Supplementary Methods.

Study population

In this register-based study, we investigated a whole-population cohort of 464,580 children born alive in Western Australia between 1 January 1980 and 31 December 2001. Children with *familial heightened risk* (of later psychosis, in adulthood) were those born to mothers diagnosed with severe mental illness (15,351 children, 7,492 mothers). Children with *generic risk* were those born to mothers with no recorded history of any psychiatric disorder (449,229 children, 238,880 mothers). Children born to mothers with a recorded history of only non-psychotic psychiatric illness were excluded from this study. Children were identified on the Midwives' Notification System [1], which includes mandatory, prospectively collected data on all infants born in Western Australia at 20 weeks gestation or greater or weighing at least 400 grams, including home births, and not restricted to live births. Mothers with a severe mental illness were identified through linkage of records on the Midwives' Notification System to the Hospital Morbidity Data Collection and Mental Health Information System which cover records of all public and private inpatient hospital admissions, as well as public outpatient and ambulatory care contacts with mental health services across the State, dating back to 1966. Maternally linked sibships on the Midwives' Notification System were identified. Additional covariates used in analyses were from State registers linked to the Midwives' Notification System. For those fathers named on the Midwives' Notification System, relevant covariate data were also extracted from linked State registers. Linkage was carried out by the Data Linkage Branch of the Western Australian Department of Health. Full details on the linked registers used to establish and characterise this birth cohort have been published elsewhere.[2]

Outcome variable: Intellectual disability. The intellectual disability status of a child was determined using three main data sources. The primary source was the Intellectual Disability Exploring Answers Database [3] which includes all Western Australians with intellectual disability registered with the Disability Services Commission since 1953, and children with intellectual disability identified through the Western Australian Department of Education from 1983 onwards. Children were identified as having intellectual disability if they met the criteria set by the American Association on Intellectual and Developmental Disabilities, including a full-scale IQ score greater than or equal to 2 standard deviations below the population mean, in combination with limitations in adaptive behaviours and skills. A small number of children with a borderline IQ were included if their limitations in adaptive behaviours and skills were sufficiently severe [3]. For children identified solely via the Western Australian Department of Education, only the IQ criterion was applied. Additional children were identified through hospital admission records for all WA hospitals for the period 1 January 1980 – 30 June

2010, and mental health ambulatory or outpatient and community mental health records for the same period (ICD-9 codes 317, 318.8, 318.2, 318.3 or 319; ICD-10 codes F70, F71, F72, F73 or F79 [4, 5]). Finally, several children were identified through the Birth Defects Registry of Western Australia [6] which records all malformations, including syndromes causing intellectual disability, occurring in live births, stillbirths and pregnancies terminated because of foetal malformation and diagnosed in children up to six years of age. Malformations were classified using the British Paediatric Association Classification of Diseases (codes included were 75880-75885 and 75888). For children registered with the Disability Services Commission, Heber diagnoses pertaining to the basis of the intellectual disability were available [7]. We classified intellectual disabilities of genetic bases (chromosomal, autosomal and X-linked) according to the categories developed by Yeargin-Allsopp *et al*. [8] which indicate the aetiological basis of biomedical original of the intellectual disability, and which we previously applied to the Heber classification system [9]. The Heber codes used to classify intellectual disability with genetic basis are as follows:

X-linked 4340, 4820, 4921, 4931, 6221, 6660, 6661, 6717, 6722, 6728, 6739, 6741, 6743, 6749, 6754, 6767, 6770, 6773, 6775, 6776, 7120, 8123, 8130

chromosomal 6400,6410, 6420, 6500, 6510, 6512, 6513, 6514, 6515, 6516, 6517, 6518, 6519, 6520, 6521, 6522, 6523, 6524, 6525, 6530, 6531, 6532, 6540, 6541, 6542, 6550, 6551, 6560, 6561, 6562, 6563, 6564, 6570, 6575, 6580, 6585, 6590, 6600, 6610, 6620, 6630, 6640, 6650

autosomal 4000, 4110, 4120, 4130, 4140, 4150, 4160, 4200, 4310, 4320, 4330, 4350, 4400, 4510, 4530, 4540, 4800, 4810, 4830, 4840, 4850, 4860, 4920, 4932, 4940, 5100, 5110, 5300, 6230, 6300, 6310, 6700, 6710, 6711, 6712, 6713, 6714, 6715, 6716, 6718, 6719, 6720, 6721, 6723, 6724, 6725, 6726, 6727, 6729, 6730, 6731, 6732, 6733, 6734, 6735, 6736, 6737, 6738, 6740, 6742, 6744, 6745, 6747, 6748, 6750, 6751, 6752, 6753, 6755, 6756, 6757, 6759, 6760, 6761, 6762, 6763, 6764, 6765, 6768, 6769, 6772, 6774, 6778, 6779, 6781, 6782, 6783, 6784, 6785, 6787, 6788, 6789, 6791, 6792, 6793, 6794, 6796, 6797, 6798, 7110, 7130, 7140, 7150, 7160, 7170, 7171, 7180, 7190, 7210, 8121, 8122

possible autosomal 4930, 6746, 6777, 6780, 6786, 6790, 6795, 6799, 6800.

Psychotic disorder in children

Psychiatric records for children were available up to June 30th, 2011. Children were classified as having a psychotic disorder if they had had any inpatient, outpatient or

community mental health record with a diagnosis of ICD-9 code 295–298, or if they had an ICD-10 diagnosis mapping to these codes.

Exposure variables:

a) Maternal severe mental illness The primary exposure variable of maternal severe mental illness identified children with familial heightened risk. Mothers with a severe mental illness were identified using the Hospital Morbidity Data Collection and Mental Health Information System. An iterative algorithm based on the most recent diagnosis was applied to inpatient and outpatient and community mental health psychiatric records to determine maternal severe mental illness, namely maternal schizophrenia (ICD-9 codes 295.x), bipolar disorder (ICD-9 codes 296.0, 296.2–296.5), unipolar major depression (ICD-9 codes 296.1, 296.6, 296.8, 296.9), paranoid states (ICD-9 codes 297.x) and other nonorganic psychoses (ICD-9 codes 298.x). (ICD-8 and ICD-10 codes used in a small number of records were mapped to ICD-9 codes). The concurrent validity of register diagnoses of schizophrenia and affective psychoses based on the algorithm used was evaluated against an independent sample assessed using a semi-structured diagnostic interview [10] with sensitivity of 0.92 and specificity of 0.88 for schizophrenia and 0.80 and 0.90 respectively for affective psychoses [11].

b) Obstetric Complications

Data were extracted from the Midwives' Notification System which includes prospectively recorded information in up to 44 relevant fields. Core data include the baby's gestational age and weight, pregnancy complications (e.g. pre-eclampsia, placenta praevia, abruption, substance misuse), labour and delivery complications (e.g. cephalopelvic disproportion, prolapsed cord, foetal distress) and early neonatal complications (e.g. intubation, low 5-minute Apgar score), as well as maternal demographic characteristics (age, marital status and ethnicity).

Obstetric complications were scored using the McNeil-Sjöström Scale for Obstetric Complications [12] adapted for automated scoring in Australian electronic databases. This clinically derived scale reflects each obstetric complication's potential for negative impact on the exposed offspring's developing central nervous system at a specific stage or stages of development – during pregnancy, labour and delivery or the neonatal period. The 6-point severity scale ranges from 1 ("not harmful or relevant") to 6 ("very great harm to or deviation in the offspring"). The same obstetric complication can contribute to the scale during more than one developmental period, with different weightings reflecting the severity of effect for

that period. The scale's capacity to discriminate histories of obstetric complications for people with and without psychiatric illness[11 13] and to identify combinations of obstetric complications and genetic factors associated with schizophrenia (for example,[14]), has been demonstrated.

The scale, which was developed in the northern hemisphere, was adapted for use in Australia: more than 300 new items were added to cover the range of obstetric complications encountered in Western Australia which includes sub-tropical regions. In addition, the scale was adapted for use with electronic databases. Obstetric complication scale scores were then automatically generated for all subjects by applying a computerised algorithm to the relevant information contained in approximately 500,000 electronic birth records for the study population. The underlying computer algorithm has been validated[11].

In the current study, children were operationally defined as having had obstetric complications of critical severity if they had at least one obstetric complication categorised at severity level 4 ("potentially clearly harmful or relevant") or greater. To enable us to examine differential impacts due to exposure at different stages of early foetal and neonatal neurodevelopment, binary scores were computed for each birth for each developmental period (pregnancy, labour and delivery, or neonatal) affected by harmful exposure as well as for the three periods combined.

c) Other factors associated with intellectual disability

A number of additional variables that, on reviewing the literature, were thought to potentially influence the relation between maternal severe mental illness, exposure to obstetric complications and intellectual disability in children, were included in adjusted models. Socio-demographic and socioeconomic factors including maternal age, maternal marital status, child's sex, order of birth among siblings and year of birth were extracted from the Midwives Notification System. Year of birth was included to account for variation in ascertainment over time. Paternal age at birth, and maternal and paternal country of birth were extracted from State birth registration records. A binary variable indicating whether the name of the child's father was registered on the child's birth record was included, as children with missing information on this variable (0.7% of the study sample) were more frequently children with heightened risk. Socioeconomic status was determined using an area-level measure derived by the Australian Bureau of Statistics using principal components analysis of census data: the Index of Relative Socio-Economic Disadvantage [15]. This index was linked to the mother's residence at the time of the child's birth. For most cases, the smallest spatial unit (the census collection district) was used to determine area-level socio-economic disadvantage.

Where the census collection district was not available, aggregated data at the corresponding postcode level was used. The index used for each child was that for the census year closest in time to the date of the child's birth. Transformation of index values to quintiles allowed comparison across different birth years. The geographical remoteness of the mother's residence at time of the child's birth was determined using the Australian Bureau of Statistics census-derived area-level measure: the Australian Standard Geographic Classification - Remoteness Area [16]. Remoteness Area categories are based on the road distance of a location from the nearest population centres providing access to goods and services, taking into account population size. They are classified as: Major City, Inner Regional, Outer Regional, Remote and Very Remote. The Indigenous status of the child was scored positive if the child or either parent were identified as being of Aboriginal or Torres Strait Islander descent in any of the data sources available.

Competing aetiological influences of parental intellectual disability and father's psychiatric morbidity completed the set of adjustment variables. The intellectual disability status of mothers and fathers was ascertained following the same process described for children. The psychiatric morbidity of fathers was ascertained through mental health inpatient admissions and ambulatory and outpatient contacts; it was coded as a severe mental illness if there was any history of schizophrenia, affective psychoses, paranoid disorders or other nonorganic psychoses (ICD-9 codes 295-298, or ICD-8 codes and ICD-10 codes which mapped to these) and as another psychiatric illness for all other disorders in the ICD-8 and ICD-9 Chapter 5 range and ICD-10 F range for mental illness. For children born to mothers with a severe mental illness, a binary variable was created that coded for whether conception occurred prior to or after the diagnosis.

Data analyses

Counts and percentages were used to describe demographic characteristics of the population cohort. We used multiple logistic regressions to examine associations between a child's exposure to obstetric complications, maternal severe mental illness (as a proxy for familial heightened risk) and intellectual disability outcome. Estimates of odds ratios with 95% confidence intervals were computed.

Unadjusted analyses modeled associations between heightened familial risk classification (maternal severe mental illness compared to no maternal psychiatric history) and the child's intellectual disability status; and mothers' specific diagnoses (schizophrenia, bipolar disorder, unipolar major depression or other psychoses) and the child's intellectual disability status. These associations were then adjusted in Model 1 for demographic and socioeconomic

variables and exposure to obstetric complications, and in Model 2, with additional adjustment for potentially competing aetiological factors. . Parallel analyses were run for intellectual disability with a genetic basis.

Simple diagnostic checks were employed to ensure any collinearity between covariates did not adversely impact the estimation of key parameters of interest. In developing Models 1 and 2, covariates were added in staged blocks. After each addition, odds ratio estimates for previously added covariates were screened for unexpected (>20%) changes when estimated in the presence of newly added covariates. No evidence of unexpected confounding between covariates was observed.

The combined effects of maternal severe mental illness and exposure to obstetric complications were further examined for evidence of statistical interaction by adding additional terms to Model 2. These terms also allowed the odds ratios for exposure to obstetric complications at each period of pregnancy, labour and delivery and neonatal to be determined separately for children at familial heightened risk and children at generic risk. We define the interaction of the two effects as the difference in effect sizes attributable to: 1) obstetric complications in children whose mothers have no known mental illness (Odds Ratio of some OC exposure relative to no exposure given the child is at generic risk); and attributable to 2) obstetric complications in children of mothers with severe mental illness (Odds Ratio of some OC exposure relative to no exposure given the child's mother has a severe mental illness). The strength of the difference between the conditional odds ratios (1) and (2) can be statistically assessed on both multiplicative and additive scales. Multiplicative interaction was assessed by adding relevant interaction terms (the product of the two binary measures: child's heightened risk classification and exposure to obstetric complications) to Model 2; separate analyses were run for each period of exposure: pregnancy, labour and delivery and neonatal. The extra variation in intellectual disability outcome explained by the addition of each of these interaction terms was assessed for statistical significance using a likelihood ratio test. Additive interaction was assessed using the relative excess risk due to interaction (RERI) [17, 18] statistic and its 95% confidence interval. Odds ratios were used in the RERI calculations as approximations to rate ratios. Given the incidence proportions of intellectual disability observed in this study, odds ratios made satisfactory approximations to rate ratios ([19]). Estimates of odds ratios for exposure to obstetric complications were determined at each period of exposure (pregnancy, labour and delivery or neonatal) separately for children at familial heightened risk and children at generic risk. Robust standard errors were computed in all analyses to protect against erroneous deflation of standard errors due to clustering of maternal sibships. Missing data levels were low and not considered to introduce any bias. Any children with a missing covariate were included in

analyses by estimating distinct parameters for ‘missing’ categories for relevant variables. Analyses were conducted with Stata version 13 [20].

The study was approved by the Western Australian Department of Health Human Research Ethics Committee (2011/75) and The University of Western Australia Human Research Ethics Committee (RA/4/1/1322).

Supplementary results

Supplementary Table 3 shows formal measures of the strengths of statistical multiplicative and additive interactions between maternal severe mental illness and exposure to obstetric complications. There was some evidence of a sub-multiplicative interaction between maternal severe mental illness in general, and maternal schizophrenia in particular, and exposure to obstetric complications in the neonatal period (likelihood ratio tests: Chi-squared = 4.5, 1df, p=0.03, chi-squared=4.4, 1df, p=0.04 respectively). The odds ratio for children of mothers with severe mental illness (or schizophrenia in particular) who were exposed to obstetric complications in the neonatal period was less than the product of the odds ratio due to maternal severe mental illness (or schizophrenia) only and the odds ratio due to exposure to obstetric complications only. There was no evidence of any other interaction between maternal severe mental illness in general, or maternal schizophrenia in particular, and exposure to obstetric complications, either additive or multiplicative.

Supplementary Table 1. Characteristics of children in the cohort by all maternal severe mental illness (SMI) categories (%, N)

	Maternal severe mental illness category						
	Schizophrenia	**Bipolar disorder**	**Unipolar major depression**	**Other psychoses**	**Height. risk (maternal SMI) Total**	**Generic risk Total**	**Full cohort Total**
	N=1,653	**N=3,332**	**N=8,795**	**N=1,571**	**N=15,351**	**N=449,229**	**N=464,580**
	% (N)	**% (N)**	**% (N)**	**% (N)**	**% (N)**	**% (N)**	**% (N)**
Child with intellectual disability	4.7 (77)	2.5 (84)	3.2 (283)	4.2 (66)	3.3 (510)	1.3 (5,707)	1.3 (6,217)
Child with intellectual disability with information on cause	(43)	(39)	(147)	(33)	(262)	(2,917)	(3,179)
Child with intellectual disability of genetic basis	0.4 (7)	0.3 (9)	0.4 (35)	0.2 (3)	0.4 (54)	0.2 (806)	0.2 (860)
Exposure to obstetric complications of critical severity							
During pregnancy	32.7 (541)	34.1 (1,139)	34.2 (3,009)	35.0 (550)	34.1 (5,239)	26.8 (120,303)	27.0 (125,542)
During labour and delivery	47.0 (777)	49.5 (1,648)	49.8 (4,376)	47.7 (750)	49.2 (7,551)	47.3 (212,383)	47.3 (219,934)
During the neonatal period	52.3 (865)	47.9 (1,597)	50.6 (4,452)	51.3 (806)	50.3 (7,720)	43.0 (192,945)	43.2 (200,665)
During any of pregnancy, labour and delivery or the neonatal period	74.5 (1,232)	74.5 (2,483)	75.6 (6,651)	75.5 (1,186)	75.3(11,552)	70.3 (315,900)	70.5 (327,452)
Sex							
Male	52.9 (875)	50.2(1,673)	52.4(4,611)	51.1 (803)	51.9 (7,962)	51.3 (230,419)	51.3(238,381)
Female	47.1 (778)	49.8(1,659)	47.6(4,184)	48.9 (768)	48.1 (7,389)	48.7 (218,810)	48.7(226,199)

	Maternal severe mental illness category						
	Schizophrenia	**Bipolar disorder**	**Unipolar major depression**	**Other psychoses**	**Height. risk (maternal SMI) Total**	**Generic risk Total**	**Full cohort Total**
	N=1,653 % (N)	**N=3,332 % (N)**	**N=8,795 % (N)**	**N=1,571 % (N)**	**N=15,351 % (N)**	**N=449,229 % (N)**	**N=464,580 % (N)**
Maternal age (years)							
<= 19	12.0 (198)	8.0 (268)	10.4 (911)	11.5 (180)	10.1 (1,557)	5.4 (24,422)	5.6 (25,979)
20 – 34	75.6(1,249)	82.6(2,752)	81.0 7,123)	77.5(1,217)	80.4(12,341)	84.0 (377,142)	83.8(389,483)
>= 35	12.5 (206)	9.4 (312)	8.7 (761)	11.1 (174)	9.5 (1,453)	10.6 (47,649)	10.6(49,102)
Unknown							0.0(16)
Maternal place of birth							
Outside Australia	23.1 (382)	26.8 (893)	22.3(1,957)	25.5 (400)	23.7 (3,632)	29.5 (132,384)	29.3(136,016)
Australia	76.6(1,267)	73.1(2,437)	77.4(6,810)	74.2(1,165)	76.1(11,679)	70.3 (315,881)	70.5(327,560)
Unknown	0.2 (4)	0.1 (2)	0.3 (28)	0.4 (6)	0.3 (40)	0.2 (964)	0.2(1,004)
Father's age (years)							
<=19	2.7 (45)	1.6 (54)	2.5 (221)	2.7 (43)	2.4 (363)	1.4 (6,190)	1.4(6,553)
20 – 54	73.3(1,211)	89.6(2,984)	87.8(7,725)	79.8(1,254)	85.8(13,174)	94.1 (422,760)	93.8(435,934)
>= 55	0.2 (3)	0.6 (21)	0.1 (8)	0.7 (11)	0.3 (43)	0.2 (991)	0.2(1,034)
Unknown	21.5 (356)	7.8 (261)	8.3 (733)	14.4 (227)	10.3 (1,577)	3.6 (16,218)	3.8(17,795)
Father unknown	2.3 (38)	0.4 (12)	1.2 (108)	2.3 (36)	1.3 (194)	0.7 (3,070)	0.7(3,264)

	Maternal severe mental illness category						
	Schizophrenia	**Bipolar disorder**	**Unipolar major depression**	**Other psychoses**	**Height. risk (maternal SMI) Total**	**Generic risk Total**	**Full cohort Total**
	N=1,653 % (N)	**N=3,332 % (N)**	**N=8,795 % (N)**	**N=1,571 % (N)**	**N=15,351 % (N)**	**N=449,229 % (N)**	**N=464,580 % (N)**
Father's place of birth, (if the father is known)							
Outside Australia	25.6 (423)	26.0 (865)	23.1(2,032)	26.8 (421)	24.4 (3,741)	30.4 (136,358)	30.2(140,099)
Australia	50.5 (835)	65.7(2,189)	67.4(5,924)	56.6 (889)	64.1 (9,837)	65.3 (293,352)	65.3(303,189)
Unknown	21.6 (357)	8.0 (266)	8.3 (731)	14.3 (225)	10.3 (1,579)	3.7 (16,449)	3.9(18,028)
Birth cohort							
1980 – 1982	16.1 (266)	12.9 (431)	11.4(1,003)	15.1 (238)	12.6 (1,938)	12.0 (54,124)	12.1(56,062)
1983 – 1986	19.8 (327)	19.7 (657)	16.7(1,473)	18.3 (287)	17.9 (2,744)	17.2 (77,453)	17.3(80,197)
1987 – 1992	30.9 (511)	32.0(1,067)	27.7(2,434)	29.7 (466)	29.2 (4,478)	28.1(126,207)	28.1(130,685)
1993 – 1996	16.8 (277)	18.3 (609)	19.6(1,723)	19.6 (308)	19.0 (2,917)	18.9 (84,791)	18.9(87,708)
1997 – 2001	16.5 (272)	17.0 (568)	24.6(2,162)	17.3 (272)	21.3 (3,274)	23.7(106,654)	23.7(109,928)
Birth order							
1	38.0 (628)	35.4(1,179)	35.4(3,117)	33.4 (525)	35.5 (5,449)	39.1(175,511)	39.0(180,960)
2	30.0 (496)	32.2(1,074)	31.2(2,745)	30.6 (480)	31.2 (4,795)	33.9(152,083)	33.8(156,878)
3	17.0 (281)	18.7 (624)	18.7(1,646)	18.5 (291)	18.5 (2,842)	17.3 (77,581)	17.3 (80,423)
≥4	15.0 (248)	13.7 (455)	14.6(1,287)	17.5 (275)	14.8 (2,265)	9.8 44,054)	10.0 (46,319)

	Maternal severe mental illness category						
	Schizophrenia	**Bipolar disorder**	**Unipolar major depression**	**Other psychoses**	**Height. risk (maternal SMI) Total**	**Generic risk Total**	**Full cohort Total**
	N=1,653 % (N)	**N=3,332 % (N)**	**N=8,795 % (N)**	**N=1,571 % (N)**	**N=15,351 % (N)**	**N=449,229 % (N)**	**N=464,580 % (N)**
Mother's marital status at time of child's birth							
Married or *de facto* marriage	67.2(1,110)	83.2(2,773)	82.0(7,212)	78.0(1,226)	80.3(12,321)	91.3(410,301)	91.0(422,622)
Single or other	32.6 (539)	16.7 (555)	17.8(1,568)	21.9 (344)	19.6 (3,006)	8.6 (38,691)	9.0 (41,697)
Unknown	0.2 (4)	0.1 (4)	0.2 (15)	0.1 (1)	0.2 (24)	0.1 (237)	0.1 (261)
Socioeconomic index of mother's residence at time of child's birth							
Lowest quintile (most disadvantaged)	35.1 (581)	25.6 (853)	26.9(2,365)	33.3 (523)	28.2 (4,322)	19.2 (86,111)	19.5 (90,433)
Second	24.1 (399)	23.8 (793)	25.4(2,238)	23.6 (371)	24.8 (3,801)	22.0 (99,054)	22.1(102,855)
Third	16.6 (274)	19.1 (638)	19.0(1,673)	18.1 (284)	18.7 (2,869)	19.5 (87,388)	19.4 (90,257)
Fourth	12.6 (208)	16.6 (552)	15.5(1,367)	12.0 (188)	15.1 (2,315)	18.1 (81,274)	18.0 (83,589)
Highest quintile (least disadvantaged)	11.1 (184)	14.3 (477)	12.6(1,109)	12.6 (198)	12.8 (1,968)	20.6 (92,534)	20.3 (94,502)
Missing data	0.4 (7)	0.6 (19)	0.5 (43)	0.4 (7)	0.5 (76)	0.6 (2,868)	0.6 2,944)
Remoteness of mother's residence at time of child's birth							
Major city	65.7(1,086)	63.0(2,100)	55.3(4,861)	60.1 (944)	58.6 (8,991)	66.7(299,529)	66.4(308,520)
Inner regional	7.4 (122)	11.8 (394)	11.1 (974)	8.6 (135)	10.6 (1,625)	9.7 (43,422)	9.7 (45,047)
Outer regional	13.4 (222)	13.9 (463)	18.8(1,657)	14.1 (222)	16.7 (2,564)	11.9 (53,572)	12.1 (56,136)

	Maternal severe mental illness category													
	Schizophrenia		**Bipolar disorder**		**Unipolar major depression**		**Other psychoses**		**Height. risk (maternal SMI) Total**		**Generic risk Total**		**Full cohort Total**	
	N=1,653 % (N)		**N=3,332 % (N)**		**N=8,795 % (N)**		**N=1,571 % (N)**		**N=15,351 % (N)**		**N=449,229 % (N)**		**N=464,580 % (N)**	
Remote	8.5	(140)	8.1	(271)	10.1	(888)	10.6	(167)	9.5	(1,466)	7.7	(34,376)	7.7	35,842)
Very remote	5.0	(82)	3.1	(104)	4.7	415)	6.6	(103)	4.6	(704)	4.0	(18,149)	4.1	(18,853)
Missing data									0.0	(1)	0.0	(181)	0.0	(182)
Indigenous status														
Of Aboriginal or Torres Strait Islander descent	21.4	(354)	7.6	(253)	12.4	(1,087)	23.0	(362)	13.4	(2,056)	6.3	28,495)	6.6	30,551)
Mother with an intellectual disability	5.9	(97)	1.8	(59)	0.7	(63)	3.4	(54)	1.8	(273)	0.1	(439)	0.2	(712)
Father with an intellectual disability	0.4	(7)	0.2	(8)	0.3	(24)	0.4	(7)	0.3	(46)	0.1	(486)	0.1	(532)
Father with any mental health contact other than for a psychotic disorder	18.5	(305)	20.2	(674)	17.4	(1,527)	18.8	(295)	18.2	(2,801)	9.5	(42,737)	9.8	(45,538)
Father with any diagnosis of a psychotic disorder	6.2	(103)	5.1	(171)	4.8	(423)	4.6	(72)	5.0	(769)	1.6	(7,010)	1.7	(7,779)
Child's conception after the mother's diagnosis of severe mental illness	40.9	(676)	25.0	(834)	13.9	(1,220)	27.4	(431)	20.6	(3,161)				

Supplementary Table 2. Child Intellectual Disability by Explanatory and Adjustment Variables[a]

	Any intellectual disability			Intellectual disability of genetic basis		
	Unadjusted N=464,580	**Model 1 N= 464,564**	**Model 2 N= 464,564**	**Unadjusted N=459,223**	**Model 1 N= 457,787**	**Model 2 N= 457,787**
Child exposed to obstetric complications of critical severity						
During pregnancy	1.7 (1.6 - 1.8)	1.4(1.3-1.5)	1.4(1.3-1.5)	2.4(2.1 -2.8)	1.9(1.6-2.1)	1.9(1.6-2.1)
During labour and delivery	1.3 (1.2 - 1.3)	1.1(1.1-1.2)	1.1(1.0-1.2)[b]	1.2(1.0-1.3)[b]	0.9(0.8-1.0)	0.9(0.8-1.0)
During the neonatal period	2.0 (1.9 - 2.2)	1.7(1.6-1.8)	1.7(1.6-1.8)	3.8(3.2 -4.4)	3.4(2.9-4.0)	3.4(2.9-3.9)
No such exposure in respective period	**Reference**	**Reference**	**Reference**	**Reference**	**Reference**	**Reference**
Child with heightened familial risk - Mother's specific psychiatric diagnosis						
Schizophrenia	3.8 (3.0 - 4.9)	2.4(1.9-3.2)	1.7(1.3-2.3)	2.4(1.2 -5.1)	2.1(1.0-4.4) [2]	1.6(0.7-3.6)
Bipolar disorder	2.0 (1.6 - 2.5)	1.6(1.3-2.1)	1.3(1.0-1.7) [2]	1.5(0.8 -2.9)	1.3(0.7-2.6)	1.2(0.6-2.3)
Unipolar major depression	2.6 (2.3 - 3.0)	2.0(1.8-2.4)	1.9(1.6-2.1)	2.3(1.5 - 3.1	2.1(1.4-3.0)	2.0(1.3-2.9)
Other psychoses	3.4 (2.5 - 4.6)	2.3(1.7-3.1)	1.8(1.3-2.4)	1.1(0.4 -3.4)	0.9(0.3-2.9)	0.8(0.3-2.5)
Child with generic risk	**Reference**	**Reference**	**Reference**	**Reference**	**Reference**	**Reference**
Sex						
Male		**Reference**	**Reference**		**Reference**	**Reference**
Female		0.6(0.6-0.6)	0.6(0.6-0.6)		0.8(0.7-0.9)	0.8(0.7-0.9)
Mother's age (years)						

≤19	1.2(1.1-1.3)	1.2(1.1-1.3)	0.9(0.6-1.3)	0.9(0.6-1.3)
20-34	**Reference**	**Reference**	**Reference**	**Reference**
≥ 35	1.1(1.0-1.2)	1.1(1.0-1.2)	1.7(1.4-2.1)	1.7(1.4-2.1)
Father's age (years)				
≤19	1.2(1.0-1.4)	1.2(1.0-1.4)	1.1(0.5-2.1)	1.0(0.5-2.0)
20-54	**Reference**	**Reference**	**Reference**	**Reference**
≥ 55	2.0(1.3-2.9)	1.7(1.2-2.6)	1.9(0.8-4.6)	1.8(0.8-4.5)
Unknown age	1.4(0.9-2.2)	1.5(1.0-2.4)	1.3(0.9-1.7)	1.3(1.0-1.7)
Father unknown	0.9(0.7-1.2)	1.1(0.8-1.4)	0.7(0.2-2.2)	0.7(0.2-2.3)
Mother's place of birth				
Australia	**Reference**	**Reference**	**Reference**	**Reference**
Outside Australia	0.9(0.8-0.9)	0.9(0.8-0.9)	1.1(0.9-1.3)	1.1(0.9-1.3)
Father's place of birth				
Australia	**Reference**	**Reference**	**Reference**	**Reference**
Outside Australia	0.9(0.9-1.0) [b]	1.0(0.9-1.0)	1.0(0.9-1.2)	1.0(0.9-1.2)
Unknown or missing data	1.0(0.6-1.5)	1.0(0.6-1.6)	0.7(0.6-0.9)	0.7(0.6-0.9)
Birth cohort				
1980-82	**Reference**	**Reference**	**Reference**	**Reference**
1983-86	2.0(1.7-2.2)	2.0(1.7-2.2)	1.1(0.9-1.4)	1.1(0.9-1.4)
1987-92	2.6(2.3-2.9)	2.6(2.3-2.9)	1.0(0.8-1.2)	1.0(0.8-1.2)
1993-96	2.0(1.8-2.2)	2.0(1.8-2.3)	0.8(0.6-1.0)	0.8(0.6-1.0)

1997-2001	1.1(1.0-1.2)	1.1(1.0-1.3)	0.7(0.5-0.9)	0.7(0.5-0.9)
Birth order				
1	**Reference**	**Reference**	**Reference**	**Reference**
2	1.1(1.0-1.2) [2]	1.1(1.1-1.2)	1.0(0.9-1.2)	1.0(0.9-1.2)
3	1.3(1.2-1.4)	1.3(1.2-1.5)	1.3(1.0-1.5) [2]	1.3(1.0-1.5) [b]
≥4	1.7(1.6-1.9)	1.7(1.5-1.8)	1.7(1.4-2.2)	1.7(1.4-2.1)
Mother's marital status at time of child's birth				
Married or *de facto* marriage	**Reference**	**Reference**	**Reference**	**Reference**
Single or other	1.3(1.2-1.4)	1.2(1.0-1.2) [b]	1.0(0.8-1.3)	1.0(0.7-1.3)
Socioeconomic index of mother's residence at time of child's birth				
Fifth quintile (least disadvantaged)	**Reference**	**Reference**	**Reference**	**Reference**
Fourth quintile	1.2(1.1-1.3)	1.2(1.1-1.3)	0.9(0.8-1.2)	0.9(0.8-1.2)
Third quintile	1.4(1.3-1.5)	1.4(1.2-1.5)	1.0(0.8-1.3)	1.0(0.8-1.2)
Second quintile	1.6(1.4-1.7)	1.5(1.4-1.6)	1.1(0.9-1.3)	1.0(0.8-1.3)
Lowest quintile (most disadvantaged)	1.9(1.8-2.1)	1.8(1.6-2.0)	1.0(0.8-1.2)	0.9(0.8-1.2)
Remoteness of mother's residence at time of child's birth				
Major city of Australia	**Reference**	**Reference**	**Reference**	**Reference**
Inner regional	0.8(0.8-0.9)	0.9(0.8-0.9)	1.0(0.8-1.2)	1.0(0.8-1.2)
Outer regional	0.9(0.8-0.9)	0.9(0.8-1.0) [b]	1.0(0.8-1.2)	1.0(0.8-1.2)
Remote	0.8(0.7-0.9)	0.8(0.7-0.9)	0.9(0.7-1.2)	0.9(0.7-1.2)

Very remote	0.6(0.5-0.7)	0.7(0.6-0.8)	0.6(0.4-1.0)	0.7(0.4-1.0)
Indigenous status of child				
Child not of Aboriginal or Torres Strait Islander descent	**Reference**	**Reference**	**Reference**	**Reference**
Child of Aboriginal or Torres Strait Islander descent	1.4(1.3-1.6)	1.4(1.2-1.5)	0.7(0.5-1.0)	0.7(0.5-1.0) [b]
Mother's intellectual disability status				
Mother not identified with an intellectual disability		**Reference**		**Reference**
Mother with an intellectual disability		8.4(6.3-11.1)		5.9(2.9-12.0)
Father's intellectual disability status				
Father not identified with an intellectual disability		**Reference**		**Reference**
Father with an intellectual disability		7.3(5.4-9.9)		5.2(2.4-11.7)
Father's mental health status				
Father not identified with any mental health contact		**Reference**		**Reference**
Father with any mental health contact other than for a psychotic disorder		1.6(1.3-1.9)		1.2(0.7-1.9)
Father with any diagnosis of a psychotic disorder		1.6(1.5-1.7)		1.3(1.0-1.5) [b]

[a] Odds ratios in model 1 were adjusted simultaneously for exposure to obstetric complications of critical severity during pregnancy, labor and delivery, and the neonatal period, and by mother's specific psychiatric diagnosis. Demographic and socioeconomic covariates included sex, year of birth, parents' ages, parents' places of birth, birth order, mother's marital status, area-level socioeconomic and remoteness measures of mother's residence, and Indigenous status. Model 2 further adjusted for potentially competing etiological factors, such as the intellectual disability status of both the mother and father and the father's psychiatric morbidity status.

[b] The boundary of the odds ratio does not contain 1 but is recorded as 1.0 when rounded to one decimal place.

Supplementary Table 3. **Measures of multiplicative interaction** (likelihood ratio test) **and additive interaction** (relative excess risk due to interaction—RERI, 95% confidence interval) **between the effects of maternal severe mental illness and exposure to obstetric complications on any intellectual disability outcome.**

	Multiplicative interaction			Additive interaction	
Maternal severe mental illness and exposure to obstetric complications	**Chi-squared statistic**	**Degrees of freedom**	**P value**	**RERI**	**95% CI**
During pregnancy	2.5	1	0.1	-0.04	-0.4 – 0.4
During labour and delivery	0.6	1	0.5	0.2	-0.2 – 0.5
During the neonatal period	4.5	1	0.03	0.05	-0.4 – 0.5
During any of the three periods	0.04	1	0.8	0.5	-0.1 – 1.0
Maternal schizophrenia and exposure to obstetric complications					
During pregnancy	0.6	1	0.5	-0.1	-1.1 – 0.9
During labour and delivery	1.1	1	0.3	0.5	-0.4 – 1.4
During the neonatal period	4.6	1	0.03	-0.7	-1.9 – 0.5
During any of the three periods	0.9	1	0.3	-0.2	-1.5 – 1.2

REFERENCES

1. Gee V, Dawes V. *Validation Study of the Western Australian Midwives' Notification System 1992. Occasional Paper 59*: Health Department of Western Australia; July 1994 1994.

2. Morgan VA, Valuri GM, Croft ML, Griffith JA, Shah S, Young DJ, Jablensky AV. Cohort Profile: Pathways of risk from conception to disease: the Western Australian schizophrenia high-risk e-Cohort. *International journal of epidemiology* Dec 2011;40(6):1477-1485.

3. Leonard H, Petterson B, Bourke J, Morgan VA, Glasson E, Bower C. *Inaugural report of the IDEA database - Intellectual disability in Western Australia.* Perth, Western Australia: Institute for Child Health Research; 2004.

4. World Health Organization. *International Classification of Diseases, 9th Revision, Clinical Modification*. Geneva: World Health Organization; 1979.

5. World Health Organization. *The ICD-10 Classification of Mental and Behavioural Disorders. Clinical descriptions and diagnostic guidelines*. Geneva: World Health Organization; 1992.

6. Bower C, Rudy E, Callaghan A, Quick J, Cosgrove P, Nassar N. *Report of the Birth Defects Registry of Western Australia 1980-2008.* Perth: King Edward Memorial Hospital, Health Department of Western Australia; 2009.

7. Heber R. A manual on terminology and classification in mental retardation. *Am J Ment Defic* Sep 1959;Suppl 64(2):1-111.

8. Yeargin-Allsopp M, Murphy CC, Cordero JF, Decoufle P, Hollowell JG. Reported biomedical causes and associated medical conditions for mental retardation among 10-year-old children, metropolitan Atlanta, 1985 to 1987. *Dev Med Child Neurol* Mar 1997;39(3):142-149.

9. Morgan VA, Leonard H, Bourke J, Jablensky AV. Intellectual disability co-occurring with schizophrenia and other psychiatric illness: a population-based study. *British Journal of Psychiatry* 2008;193:364–372.

10. Castle D, Jablensky A, McGrath J, et al. The Diagnostic Interview for Psychoses (DIP): Development, reliability and applications. *Psychological Medicine* 2006;36:69-80.

11. Jablensky A, Morgan VA, Zubrick S, Bower C, Yellachich L. Pregnancy, delivery, and neonatal complications in a population cohort of women with schizophrenia and major affective disorders. *American Journal of Psychiatry* 2005;162:79-91.

12. McNeil TF, Sjöström K. McNeil-Sjöström Scale for Obstetric Complications. Version B: 95 03 01b. 1995, Malmö.

13. McNeil T, Cantor-Graae E, Sjöström K. Obstetric complications as antecedents of schizophrenia: empirical effects of using different obstetric complication scales. *Journal of Psychiatric Research* 1994;28:519-530.

14. Haukvik UK, Schaer M, Nesvag R, McNeil T, Hartberg CB, Jonsson EG, Eliez S, Agartz I. Cortical folding in Broca's area relates to obstetric complications in schizophrenia patients and healthy controls. *Psychol Med* Jun 2012;42(6):1329-1337.

15. Australian Bureau of Statistics. *Socio-Economic Indexes for Areas (SEIFA) - Technical Paper 2006. Catalogue no. 2039.0.55.001.* Canberra: Australian Bureau of Statistics; 2008.

16. Australian Bureau of Statistics. *Statistical Geography Volume 1 - Australian Standard Geographical Classification (ASGC), Jul 2006. Catalogue no. 1216.0.* Canberra: Australian Bureau of Statistics; 2006.

17. Hosmer DW, Lemeshow S. Confidence interval estimation of interaction. *Epidemiology (Cambridge, Mass)* Sep 1992;3(5):452-456.

18. Knol MJ, van der Tweel I, Grobbee DE, Numans ME, Geerlings MI. Estimating interaction on an additive scale between continuous determinants in a logistic regression model. *International journal of epidemiology* October 1, 2007 2007;36(5):1111-1118.
19. Cummings P. The relative merits of risk ratios and odds ratios. *Archives of Pediatrics & Adolescent Medicine* 2009;163(5):438-445.
20. StataCorp. Stata: Release 13. *Statistical Software*. College Station, TX: StataCorp LP; 2013.