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Associations between biological and sociodemographic risks for developmental vulnerability in twins at age 5: a population data linkage study in Western Australia

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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 5.

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 13.5% as DV2. In the multivariable model, risk factors for DV1 were maternal age <25 years (adjusted OR (aOR): 7.06, 95% CI: 2.29 to 21.76), child speaking a language other than English at home (aOR: 6.45, 95% CI: 2.17 to 19.17), male child (aOR: 5.08, 95% CI: 2.89 to 8.92), age younger than the reference category for the study sample (≥5 years 1 month to <5 years 10 months) at time of AEDC completion (aOR: 3.34, 95% CI: 1.55 to 7.22) and having a proportion of optimal birth weight (POBW) <15th percentile of the study sample (aOR: 2.06, 95% CI 1.07 to 3.98). Risk factors for DV2 were male child (aOR: 7.87, 95% CI: 3.45 to 17.97), maternal age <25 (aOR: 5.60, 95% CI: 1.30 to 24.10), age younger than the reference category (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 a POBW <15th percentile (aOR: 3.11, 95% CI: 1.26 to 7.64).

Conclusion Both biological and sociodemographic risk factors are associated with developmental vulnerability in twins at 5 years of age.

Strengths and limitations of this study

- The study is based on a large population-level sample of 1656 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 ORs was performed to explore the associations between a large range of prenatal and perinatal risk factors.
- Twin pairs for which data were complete were used for the analysis.
- The data sets used in this study did not report on twin zygosity nor on complications of pregnancy that are specific to multiple pregnancies (eg, twin reversed arterial perfusion, twin-twin transfusion syndrome).

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 with 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 birth weight[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 2.[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 5 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 also reported that twins are more likely to have poorer neurodevelopmental outcomes compared with singletons, even after controlling for gestational age and birth weight.[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 4 and 5.[38] Likewise, twin studies have also reported sex differences, with girls scoring higher than boys at ages 4 and 5.[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 birth weight 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 5, 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

This study used anonymised individual-level data from the Midwives Notification System (MNS), which is a statutory record of all births (still-born or live-born) in Western Australia (WA) with either a birth weight >400 g 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% and 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 5. Statistical linkage of all records, by matching identifiers (eg, 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 data sets (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=1656 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)

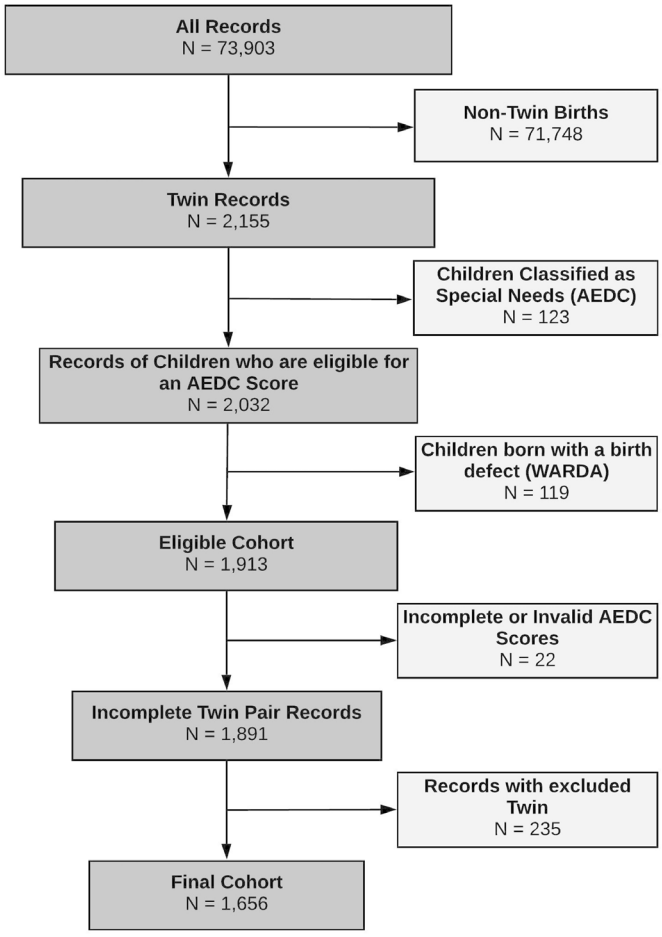

Figure 1 Eligible cohort and numbers included for analyses. AEDC, Australian Early Development Census; WARDA, Western Australian register of developmental anomalies.

Physical Health and Well-being, (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 3 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 to 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 (ie, AUSEI06 (0–20)) and greater than the most disadvantaged quintile (ie, 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, placenta praevia, placental abruption, fetal distress, cephalopelvic disproportion, prolapsed cord, precipitate delivery, postpartum haemorrhage (PPH), intubation status, early preterm birth (<34 weeks of gestational age) and time to spontaneous respiration (TSR); with a TSR of ≥2 min forming the 'at risk' group, and 5-min Apgar score; with a 5-min Apgar score of <7 forming the 'at risk' group.

The proportion of optimal birth weight (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,[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 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, prelabour 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 and <6 years 10 months, with a mean of age category of ≥5 years 1 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 1 month, (2) ≥5 years 1 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 (ie, mode of separation post-birth from the hospital was death) were excluded in the calculations for the 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 (ie, ISRD quintile 1) and greater than the most disadvantaged quintile (ie, ISRD quintiles 2–5).

Statistical modelling

For each risk variable, the 'least risk' category (eg, 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 5-min Apgar score of <7. All variables were added simultaneously to the models. OR and the associated 95% CIs were estimated for both unadjusted and adjusted models. All analyses were undertaken using PROC GLIMMIX in SAS V.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 years at time of twins' birth (adjusted OR (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% CI: 2.89 to 8.92), child's age younger than the reference category for the study sample (≥5 years 1 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 (13.5%) twins were classified as DV2 (table 2). In 95 (11.5%) twin pairs, one twin was identified as DV2 and in 64 twin pairs (7.7%), 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 years 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 DV for the domains of: Physical Health and Well-being, 151 (9.1%) for Social Competence, 147 (8.9%) for Emotional Maturity, 195 (11.8%) for Language and Cognitive Skills (school-based) and 200 (12.1%) for Communication Skills and General Knowledge (see online supplemental 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 the best of our knowledge, our study is the first of this scale (population-level sample of twins; n>1600) 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

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

	DV1	NDV1	Bivariate		Multivariable	
	(N=431)	(N=1225)			(N=1352)	
Characteristic	**N (%)**	**N (%)**	**OR (95% CI)**	**P value**	**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 to 25.32)**	**<0.001**	**7.06 (2.29 to 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 to 1.72)	0.576	0.89 (0.38 to 2.07)	0.780
≥35	106 (24.59)	338 (27.59)	1.06 (0.48 to 2.36)	0.886	1.19 (0.47 to 2.99)	0.715
			Overall P value	**<0.001**	Overall P value	**0.003**
Marital status						
Married (inc. de facto)	357 (82.83)	1123 (91.67)	1 (referent)		1 (referent)	
All Other	72 (16.71)	98 (8.00)	**5.99 (2.43 to 14.75)**	**<0.001**	2.26 (0.76 to 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 to 11.46)**	**<0.001**	1.83 (0.79 to 4.26)	0.159
>20–100	279 (64.73)	1006 (82.12)	1 (referent)		1 (referent)	
Unavailable	30 (6.96)	32 (2.61)				
Pregnancy and birth						
Fertility treatments						
No	377 (87.47)	1011 (82.53)	1 (referent)		1 (referent)	
Yes	54 (12.53)	214 (17.47)	0.43 (0.19 to 0.97)	0.042	0.84 (0.32 to 2.23)	0.729
Smoking status during pregnancy						
No	339 (78.65)	1079 (88.08)	1 (referent)		1 (referent)	
Yes	92 (21.35)	146 (11.92)	**4.31 (1.95 to 9.53)**	**<0.001**	0.87 (0.34 to 2.27)	0.779
Pre-eclampsia						
No	375 (87.01)	1085 (88.57)	1 (referent)		1 (referent)	
Yes	56 (12.99)	140 (11.43)	1.40 (0.59 to 3.34)	0.444	1.82 (0.68 to 4.88)	0.237
Gestational diabetes						
No	402 (93.27)	1152 (94.04)	1 (referent)		1 (referent)	
Yes	29 (6.73)	73 (5.96)	1.30 (0.40 to 4.22)	0.657	1.15 (0.33 to 4.09)	0.826
Threatened abortion						
No	416 (96.52)	1156 (94.37)	1 (referent)		1 (referent)	
Yes	15 (3.48)	69 (5.63)	0.36 (0.09 to 1.45)	0.151	0.23 (0.04 to 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 to 3.85)**	**0.020**	1.79 (0.85 to 3.79)	0.129
Threatened preterm labour						
No	376 (87.24)	1088 (88.82)	1 (referent)		1 (referent)	
Yes	55 (12.76)	137 (11.18)	1.34 (0.55 to 3.24)	0.519	0.68 (0.25 to 1.83)	0.446
APH						
No	411 (95.36)	1187 (96.90)	1 (referent)		1 (referent)	
Yes	20 (4.64)	38 (3.10)	2.38 (0.53 to 10.73)	0.260	0.67 (0.12 to 3.85)	0.650
Placenta praevia*						
No	429 (99.54)	1217 (99.35)				
Yes	2 (0.46)	8 (0.65)				
Placental abruption*						

Continued

Table 1 Continued

Characteristic	DV1 (N=431) N (%)	NDV1 (N=1225) N (%)	Bivariate OR (95% CI)	P value	Multivariable (N=1352) aOR (95% CI)	P value
No	427 (99.07)	1223 (99.84)				
Yes	4 (0.93)	2 (0.16)				
Fetal distress						
No	382 (88.63)	1136 (92.73)	1 (referent)		1 (referent)	
Yes	49 (11.37)	89 (7.27)	**2.92 (1.13 to 7.58)**	**0.028**	1.76 (0.60 to 5.13)	0.301
Cephalopelvic disproportion*						
No	431 (100.00)	1221 (99.67)				
Yes	0 (0.00)	4 (0.33)				
Prolapsed cord*						
No	428 (99.30)	1215 (99.18)				
Yes	3 (0.70)	10 (0.82)				
Precipitate delivery*						
No	424 (98.38)	1206 (98.45)				
Yes	7 (1.62)	19 (1.55)				
PPH ≥500 mL						
No	281 (65.20)	918 (74.94)	1 (referent)		1 (referent)	
Yes	150 (34.80)	307 (25.06)	**2.59 (1.39 to 4.82)**	**0.003**	1.52 (0.73 to 3.16)	0.260
TSR ≥2 min						
No	364 (84.45)	1060 (86.53)	1 (referent)		1 (referent)	
Yes	67 (15.55)	165 (13.47)	1.06 (0.56 to 1.99)	0.863	0.52 (0.22 to 1.21)	0.128
Apgar 5 min<7*						
No	425 (98.61)	1198 (97.80)				
Yes	6 (1.39)	27 (2.20)				
Intubation						
No	353 (81.90)	1036 (84.57)	1 (referent)		1 (referent)	
Yes	78 (18.10)	189 (15.43)	1.36 (0.75 to 2.45)	0.313	1.54 (0.71 to 3.37)	0.277
Early preterm birth						
No	352 (81.67)	1058 (86.37)	1 (referent)		1 (referent)	
Yes	79 (18.33)	167 (13.63)	2.08 (0.94 to 4.56)	0.069	1.29 (0.53 to 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 to 3.84)**	**0.017**	**2.06 (1.07 to 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 to 3.16)	0.158	1.96 (0.77 to 5.00)	0.159
≥2	127 (29.47)	284 (23.18)	**2.50 (1.20 to 5.22)**	**0.015**	2.03 (0.55 to 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 to 7.36)**	**<0.001**	**5.08 (2.89 to 8.92)**	**<0.001**
Ethnicity						
Other	385 (89.33)	1187 (96.90)	1 (referent)		1 (referent)	

Continued

Table 1 Continued

Characteristic	DV1 (N=431) N (%)	NDV1 (N=1225) N (%)	Bivariate OR (95% CI)	P value	Multivariable (N=1352) aOR (95% CI)	P value
Indigenous Australian	46 (10.67)	38 (3.10)	**16.98 (4.85 to 59.46)**	**<0.001**	2.46 (0.46 to 13.03)	0.291
Child speaks language other than English at home						
No	367 (85.15)	1149 (93.80)	1 (referent)		1 (referent)	
Yes	64 (14.85)	76 (6.20)	**6.28 (2.48 to 15.90)**	**<0.001**	**6.45 (2.17 to 19.17)**	**<0.001**
Age category at time of AEDC completion †						
1	109 (25.29)	212 (17.31)	**2.93 (1.45 to 5.90)**	**0.003**	**3.34 (1.55 to 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 to 3.27)	0.746	0.77 (0.23 to 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 to 2.30)	0.685	0.70 (0.27 to 1.83)	0.461
3	74 (17.17)	240 (19.59)	1.04 (0.45 to 2.41)	0.926	0.44 (0.13 to 1.55)	0.120
>3	78 (18.10)	102 (8.33)	**7.28 (2.73 to 19.45)**	**<0.001**	2.71 (0.60 to 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)	1046 (85.39)	**3.55 (1.62 to 7.78)**	**0.002**	1.63 (0.66 to 4.02)	0.287
>Lowest quintile	87 (20.19)	150 (12.24)	1 (referent)		1 (referent)	
Unavailable	17 (3.94)	29 (2.37)				

*Excluded from multivariable analysis due to small N.
†Age categories classified as (1) ≥3 years 10 months to <5 years and 1 month, (2) ≥5 years and 1 month to <5 years and 10 months (reference category), (3) ≥5 years and 10 months to <6 years 10 months.
AEDC, Australian Early Development Census; aOR, adjusted OR; APH, antepartum haemorrhage; DV1, developmentally vulnerable on one or more AEDC domains; NDV1, not developmentally vulnerable on one or more AEDC domains; POBW, proportion of optimal birth weight; PPH, postpartum haemorrhage; TSR, time to spontaneous respiration.

reported that twins are more likely to have poorer performance, in comparison to singletons, at the age of 2,[10 11] it was pertinent to assess if the prevalence rates of developmental vulnerabilities are higher in twins at age 5. We reported that in the WA population, 26.0% of twins were classified as DV1 and 13.5% 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 WA 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 4 and 5 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 with the general Australian population, suggests that healthy twins are more likely to be classified as DV on AEDC domains at school starting age when compared with 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 DV 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% were twins, also reported that male twins were more likely to be classified as DV2 when compared with 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 4 and 5, however, scores tended to converge at 6 years of age.[38]

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

	DV2	NDV2	Bivariate		Multivariable	
	(N=223)	(N=1433)			(N=1352)	
Characteristic	N (%)	N (%)	OR (95% CI)	P value	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 to 23.45)**	**<0.001**	**5.60 (1.30 to 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 to 1.63)	0.356	0.92 (0.29 to 2.91)	0.885
≥35	48 (21.52)	396 (27.63)	0.67 (0.25 to 1.81)	0.434	0.77 (0.22 to 2.76)	0.689
			Overall P value	**<0.001**	Overall P value	0.072
Marital status						
Married (inc. de facto)	172 (77.13)	1308 (91.28)	1 (referent)		1 (referent)	
All other	49 (21.97)	121 (8.44)	**9.91 (3.54 to 27.77)**	**<0.001**	**4.59 (1.13 to 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 to 20.89)**	**<0.001**	**3.30 (1.11 to 9.81)**	**0.032**
>20–100	130 (58.30)	1155 (80.60)	1 (referent)		1 (referent)	
Unavailable	15 (6.73)	47 (3.28)				
Pregnancy and birth						
Fertility treatments						
No	200 (89.69)	1188 (82.90)	1 (referent)		1 (referent)	
Yes	23 (10.31)	245 (17.10)	**0.35 (0.13 to 0.97)**	**0.042**	0.67 (0.17 to 2.69)	0.567
Smoking status during pregnancy						
No	166 (74.44)	1252 (87.37)	1 (referent)		1 (referent)	
Yes	57 (25.56)	181 (12.63)	**5.83 (2.32 to 14.65)**	**<0.001**	1.27 (0.38 to 4.30)	0.700
Pre-eclampsia						
No	195 (87.44)	1265 (88.28)	1 (referent)		1 (referent)	
Yes	28 (12.56)	168 (11.72)	1.25 (0.41 to 3.86)	0.693	2.45 (0.65 to 9.17)	0.184
Gestational diabetes						
No	208 (93.27)	1346 (93.93)	1 (referent)		1 (referent)	
Yes	15 (6.73)	87 (6.07)	1.44 (0.32 to 6.42)	0.635	2.29 (0.46 to 11.44)	0.312
Threatened abortion						
No	214 (95.96)	1358 (94.77)	1 (referent)		1 (referent)	
Yes	9 (4.04)	75 (5.23)	0.54 (0.10 to 2.94)	0.478	0.24 (0.02 to 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 to 5.69)**	**0.014**	1.64 (0.58 to 4.61)	0.351
Threatened preterm labour						
No	191 (85.65)	1273 (88.83)	1 (referent)		1 (referent)	
Yes	32 (14.35)	160 (11.17)	2.04 (0.66 to 6.29)	0.216	0.72 (0.20 to 2.61)	0.613
APH						
No	209 (93.72)	1389 (96.93)	1 (referent)		1 (referent)	
Yes	14 (6.28)	44 (3.07)	5.96 (0.95 to 37.40)	0.057	1.45 (0.36 to 5.87)	0.599
Placenta praevia*						
No	223 (100.00)	1423 (99.30)				
Yes	0 (0.00)	10 (0.70)				

Continued

Table 2 Continued

Characteristic	DV2 (N=223) N (%)	NDV2 (N=1433) N (%)	Bivariate OR (95% CI)	P value	Multivariable (N=1352) aOR (95% CI)	P value
Placental abruption*						
No	221 (99.10)	1429 (99.72)				
Yes	2 (0.90)	4 (0.28)				
Fetal distress						
No	195 (87.44)	1323 (92.32)	1 (referent)		1 (referent)	
Yes	28 (12.56)	110 (7.68)	3.03 (0.90 to 10.23)	0.074	1.56 (0.59 to 4.15)	0.368
Cephalopelvic disproportion*						
No	223 (100.00)	1429 (99.72)				
Yes	0 (0.00)	4 (0.28)				
Prolapsed cord*						
No	220 (98.65)	1423 (99.30)				
Yes	3 (1.35)	10 (0.70)				
Precipitate delivery*						
No	219 (98.21)	1411 (98.46)				
Yes	4 (1.79)	22 (1.54)				
PPH ≥500 mL						
No	141 (63.23)	1058 (73.83)	1 (referent)		1 (referent)	
Yes	82 (36.77)	375 (26.17)	**3.43 (1.49 to 7.94)**	**0.004**	1.38 (0.16 to 11.79)	0.766
TSR ≥2 min						
No	183 (82.06)	1241 (86.60)	1 (referent)		1 (referent)	
Yes	40 (17.94)	192 (13.40)	1.78 (0.81 to 3.89)	0.149	0.91 (0.30 to 2.72)	0.863
Apgar 5 min<7*						
No	219 (98.21)	1404 (97.98)				
Yes	4 (1.79)	29 (2.02)				
Intubation						
No	178 (79.82)	1211 (84.51)	1 (referent)		1 (referent)	
Yes	45 (20.18)	222 (15.49)	1.91 (0.90 to 4.05)	0.093	1.53 (0.54 to 4.35)	0.429
Early preterm birth						
No	172 (77.13)	1238 (86.39)	1 (referent)		1 (referent)	
Yes	51 (22.87)	195 (13.61)	**4.18 (1.50 to 11.67)**	**0.006**	2.06 (0.64 to 6.58)	0.224
POBW <15th percentile						
No	162 (72.65)	1069 (74.60)	1 (referent)		1 (referent)	
Yes	42 (18.83)	175 (12.21)	**2.72 (1.25 to 5.93)**	**0.012**	**3.11 (1.26 to 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 to 2.76)	0.700	1.12 (0.31 to 4.04)	0.861
≥2	71 (31.84)	340 (23.73)	**2.66 (1.04 to 6.83)**	**0.042**	3.61 (0.61 to 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 to 10.55)**	**<0.001**	**7.87 (3.45 to 17.97)**	**<0.001**

Continued

Table 2 Continued

Characteristic	DV2 (N=223) N (%)	NDV2 (N=1433) N (%)	Bivariate OR (95% CI)	P value	Multivariable (N=1352) aOR (95% CI)	P value
Ethnicity						
Other	197 (88.34)	1375 (95.95)	1 (referent)		1 (referent)	
Indigenous Australian	26 (11.66)	58 (4.05)	**11.00 (2.78 to 43.60)**	**<0.001**	2.32 (0.32 to 16.84)	0.404
Child speaks language other than English at home						
No	192 (86.10)	1324 (92.39)	1 (referent)		1 (referent)	
Yes	31 (13.90)	109 (7.61)	3.19 (0.96 to 10.63)	0.059	**4.65 (1.14 to 19.03)**	**0.033**
Age category at time of AEDC completion						
1	66 (29.60)	255 (17.79)	**4.11 (1.80 to 9.39)**	**<0.001**	**5.36 (1.94 to 14.82)**	**0.001**
2	142 (63.68)	1057 (73.76)	1 (referent)		1 (referent)	
3	15 (6.73)	121 (8.44)	0.95 (0.26 to 3.46)	0.942	0.28 (0.05 to 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 to 3.19)	0.489	1.26 (0.34 to 4.71)	0.733
3	38 (17.04)	276 (19.26)	1.14 (0.40 to 3.24)	0.810	0.47 (0.08 to 2.70)	0.395
>3	43 (19.28)	137 (9.56)	**7.14 (2.24 to 22.72)**	**<0.001**	2.52 (0.34 to 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)	1198 (83.60)	2.14 (0.76 to 6.02)	0.151	0.68 (0.21 to 2.25)	0.529
>Lowest quintile	39 (17.49)	198 (13.82)	1 (referent)		1 (referent)	
Unavailable	9 (4.04)	37 (2.58)				

All bold face values are statistically signficant.
*Excluded from multivariable analysis due to small N.
†Age categories classified as: (1) ≥3 years 10 months to <5 years and 1 month, (2) ≥5 years and 1 month to <5 years and 10 months (reference category), (3) ≥5 years and 10 months to <6 years 10 months.
AEDC, Australian Early Development Census; aOR, adjusted OR; APH, antepartum haemorrhage; DV2, developmentally vulnerable on two or more AEDC domains; NDV2, not developmentally vulnerable on two or more AEDC domains; POBW, proportion of optimal birth weight; PPH, postpartum haemorrhage; TSR, time to spontaneous respiration.

We also reported that twins younger than the reference category for this sample were more likely to be classified as DV in their first year of full-time school. A study of 840 Canadian 5-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 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 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 with 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 2.[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 5, 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 2. 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 5.[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 5 compared with at the age of 2. This hypothesis is supported by a subsequent study of twins aged 4 and 6, 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 do not contain information on zygosity. Furthermore, we did not aim to assess the impact of within twin-pair discordance in regard to developmental vulnerabilities at age 5. 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 birth weight 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 5. An Australian cohort study of 1922 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-min 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 with 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 5 in twins remain not well established.

Preventative intervention studies have reported that programmes 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 5 in twins. The findings of our study suggest that twins

are more likely to be classified as DV at school starting age when compared with 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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Contributors 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. 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 agreed to be accountable for all aspects of the work.

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Data availability statement No data are available. 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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