). There was a statistically significant association between an increased risk of a twin being classified as DV2 and the age category at the time of ADEC completion (p=0.001).

Associations with domain-specific developmental vulnerability

A total of, 188 (11.4%) children were classified as developmentally vulnerable (DV) for the domains of; Physical Health and Wellbeing, 151 (9.1%) for Social Competence, 147 (8.9%) for Emotional Maturity, 195 (11.8%) for Language and Cognitive Skills (school-based), and 200 (12.0%) for Communication Skills and General Knowledge (Supplementary Tables 1-5, respectively). These results were broadly consistent with the findings for the aggregate measures of developmental vulnerability (DV1 and DV2). All variables that were statistically significant in the aggregated measures of developmental vulnerability were statistically significant for the domains.

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Discussion

This study examined the associations between biological and sociodemographic risk factors and developmental vulnerability in twins in their first year of full-time school. To our knowledge, our study is the first of this scale (population-level sample of twins; N>1,600) to report on the prevalence of developmental vulnerabilities, in an otherwise healthy sample of twins, at the time of their first year of full-time school. As studies have reported that twins are more likely to have poorer performance, in comparison to singletons, at the age of two[10,11] it was pertinent to assess if the prevalence rates of developmental vulnerabilities are higher in twins at age five. We reported that in the WA population, 26.0% of twins were classified as DV1 and 14.1% as DV2 across the 2009, 2012, and 2015 AEDC cycles. In the general WA population, which includes twins and higher-order multiples, 23.0% of children were classified as DV1 and 11.3% of children were classified as DV2, across these AEDC cycles.[50] A large cohort study of 99,530 singleton children from New South Wales reported that 20.8% were classified as DV1 across the 2009 and 2012 AEDC cycles.[56] Thus, we found that twins are at an elevated risk of developmental vulnerability relative to a general population of children in the state of Western Australia and in a singleton population in New South Wales. This is consistent with findings from a study of 142 twin pairs from the Louisville Twin Study, that reported twins scored lower than singletons in both the Verbal and Performance IQ domains of the Wechsler Preschool and Primary Scale of Intelligence at both four and five years of age.[38] As our results were obtained from a sample of twins without any diagnosed developmental disabilities, the higher prevalence rates of twins being classified as DV1 and DV2 observed in our study, when compared to the general Australian population, suggests that healthy twins are more likely to be classified as developmentally vulnerable on AEDC domains at school starting age when compared to their singleton counterparts.

The biological factors associated with developmental vulnerability in twins were; male sex, fetal growth restriction, and younger chronological age at the time of AEDC completion. These results are in line with singleton studies[31,57] which have reported that male children are more likely to be classified as developmentally vulnerable in their first year of full-time school, in comparison to female

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children. A study conducted in South Australia of 13,827 children, of which 3.4% were twins, also reported that male twins were more likely to be classified as DV2 when compared to female twins, however, this finding was not statistically significant.[58] The Louisville Twin Study also reported sex differences, with females scoring higher on Full Scale, Verbal, and Performance IQ, than males at ages four and five years, however, scores tended to converge at six years of age.[38]

We also reported that twins younger than the reference category for this sample were more likely to be classified as developmentally vulnerable in their first year of full-time school. A study of 840 Canadian five-year-old twins, aiming to assess the genetic and environmental factors influencing school readiness, reported that in the preliminary models age was positively correlated with the spatial recognition, numbers, and letters components of the Lollipop test.[59] Furthermore, a recent discussion paper identified the need for further research to assess the effects of delaying school entry for twins[60] thus, highlighting that further research is required to better understand if delaying school entry is beneficial for both short-term and long-term academic outcomes in twins.

The sociodemographic risk factors associated with developmental vulnerability in twins included; maternal age, maternal occupational status, and a not married maternal marital status, at the time of twins' birth, and the child speaking a language other than English at home. These results are supported by the South Australian study, which examined a range of variables also included in our study.[58] This study reported that maternal age, marital status, and maternal occupation were associated with an increased risk of children being classified as DV2 on the AEDC.[58] The South Australian study also reported that parity and smoking during pregnancy were also associated with an increased risk of children being classified as DV2.[58] In our study, we observed an increased but statistically insignificant association between these risk variables and twins being classified as either DV1 or DV2.

An interesting finding from our study was that speaking a language other than English at home was associated with an increased risk for twins being classified as DV1 and DV2. Previous studies have reported that approximately a fifth of Australian children are bilingual,[61] and the prevalence of twins speaking a language other than English at home in our study were in line with these results. Results

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from an Australia-wide study of 261,147 children (including singletons and multiples) from the 2009 AEDC cycle, reported that bilingual children proficient in English have an equal or slightly lower odds of being classed as DV1 when compared to their English-speaking background peers.[61] However, unlike our study, this study[61] did not report differences in developmental vulnerability based on plurality. Additionally, a Canadian study examining the school readiness profiles of 95,537 children in British Columbia[62] reported that bilingualism was associated with positive social, emotional, and cognitive development, as measured by the Early Development Index.[34] Differences in results may be attributed to the fact bilingualism may be a risk factor for twins, however, it may not be a significant risk factor in a general population sample. The language groups most commonly spoken in WA after English (Mandarin, Italian and Vietnamese)[63] are different to those most prevalent in British Colombia (Punjabi, Chinese and German).[64] Thus, the difference in findings between the Canadian study and our results may be attributable to this fact.

Our findings have some accord with a cohort study examining the associations between biological and sociodemographic risk factors on late language emergence in 473 twins pairs at the age of two years.[9] Taylor et al. reported that the risk factors for late language emergence in twins, without developmental disabilities, include fetal growth restriction.[9] Interestingly, our study also identified fetal growth restriction as a risk factor for developmental vulnerability at age five, suggesting that the biological implications of a suboptimal intrauterine environment may persist beyond infancy and into early childhood in twins not diagnosed developmental disabilities. In contrast to our study, the Taylor et al. twin sample excluded twins with exposure to languages other than English. This study reported that sociodemographic risk factors (low maternal education, socioeconomic area disadvantage) were not associated with late language emergence at age two years. Our results suggest that sociodemographic factors including, maternal; age, marital status and occupational status, at time of twins' birth, and the child speaking a language other than English at home are associated with an increased risk of developmental vulnerability at age five.[9] The differences in findings between this study and our study suggest that sociodemographic characteristics may play a more significant role as risk variables at age five years compared to at the age of two years. This hypothesis is supported by a subsequent study of

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twins aged four and six years, which reported that higher maternal education and older maternal age showed positive effects on language and non-verbal phenotypes.[6] Furthermore, a study of a twin sample from the Quebec Newborn Twin Study reported that environmental factors, such as socioeconomic status, rather than genetic factors were attributable to the predictive association observed between early language skills and school readiness, as measured by the Lollipop Test, in twins 63-months of age.[45] In our study, the zygosity of twins could not be established as WA administrative data does not contain information on zygosity. Furthermore, we did not aim to assess the impact of within twin-pair discordance in regards to developmental vulnerabilities at age five. Thus, further research is required to better elucidate the impact and interplay of biological and sociodemographic risk variables at different stages of development in twins.

Studies assessing twin-singleton differences often control for or select for factors such as prematurity, low birthweight, or parental socioeconomic status.[57,65,66] Our study, however, draws attention to the adverse effects of other risk factors, including POBW and maternal marital status, on child development outcomes at age five. An Australian cohort study of 1,922 children from the Northern Territory using linked administrative data, reported an increased, but non-statistically significant, risk of twins being classified as DV1 on the AEDC, after controlling for a range of biological and sociodemographic variables used in our study including; sex, 5-minute Apgar score <7, area remoteness, ethnicity, child speaks a language other than English at home and maternal age at the time of the child's birth.[57] Although this study gave consideration to plurality as a risk factor for developmental vulnerability, it did not aim to assess the association between a comprehensive set of biological and sociodemographic risk factors. A Canadian study of 5-year old twins reported that shared environmental factors substantially accounted for cognitive school readiness (as measured by the Lollipop Test) as compared to genetic effects.[59] Likewise, other studies have also reported that a range of family factors, which would be assumed to be shared by both twins, such as family income, maternal occupation, and employment status are associated with cognitive school readiness.[67,68] Further studies in this area are required, as the extent and nature of the risk factors associated with developmental vulnerability at age five in twins remain not well-established.

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Preventative intervention studies have reported that programs designed to improve school readiness and high-quality early childhood education and care, are effective for at-risk populations and can have significant long-term results.[69,70] The higher prevalence rates of DV1 and DV2 in twins observed in this study are indicative of the fact that twins form an at-risk group in terms of developmental vulnerability at the time at which children commence full-time school. Therefore, it is pertinent for those working in the early childhood education sector and for parents to be aware of the developmental vulnerabilities present in twins at the age at which children begin full-time school. In Australia, there has been a call to provide increased quantity and quality of support service and resources for twins and their families due to increased vulnerability,[60] and the results of our study highlight this need.

Conclusions

Both biological and sociodemographic risk factors are associated with developmental vulnerability at the age of five in twins. The findings of our study suggest that twins are more likely to be classified as developmentally vulnerable at school starting age when compared to their singleton counterparts. In particular, the results draw attention to the hypothesis that prenatal, and more significantly perinatal, risk factors and the sociodemographic environments in which twins are raised can impact developmental vulnerability in early childhood.

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Acknowledgements:

We gratefully acknowledge the WA Data Linkage Branch and the data custodians who provided data for this study and the people of Western Australia for the use of their administrative data. This study does not necessarily reflect their views. This study uses data from the Australian Early Development Census (AEDC). The AEDC is funded by the Australian Government Department of Education and Training. The findings and views reported are those of the authors and should not be attributed to the Department or the Australian Government.

Ethics Approval:

Ethics approval for this study was granted by the Western Australian Department of Health Human Research Ethics Committee (2016/51) and the University of Western Australia Human Research Ethics Committee (RA/4/20/4776).

Declaration of interests:

The authors declare that they have no competing interests, no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Funding:

This study was supported by National Health and Medical Research Grants (GNT1173991 and GNT1099655 to GP), the Research Council of Norway through its Centres of Excellence funding scheme (#262700 to GP) and the Australian Research Council Centre of Excellence for Children and Families over the Life Course (CE140100027 to CLT and DC). GKD was supported by the ARC Centre of Excellence for Children and Families over the Life Course Scholarship, the ARC Centre of Excellence for Children and Families over the Life Course Top-Up Scholarship and the Stan and Jean Perron Top-Up Scholarship.

Author Contributions:

GKD: led study conceptualisation and design, conducted the literature review, performed data manipulation, analysis and interpretation of findings, drafted the initial manuscript and reviewed and revised the manuscript critically for important intellectual content.

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DC, GP and CLT: contributed to the study inception, the development of the design, interpretation of the results, manuscript revisions, the interpretation of the results and revised the manuscript critically for important intellectual content.

GKD, DC, GP and CLT: approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Data Sharing:

The linked administrative data are owned by the government departments who approved the linkage and use of the data for this study. Use of the study data is restricted to named researchers. The current Human Research Ethics Committee approvals were obtained for public sharing and presentation of data on group level only, meaning the data used in this study cannot be shared by the authors. Collaborative research may be conducted according to the ethical requirements and relevant privacy legislations. Potential collaborators should contact author GP with their expression of interest. The steps involved in seeking permission for linkage and use of the data used in this study are the same for all researchers.

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Figures & Tables: (Total 1 Figure & 2 Tables)

Figure 1. Eligible Cohort and Numbers Included for Analyses.
AEDC = Australian Early Development Census. WARDA= Western Australian Register of Developmental Anomalies.

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Table 1. Risk factors for children who are developmentally vulnerable on one or more AEDC domains (DV1).

Characteristic	DV1 (N=431) N (%)	NDV1 (N=1,225) N (%)	Bivariate OR [95% CI]	p-value	Multivariable (N=1,352) aOR [95% CI]	p-value
Maternal						
Age at Time of Child's Birth (years)						
<25	105 (24.36)	117 (9.55)	**9.66 [3.68-25.32]**	**<0.001**	**7.06 [2.29-21.76]**	**<0.001**
25-29	90 (20.88)	294 (24.00)	1 [referent]		1 [referent]	
30-34	130 (30.16)	476 (38.86)	0.81 [0.38-1.72]	0.576	0.89 [0.38-2.07]	0.780
≥35	106 (24.59)	338 (27.59)	1.06 [0.48-2.36]	0.886	1.19 [0.47-2.99]	0.715
			Overall p-value	**<0.001**	Overall p-value	**0.003**
Marital Status						
Married (inc. de facto)	357 (82.83)	1,123 (91.67)	1 [referent]		1 [referent]	
All Other	72 (16.71)	98 (8.00)	**5.99 [2.43-14.75]**	**<0.001**	2.26 [0.76-6.71]	0.140
Unavailable	2 (0.46)	4 (0.33)				
Occupational Status Scale at Time of Child's Birth						
0-20	122 (28.31)	187 (15.27)	**5.58 [2.71-11.46]**	**<0.001**	1.83 [0.79-4.26]	0.159
>20-100	279 (64.73)	1,006 (82.12)	1 [referent]		1 [referent]	
Unavailable	30 (6.96)	32 (2.61)				
Pregnancy & Birth						
Fertility Treatments						
No	377 (87.47)	1,011 (82.53)	1 [referent]		1 [referent]	
Yes	54 (12.53)	214 (17.47)	0.43 [0.19-0.97]	0.042	0.84 [0.32-2.23]	0.729
Smoking Status During Pregnancy						
No	339 (78.65)	1,079 (88.08)	1 [referent]		1 [referent]	
Yes	92 (21.35)	146 (11.92)	**4.31 [1.95-9.53]**	**<0.001**	0.87 [0.34-2.27]	0.779
Pre-eclampsia						
No	375 (87.01)	1,085 (88.57)	1 [referent]		1 [referent]	
Yes	56 (12.99)	140 (11.43)	1.40 [0.59-3.34]	0.444	1.82 [0.68-4.88]	0.237
Gestational Diabetes						
No	402 (93.27)	1,152 (94.04)	1 [referent]		1 [referent]	
Yes	29 (6.73)	73 (5.96)	1.30 [0.40-4.22]	0.657	1.15 [0.33-4.09]	0.826
Threatened Abortion						
No	416 (96.52)	1,156 (94.37)	1 [referent]		1 [referent]	
Yes	15 (3.48)	69 (5.63)	0.36 [0.09-1.45]	0.151	0.23 [0.04-1.35]	0.103
Other Pregnancy Related Complications						
No	125 (29.00)	451 (36.82)	1 [referent]		1 [referent]	
Yes	306 (71.00)	774 (63.18)	**2.08 [1.12-3.85]**	**0.020**	1.79 [0.85-3.79]	0.129
Threatened Preterm Labour						
No	376 (87.24)	1,088 (88.82)	1 [referent]		1 [referent]	
Yes	55 (12.76)	137 (11.18)	1.34 [0.55-3.24]	0.519	0.68 [0.25-1.83]	0.446
APH						
No	411 (95.36)	1,187 (96.90)	1 [referent]		1 [referent]	
Yes	20 (4.64)	38 (3.10)	2.38 [0.53-10.73]	0.260	0.67 [0.12-3.85]	0.650
Placenta Praevia [a]						
No	429 (99.54)	1,217 (99.35)				
Yes	2 (0.46)	8 (0.65)				
Placental Abruption [a]						
No	427 (99.07)	1,223 (99.84)				
Yes	4 (0.93)	2 (0.16)				
Fetal Distress						
No	382 (88.63)	1,136 (92.73)	1 [referent]		1 [referent]	
Yes	49 (11.37)	89 (7.27)	**2.92 [1.13-7.58]**	**0.028**	1.76 [0.60-5.13]	0.301
Cephalopelvic Disproportion [a]						
No	431 (100.00)	1,221 (99.67)				
Yes	0 (0.00)	4 (0.33)				

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Prolapsed Cord [a]						
No	428 (99.30)	1,215 (99.18)				
Yes	3 (0.70)	10 (0.82)				
Precipitate Delivery [a]						
No	424 (98.38)	1,206 (98.45)				
Yes	7 (1.62)	19 (1.55)				
PPH ≥500mls						
No	281 (65.20)	918 (74.94)	1 [referent]		1 [referent]	
Yes	150 (34.80)	307 (25.06)	**2.59 [1.39-4.82]**	**0.003**	1.52 [0.73-3.16]	0.260
TSR ≥2mins						
No	364 (84.45)	1,060 (86.53)	1 [referent]		1 [referent]	
Yes	67 (15.55)	165 (13.47)	1.06 [0.56-1.99]	0.863	0.52 [0.22-1.21]	0.128
Apgar 5-minutes <7 [a]						
No	425 (98.61)	1,198 (97.80)				
Yes	6 (1.39)	27 (2.20)				
Intubation						
No	353 (81.90)	1,036 (84.57)	1 [referent]		1 [referent]	
Yes	78 (18.10)	189 (15.43)	1.36 [0.75-2.45]	0.313	1.54 [0.71-3.37]	0.277
Early Preterm Birth						
No	352 (81.67)	1,058 (86.37)	1 [referent]		1 [referent]	
Yes	79 (18.33)	167 (13.63)	2.08 [0.94-4.56]	0.069	1.29 [0.53-3.15]	0.579
POBW <15th Percentile						
No	305 (70.77)	926 (75.59)	1 [referent]		1 [referent]	
Yes	81 (18.79)	136 (11.10)	**2.09 [1.14-3.84]**	**0.017**	**2.06 [1.07-3.98]**	**0.031**
Unavailable	45 (10.44)	163 (13.31)				
Parity						
0	150 (34.80)	512 (41.80)	1 [referent]		1 [referent]	
1	154 (35.73)	429 (35.02)	1.62 [0.83-3.16]	0.158	1.96 [0.77-5.00]	0.159
≥2	127 (29.47)	284 (23.18)	**2.50 [1.20-5.22]**	**0.015**	2.03 [0.55-7.48]	0.288
			Overall p-value	**0.048**	Overall p-value	0.351
Child						
Sex						
Female	176 (40.84)	674 (55.02)	1 [referent]		1 [referent]	
Male	255 (59.16)	551 (44.98)	**4.44 [2.68-7.36]**	**<0.001**	**5.08 [2.89-8.92]**	**<0.001**
Ethnicity						
Other	385 (89.33)	1,187 (96.90)	1 [referent]		1 [referent]	
Indigenous Australian	46 (10.67)	38 (3.10)	**16.98 [4.85-59.46]**	**<0.001**	2.46 [0.46-13.03]	0.291
Child Speaks Language Other Than English at Home						
No	367 (85.15)	1,149 (93.80)	1 [referent]		1 [referent]	
Yes	64 (14.85)	76 (6.20)	**6.28 [2.48-15.90]**	**<0.001**	**6.45 [2.17-19.17]**	**<0.001**
Age Category at Time of AEDC Completion [b]						
1	109 (25.29)	212 (17.31)	**2.93 [1.45-5.90]**	**0.003**	**3.34 [1.55-7.22]**	**0.002**
2	288 (66.82)	911 (74.37)	1 [referent]		1 [referent]	
3	34 (7.89)	102 (8.33)	1.18 [0.43-3.27]	0.746	0.77 [0.23-2.54]	0.666
			Overall p-value	**0.011**	Overall p-value	**0.006**
Total Number of Siblings						
1	119 (27.61)	389 (31.76)	1 [referent]		1 [referent]	
2	160 (37.12)	494 (40.33)	1.15 [0.58-2.30]	0.685	0.70 [0.27-1.83]	0.461
3	74 (17.17)	240 (19.59)	1.04 [0.45-2.41]	0.926	0.44 [0.13-1.55]	0.120
>3	78 (18.10)	102 (8.33)	**7.28 [2.73-19.45]**	**<0.001**	2.71 [0.60-12.22]	0.194
			Overall p-value	**<0.001**	Overall p-value	**0.025**
Sociodemographic						
Index of Relative Socioeconomic Disadvantage						
Lowest Quintile	327 (75.87)	1,046 (85.39)	**3.55 [1.62-7.78]**	**0.002**	1.63 [0.66-4.02]	0.287
> Lowest Quintile	87 (20.19)	150 (12.24)	1 [referent]		1 [referent]	
Unavailable	17 (3.94)	29 (2.37)				

[a] Excluded from multivariable analysis due to small N.

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[b] Age categories classified as; 1) ≥3 years 10 months to <5 years and one month, 2) ≥5 years and one month to <5 years and 10 months (reference category), 3) ≥5 years and 10 months to <6 years 10 months.

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Table 2. Risk factors for children who are developmentally vulnerable on two or more AEDC domains (DV2).

Characteristic	DV2 (N=223) N (%)	NDV2 (N=1,433) N (%)	Bivariate OR [95% CI]	p-value	Multivariable (N=1,352) aOR [95% CI]	p-value
Maternal						
Age at Time of Child's Birth (years)						
<25	63 (28.25)	159 (11.10)	**7.81 [2.60-23.45]**	**<0.001**	**5.60 [1.30-24.10]**	**0.021**
25-29	48 (21.52)	336 (23.45)	1 [referent]		1 [referent]	
30-34	64 (28.70)	542 (37.82)	0.65 [0.26-1.63]	0.356	0.92 [0.29-2.91]	0.885
≥35	48 (21.52)	396 (27.63)	0.67 [0.25-1.81]	0.434	0.77 [0.22-2.76]	0.689
			Overall p-value	**<0.001**	Overall p-value	0.072
Marital Status						
Married (inc. de facto)	172 (77.13)	1,308 (91.28)	1 [referent]		1 [referent]	
All Other	49 (21.97)	121 (8.44)	**9.91 [3.54-27.77]**	**<0.001**	**4.59 [1.13-18.55]**	**0.033**
Unavailable	2 (0.90)	4 (0.28)				
Occupational Status Scale at Time of Child's Birth						
0-20	78 (34.98)	231 (16.12)	**8.82 [3.72-20.89]**	**<0.001**	**3.30 [1.11-9.81]**	**0.032**
>20-100	130 (58.30)	1,155 (80.60)	1 [referent]		1 [referent]	
Unavailable	15 (6.73)	47 (3.28)				
Pregnancy & Birth						
Fertility Treatments						
No	200 (89.69)	1,188 (82.90)	1 [referent]		1 [referent]	
Yes	23 (10.31)	245 (17.10)	**0.35 [0.13-0.97]**	**0.042**	0.67 [0.17-2.69]	0.567
Smoking Status During Pregnancy						
No	166 (74.44)	1,252 (87.37)	1 [referent]		1 [referent]	
Yes	57 (25.56)	181 (12.63)	**5.83 [2.32-14.65]**	**<0.001**	1.27 [0.38-4.30]	0.700
Pre-eclampsia						
No	195 (87.44)	1,265 (88.28)	1 [referent]		1 [referent]	
Yes	28 (12.56)	168 (11.72)	1.25 [0.41-3.86]	0.693	2.45 [0.65-9.17]	0.184
Gestational Diabetes						
No	208 (93.27)	1,346 (93.93)	1 [referent]		1 [referent]	
Yes	15 (6.73)	87 (6.07)	1.44 [0.32-6.42]	0.635	2.29 [0.46-11.44]	0.312
Threatened Abortion						
No	214 (95.96)	1,358 (94.77)	1 [referent]		1 [referent]	
Yes	9 (4.04)	75 (5.23)	0.54 [0.10-2.94]	0.478	0.24 [0.02-3.08]	0.274
Other Pregnancy Related Complications						
No	57 (25.56)	519 (36.22)	1 [referent]		1 [referent]	
Yes	166 (74.44)	914 (63.78)	**2.64 [1.22-5.69]**	**0.014**	1.64 [0.58-4.61]	0.351
Threatened Preterm Labour						
No	191 (85.65)	1,273 (88.83)	1 [referent]		1 [referent]	
Yes	32 (14.35)	160 (11.17)	2.04 [0.66-6.29]	0.216	0.72 [0.20-2.61]	0.613
APH						
No	209 (93.72)	1,389 (96.93)	1 [referent]		1 [referent]	
Yes	14 (6.28)	44 (3.07)	5.96 [0.95-37.40]	0.057	1.45 [0.36-5.87]	0.599
Placenta Praevia [a]						
No	223 (100.00)	1,423 (99.30)				
Yes	0 (0.00)	10 (0.70)				
Placental Abruption [a]						
No	221 (99.10)	1,429 (99.72)				
Yes	2 (0.90)	4 (0.28)				
Fetal Distress						
No	195 (87.44)	1,323 (92.32)	1 [referent]		1 [referent]	
Yes	28 (12.56)	110 (7.68)	3.03 [0.90-10.23]	0.074	1.56 [0.59-4.15]	0.368
Cephalopelvic Disproportion [a]						
No	223 (100.00)	1,429 (99.72)				
Yes	0 (0.00)	4 (0.28)				

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Prolapsed Cord [a]						
No	220 (98.65)	1,423 (99.30)				
Yes	3 (1.35)	10 (0.70)				
Precipitate Delivery [a]						
No	219 (98.21)	1,411 (98.46)				
Yes	4 (1.79)	22 (1.54)				
PPH ≥500mls						
No	141 (63.23)	1,058 (73.83)	1 [referent]		1 [referent]	
Yes	82 (36.77)	375 (26.17)	**3.43 [1.49-7.94]**	**0.004**	1.38 [0.16-11.79]	0.766
TSR ≥2mins						
No	183 (82.06)	1,241 (86.60)	1 [referent]		1 [referent]	
Yes	40 (17.94)	192 (13.40)	1.78 [0.81-3.89]	0.149	0.91 [0.30-2.72]	0.863
Apgar 5-minutes <7 [a]						
No	219 (98.21)	1,404 (97.98)				
Yes	4 (1.79)	29 (2.02)				
Intubation						
No	178 (79.82)	1,211 (84.51)	1 [referent]		1 [referent]	
Yes	45 (20.18)	222 (15.49)	1.91 [0.90-4.05]	0.093	1.53 [0.54-4.35]	0.429
Early Preterm Birth						
No	172 (77.13)	1,238 (86.39)	1 [referent]		1 [referent]	
Yes	51 (22.87)	195 (13.61)	**4.18 [1.50-11.67]**	**0.006**	2.06 [0.64-6.58]	0.224
POBW <15th Percentile						
No	162 (72.65)	1,069 (74.60)	1 [referent]		1 [referent]	
Yes	42 (18.83)	175 (12.21)	**2.72 [1.25-5.93]**	**0.012**	**3.11 [1.26-7.64]**	**0.014**
Unavailable	19 (8.52)	189 (13.19)				
Parity						
0	79 (35.43)	583 (40.68)	1 [referent]		1 [referent]	
1	73 (32.74)	510 (35.59)	1.18 [0.51-2.76]	0.700	1.12 [0.31-4.04]	0.861
≥2	71 (31.84)	340 (23.73)	**2.66 [1.04-6.83]**	**0.042**	3.61 [0.61-21.22]	0.155
			Overall p-value	0.109	Overall p-value	0.283
Child						
Sex						
Female	83 (37.22)	767 (53.52)	1 [referent]		1 [referent]	
Male	140 (62.78)	666 (46.48)	**5.42 [2.79-10.55]**	**<0.001**	**7.87 [3.45-17.97]**	**<0.001**
Ethnicity						
Other	197 (88.34)	1,375 (95.95)	1 [referent]		1 [referent]	
Indigenous Australian	26 (11.66)	58 (4.05)	**11.00 [2.78-43.60]**	**<0.001**	2.32 [0.32-16.84]	0.404
Child Speaks Language Other Than English at Home						
No	192 (86.10)	1,324 (92.39)	1 [referent]		1 [referent]	
Yes	31 (13.90)	109 (7.61)	3.19 [0.96-10.63]	0.059	**4.65 [1.14-19.03]**	**0.033**
Age Category at Time of AEDC Completion						
1	66 (29.60)	255 (17.79)	**4.11 [1.80-9.39]**	**<0.001**	**5.36 [1.94-14.82]**	**0.001**
2	142 (63.68)	1,057 (73.76)	1 [referent]		1 [referent]	
3	15 (6.73)	121 (8.44)	0.95 [0.26-3.46]	0.942	0.28 [0.05-1.70]	0.167
			Overall p-value	**0.003**	Overall p-value	**0.001**
Total Number of Siblings						
1	58 (26.01)	450 (31.40)	1 [referent]		1 [referent]	
2	84 (37.67)	570 (39.78)	1.35 [0.57-3.19]	0.489	1.26 [0.34-4.71]	0.733
3	38 (17.04)	276 (19.26)	1.14 [0.40-3.24]	0.810	0.47 [0.08-2.70]	0.395
>3	43 (19.28)	137 (9.56)	**7.14 [2.24-22.72]**	**<0.001**	2.52 [0.34-18.73]	0.366
			Overall p-value	**0.006**	Overall p-value	0.175
Sociodemographic						
Index of Relative Socioeconomic Disadvantage						
Lowest Quintile	175 (78.48)	1,198 (83.60)	2.14 [0.76-6.02]	0.151	0.68 [0.21-2.25]	0.529
> Lowest Quintile	39 (17.49)	198 (13.82)	1 [referent]		1 [referent]	
Unavailable	9 (4.04)	37 (2.58)				

[a] Excluded from multivariable analysis due to small N.

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[b] Age categories classified as; 1) ≥3 years 10 months to <5 years and one month, 2) ≥5 years and one month to <5 years and 10 months (reference category), 3) ≥5 years and 10 months to <6 years 10 months.

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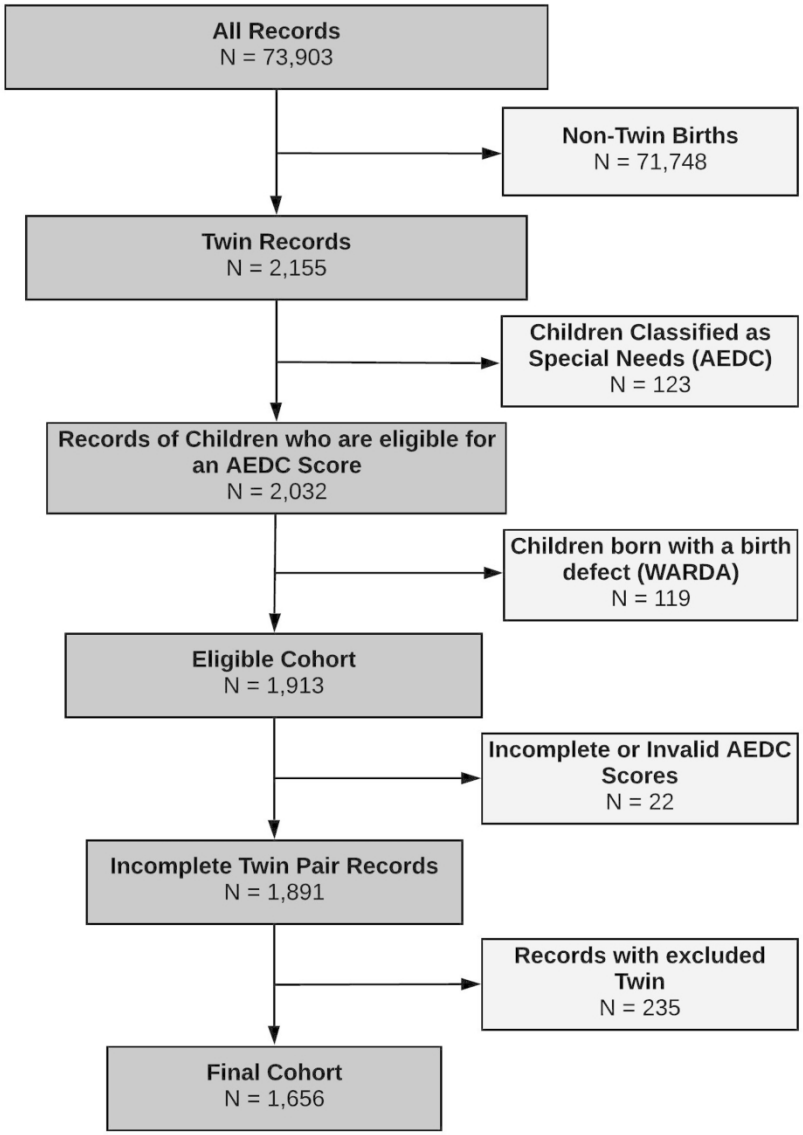

Figure 1. Eligible Cohort and Numbers Included for Analyses.AEDC = Australian Early Development Census. WARDA= Western Australian Register of Developmental Anomalies.

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Supplementary Tables

Table 1. Risk Factors for Developmental Vulnerability on the Physical Health & Wellbeing Domain.

Characteristic	DV (N=188) N (%)	NDV (N=1,468) N (%)	Bivariate OR [95% CI]	p-value	Multivariable (N=1,352) aOR [95% CI]	p-value
Maternal						
Age at Time of Child's Birth (years)						
<25	46 (24.47)	176 (11.99)	**5.36 [1.64-17.48]**	**0.002**	3.59 [0.93-13.90]	0.065
25-29	39 (20.74)	345 (23.50)	1 [referent]		1 [referent]	
30-34	62 (32.98)	544 (37.06)	1.08 [0.41-2.87]	0.646	1.13 [0.39-3.25]	0.821
≥35	41 (21.81)	403 (27.45)	0.83 [0.29-2.38]	0.776	0.97 [0.30-3.13]	0.959
			Overall p-value	**0.009**	Overall p-value	0.269
Marital Status						
Married (inc. de facto)	152 (80.85)	1,328 (90.46)	1 [referent]		1 [referent]	
All Other	36 (19.15)	134 (9.13)	**5.54 [1.87-16.35]**	**0.002**	2.39 [0.66-8.70]	0.185
Unavailable	0 (0.00)	6 (0.41)				
Occupational Status Scale at Time of Child's Birth						
0-20	52 (27.66)	257 (17.51)	**3.29 [1.40-7.75]**	**0.025**	0.79 [0.28-2.27]	0.663
>20-100	119 (63.30)	1,166 (79.43)	1 [referent]		1 [referent]	
Unavailable	17 (9.04)	45 (3.07)				
Pregnancy & Birth						
Fertility Treatments						
No	163 (86.70)	1,225 (83.45)	1 [referent]		1 [referent]	
Yes	25 (13.30)	243 (16.55)	0.61 [0.21-1.75]	0.359	1.07 [0.32-3.62]	0.914
Smoking Status During Pregnancy						
No	134 (71.28)	1,284 (87.47)	1 [referent]		1 [referent]	
Yes	54 (28.72)	184 (12.53)	**7.19 [2.76-18.70]**	**<0.001**	2.49 [0.83-7.51]	0.105
Pre-eclampsia						
No	163 (86.70)	1,297 (88.35)	1 [referent]		1 [referent]	
Yes	25 (13.30)	171 (11.65)	1.56 [0.46-5.24]	0.475	2.99 [0.90-9.91]	0.074
Gestational Diabetes						
No	173 (92.02)	1,381 (94.07)	1 [referent]		1 [referent]	
Yes	15 (7.98)	87 (5.93)	1.87 [0.36-9.87]	0.460	2.26 [0.50-10.20]	0.290
Threatened Abortion						
No	182 (96.81)	1,390 (94.69)	1 [referent]		1 [referent]	
Yes	6 (3.19)	78 (5.31)	0.45 [0.07-2.71]	0.379	0.43 [0.05-3.77]	0.443
Other Pregnancy Related Complications						
No	51 (27.13)	525 (35.76)	1 [referent]		1 [referent]	
Yes	137 (72.87)	943 (64.24)	1.96 [0.87-4.42]	0.103	1.69 [0.65-4.42]	0.284
Threatened Preterm Labour						
No	161 (85.64)	1,303 (88.76)	1 [referent]		1 [referent]	
Yes	27 (14.36)	165 (11.24)	1.68 [0.49-5.81]	0.411	0.86 [0.26-2.82]	0.797
APH						
No	178 (94.68)	1,420 (96.73)	1 [referent]		1 [referent]	
Yes	10 (5.32)	48 (3.27)	3.27 [0.37-28.63]	0.285	0.73 [0.09-5.96]	0.766
Placenta Praevia [a]						
No	187 (99.47)	1,459 (99.39)				
Yes	1 (0.53)	9 (0.61)				
Placental Abruption [a]						
No	185 (98.40)	1,465 (99.8)				
Yes	3 (1.60)	3 (0.20)				
Fetal Distress						
No	162 (86.17)	1,356 (92.37)	1 [referent]		1 [referent]	
Yes	26 (13.83)	112 (7.63)	**4.89 [1.20-19.90]**	**0.027**	2.57 [0.72-9.19]	0.145
Cephalopelvic Disproportion [a]						
No	188 (100.00)	1,464 (99.73)				
Yes	0 (0.00)	4 (0.27)				
Prolapsed Cord [a]						

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No	188 (100.00)	1,455 (99.11)				
Yes	0 (0.00)	13 (0.89)				
Precipitate Delivery [a]						
No	186 (98.94)	1,444 (98.37)				
Yes	2 (1.06)	24 (1.63)				
PPH ≥500mls						
No	124 (65.96)	1,075 (73.23)	1 [referent]		1 [referent]	
Yes	64 (34.04)	393 (26.77)	2.16 [0.90-5.18]	0.084	0.90 [0.36-2.25]	0.826
TSR ≥2mins						
No	152 (80.85)	1,272 (86.65)	1 [referent]		1 [referent]	
Yes	36 (19.15)	196 (13.35)	1.48 [0.64-3.44]	0.363	0.55 [0.19-1.55]	0.258
Apgar 5-minutes <7 [a]						
No	182 (96.81)	1,441 (98.16)				
Yes	6 (3.19)	27 (1.84)				
Intubation						
No	147 (78.19)	1,242 (84.60)	1 [referent]		1 [referent]	
Yes	41 (21.81)	226 (15.40)	**2.33 [1.03-5.28]**	**0.043**	1.96 [0.75-5.10]	0.167
Early Preterm Birth						
No	146 (77.66)	1,264 (86.1)	1 [referent]		1 [referent]	
Yes	42 (22.34)	204 (13.9)	**3.76 [1.21-11.68]**	**0.022**	2.15 [0.76-6.11]	0.151
POBW <15th Percentile						
No	125 (66.49)	1,106 (75.34)	1 [referent]		1 [referent]	
Yes	42 (22.34)	175 (11.92)	**3.44 [1.53-7.74]**	**0.003**	**2.58 [1.15-5.77]**	**0.022**
Unavailable	21 (11.17)	187 (12.74)				
Parity						
0	67 (35.64)	595 (40.53)	1 [referent]		1 [referent]	
1	65 (34.57)	518 (35.29)	1.18 [0.48-2.86]	0.721	1.29 [0.41-4.08]	0.665
≥2	56 (29.79)	355 (24.18)	1.81 [0.67-4.91]	0.244	1.53 [0.29-8.17]	0.617
			Overall p-value	0.503	Overall p-value	0.866
Child						
Sex						
Female	82 (43.62)	768 (52.32)	1 [referent]		1 [referent]	
Male	106 (56.38)	700 (47.68)	**2.50 [1.36-4.61]**	**0.003**	**3.31 [1.64-6.69]**	**<0.001**
Ethnicity						
Other	167 (88.83)	1,405 (95.71)	1 [referent]		1 [referent]	
Indigenous Australian	21 (11.17)	63 (4.29)	**12.56 [2.12-74.52]**	**0.005**	0.80 [0.12-5.40]	0.816
Child Speaks Language Other Than English at Home						
No	159 (84.57)	1,357 (92.44)	1 [referent]		1 [referent]	
Yes	29 (15.43)	111 (7.56)	**4.62 [1.24-17.26]**	**0.023**	**4.84 [1.34-17.48]**	**0.016**
Age Category at Time of AEDC Completion						
1	50 (26.60)	271 (18.46)	**2.76 [1.02-7.46]**	**<0.001**	2.22 [0.88-5.60]	0.092
2	129 (68.62)	1,070 (72.89)	1 [referent]		1 [referent]	
3	9 (4.79)	127 (8.65)	0.44 [0.10-1.93]	0.942	0.19 [0.03-1.18]	0.074
			Overall p-value	**0.049**	Overall p-value	**0.033**
Total Number of Siblings						
1	51 (27.13)	457 (31.13)	1 [referent]		1 [referent]	
2	69 (36.70)	585 (39.85)	1.10 [0.46-2.63]	0.827	0.98 [0.30-3.15]	0.970
3	24 (12.77)	290 (19.75)	0.51 [0.16-1.57]	0.239	0.41 [0.08-2.10]	0.284
>3	44 (23.40)	136 (9.26)	**8.32 [2.57-26.96]**	**<0.001**	6.47 [0.98-42.75]	0.053
			Overall p-value	**<0.001**	Overall p-value	**0.008**
Sociodemographic						
Index of Relative Socioeconomic Disadvantage						
Lowest Quintile	138 (73.40)	1,235 (84.13)	**3.78 [1.17-12.22]**	**0.026**	1.85 [0.63-5.44]	0.264
> Lowest Quintile	40 (21.28)	197 (13.42)	1 [referent]		1 [referent]	
Unavailable	10 (5.32)	36 (2.45)				

[a] Excluded from multivariable analysis due to small N.

[b] Age categories classified as; 1) ≥3 years 10 months to <5 years and one month, 2) ≥5 years and one month to <5 years and 10 months (reference category), 3) ≥5 years and 10 months to <6 years 10 months.

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Table 2. Risk Factors for Developmental Vulnerability on the Social Competence Domain.

Characteristic	DV (N=151) N (%)	NDV (N=1,505) N (%)	Bivariate OR [95% CI]	p-value	Multivariable (N=1,352) aOR [95% CI]	p-value
Maternal						
Age at Time of Child's Birth (years)						
<25	43 (28.48)	179 (11.89)	**6.32 [1.91-20.95]**	**0.003**	3.13 [0.74-13.30]	0.122
25-29	31 (20.53)	353 (23.46)	1 [referent]		1 [referent]	
30-34	44 (29.14)	562 (37.34)	0.78 [0.29-2.15]	0.634	1.36 [0.43-4.36]	0.604
≥35	33 (21.85)	411 (27.31)	0.81 [0.27-2.37]	0.696	0.99 [0.27-3.59]	0.982
			Overall p-value	**0.002**	Overall p-value	0.431
Marital Status						
Married (inc. de facto)	113 (74.83)	1,367 (90.83)	1 [referent]		1 [referent]	
All Other	36 (23.84)	134 (8.90)	**9.65 [3.20-29.05]**	**<0.001**	**10.16 [2.56-40.41]**	**0.001**
Unavailable	2 (1.32)	4 (0.27)				
Occupational Status Scale at Time of Child's Birth						
0-20	50 (33.11)	259 (17.21)	**5.05 [2.07-12.29]**	**<0.001**	1.93 [0.64-5.79]	0.241
>20-100	94 (62.25)	1,191 (79.14)	1 [referent]		1 [referent]	
Unavailable	7 (4.64)	55 (3.65)				
Pregnancy & Birth						
Fertility Treatments						
No	132 (87.42)	1,256 (83.46)	1 [referent]		1 [referent]	
Yes	19 (12.58)	249 (16.54)	0.54 [0.18-1.60]	0.269	1.38 [0.37-5.17]	0.635
Smoking Status During Pregnancy						
No	116 (76.82)	1,302 (86.51)	1 [referent]		1 [referent]	
Yes	35 (23.18)	203 (13.49)	**3.70 [1.06-12.91]**	**0.041**	1.22 [0.35-4.20]	0.753
Pre-eclampsia						
No	134 (88.74)	1,326 (88.11)	1 [referent]		1 [referent]	
Yes	17 (11.26)	179 (11.89)	0.98 [0.31-3.14]	0.975	1.84 [0.49-6.84]	0.365
Gestational Diabetes						
No	140 (92.72)	1,414 (93.95)	1 [referent]		1 [referent]	
Yes	11 (7.28)	91 (6.05)	1.46 [0.32-6.60]	0.627	2.11 [0.41-10.74]	0.369
Threatened Abortion						
No	144 (95.36)	1,428 (94.88)	1 [referent]		1 [referent]	
Yes	7 (4.64)	77 (5.12)	0.66 [0.11-4.10]	0.658	0.13 [0.01-2.43]	0.171
Other Pregnancy Related Complications						
No	38 (25.17)	538 (35.75)	1 [referent]		1 [referent]	
Yes	113 (74.83)	967 (64.25)	2.15 [0.89-5.19]	0.088	2.00 [0.70-5.74]	0.196
Threatened Preterm Labour						
No	131 (86.75)	1,333 (88.57)	1 [referent]		1 [referent]	
Yes	20 (13.25)	172 (11.43)	1.32 [0.42-4.17]	0.640	0.69 [0.19-2.59]	0.584
APH						
No	142 (94.04)	1,456 (96.74)	1 [referent]		1 [referent]	
Yes	9 (5.96)	49 (3.26)	3.74 [0.62-22.66]	0.151	2.12 [0.27-16.50]	0.473
Placenta Praevia [a]						
No	151 (100.00)	1,495 (99.34)				
Yes	0 (0.00)	10 (0.66)				
Placental Abruption [a]						
No	149 (98.68)	1,501 (99.73)				
Yes	2 (1.32)	4 (0.27)				
Fetal Distress						
No	132 (87.42)	1,386 (92.09)	1 [referent]		1 [referent]	
Yes	19 (12.58)	119 (7.91)	2.77 [0.81-9.50]	0.105	1.39 [0.33-5.82]	0.656
Cephalopelvic Disproportion [a]						
No	151 (100.00)	1,501 (99.73)				
Yes	0 (0.00)	4 (0.27)				
Prolapsed Cord [a]						
No	148 (98.01)	1,495 (99.34)				

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Yes	3 (1.99)	10 (0.66)				
Precipitate Delivery [a]						
No	149 (98.68)	1,481 (98.41)				
Yes	2 (1.32)	24 (1.59)				
PPH ≥500mls						
No	96 (63.58)	1,103 (73.29)	1 [referent]		1 [referent]	
Yes	55 (36.42)	402 (26.71)	**2.61 [1.14-5.97]**	**0.023**	1.42 [0.54-3.76]	0.477
TSR ≥2mins						
No	119 (78.81)	1,305 (86.71)	1 [referent]		1 [referent]	
Yes	32 (21.19)	200 (13.29)	1.76 [0.80-3.89]	0.161	0.80 [0.26-2.46]	0.697
Apgar 5-minutes <7 [a]						
No	147 (97.35)	1,476 (98.07)				
Yes	4 (2.65)	29 (1.93)				
Intubation						
No	112 (74.17)	1,277 (84.85)	1 [referent]		1 [referent]	
Yes	39 (25.83)	228 (15.15)	2.31 [1.00-5.33]	0.051	2.48 [0.86-7.20]	0.093
Early Preterm Birth						
No	123 (81.46)	1,287 (85.51)	1 [referent]		1 [referent]	
Yes	28 (18.54)	218 (14.49)	1.64 [0.59-4.57]	0.345	0.68 [0.20-2.27]	0.525
POBW <15th Percentile						
No	114 (75.5)	1,117 (74.22)	1 [referent]		1 [referent]	
Yes	23 (15.23)	194 (12.89)	1.51 [0.65-3.54]	0.341	1.65 [0.63-4.30]	0.304
Unavailable	14 (9.27)	194 (12.89)				
Parity						
0	58 (38.41)	604 (40.13)	1 [referent]		1 [referent]	
1	49 (32.45)	534 (35.48)	1.06 [0.44-2.56]	0.906	0.87 [0.25-3.08]	0.827
≥2	44 (29.14)	367 (24.39)	1.73 [0.67-4.50]	0.259	2.02 [0.35-11.63]	0.432
			Overall p-value	0.481	Overall p-value	0.554
Child						
Sex						
Female	51 (33.77)	799 (53.09)	1 [referent]		1 [referent]	
Male	100 (66.23)	706 (46.91)	**5.21 [2.58-10.52]**	**<0.001**	**5.35 [2.38-12.00]**	**<0.001**
Ethnicity						
Other	137 (90.73)	1,435 (95.35)	1 [referent]		1 [referent]	
Indigenous Australian	14 (9.27)	70 (4.65)	3.96 [0.86-18.29]	0.078	2.43 [0.36-16.63]	0.364
Child Speaks Language Other Than English at Home						
No	139 (92.05)	1,377 (91.50)	1 [referent]		1 [referent]	
Yes	12 (7.95)	128 (8.50)	0.67 [0.17-2.62]	0.567	1.13 [0.24-5.18]	0.880
Age Category at Time of AEDC Completion [b]						
1	40 (26.49)	281 (18.67)	2.42 [0.98-5.94]	0.055	**2.84 [1.05-7.73]**	**0.041**
2	98 (64.9)	1,101 (73.16)	1 [referent]		1 [referent]	
3	13 (8.61)	123 (8.17)	1.73 [0.46-6.48]	0.417	0.51 [0.09-2.75]	0.431
			Overall p-value	0.145	Overall p-value	0.065
Total Number of Siblings						
1	41 (27.15)	467 (31.03)	1 [referent]		1 [referent]	
2	57 (37.75)	597 (39.67)	1.27 [0.50-3.23]	0.613	1.97 [0.52-7.49]	0.322
3	27 (17.88)	287 (19.07)	1.27 [0.41-3.91]	0.678	0.91 [0.16-5.21]	0.915
>3	26 (17.22)	154 (10.23)	**4.06 [1.14-14.39]**	**0.030**	2.53 [0.33-19.66]	0.374
			Overall p-value	0.172	Overall p-value	0.417
Sociodemographic						
Index of Relative Socioeconomic Disadvantage						
Lowest Quintile	118 (78.15)	1,255 (83.39)	1.67 [0.59-4.74]	0.336	0.72 [0.21-2.45]	0.596
> Lowest Quintile	26 (17.22)	211 (14.02)	1 [referent]		1 [referent]	
Unavailable	7 (4.64)	39 (2.59)				

[a] Excluded from multivariable analysis due to small N.

[b] Age categories classified as; 1) ≥3 years 10 months to <5 years and one month, 2) ≥5 years and one month to <5 years and 10 months (reference category), 3) ≥5 years and 10 months to <6 years 10 months.

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Table 3. Risk Factors for Developmental Vulnerability on the Emotional Maturity Domain.

Characteristic	DV (N=147) N (%)	NDV (N=1,509) N (%)	Bivariate OR [95% CI]	p-value	Multivariable (N=1,352) aOR [95% CI]	p-value
Maternal						
Age at Time of Child's Birth (years)						
<25	39 (26.53)	183 (12.13)	**3.14 [1.44-6.89]**	**0.004**	1.89 [0.70-5.05]	0.206
25-29	31 (21.09)	353 (23.39)	1 [referent]		1 [referent]	
30-34	38 (25.85)	568 (37.64)	0.70 [0.35-1.40]	0.311	1.03 [0.46-2.34]	0.937
≥35	39 (26.53)	405 (26.84)	1.12 [0.55-2.27]	0.762	1.16 [0.48-2.81]	0.742
			Overall p-value	**0.001**	Overall p-value	0.611
Marital Status						
Married (inc. de facto)	111 (75.51)	1,369 (90.72)	1 [referent]		1 [referent]	
All Other	34 (23.13)	136 (9.01)	**4.58 [2.26-9.27]**	**<0.001**	**3.77 [1.48-9.58]**	**0.006**
Unavailable	2 (1.36)	4 (0.27)				
Occupational Status Scale at Time of Child's Birth						
0-20	45 (30.61)	264 (17.50)	**2.62 [1.46-4.72]**	**0.001**	1.85 [0.86-3.97]	0.113
>20-100	95 (64.63)	1,190 (78.86)	1 [referent]		1 [referent]	
Unavailable	7 (4.76)	55 (3.64)				
Pregnancy & Birth						
Fertility Treatments						
No	126 (85.71)	1,262 (83.63)	1 [referent]		1 [referent]	
Yes	21 (14.29)	247 (16.37)	0.81 [0.40-1.66]	0.567	1.03 [0.42-2.53]	0.957
Smoking Status During Pregnancy						
No	118 (80.27)	1,300 (86.15)	1 [referent]		1 [referent]	
Yes	29 (19.73)	209 (13.85)	1.70 [0.86-3.36]	0.130	0.82 [0.33-2.02]	0.662
Pre-eclampsia						
No	129 (87.76)	1,331 (88.20)	1 [referent]		1 [referent]	
Yes	18 (12.24)	178 (11.80)	1.09 [0.50-2.40]	0.827	1.87 [0.75-4.63]	0.176
Gestational Diabetes						
No	138 (93.88)	1,416 (93.84)	1 [referent]		1 [referent]	
Yes	9 (6.12)	93 (6.16)	1.02 [0.35-2.97]	0.975	1.18 [0.37-3.76]	0.785
Threatened Abortion						
No	140 (95.24)	1,432 (94.90)	1 [referent]		1 [referent]	
Yes	7 (4.76)	77 (5.10)	0.91 [0.28-3.03]	0.882	0.09 [0.01-1.06]	0.055
Other Pregnancy Related Complications						
No	35 (23.81)	541 (35.85)	1 [referent]		1 [referent]	
Yes	112 (76.19)	968 (64.15)	**2.13 [1.20-3.80]**	**0.010**	1.80 [0.86-3.78]	0.121
Threatened Preterm Labour						
No	125 (85.03)	1,339 (88.73)	1 [referent]		1 [referent]	
Yes	22 (14.97)	170 (11.27)	1.52 [0.72-3.25]	0.274	1.21 [0.51-2.85]	0.664
APH						
No	139 (94.56)	1,459 (96.69)	1 [referent]		1 [referent]	
Yes	8 (5.44)	50 (3.31)	2.13 [0.62-7.31]	0.230	0.67 [0.13-3.31]	0.618
Placenta Praevia [a]						
No	146 (99.32)	1,500 (99.40)				
Yes	1 (0.68)	9 (0.60)				
Placental Abruption [a]						
No	145 (98.64)	1,505 (99.73)				
Yes	2 (1.36)	4 (0.27)				
Fetal Distress						
No	128 (87.07)	1,390 (92.11)	1 [referent]		1 [referent]	
Yes	19 (12.93)	119 (7.89)	1.95 [0.86-4.44]	0.111	1.09 [0.40-2.93]	0.869
Cephalopelvic Disproportion [a]						
No	147 (100.00)	1,505 (99.73)				
Yes	0 (0.00)	4 (0.27)				
Prolapsed Cord [a]						
No	145 (98.64)	1,498 (99.27)				

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Yes	2 (1.36)	11 (0.73)				
Precipitate Delivery [a]						
No	146 (99.32)	1,484 (98.34)				
Yes	1 (0.68)	25 (1.66)				
PPH ≥500mls						
No	95 (64.63)	1,104 (73.16)	1 [referent]		1 [referent]	
Yes	52 (35.37)	405 (26.84)	**1.75 [1.01-3.05]**	**0.047**	1.03 [0.52-2.03]	0.932
TSR ≥2mins						
No	119 (80.95)	1,305 (86.48)	1 [referent]		1 [referent]	
Yes	28 (19.05)	204 (13.52)	1.69 [0.91-3.15]	0.096	1.12 [0.45-2.74]	0.812
Apgar 5-minutes <7 [a]						
No	143 (97.28)	1,480 (98.08)				
Yes	4 (2.72)	29 (1.92)				
Intubation						
No	114 (77.55)	1,275 (84.49)	1 [referent]		1 [referent]	
Yes	33 (22.45)	234 (15.51)	1.78 [0.98-3.21]	0.057	1.48 [0.63-3.49]	0.366
Early Preterm Birth						
No	119 (80.95)	1,291 (85.55)	1 [referent]		1 [referent]	
Yes	28 (19.05)	218 (14.45)	1.51 [0.76-3.00]	0.237	0.95 [0.42-2.13]	0.897
POBW <15th Percentile						
No	106 (72.11)	1,125 (74.55)	1 [referent]		1 [referent]	
Yes	24 (16.33)	193 (12.79)	1.48 [0.76-2.87]	0.252	1.59 [0.77-3.30]	0.210
Unavailable	17 (11.56)	191 (12.66)				
Parity						
0	61 (41.5)	601 (39.83)	1 [referent]		1 [referent]	
1	52 (35.37)	531 (35.19)	0.99 [0.55-1.78]	0.968	0.86 [0.36-2.03]	0.723
≥2	34 (23.13)	377 (24.98)	0.89 [0.46-1.72]	0.727	0.84 [0.24-2.95]	0.786
			Overall p-value	0.934	Overall p-value	0.935
Child						
Sex						
Female	32 (21.77)	818 (54.21)	1 [referent]		1 [referent]	
Male	115 (78.23)	691 (45.79)	**10.13 [4.94-20.79]**	**<0.001**	**9.37 [4.42-19.87]**	**<0.001**
Ethnicity						
Other	131 (89.12)	1,441 (95.49)	1 [referent]		1 [referent]	
Indigenous Australian	16 (10.88)	68 (4.51)	**3.62 [1.36-9.62]**	**0.010**	**5.61 [1.48-21.31]**	**0.012**
Child Speaks Language Other Than English at Home						
No	135 (91.84)	1,381 (91.52)	1 [referent]		1 [referent]	
Yes	12 (8.16)	128 (8.48)	1.00 [0.40-2.49]	0.994	1.02 [0.34-3.04]	0.975
Age Category at Time of AEDC Completion [b]						
1	37 (25.17)	284 (18.82)	1.57 [0.85-2.90]	0.148	1.38 [0.68-2.80]	0.377
2	102 (69.39)	1,097 (72.7)	1 [referent]		1 [referent]	
3	8 (5.44)	128 (8.48)	0.62 [0.22-1.77]	0.372	0.31 [0.08-1.17]	0.085
			Overall p-value	0.187	Overall p-value	0.122
Total Number of Siblings						
1	45 (30.61)	463 (30.68)	1 [referent]		1 [referent]	
2	59 (40.14)	595 (39.43)	1.05 [0.57-1.95]	0.873	1.72 [0.69-4.25]	0.241
3	22 (14.97)	292 (19.35)	0.71 [0.32-1.57]	0.400	0.95 [0.28-3.24]	0.935
>3	21 (14.29)	159 (10.54)	1.62 [0.69-3.80]	0.270	1.93 [0.46-8.19]	0.370
			Overall p-value	0.423	Overall p-value	0.356
Sociodemographic						
Index of Relative Socioeconomic Disadvantage						
Lowest Quintile	118 (80.27)	1,255 (83.17)	1.08 [0.54-2.17]	0.835	0.58 [0.24-1.43]	0.238
> Lowest Quintile	22 (14.97)	215 (14.25)	1 [referent]		1 [referent]	
Unavailable	7 (4.76)	39 (2.58)				

[a] Excluded from multivariable analysis due to small N.

[b] Age categories classified as; 1) ≥3 years 10 months to <5 years and one month, 2) ≥5 years and one month to <5 years and 10 months (reference category), 3) ≥5 years and 10 months to <6 years 10 months.

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Table 4. Risk Factors for Developmental Vulnerability on the Language & Cognitive Skills (school-based) Domain.

Characteristic	DV (N=195) N (%)	NDV (N=1,461) N (%)	Bivariate OR [95% CI]	p-value	Multivariable (N=1,352) aOR [95% CI]	p-value
Maternal						
Age at Time of Child's Birth (years)						
<25	68 (34.87)	154 (10.54)	**18.41 [5.21-65.05]**	**<0.001**	**12.90 [2.81-59.16]**	**0.001**
25-29	38 (19.49)	346 (23.68)	1 [referent]		1 [referent]	
30-34	52 (26.67)	554 (37.92)	0.72 [0.25-2.02]	0.528	0.80 [0.24-2.67]	0.716
≥35	37 (18.97)	407 (27.86)	0.70 [0.23-2.13]	0.528	0.98 [0.27-3.57]	0.970
			Overall p-value	**<0.001**	Overall p-value	**0.003**
Marital Status						
Married (inc. de facto)	145 (74.36)	1,335 (91.38)	1 [referent]		1 [referent]	
All Other	50 (25.64)	120 (8.21)	**18.44 [5.70-59.63]**	**<0.001**	**5.92 [1.43-24.59]**	**0.014**
Unavailable	0 (0.00)	6 (0.41)				
Occupational Status Scale at Time of Child's Birth						
0-20	70 (35.90)	239 (16.36)	**12.68 [4.58-35.09]**	**<0.001**	**3.61 [1.19-10.95]**	**0.024**
>80-100	105 (53.85)	1,180 (80.77)	1 [referent]		1 [referent]	
Unavailable	20 (10.26)	42 (2.87)				
Pregnancy & Birth						
Fertility Treatments						
No	180 (92.31)	1,208 (82.68)	1 [referent]		1 [referent]	
Yes	15 (7.69)	253 (17.32)	0.16 [0.04-0.55]	0.004	0.42 [0.09-1.95]	0.264
Smoking Status During Pregnancy						
No	145 (74.36)	1,273 (87.13)	1 [referent]		1 [referent]	
Yes	50 (25.64)	188 (12.87)	**6.35 [2.24-18.01]**	**<0.001**	0.28 [0.07-1.09]	0.066
Pre-eclampsia						
No	176 (90.26)	1,284 (87.89)	1 [referent]		1 [referent]	
Yes	19 (9.74)	177 (12.11)	0.61 [0.18-2.10]	0.434	1.09 [0.26-4.60]	0.908
Gestational Diabetes						
No	184 (94.36)	1,370 (93.77)	1 [referent]		1 [referent]	
Yes	11 (5.64)	91 (6.23)	0.84 [0.16-4.44]	0.836	0.66 [0.11-4.01]	0.651
Threatened Abortion						
No	189 (96.92)	1,383 (94.66)	1 [referent]		1 [referent]	
Yes	6 (3.08)	78 (5.34)	0.36 [0.05-2.41]	0.291	0.20 [0.01-3.32]	0.258
Other Pregnancy Related Complications						
No	53 (27.18)	523 (35.80)	1 [referent]		1 [referent]	
Yes	142 (72.82)	938 (64.20)	1.96 [0.84-4.54]	0.119	1.29 [0.45-3.71]	0.635
Threatened Preterm Labour						
No	162 (83.08)	1,302 (89.12)	1 [referent]		1 [referent]	
Yes	33 (16.92)	159 (10.88)	3.21 [0.80-12.92]	0.100	1.20 [0.32-4.48]	0.782
APH						
No	183 (93.85)	1,415 (96.85)	1 [referent]		1 [referent]	
Yes	12 (6.15)	46 (3.15)	6.80 [0.62-74.13]	0.116	4.92 [0.62-39.01]	0.131
Placenta Praevia						
No	195 (100.00)	1,451 (99.32)				
Yes	0 (0.00)	10 (0.68)				
Placental Abruption						
No	195 (100.00)	1,455 (99.59)				
Yes	0 (0.00)	6 (0.41)				
Fetal Distress						
No	173 (88.72)	1,345 (92.06)	1 [referent]		1 [referent]	
Yes	22 (11.28)	116 (7.94)	2.04 [0.45-9.17]	0.353	0.56 [0.11-2.76]	0.475
Cephalopelvic Disproportion [a]						
No	195 (100.00)	1,457 (99.73)				
Yes	0 (0.00)	4 (0.27)				
Prolapsed Cord [a]						

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No	192 (98.46)	1,451 (99.32)				
Yes	3 (1.54)	10 (0.68)				
Precipitate Delivery [a]						
No	190 (97.44)	1,440 (98.56)				
Yes	5 (2.56)	21 (1.44)				
PPH ≥500mls						
No	123 (63.08)	1,076 (73.65)	1 [referent]		1 [referent]	
Yes	72 (36.92)	385 (26.35)	**3.13 [1.22-8.05]**	**0.018**	1.84 [0.67-5.03]	0.237
TSR ≥2mins						
No	163 (83.59)	1,261 (86.31)	1 [referent]		1 [referent]	
Yes	32 (16.41)	200 (13.69)	0.95 [0.39-2.30]	0.908	0.62 [0.20-1.91]	0.399
Apgar 5-minutes <7 [a]						
No	193 (98.97)	1,430 (97.88)				
Yes	2 (1.03)	31 (2.12)				
Intubation						
No	159 (81.54)	1,230 (84.19)	1 [referent]		1 [referent]	
Yes	36 (18.46)	231 (15.81)	1.13 [0.49-2.58]	0.779	1.68 [0.59-4.81]	0.333
Early Preterm Birth						
No	155 (79.49)	1,255 (85.90)	1 [referent]		1 [referent]	
Yes	40 (20.51)	206 (14.10)	2.57 [0.75-8.80]	0.133	0.79 [0.23-2.80]	0.720
POBW <15th Percentile						
No	142 (72.82)	1,089 (74.54)	1 [referent]		1 [referent]	
Yes	36 (18.46)	181 (12.39)	1.62 [0.72-3.66]	0.246	1.74 [0.71-4.25]	0.222
Unavailable	17 (8.72)	191 (13.07)				
Parity						
0	51 (26.15)	611 (41.82)	1 [referent]		1 [referent]	
1	81 (41.54)	502 (34.36)	**4.67 [1.71-12.70]**	**0.003**	**5.12 [1.25-20.99]**	**0.023**
≥2	63 (32.31)	348 (23.82)	**6.18 [2.09-18.27]**	**0.001**	6.37 [1.00-40.66]	**0.050**
			Overall p-value	**0.002**	Overall p-value	**0.060**
Child						
Sex						
Female	85 (43.59)	765 (52.36)	1 [referent]		1 [referent]	
Male	110 (56.41)	696 (47.64)	**3.03 [1.60-5.71]**	**<0.001**	**3.57 [1.66-7.65]**	**0.001**
Ethnicity						
Other	165 (84.62)	1,407 (96.30)	1 [referent]		1 [referent]	
Indigenous Australian	30 (15.38)	54 (3.70)	**34.27 [7.49-156.82]**	**<0.001**	2.22 [0.32-15.52]	0.420
Child Speaks Language Other Than English at Home						
No	167 (85.64)	1,349 (92.33)	1 [referent]		1 [referent]	
Yes	28 (14.36)	112 (7.67)	3.82 [0.89-16.47]	0.072	2.14 [0.49-9.35]	0.313
Age Category at Time of AEDC Completion [b]						
1	48 (24.62)	273 (18.69)	2.09 [0.74-5.89]	0.164	2.18 [0.77-6.16]	0.140
2	128 (65.64)	1,071 (73.31)	1 [referent]		1 [referent]	
3	19 (9.74)	117 (8.01)	2.56 [0.56-11.82]	0.227	1.06 [0.22-5.19]	0.943
			Overall p-value	0.234	Overall p-value	0.329
Total Number of Siblings						
1	41 (21.03)	467 (31.96)	1 [referent]		1 [referent]	
2	79 (40.51)	575 (39.36)	**2.82 [1.01-7.88]**	**0.048**	0.63 [0.15-2.60]	0.523
3	35 (17.95)	279 (19.10)	2.40 [0.71-8.13]	0.160	0.23 [0.04-1.40]	0.110
>3	40 (20.51)	140 (9.58)	**17.34 [4.37-68.74]**	**<0.001**	2.14 [0.29-15.84]	0.455
			Overall p-value	**<0.001**	Overall p-value	**0.044**
Sociodemographic						
Index of Relative Socioeconomic Disadvantage						
Lowest Quintile	141 (72.31)	1,232 (84.33)	**6.87 [1.80-26.28]**	**0.005**	1.52 [0.47-4.94]	0.486
> Lowest Quintile	46 (23.59)	191 (13.07)	1 [referent]		1 [referent]	
Unavailable	8 (4.10)	38 (2.60)				

[a] Excluded from multivariable analysis due to small N.

[b] Age categories classified as; 1) ≥3 years 10 months to <5 years and one month, 2) ≥5 years and one month to <5 years and 10 months (reference category), 3) ≥5 years and 10 months to <6 years 10 months.

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Table 5. Risk Factors for Developmental Vulnerability on the Communication Skills & General Knowledge Domain.

Characteristic	DV (N=200) N (%)	NDV (N=1,456) N (%)	Bivariate OR [95% CI]	p-value	Multivariable (N=1,352) aOR [95% CI]	p-value
Maternal						
Age at Time of Child's Birth (years)						
<25	59 (29.50)	163 (11.20)	**13.25 [3.50-50.17]**	**<0.001**	**10.96 [2.24-53.75]**	**0.003**
25-29	40 (20.00)	344 (23.63)	1 [referent]		1 [referent]	
30-34	59 (29.50)	547 (37.57)	0.74 [0.24-2.28]	0.602	1.17 [0.33-4.09]	0.811
≥35	42 (21.00)	402 (27.61)	0.75 [0.23-2.47]	0.632	1.34 [0.34-5.26]	0.675
			Overall p-value	**<0.001**	Overall p-value	**0.020**
Marital Status						
Married (inc. de facto)	160 (80.00)	1,320 (90.66)	1 [referent]		1 [referent]	
All Other	40 (20.00)	130 (8.93)	**14.40 [2.74-75.72]**	**0.002**	2.28 [0.52-10.04]	0.276
Unavailable	0 (0.00)	6 (0.41)				
Occupational Status Scale at Time of Child's Birth						
0-20	68 (34.00)	241 (16.55)	**11.20 [3.86-32.50]**	**<0.001**	2.11 [0.67-6.65]	0.203
>20-100	117 (58.50)	1,168 (80.22)	1 [referent]		1 [referent]	
Unavailable	15 (7.50)	47 (3.23)				
Pregnancy & Birth						
Fertility Treatments						
No	188 (94.00)	1,200 (82.42)	1 [referent]		1 [referent]	
Yes	12 (6.00)	256 (17.58)	**0.10 [0.02-0.39]**	**<0.001**	0.32 [0.06-1.64]	0.172
Smoking Status During Pregnancy						
No	148 (74.00)	1,270 (87.23)	1 [referent]		1 [referent]	
Yes	52 (26.00)	186 (12.77)	**7.79 [2.61-23.28]**	**<0.001**	1.51 [0.42-5.45]	0.532
Pre-eclampsia						
No	175 (87.50)	1,285 (88.26)	1 [referent]		1 [referent]	
Yes	25 (12.50)	171 (11.74)	1.07 [0.29-3.90]	0.924	0.95 [0.21-4.20]	0.944
Gestational Diabetes						
No	187 (93.50)	1,367 (93.89)	1 [referent]		1 [referent]	
Yes	13 (6.50)	89 (6.11)	1.16 [0.20-6.72]	0.870	1.39 [0.23-8.50]	0.724
Threatened Abortion						
No	192 (96.00)	1,380 (94.78)	1 [referent]		1 [referent]	
Yes	8 (4.00)	76 (5.22)	0.55 [0.09-3.48]	0.524	0.37 [0.02-5.73]	0.477
Other Pregnancy Related Complications						
No	51 (25.50)	525 (36.06)	1 [referent]		1 [referent]	
Yes	149 (74.50)	931 (63.94)	**2.53 [1.07-6.00]**	**0.035**	1.61 [0.53-4.90]	0.404
Threatened Preterm Labour						
No	178 (89.00)	1,286 (88.32)	1 [referent]		1 [referent]	
Yes	22 (11.00)	170 (11.68)	1.00 [0.27-3.61]	0.994	0.45 [0.11-1.88]	0.272
APH						
No	188 (94.00)	1,410 (96.84)	1 [referent]		1 [referent]	
Yes	12 (6.00)	46 (3.16)	9.09 [0.70-117.63]	0.091	1.15 [0.12-11.44]	0.905
Placenta Praevia [a]						
No	200 (100.00)	1,446 (99.31)				
Yes	0 (0.00)	10 (0.69)				
Placental Abruption [a]						
No	199 (99.50)	1,451 (99.66)				
Yes	1 (0.50)	5 (0.34)				
Fetal Distress						
No	172 (86.00)	1,346 (92.45)	1 [referent]		1 [referent]	
Yes	28 (14.00)	110 (7.55)	4.73 [1.00-22.38]	0.050	2.21 [0.52-9.41]	0.285
Cephalopelvic Disproportion [a]						
No	200 (100.00)	1,452 (99.73)				
Yes	0 (0.00)	4 (0.27)				
Prolapsed Cord [a]						

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No	200 (100)	1,443 (99.11)				
Yes	0 (0.00)	13 (0.89)				
Precipitate Delivery [a]						
No	195 (97.50)	1,435 (98.56)				
Yes	5 (2.50)	21 (1.44)				
PPH ≥500mls						
No	122 (61.00)	1,077 (73.97)	1 [referent]		1 [referent]	
Yes	78 (39.00)	379 (26.03)	**3.72 [1.41-9.86]**	**0.008**	2.38 [0.84-6.74]	0.104
TSR ≥2mins						
No	163 (81.50)	1,261 (86.61)	1 [referent]		1 [referent]	
Yes	37 (18.50)	195 (13.39)	**2.80 [1.08-7.22]**	**0.034**	1.55 [0.50-4.86]	0.448
Apgar 5-minutes <7 [a]						
No	198 (99.00)	1,425 (97.87)				
Yes	2 (1.00)	31 (2.13)				
Intubation						
No	162 (81.00)	1,227 (84.27)	1 [referent]		1 [referent]	
Yes	38 (19.00)	229 (15.73)	1.91 [0.80-4.56]	0.147	1.32 [0.45-3.90]	0.614
Early Preterm Birth						
No	157 (78.50)	1,253 (86.06)	1 [referent]		1 [referent]	
Yes	43 (21.50)	203 (13.94)	3.73 [0.99-14.09]	0.053	1.68 [0.48-5.82]	0.413
POBW <15th Percentile						
No	146 (73.00)	1,085 (74.52)	1 [referent]		1 [referent]	
Yes	36 (18.00)	181 (12.43)	1.83 [0.78-4.33]	0.166	1.77 [0.72-4.32]	0.211
Unavailable	18 (9.00)	190 (13.05)				
Parity						
0	65 (32.50)	597 (41.00)	1 [referent]		1 [referent]	
1	68 (34.00)	515 (35.37)	1.51 [0.59-3.86]	0.385	1.56 [0.38-6.42]	0.536
≥2	67 (33.50)	344 (23.63)	**4.54 [1.47-14.09]**	**0.009**	2.48 [0.38-15.95]	0.340
			Overall p-value	0.032	Overall p-value	0.633
Child						
Sex						
Female	87 (43.50)	763 (52.40)	1 [referent]		1 [referent]	
Male	113 (56.50)	693 (47.60)	**3.00 [1.56-5.79]**	**0.001**	**3.26 [1.49-7.10]**	**0.003**
Ethnicity						
Other	179 (89.50)	1,393 (95.67)	1 [referent]		1 [referent]	
Indigenous Australian	21 (10.50)	63 (4.33)	**21.66 [2.34-200.50]**	**0.007**	0.81 [0.10-6.68]	0.842
Child Speaks Language Other Than English at Home						
No	161 (80.50)	1,355 (93.06)	1 [referent]		1 [referent]	
Yes	39 (19.50)	101 (6.94)	**11.16 [3.30-37.77]**	**<0.001**	**17.83 [4.10-77.61]**	**<0.001**
Age Category at Time of AEDC Completion [b]						
1	57 (28.50)	264 (18.13)	**5.60 [1.73-18.09]**	**0.004**	**6.01 [1.97-18.31]**	**0.002**
2	125 (62.50)	1,074 (73.76)	1 [referent]		1 [referent]	
3	18 (9.00)	118 (8.10)	1.91 [0.44-8.30]	0.387	1.30 [0.24-6.95]	0.762
			Overall p-value	**0.017**	Overall p-value	**0.007**
Total Number of Siblings						
1	49 (24.50)	459 (31.52)	1 [referent]		1 [referent]	
2	77 (38.50)	577 (39.63)	1.54 [0.58-4.13]	0.387	0.88 [0.20-3.81]	0.864
3	37 (18.50)	277 (19.02)	1.64 [0.49-5.44]	0.419	1.11 [0.18-6.78]	0.913
>3	37 (18.50)	143 (9.82)	**15.85 [2.91-86.42]**	**0.001**	4.07 [0.48-34.47]	0.198
			Overall p-value	**0.015**	Overall p-value	0.371
Sociodemographic						
Index of Relative Socioeconomic Disadvantage						
Lowest Quintile	153 (76.50)	1,220 (83.79)	**4.24 [1.12-16.03]**	**0.033**	0.92 [0.26-3.26]	0.890
> Lowest Quintile	42 (21.00)	195 (13.39)	1 [referent]		1 [referent]	
Unavailable	5 (2.50)	41 (2.82)				

[a] Excluded from multivariable analysis due to small N.

[b] Age categories classified as; 1) ≥3 years 10 months to <5 years and one month, 2) ≥5 years and one month to <5 years and 10 months (reference category), 3) ≥5 years and 10 months to <6 years 10 months.

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3 and 7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-10
Bias	9	Describe any efforts to address potential sources of bias	6-10
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10
		(*b*) Describe any methods used to examine subgroups and interactions	10
		(*c*) Explain how missing data were addressed	10
		(*d*) If applicable, explain how loss to follow-up was addressed	10
		(*e*) Describe any sensitivity analyses	10
Results			

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Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7-11
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10-11 and 26-29
		(b) Indicate number of participants with missing data for each variable of interest	26-31
		(c) Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	Report numbers of outcome events or summary measures over time	26-29
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-11 and 26-29
		(*b*) Report category boundaries when continuous variables were categorized	10-11
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	4 and 14
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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