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Meta-analysis of adult height and birth length in schizophrenia

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ABSTRACT

Objective: As a group, people with schizophrenia have a number of subtle anatomical abnormalities as well as physiological abnormalities that precede antipsychotic treatment. Some studies have also found shorter birth length or shorter adult height in people with schizophrenia compared to control subjects. We performed a systematic review and meta-analysis of studies of birth length and adult height in schizophrenia, following PRISMA guidelines (Prospero Registration # CRD42016043718).
Data sources: We searched the PsycInfo, Web of Science, and PubMed databases for articles published 1947–2016.
Study selection: Articles were included if they had data for patients diagnosed with schizophrenia and a matched control group of subjects without a psychotic disorder; both groups were measured for birth length and/or adult height (18 years or older); and the paper was published in English.
Data extraction: One author extracted the data, which was verified by the other.
Results: For adult height, six studies with 1,122 patients and 250,200 control subjects were included in analyses. There were six birth length studies, which included 984 patients and 976,296 controls. The patients did not differ from comparison subjects in birth length (effect size estimate = −0.03; CI: −0.09, 0.03), but adults were slightly shorter than comparison subjects (−0.15; −0.24, −0.06). In meta-regression of adult studies, the variables of first episode versus clinical sample, and population registry versus non-registry were not significant. Matching for several important variables was usually lacking in these studies.
Conclusions: While there appears to be no difference in birth length between people with schizophrenia and comparison subjects, the former may be slighter shorter in adult life. The cause of such a discrepancy, if confirmed, is not clear, and lack of matching on potentially confounding variables undermines confidence in any conclusion.
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1. Introduction

There is now an extensive literature on prenatal risk factors for adult disease, including cardiovascular disease, diabetes, and hypertension (Barker, 2003; Gluckman et al., 2007; Lawlor and Smith, 2005). A number of obstetric and prenatal problems are risk factors for schizophrenia (Cannon et al., 2002; Khandaker et al., 2013a, 2013b; Susser and St Clair, 2013; Knuesel et al., 2014). Consistent with that evidence, people with schizophrenia have an increased prevalence of minor physical anomalies, which are subtle anatomical abnormalities that have their origin in gestation (Franco et al., 2010; Xu et al., 2011). They also have several metabolic abnormalities, including abnormal glucose tolerance, increased inflammation, an elevated pulse pressure, increase prolactin, and decreased androgens in men, which are present prior to antipsychotic exposure (Miller et al., 2011; González-Blanco et al., 2016; Greenhalgh et al., 2017; Fernandez-Egea et al., 2009, 2011). These abnormalities are consistent with the concept that for many patients, the pathophysiology of schizophrenia is related to difficulties in gestation.

Prenatal events help determine adult height and birth length. While people with schizophrenia have been the subject of several studies of these variables, the results have not been consistent. The easily obtained measure of adult height would be a convenient measure that might be of theoretical interest for some areas of research. We performed a systematic review and meta-analysis of these studies to test the hypothesis that stature—adult height and birth length—is also abnormal in people with schizophrenia.

2. Materials and methods

2.1. Search strategy

We followed PRISMA guidelines (Moher et al., 2009) and registered the meta-analysis through PROSPERO (https://www.crd.york.ac.uk/PROSPERO/) as "Height in Schizophrenia Spectrum Disorders," registration number CRD42016043718. The literature search included articles from 1947 to 2016 on PsycInfo, Web of Science, and PubMed databases,

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using search terms of "schizophrenia" crossed with "body height". The bibliographies of the articles found by computer search were then examined for other relevant articles. Both authors (KL and BK) examined the titles and abstracts to find possibly relevant articles by both authors; they then inspected these articles to determine which fulfilled the inclusion and exclusion criteria.

2.2. Inclusion/exclusion criteria

To meet inclusion criteria a study had to include data for patients diagnosed with schizophrenia or schizoaffective disorder and a matched control group of subjects without a psychotic disorder; these two groups were measured for birth length, adult height (18 years or older), or both; and the paper was published in English.

2.3. Data analysis

One author (KL) recorded the data from the studies, which was verified by the second (BK). All analyses were conducted separately for birth length and adult height and were performed using Stata 13.1 software program. Effect size (ES) estimates using Hedges' g were calculated separately for adult height and birth length. This statistic quantifies the size of the difference between group means relative to their standard deviations (http://www.statisticshowto.com/hedges-g/). Random effects, pooled ES estimates and 95% confidence intervals were calculated using the method of DerSimonian and Laird (1986); p-values were considered statistically significant at the $p < 0.05$ level. We also examined forest and funnel plots for adult height and birth length.

For adult height, meta-regression was conducted for the variables of 1) first-episode patients (2 studies) vs. a clinic sample (4 studies), and 2) the use of registry (2 studies) vs. non-registry subjects (4 studies).

We also compared the ES estimate of 1) the two studies (one of adult height, one of birth length; respectively Sugawara et al., 2012 and Perrin et al., 2007) that included schizoaffective disorder patients to the ES estimate of the other five adult height or birth length studies, and 2) the two birth length studies (Haukka et al., 2008; Woerner et al., 1971) that used siblings as control subjects, to the other four birth length studies.

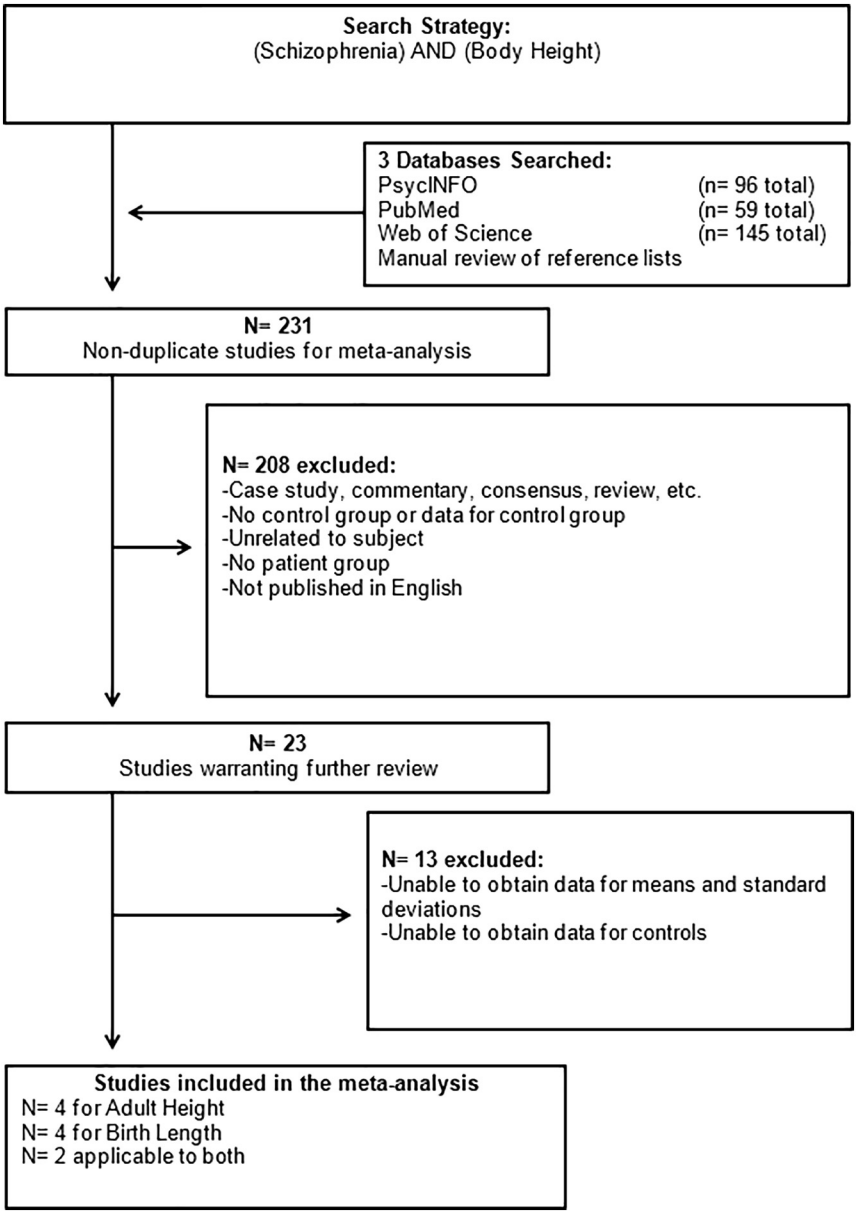

Fig. 1. Selection of studies for meta-analysis.

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