



Height and Body Mass

Introduction

Subtle deviations in various developmental trajectories during childhood and adolescence may foreshadow the later development of schizophrenia. Studies exploring these deviations (antecedents) are ideally based on representative, population-based samples that follow the cohort from birth through childhood and adolescence to adulthood. These studies can provide unique insights into the changes in developmental trajectories that may be associated with later development of schizophrenia.

Method

We have included only systematic reviews (systematic literature search, detailed methodology with inclusion/exclusion criteria) published in full text, in English, from the year 2000 that report results separately for people with a diagnosis of schizophrenia, schizoaffective disorder, schizophreniform disorder or first episode schizophrenia. Reviews were identified by searching the databases MEDLINE, EMBASE, CINAHL, Current Contents, PsycINFO and the Cochrane library. Hand searching reference lists of identified reviews was also conducted. When multiple copies of reviews were found, only the most recent version was included. Reviews with pooled data are given priority for inclusion.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist that describes a preferred way to present a meta-analysis¹. Reviews with less than 50% of items checked have been excluded from the library. The PRISMA flow diagram is a suggested way of providing information about studies included and excluded with reasons for exclusion. Where no flow diagram has been presented by individual reviews, but identified studies have been described in the text, reviews have been

checked for this item. Note that early reviews may have been guided by less stringent reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines.

Evidence was graded using the Grading of Recommendations Assessment, Development and Evaluation ([GRADE](#)) Working Group approach where high quality evidence such as that gained from randomised controlled trials (RCTs) may be downgraded to moderate or low review and study quality is limited, if there is inconsistency in results, indirect comparisons, imprecise or sparse data and high probability of reporting bias. It may also be downgraded if risks associated with the intervention or other matter under review are high. Conversely, low quality evidence such as that gained from observational studies may be upgraded if effect sizes are large, there is a dose dependent response or if results are reasonably consistent, precise and direct with low associated risks (see end of table for an explanation of these terms)². The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

Results

We found four systematic reviews that met our inclusion criteria³⁻⁶.

- Moderate quality evidence suggests a small increased risk of schizophrenia in men who were underweight or shorter than average around 5 years prior to the onset of schizophrenia.
- Moderate to low quality evidence suggests a medium effect of less leanness at birth, shorter height at 2.5 and 9 years, and higher body mass index (BMI) at 7 years, although



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no differences in BMI were reported at 2.5 and 9 years in a separate study.

- Moderate to low quality evidence suggests there may be slower growth in early childhood in females who later develop schizophrenia, with no differences in growth rate in males.
- High quality evidence shows no differences in birth length between people with schizophrenia and controls.



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Harper S, Towers-Evans H, MacCabe J

The aetiology of schizophrenia: what have the Swedish Medical Registers taught us?

Social Psychiatry and Psychiatric Epidemiology 2015; 50: 1471- 479

[View review abstract online](#)

Comparison	Childhood height and body mass index (BMI) in Swedish populations with schizophrenia vs. Swedish population without schizophrenia.
Summary of evidence	Moderate quality evidence (precise, direct, large sample) suggests a small increased risk of schizophrenia in men who were underweight or shorter than average around 5 years prior to onset of schizophrenia.
Childhood height and BMI	
<p><i>Significant, small effect of increased risk of schizophrenia in young adults who were underweight or shorter than average ~5 years before onset of the disorder;</i></p> <p>Underweight vs. normal: 1 study, N = 1,347,520 men, HR 1.30, 95%CI 1.20 to 1.42, $p < 0.05$</p> <p>Taller (reduced risk for 182 cm vs. 177 cm): HR 0.85, 95%CI 0.80 to 0.92, $p < 0.05$</p>	
Consistency in results [†]	Not applicable (one study)
Precision in results [§]	Precise
Directness of results	Direct

Latham K, Kirkpatrick B

Meta-analysis of adult height and birth length in schizophrenia

Schizophrenia Research 2018; 195: 110-4

[View review abstract online](#)

Comparison	Birth length in people with schizophrenia vs. controls.
Summary of evidence	High quality evidence (large samples, consistent, precise, direct) shows no differences in birth length.



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Birth length	
<p><i>No significant differences between groups;</i> 6 studies, N = 977,280, ES = -0.03, 95%CI -0.09 to 0.03, $p > 0.05$, $I^2 = 0\%$, $p = 0.932$</p>	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

Laurens KR, Luo L, Matheson SL, Carr VJ, Raudino A, Harris F, Green MJ

Common or distinct pathways to psychosis? A systematic review of evidence from prospective studies for developmental risk factors and antecedents of the schizophrenia spectrum disorders and affective psychoses

BMC Psychiatry 2015; 15: 205. DOI 10.1186/s12888-015-0562-2

[View review abstract online](#)

Comparison	Childhood height and BMI in people with schizophrenia vs. controls.
Summary of evidence	Moderate to low quality evidence (medium to large samples, direct, imprecise, unable to assess consistency) suggests a medium effect of less leanness at birth, shorter height at 2.5 and 9 years, and higher BMI at 7 years, although no differences in BMI were reported at 2.5 and 9 years.

Childhood height and BMI

1 prospective study (N = 112) reported a large effect of less leanness at birth and high BMI at 7 years in people with schizophrenia in adulthood (adjusted for sex and SES);

OR 22.8, 95%CI 2.0 to >100, $p < 0.05$

1 prospective study (N = 7,780) reported a medium effect of shorter height at 2.5 years and at 9 years in people with schizophrenia in adulthood;

Shorter height at 2.5 years: OR 2.32, 95%CI 1.51 to 3.56, $p < 0.01$

Shorter height at 9 years; OR 3.47, 95%CI 2.26 to 5.32, $p < 0.01$

No significant differences were reported for BMI;



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BMI at 2.5 years: OR 1.21, 95%CI 0.79 to 1.86, $p > 0.05$

BMI at 9 years: OR 1.42, 95%CI 0.92 to 2.17, $p > 0.05$

Consistency in results	Appears inconsistent, but unable to statistically assess as no pooled data are reported.
Precision in results	Imprecise
Directness of results	Direct

Welham J, Isohanni M, Jones P, McGrath J

The Antecedents of Schizophrenia: A Review of Birth Cohort Studies

Schizophrenia Bulletin 2009; 35(3):603-623

[View review abstract online](#)

Comparison	Prospective assessment of childhood height, BMI, and growth trajectories and the later development of schizophrenia.
Summary of evidence	Moderate to low quality evidence (large samples, direct, unable to assess precision or consistency) suggests there may be slower growth in early childhood in females who later develop schizophrenia, with no differences in growth rate for males. Males, however may show lower BMI prior to onset of schizophrenia.

Childhood height, BMI, and growth trajectories

2 birth cohorts (N = 5 362, and N = 12 537) reported no differences in childhood height, weight or pubertal development in people with schizophrenia compared to people without schizophrenia.

1 birth cohort (N ~ 19,000) reported females with schizophrenia grew slower in early childhood by approximately 1cm per year than females without schizophrenia. No differences were reported for males.

1 birth cohort (N = 9,125) reported mean BMI in men prior to schizophrenia onset was lower than average, controlling for maternal pre-pregnancy BMI, parental SES, and birth weight and length.

Consistency in results	Appears inconsistent, but unable to statistically assess as no pooled data are reported.
Precision in results	Unable to assess, no data reported



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Directness of results	Direct
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Explanation of acronyms

BMI = body mass index, CI = Confidence Interval, cm = centimeters, HR = hazard ratio, N = number of participants, OR = odds ratio, p = probability of obtaining that result ($p < 0.05$ generally regarded as significant), SD = standard deviation. SES = socio-economic status



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Explanation of technical terms

* Bias has the potential to affect reviews of both RCT and observational studies. Forms of bias include; reporting bias – selective reporting of results, publication bias - trials that are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias – only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias - including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small⁷.

† Different effect measures are reported by different reviews.

Odds ratio (OR) or relative risk (RR) refers to the probability of a reduction (< 1) or an increase (> 1) in a particular outcome in a treatment group, or a group exposed to a risk factor, relative to the comparison group. For example, a RR of 0.75 translates to a reduction in risk of an outcome of 25% relative to those not receiving the treatment or not exposed to the risk factor. Conversely, an RR of 1.25 translates to an increased risk of 25% relative to those not receiving treatment or not having been exposed to a risk factor. An RR or OR of 1.00 means there is no difference between groups. A medium effect is considered if $RR > 2$ or < 0.5 and a large effect if $RR > 5$ or < 0.2 ⁸. InOR stands for

logarithmic OR where a InOR of 0 shows no difference between groups. Hazard ratios measure the effect of an explanatory variable on the hazard or risk of an event.

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) which allows results from different scales to be combined and compared. Each study's mean difference is then given a weighting depending on the size of the sample and the variability in the data. 0.2 represents a small effect, 0.5 a medium effect, and 0.8 and over represents a large treatment effect⁷.

Prevalence refers to how many existing cases there are at a particular point in time. Incidence refers to how many new cases there are per population in a specified time period. Incidence is usually reported as the number of new cases per 100,000 people per year. Alternatively some studies present the number of new cases that have accumulated over several years against a person-years denominator. This denominator is the sum of individual units of time that the persons in the population are at risk of becoming a case. It takes into account the size of the underlying population sample and its age structure over the duration of observation.

Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives that are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives that are correctly



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identified (100% specificity = not identifying anyone as positive if they are truly not).

Correlation coefficients (eg, r) indicate the strength of association or relationship between variables. They are an indication of prediction, but do not confirm causality due to possible and often unforeseen confounding variables. An r of 0.10 represents a weak association, 0.25 a medium association and 0.40 and over represents a strong association. Unstandardised (b) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in the independent variable, statistically controlling for the other independent variables. Standardised regression coefficients represent the change being in units of standard deviations to allow comparison across different scales.

‡ Inconsistency refers to differing estimates of treatment effect across studies (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I^2 is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent substantial heterogeneity and 75% to 100%: considerable heterogeneity. I^2 can be calculated from Q (chi-square) for the test of heterogeneity with the following formula⁷;

$$I^2 = \left(\frac{Q - df}{Q} \right) \times 100\%$$

§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the

effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also recommends downgrading the evidence when sample size is smaller than 300 (for binary data) and 400 (for continuous data), although for some topics, this criteria should be relaxed⁹.

|| Indirectness of comparison occurs when a comparison of intervention A versus B is not available but A was compared with C and B was compared with C that allows indirect comparisons of the magnitude of effect of A versus B. Indirectness of population, comparator and or outcome can also occur when the available evidence regarding a particular population, intervention, comparator, or outcome is not available so is inferred from available evidence. These inferred treatment effect sizes are of lower quality than those gained from head-to-head comparisons of A and B.



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