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Cohort Profile

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Cohort Profile: The Western Australian Pregnancy Cohort (Raine) Study–Generation 2

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Why was the cohort set up?

The Western Australian Pregnancy Cohort (Raine) Study (www.rainestudy.org.au) was established 1989-1991 with the then stated purpose:

to develop a large cohort of Western Australian children studied from 18 weeks' gestation to ascertain the relative contributions of familial risk factors, fetal growth, placental development and environmental insults to outcome in infancy and to the precursors of adult morbidity. This cohort, with complete intrauterine, perinatal and childhood data, will enable evaluation of the interaction between these factors, subsequent lifestyle patterns and environmental exposures which contribute to ill health during life.[1]

Establishment of the cohort involved combining funding for 'a randomised controlled trial of the influence of serial fetal ultrasounds on birth outcomes' from the National Health and Medical Research Council of Australia[2] and funding to investigate 'the origins of disease in the fetus, the child and the young adult' from the Raine Medical Research Foundation.[1]

The conceptual framework for the study was initially based around the developmental origins of health and disease, but has since evolved into a life-course framework taking into account the multiple interacting domains of genetics, phenotypes (cardiometabolic, respiratory, immunological, hormonal, musculoskeletal, psychological, vision and hearing, body composition and growth), behaviours (physical activity, sedentary behaviour, sleep, diet, drug use, risk taking), the environment (sunlight, chemical exposures, spatial environment) and other developmental outcomes (education, work).

Who is in the cohort?

Pregnant women presenting at the public antenatal clinic at King Edward Memorial Hospital (at that time it was the only tertiary women's and infants' hospital in Perth, Western Australia) and nearby private practice clinics between May 1989 and November 1991[3] were invited to participate. Women were invited if they were between 16 and 20 weeks pregnant, had sufficient proficiency in

English, were expected to deliver at the hospital and intended to remain in Western Australia. A total of 2900 women ('Generation 1') were enrolled into the study. There were 2868 live births–the index participants of 'Generation 2'–including 60 sets of twins ($n = 120$) and two sets of triplets ($n = 6$), from 2826 mothers (see Figure 1).

The cohort has been regularly followed up since birth. The number of participants has gradually decreased over time (Figure 1) and the proportion of eligible participants (those who have not died, withdrawn, been lost or deferred) providing data at each assessment remained relatively constant across childhood and adolescence, but has reduced in young adulthood (Figure 2). The reduced participation rate at the 2-year follow-up was due to the study running out of resources to complete data collection of the whole cohort.

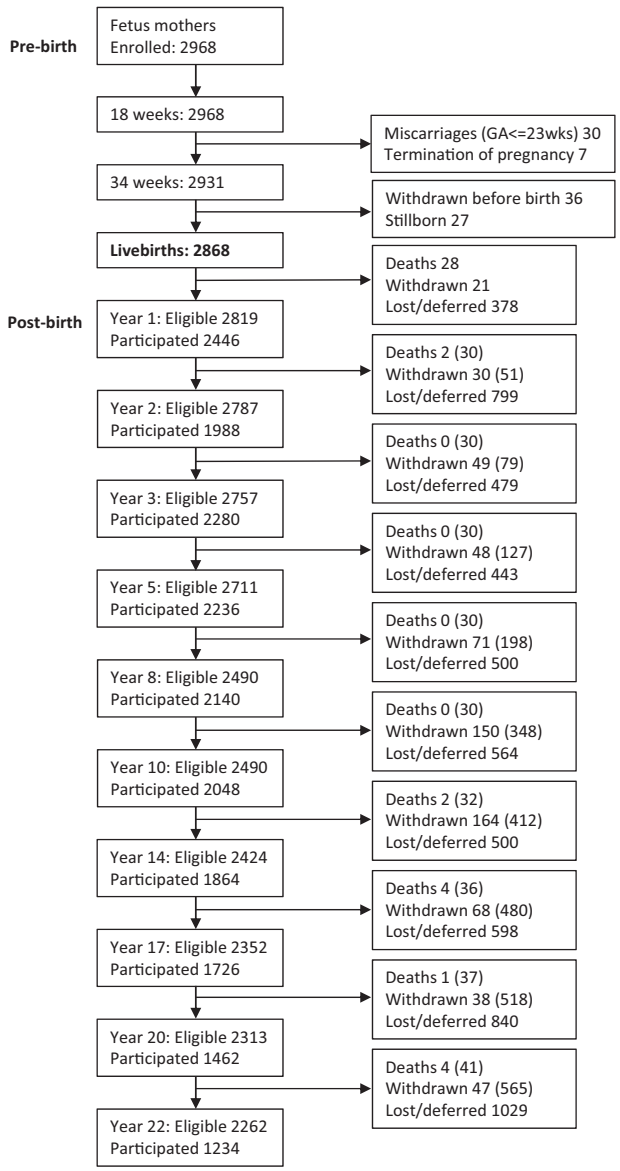

Figure 1. Flow diagram of Raine Study cohort participation.

Representativeness of the cohort

The representativeness and presence of potential biases in the cohort have been examined with three sets of analyses. Eligibility and consent rates at the recruiting clinics were evaluated. Comparisons were made between the cohort participants and the Western Australian population at birth, childhood (year 8), adolescence (years 14 and 17) and young adulthood (years 20 and 22). Comparisons were also made between cohort participants and non-participants for all follow-ups.

At the time of recruitment, to assess whether the Raine Study cohort was representative of the population presenting at the recruitment sites, 6 months of clinic records in the middle of the recruitment period were audited. In the 131 clinic sessions, 1420 women presented as new attendees and 707 (50%) were eligible. Reasons for ineligibility were: 36% were > 20 weeks' gestation; 8% had language difficulties; 4% planned to deliver elsewhere; and 2% had psychosocial problems precluding long-term follow-up. Of the 707 eligible, 633 (90%) agreed to participate during the audited period.[3]

At birth, the characteristics of the Raine cohort were compared with those of all live births (excluding Raine births) in Western Australia during the 3-year recruitment period, using data from the WA Department of Health Midwives Notification System and Hospital Morbidity Database. Comparisons were made of birthweight, gestation age, neonatal nursery admission, pregnancy complications, caesarean sections, maternal age, parity, marital status and race. Overall, the characteristics of Raine participants were similar to all Western Australian contemporaneous births except that Raine Study participants had slightly more pregnancies with complications and caesarean deliveries, and had more first-time mothers and unmarried mothers (see Table 1).

At the 8-year follow-up, the characteristics of participating cohort families were compared with the Year 2001 Western Australian Population Census data (see Table 2). Demographic factors compared included family structure, state of residence, parents' place of birth, education, labour force participation and occupational status, income level and language spoken at home. Overall differences between Raine Study and WA population families were small except for more Raine parents residing in WA, being born overseas, more with post-secondary and tertiary education and in clerical/retail occupations, and less parents having low incomes.

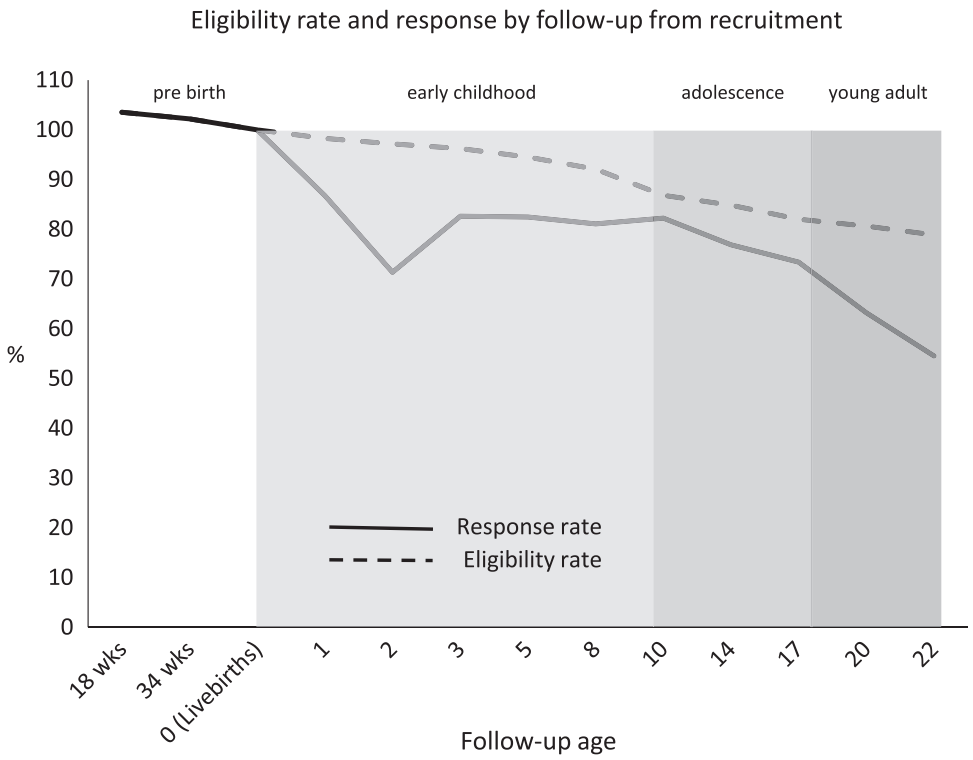

Figure 2. Raine Study cohort participation rates across life-course periods.

At the 14- and 17-year follow-ups, the cohort family characteristics of participants were compared with Year 2006 Western Australian Population Census data of families living in Western Australian with 15-17 year old children, as this was the most appropriately representative Western Australian demographic for comparison for either follow-up (see Table 3). Demographic factors compared included family structure, parents' place of birth, education, labour force and occupational status, income level and an index of advantage/disadvantage. Overall, the characteristics of the Raine families were similar to contemporaneous Western Australian families. There were no substantial differences in proportions of family structure or index of socioeconomic advantage/disadvantage. There were more Raine families living in urban areas and with tertiary education. At 14 years, there were more Raine parents in clerical/administrative occupations and middle incomes, and at 17 these differences were reduced with a shift of Raine parents to technical and professional occupations and higher incomes.

At the 20- and 22-year follow-ups, the characteristics of cohort members participating in data collection were compared with contemporaneous Year 2011 Western Australian Census Data of 20- and 22-year-old males and females living in Western Australia as the most appropriately representative Western Australian demographic for comparison (see Table 4; and Supplementary Tables 1 and 2, showing sex-specific comparisons, are available as Supplementary data at *IJE* online). Demographic factors compared included family structure, education completed, labour force status, occupation, work hours and income level. Overall, most comparisons showed the Raine cohort had similar proportions as all Western Australian young adults. Exceptions with more marked proportional differences (> 10%) indicated that the Raine cohort at 17 years had more employed in clerical/retail, more working 40 or more hours a week and more with higher incomes.

To assess any attrition bias, the characteristics at infancy of participants and non-participants were compared at each follow-up (see Tables 5, 6 and 7). In general, the proportions of participants and non-participants across a number of infant characteristics remained constant across all follow-ups. An exception was a gradual reduction in participation of infants of Aboriginal and Torres Strait Islander ethnicity.

How often have they been followed up? What has been measured?

The cohort has been assessed on 14 separate occasions. Initial assessment was at 18 weeks gestation, and subsequent assessments were undertaken at 34 weeks, at birth and at ages 1, 2, 3, 5, 8, 10, 14, 17, 18, 20 and 22 years.

Table 1. Comparison of Raine Study cohort families at birth with the Western Australian (WA) population of babies born contemporaneously, using linked data derived from the Western Australian Department of Health Midwives Notification System and Hospital Morbidity Database

	Birth	
	Raine $n = 2868$	WA $n = 99\,141$
Mothers		
Age (mean years)	27.5	27.7
Married (%)	82.1	89.4
Caucasian (%)	89.6	87.4
Parity (%)		
0	48.1	39.0
1	28.7	32.7
2-3	20.6	24.5
≥ 4	2.5	3.8
Socioeconomic status:		
IRSD[a] (mean)	1021	1022
Pregnancies		
Complications (%)	38.6	30.0
Mode of delivery:		
Spontaneous vertex	61.1	63.6
Breech	1.2	1.1
Instrumental	17.7	17.5
Caesarean section	21.1	18.9
Infants		
Birthweight (g)	3283	3344
Birth length (cm)	48.8	49.9
Ponderal index (kg/m^3)	27.9	26.7
Gestation (weeks)	39.0	39.1
Nursery admissions (%)	9.7	7.6

[a]Index of Relative Soci-economic Disadvantage.

Table 2. Comparison of Raine Study cohort families at childhood (age 8 years) with contemporaneous Western Australian (WA) Census population (2001 census data)

	Age 8 follow-up	
	Raine %	WA %
Family structure		
Single parent family	19.5	22.2
Couple family	80.5	77.8
Family state of residence		
WA	84.3	74.6
Interstate	15.7	25.4
Parents' place of birth		
Australia (≥ 1 parent)	73.4	83.8
Overseas	26.6	16.2
Maternal education[a]		
Secondary	41.7	63.2
Post-secondary	36.3	15.3
Tertiary	19.7	9.1
Parent labour force/occupation[b]		
Professional/managerial	38.8	36.0
Clerical/retail	32.1	20.2
Technical/trade/labour	23.5	34.9
Not in labour force[c]	5.6	8.8
Family income levels[d]		
Low	20.1	40.7
Medium	47.2	30.9
High	30.1	28.4
Language spoken at home		
English	94.6	94.6
Other	5.4	5.4

[a]Maternal education: WA 2001 Census data based on adult female education levels; Raine data based on maternal education levels attained by 8 years.

[b]Parent occupation: WA 2001 Census data based on 35-44 age category for all persons to correspond to median maternal age and available paternal age at 8 years [Raine: parent age median (interquartile range): maternal = 37.2 (33.1, 41.2); paternal = 39.9 (36.2, 43.8)]; Raine data based on highest level occupation of either parent at 8 years.

[c]Not in labour force or not stated.

[d]Family income: WA 2001 Census data based on weekly family income for single and couple parent families: low, < \$400 per week (pw); medium, \$400-\$800 pw; high, > \$800 pw; Raine family income level at 8 years: low, < \$25K per annum (pa); medium, \$25K-\$60K pa; high, > \$60K pa.

Currently assessment of participants at age 27 years is under way.

Early assessments typically included primary and secondary caregiver reporting via questionnaire and clinical assessments of the child participant. For the 14- and 17-year follow-ups, index participants provided self-report information to complement caregiver reporting and continued to perform clinical assessments. From the 18-year follow-up onwards, index participants provided self-report information along with performing clinical assessments. Specific assessments of reproduction were undertaken in females at the 14-year follow-up and in males at the 20-year follow-up. At the 18-year follow-up, participants with mobility problems or a history of mental health issues were not invited due to the social stressor assessment.

Currently the database holds >70 000 phenotypic measures and > 20 million genetic variants on each participant, as well as over 170 000 biological samples in storage.

A list of measurements obtained at each follow-up is presented in Tables 8-11.

What has it found? Key findings and publications

Since its genesis in 1989, over 400 peer-reviewed journal papers have been published using the Raine Study data; a full list is available on website [http://www.rainestudy.org.au/research-findings/publications/], along with brief lay

Table 3. Comparison of Raine Study cohort families at adolescence (ages 14 and 17 years) with contemporaneous Western Australian (WA) Census population (2006 Census data)

	Age 14 follow-up		Age 17 follow-up	
	Raine %	WA %	Raine %	WA %
Family structure				
Single parent family	23	24	22	24
Couple family	77	76	78	76
Family area of residence				
Rural	22	34	18	34
Urban	78	66	82	66
Family socioeconomic status[a]				
Lowest tertile	3.0	3.0	3.5	5.0
Middle tertile	78.5	80.0	83.5	83.5
Highest tertile	18.5	17.0	13.0	11.0
Parent place of birth				
Australia (≥ 1 parent)	70.9	69.5	69.5	69.5
Overseas	29.1	30.5	30.4	30.5
Parent education				
Secondary	50.8	49.6	48.9	49.6
Post-secondary	27.6	32.6	28.7	32.6
Tertiary	21.7	17.8	22.5	17.8
Parent labour force/occupation				
Professional/managerial[b]	35.3	33.4	42.1	33.4
Clerical/retail[b]	34.8	24.7	25.9	24.7
Technical/trade/labour[b]	14.2	23.6	20.1	23.6
Not in labour force[c]	15.8	18.3	11.7	18.3
Parent income levels				
Low	13	11	8	11
Medium	69	55	58	55
High	18	34	34	34

[a]Index of Relative Socioeconomic Advantage and Disadvantage.
[b]Out of % in labour force.
[c]By choice.

Table 4. Comparison of Raine Study cohort participants at young adulthood (ages 20 and 22 years) with contemporaneous Western Australian (WA) Census population (2011 Census data)

	Age 20 follow-up		Age 22 follow-up	
	Raine %	WA %	Raine %	WA %
Family structure				
Not married	88.5	87.4	77.7	78
De facto married	11.6	12.7	22.4	22
Any children	4.3	1.2	7.5	2.6
Education completed				
Secondary > year 10	88.1	83.2	88.4	83.2
Post-secondary/ = tertiary study	21.5	27.0	40.2	46.5
Labour force/occupation				
Professional/managerial[a]	4.2	8.2	16.8	17.9
Clerical/retail[a]	56.0	49.8	54.3	41.5
Technical/trade/ labour[a]	39.6	40.6	29.4	39.3
Unemployed/not in labour force	19.2	26.6	17.5	23.7
Work hours per week				
< 40	66.6	73.5	55.9	65.2
40+	33.5	26.6	44.2	34.9
Income levels				
Low	18.5	18.5	44.3	52.0
Medium	46.4	43	32.7	35.5
High	35.2	38.5	23.1	12.6

[a]Out of total *n* employed in labour force.

summaries of these papers [http://www.rainestudy.org.au/research-findings/highlights/]. The publications used measurements collected during the antenatal/perinatal, infancy, childhood, adolescent and early adulthood periods. Broadly, the nature of the measurements collected over the years and used in these papers can be characterized as being either: (i) genetic; (ii) phenotypic; (iii) behavioural; (iv) environmental; or (iv) educational or work-related.

Obstetric

- The randomized controlled trial demonstrated that a protocol of five prenatal scans, compared with a single mid-pregnancy morphology scan alone, does not prevent preterm birth or improve pregnancy outcomes.[3]
- Follow-up to 8 years of age from the multiple and single prenatal ultrasound groups provided strong evidence that ultrasound imaging studies are safe,[4] as did follow-up of eye structure and function at 20 years of age.[5]
- The unique serial fetal biometry measures have been used to develop customized fetal growth charts.[6]

Genetic

- Genome-wide association studies have identified genetic variants associated with fetal growth,[7] birthweight,[8] asthma,[9] obesity,[10] cognition[11] in childhood, vitamin D levels in adolescence[12] and myopia in young adulthood.[13]
- Exome array analysis has identified mutations in a number of genes associated with a later age of menarche.[14]
- Epigenetic studies have identified DNA methylation that is related to adiposity in young adulthood.[15]

Cardiometabolic

- Maternal exposure to life stresses during pregnancy predicts increased weight but lower blood pressure in offspring at 20 years of age.[16]

Table 5. Comparison of participants and non-participants across childhood follow-ups by infant characteristics at birth

	Age 1 follow-up		Age 2 follow-up		Age 3 follow-up		Age 5 follow-up		Age 8 follow-up		Age 10 follow-up	
	Participant		Participant		Participant		Participant		Participant		Participant	
	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
	422 (14.7)	2446 (85.3)	880 (30.7)	1988 (69.3)	588 (20.5)	2280 (79.5)	632 (22.0)	2236 (78.0)	728 (25.4)	2140 (74.6)	820 (28.6)	2048 (71.4)
	n (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Gestational age: missing $n = 11$ (0.4%)												
Term ($\geq$ 37 weeks)	359 (85.1)	2182* (89.2)	756 (85.9)	1785 (89.8)	517 (87.9)	2024 (88.8)	553 (87.5)	1988 (88.9)	630 (86.5)	1911 (89.3)	715 (87.2)	1826 (89.2)
Premature	58 (13.7)	258 (10.5)	120 (13.6)	196 (9.9)	68 (11.6)	248 (10.9)	77 (12.2)	239 (10.7)	91 (12.5)	225 (10.5)	100 (12.2)	216 (10.5)
Birthweight[a]												
< 100%	218 (51.7)	1216 (49.7)	438 (49.8)	996 (50.1)	302 (51.4)	1132 (49.6)	327 (51.7)	1107 (49.5)	369 (50.7)	1065 (49.8)	438 (53.4)	996 (48.6)
100-110%	116 (27.5)	779 (31.8)	282 (32.0)	613 (30.8)	168 (28.6)	727 (31.9)	184 (29.1)	711 (31.8)	219 (30.1)	676 (31.6)	232 (28.3)	663 (32.4)
> 110%	82 (19.4)	445 (18.2)	156 (17.7)	371 (18.7)	114 (19.4)	413 (18.1)	118 (18.7)	409 (18.3)	133 (18.3)	394 (18.4)	145 (17.7)	382 (18.7)
Small for GA[b]	47 (11.1)	257 (10.5)	93 (10.6)	211 (10.6)	60 (10.2)	244 (10.7)	74 (11.7)	230 (10.3)	77 (10.6)	227 (10.6)	97 (11.8)	207 (10.1)
Large for GA[c]	44 (10.4)	230 (9.4)	78 (8.9)	196 (9.9)	59 (10.0)	215 (9.4)	63 (10.0)	211 (9.4)	64 (8.8)	210 (9.8)	66 (8.0)	208 (10.2)
High-risk birth[d]	46 (10.9)	213 (8.7)	88 (10.0)	171 (8.6)	67 (11.4)	192 (8.4)	55 (8.7)	204 (9.1)	58 (8.0)	201 (9.4)	72 (8.8)	187 (9.1)
Ethnicity												
Caucasian	308 (73.0)	2060* (84.2)	670* (76.1)	1698* (85.4)	441 (75.0)	1927* (84.5)	481 (76.1)	1887* (84.4)	558 (76.6)	1810* (84.6)	622 (75.9)	1746* (85.3)
ATSI[e]	56 (13.3)	56 (2.3)	76 (8.6)	36 (1.8)	64 (10.9)	48 (2.1)	55 (8.7)	57 (2.5)	63 (8.7)	49 (2.3)	72 (8.8)	40 (2.0)
Other	58 (13.7)	330 (13.5)	134 (15.2)	254 (12.8)	83 (14.1)	305 (13.4)	96 (15.2)	292 (13.1)	107 (14.7)	281 (13.1)	126 (15.4)	262 (12.8)

[a]% of mean birthweight for gestational age based on WA norms (Roberts 1999).
[b]Small for gestational age (GA): < 90% expected birthweight.
[c]Large for GA: > 110% expected birthweight (both based on Australian birthweight norms).
[d]Emergency caesarean section.
[e]ATSI: Aboriginal or Torres Strait Islander.
*$P < 0.001$.

Table 6. Comparison of participants and non-participants across adolescent follow-ups by infant characteristics at birth

	Age 14 follow-up		Age 17 follow-up	
	Participant		Participant	
	No 1004 (35.0) *n* (%)	Yes 1864 (65.0) *n* (%)	No 1142 (39.8) *n* (%)	Yes 1726 (60.2) *n* (%)
Gestational age: missing $n = 11$ (0.4%)				
Term ($\geq$ 37 weeks)	878 (87.5)	1663 (89.2)	1003 (87.8)	1538 (89.1)
Premature	118 (11.8)	198 (10.6)	133 (11.6)	183 (10.6)
Birthweight[a]				
< 100%	532 (53.0)	902** (48.4)	598 (52.4)	836 (48.4)
100-110%	284 (28.3)	611 (32.8)	339 (29.7)	556 (32.2)
> 110%	180 (17.9)	347 (18.6)	199 (17.4)	328 (19.0)
Small for GA[b]	116 (11.6)	188 (10.1)	132 (11.6)	172 (10.0)
Large for GA[c]	91 (9.1)	183 (9.8)	93 (8.1)	181 (10.5)
High-risk birth[d]	83 (8.3)	176 (9.4)	95 (8.3)	164 (9.5)
Ethnicity:				
Caucasian	774 (77.1)	1594* (85.5)	901 (78.9)	1467* (85.0)
ATSI[e]	77 (7.7)	35 (1.9)	82 (7.2)	30 (1.7)
Other	153 (15.2)	235 (12.6)	159 (13.9)	229 (13.3)

[a]% of mean birthweight for gestational age based on WA norms (Roberts 1999).
[b]Small for gestational age (GA): < 90% expected birthweight (based on Australian birthweight norms).
[c]Large for GA: > 110% expected birthweight (based on Australian birthweight norms).
[d]Emergency caesarean section.
[e]ATSI: Aboriginal or Torres Strait Islander.
*$P < 0.001$, ** < 0.01 for differences between participants and non-participants (comparisons based on chi-square tests).

Table 7. Comparison of participants and non-participants across young adult follow-ups by infant characteristics at birth

	Age 20 follow-up		Age 22 follow-up	
	Participant		Participant	
	No 1406 (49.0) *n* (%)	Yes 1462 (51.0) *n* (%)	No 1634 (57.0) *n* (%)	Yes 1234 (43.0) *n* (%)
Gestational age: missing $n = 11$ (0.4%)				
Term ($\geq$ 37 weeks)	1234 (87.8)	1307 (89.4)	1433 (87.7)	1108 (89.8)
Premature	165 (11.7)	151 (10.3)	191 (11.7)	125 (10.1)
Birthweight[a]				
< 100%	716 (50.9)	718 (49.1)	831 (50.9)	603 (48.9)
100-110%	426 (30.3)	469 (32.1)	486 (29.7)	409 (33.1)
> 110%	257 (18.3)	270 (18.5)	307 (18.8)	220 (17.8)
Small for GA[b]	157 (11.2)	147 (10.1)	182 (11.1)	122 (9.9)
Large for GA[c]	129 (9.2)	145 (9.9)	156 (9.5)	118 (9.6)
High-risk birth[d]	115 (8.2)	144 (9.8)	135 (8.3)	124 (10.0)
Ethnicity:				
Caucasian	1118 (79.5)	1250* (85.5)	1319 (80.7)	1049* (85.0)
ATSI[e]	94 (6.7)	18 (1.2)	101 (6.2)	11 (0.9)
Other	194 (13.8)	194 (13.3)	214 (13.1)	174 (14.1)

[a]% of mean birthweight for gestational age based on Western Australian norms (Roberts 1999).
[b]Small for gestational age (GA): < 90% expected birthweight (based on Australian birthweight norms).
[c]Large for GA: > 110% expected birthweight (based on Australian birthweight norms).
[d]Emergency caesarean section.
[e]ATSI: Aboriginal or Torres Strait Islander.
*$P < 0.001$.

Table 8. Raine Study measurements in perinatal period

Follow-up	Measurements
18 weeks	Clinical assessment: mother weight, height, doppler, ultrasound, head circumference
	Mother questionnaire: education, income, occupation, activity, stress, smoking, alcohol, caffeine, non-prescription drugs, substance exposure, medical history
	Father questionnaire: education, occupation, toxin exposure
	Mother blood sample: Vitamin D, thyroid stimulating hormone, phthalates
34 weeks	Mother questionnaire: life stress, caffeine, smoking, alcohol, non-prescription drugs, toxin exposure
	Mother blood sample: phthalates, thyroid stimulating hormone (stored)
	Antenatal information, maternal medical records: diabetes, hypertension, post-partum complications, labour details, placental weight and shape
	Fetus information, mother's medical records: presentation, delivery, antenatal testing
Birth	Neonatal assessment: weight, length, head circumference, mid-arm, chest and abdominal circumferences, skinfold thickness, dysmorphology, perinatal morbidity
	3 days post birth: mother questionnaire: postnatal blues
	Cord blood sample: cord, cytokines, androgens
	Placental sample: (stored)

Table 9. Raine Study measurements in childhood period (age in years)

Follow-up	Measurements
Age 1	Clinical assessment: weight, height, rump to crown, head, mid-arm and chest circumferences, dysmorphology, skinfolds, blood pressure, lung function, vision test
	Questionnaire: employment, occupation, income, social benefits, home details, family structure, medical history, asthma, allergy, life stress, smoking, breastfeeding, child care, immunizations
Age 2	Clinical assessment: weight, height, rump to crown, head, mid-arm and chest circumferences, dysmorphology, skinfolds, blood pressure, vision test
	Questionnaire: employment, occupation, income, social benefits, home details, family structure, medical history, asthma, allergy, life stress, Child Behaviour Checklist, smoking, breastfeeding, child care, immunizations
Age 3	Clinical assessment: weight, height, rump to crown, head, mid-arm and chest circumferences, dysmorphology, skinfolds, blood pressure, vision test
	Questionnaire: employment, occupation, income, social benefits, home details, family structure, medical history, asthma, allergy, life stress, smoking, breastfeeding, child care, immunizations
Age 5	Clinical assessment: weight, height, head, mid-arm and chest circumferences, dysmorphology, skinfolds, blood pressure, lung function, allergy
	Questionnaire: education, employment, occupation, income, social benefits, home details, family structure, medical history, asthma, allergy, life stress, Child Behaviour Checklist, physical activity, TV, smoking, child care, immunizations
	Blood sample: Vitamin D, eosinophilic cationic protein and IgE, relative light transmission, (stored)Milk teeth: (stored)
Age 8	Clinical assessment: weight, height, head, mid-arm and chest circumferences, dysmorphology, blood pressure, fitness, lung function
	Questionnaire: education, employment, occupation, income, social benefits, home details, family structure, medical history, asthma, allergy, life stress, Child Behaviour Checklist, physical activity, TV, smoking
	Blood sample: full blood count, glucose, insulin, lipids, International Normalized Ratio
Age 10	Clinical assessment: weight, height, head and mid-arm circumferences, skinfolds, blood pressure, motor control
	Questionnaire: education, employment, occupation, income, social benefits, home details, family structure, medical history, asthma, allergy, life stress, Child Behaviour Checklist, Depression Anxiety Stress Scales, physical activity, TV, smoking

- Passive smoking exposure over childhood and adolescence predicts reduced HDL-cholesterol during adolescence in girls but not boys.[17]
- An adiposity trajectory characterized by an accelerated rate of growth in infancy predicts greater insulin resistance in adolescence.[18]

Respiratory

- Maternal smoking during pregnancy predicts decreased offspring respiratory function in infancy[19] and asthma in adolescence.[20]
- Low cytokine levels at birth predict increased risk of asthma, wheeze and allergy in childhood.[21]

Table 10. Raine Study measurements in adolescent period (age in years)

Follow-up	Measurements
Age 14	Clinical assessment: weight, height, mid arm, waist, hip, blood pressure, fitness, lung function, allergy, motor control, posture Questionnaire: education, employment, occupation, income, social benefits, home details, family structure, medical history, asthma, allergy, back pain, life stress, Child Behaviour Checklist, Depression Anxiety Stress Scales, physical activity, TV, computer use, food frequency, smoking, alcohol, drug use Blood sample: full blood count, glucose, insulin, lipids, fatty acids, Vitamin D, C-reactive protein, polychlorinated biphenyl, (stored) Urine sample: (stored)
Age 17	Clinical assessment: weight, height, mid arm, waist, hip, skinfolds, blood pressure, fitness, liver scan, motor control, cognition, posture Questionnaire: education, employment, occupation, income, social benefits, home details, family structure, medical history, asthma, allergy, back pain, life stress, Child Behaviour Checklist, Depression Anxiety Stress Scales, physical activity, TV, computer use, food frequency, smoking, alcohol, drug use Blood sample: full blood count, glucose, insulin, lipids, fatty acids, iron, Vitamin D, C-reactive protein, leptin, adiponectin, corticosteroid-binding globulin Saliva sample: basal cortisol Urine sample: urea, (stored)
Age 18	Clinical assessment: weight, height, Trier Social Stress Test Blood and/or saliva samples: blood and saliva cortisol collected pre-test and 1, 10, 20, 30, 45, 60 and 90 min post-test

Table 11. Raine Study measurements in early adulthood period (age in years)

Follow-up	Measurements
Age 20	Clinical assessment: weight, height, waist, hip, skinfolds, blood pressure, liver scan, DXA scan, eye tests, accelerometry Questionnaire: education, employment, occupation, income, social benefits, home details, family structure, medical history, asthma, allergy, back pain, Depression Anxiety Stress Scales, physical activity, TV, computer use, mobile phone, food frequency, smoking, alcohol, drug use Blood sample: glucose, insulin, lipids, iron, Vitamin D, C-reactive protein, male hormone, metabolomics, (stored) Urine sample: urea, (stored) Semen sample: count, motility, morphology
Age 22	Clinical assessment: weight, height, waist, hip, skinfolds, blood pressure, lung function, allergy, cognition, accelerometry, sleep study Questionnaire: education, employment, occupation, income, social benefits, home details, family structure, medical history, asthma, allergy, back pain, Depression Anxiety Stress Scales, physical activity, TV, computer use, mobile phone, food frequency, smoking, alcohol, drug use Blood sample: full blood count, glucose, insulin, lipids, iron, C-reactive protein, (stored)Urine sample: urea, (stored)

Hormonal

- Metabolic risks are increased in girls with polycystic ovary syndrome.[22]
- Menstrual irregularity was common in adolescent girls regardless of polycystic ovary syndrome status.[23]
- Over one-quarter of young men do not meet World Health Organization reference criteria for morphologically normal sperm.[24]
- Acute response patterns to social stress have been characterized and related to gender, health-related behaviours and adiposity.[25]

Musculoskeletal

- Maternal vitamin D deficiency during pregnancy predicts lower bone mass of offspring in young adulthood.[26]
- The presence of back pain in adolescence is associated with the presence of back pain in their carers.[27]
- Depressed mood in adolescence is associated with neck pain in adolescence.[28]

Psychological

- High concentrations of testosterone in cord blood predicts language impairment in early childhood.[29]
- Gestational hypertension predicts poorer mental ill-health trajectories across childhood and adolescence.[30]
- Being perceived as overweight by one's parents in middle childhood predicts increased risk of eating disorder in early adolescence.[31]

Vision and hearing

- Increased life-course sun exposure, as quantified by conjunctival UV autofluorescence, is related to reduced risk of myopia in young adulthood.[32]
- There was no evidence to suggest that exposure to anaesthesia as a child reduces visual acuity or increases myopia in young adulthood.[33]
- Breastfeeding for more than 6 months is protective against otitis media at 3 years of age.[34]

Physical activity and sedentary behaviour

- A trajectory characterized by less than 14 h/week TV viewing across childhood and adolescence predicts lower body fat in young adulthood.[35]
- Trajectories characterized by participation in sports across childhood and adolescence predict better physical health in young adulthood.[36]
- Higher screen time exposure in early childhood predicts lower physical activity and higher BMI in later childhood but not in adolescence.[37]

Diet

- Breastfeeding reduces the risk of asthma in childhood.[38]
- A good quality breakfast is associated with better mental health in adolescence.[39]
- Higher consumption of energy drinks is associated with higher anxiety in young adult males.[40]

Risky behaviour

- Contrary to expectations, earlier age of menarche is not related to age at first sexual intercourse.[41]

Environmental

- Antenatal exposure to phthalates is related to reduced ovarian reserve in adolescent girls.[42]
- Higher sun exposure is related to pterygium presence in young adults.[43]

Education and work

- A better quality diet in early childhood predicts better middle school achievement.[44]
- A better quality diet in adolescence is related to better school achievement.[45]
- Work absenteeism is identified as a significant issue for young adults and is associated with spinal pain and mental ill health.[46]

What are the main strengths and weaknesses?

A major strength of the Raine Study is the breadth, depth and duration of longitudinal data gathered from 14 separate follow-up assessments over 25 years. Specifically, these data included objective clinical assessments at nearly every follow-up in addition to subjective questionnaire assessments. The data include extensive phenotypic, behavioural and education/work measures along with extensive genetic data including GWAS, telomere, exome and epigenetic data. The data also include matched longitudinal data on parents, over 25 years. Additional strengths include the continued engagement of a representative cohort of participants, the strong multidisciplinary focus of investigators and clear governance and research administration procedures.

The main weaknesses of the Raine Study relate to the mainly Caucasian ethnicity of its participants, the moderate size of the cohort and the gradual attrition of its participants.

Can I get hold of the data? Where can I find out more?

The Raine Study encourages researchers to collaborate and use the available data. Details about the study, data avail-

Profile in a nutshell

- The Raine Study is a prospective observational study examining health and well-being across the life course from before birth through to young adulthood.
- Index participants were 2868 live births from 2900 mothers recruited at around 18 weeks' gestation who were attending the state's tertiary perinatal hospital and surrounding private clinics in Perth, Western Australia, between May 1999 and November 1991.
- Detailed assessments involving questionnaires and clinical measurements were undertaken at 18 and 36 weeks of gestation, birth and 1, 2, 3, 5, 8, 10, 14, 17, 18, 20 and 22 years of age. A follow-up is currently under way at 27 years of age. Over 2200 index participants remain active and eligible for future follow-up.
- Data on genetics (GWAS, exomes, telomeres, epigenetics) and an extensive range of phenotypic, behavioural, environmental, educational and occupational factors have been collected. Curated biological samples include blood, urine, saliva, semen and teeth.
- Over 400 papers have been published in international scientific and medical journals on Raine Study discoveries from the antenatal to young adulthood periods.
- Through its access processes, the Raine Study encourages collaboration and appropriate utilization of its resources–see [http://www.rainestudy.org.au/for-researchers].

ability and access are published on the study website [www.rainestudy.org.au].

Supplementary Data

Supplementary data are available at *IJE* online.

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