Prevalence of nonaffective psychosis in intellectually disabled clients: systematic review and meta-analysis

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Abstract

Epidemiological studies report high rates of schizophrenia in individuals with intellectual disability (ID). However, this subject has not been reviewed systematically. We aim to review studies that report the prevalence of nonaffective psychosis in a population with ID and estimate the prevalence of schizophrenia in this population. We performed a literature search using the PsychINFO, MEDLINE and EMBASE (from inception to 2 October 2014). We performed a manual search of citations from relevant papers identified through the databases. We identified 887 titles and after screening abstracts, identified 60 full-text articles. We identified 25 studies with 27 datasets for inclusion in the systematic review and meta-analysis. The prevalence rate was at least three times higher than the general population. There was a wide variation in the methodology, setting and sample size of the studies. Only one study reported a prevalence rate lower than the general population. The prevalence of psychosis in a population with ID is at least three times higher than that in the general population.

Keywords: epidemiology, intellectual disability, prevalence, psychosis, schizophrenia

Introduction

Over the last five decades, epidemiological studies have reported high rates of schizophrenia in individuals with intellectual disability (ID) compared with that reported in the general population (Penrose, 1938; Reid, 1972; Cooper et al., 2007). The relationship between ID and schizophrenia is complex. A number of studies suggest that individuals who later develop schizophrenia have lower IQ scores (Jones et al., 1994; David et al., 1997; Kremen et al., 1998; Davidson et al., 1999; Cannon et

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al., 2000; Zammit et al., 2004; Bilder et al., 2006; Woodberry et al., 2008). These individuals score about 0.5 SD below normal (Woodberry et al., 2008). The evidence also suggests that IQ scores decline in adolescents who later develop psychosis (Kremen et al., 1998; Fuller et al., 2002) and that the greatest deficit is just before the onset of illness (Rabinowitz et al., 2000; Gunnell et al., 2002). It has also been suggested that IQ scores tend to deteriorate during transition to illness (Cosway et al., 2000; Caspi et al., 2003; Lencz et al., 2006). Similarly, data from the follow-up studies suggest that there is a deterioration of up to 10 points on IQ scores, after onset of psychosis, in a proportion of affected individuals (Aylward et al., 1984; Reichenberg et al., 2005, 2010). Recent studies of individuals at high risk of developing psychosis indicate that a significant proportion have problems with learning and have low IQ scores before the onset of illness (Keshavan et al., 2004, 2005; Johnstone et al., 2005). Some of the syndromes linked to ID have a strong association with schizophrenia (Shprintzen, 2008).

The prevalence of schizophrenia and its correlates in the general population have been studied extensively. A systematic review of 188 studies from 46 countries examined the prevalence of schizophrenia in different populations, age groups and other strata. However, none of these studies have examined the prevalence of psychosis in individuals with ID (Saha et al., 2005). It is important to study the prevalence of psychosis in a population with ID because it can inform the service planning for this population as well as potentially help in understanding the biology of both schizophrenia and ID. Therefore, we aimed to systematically review the studies that examined the prevalence of psychosis in ID.

Our aim was to determine the prevalence of psychosis in a population that had an existing diagnosis of ID. A longitudinal study design providing information on the time of onset of psychosis in individuals already diagnosed with ID would have best answered this question. However, only one study with a longitudinal design examined the development of psychosis in a cohort of individuals

with ID. This review has relied on cross-sectional studies of populations with ID in whom the prevalence of psychosis was examined.

Materials and methods

We used the following inclusion criteria:

(1) Studies reporting psychosis in a community or an institutional sample with ID.

(2) ID diagnosed by an assessment of intelligence quotient and impaired adaptive functioning or assumed because individuals are in receipt of service for ID or live in an institution for populations with ID.

(3) Studies reporting the prevalence of psychosis where the diagnosis of psychosis is made by a clinician or a standardized instrument is used to make a diagnosis.

(4) Sample aged 14 years or older.

We decided to include both community and institutional samples because individuals with ID lived in institutions during most of the 20th century, but toward the later part of the century, institutions were closed. ID is diagnosed using an intelligence quotient test and by assessment of adaptive functioning. In older studies, the intelligence quotient and adaptive functioning were not consistently reported and we believed that it was safe to assume that individuals living in ID institutions will have ID. Similarly, individuals receiving services for ID in the community go through an assessment and it is a reasonable assumption that they have ID. The practice of diagnosis of psychosis has changed over time and we have considered different methods used for diagnosis. We used a 14-year cut-off as autism was not well established as a diagnosis until recent decades. In the older studies from institutions, it could potentially be a confounder in younger age groups.

Exclusion criterion was as follows:

(1) Affective disorders apart from schizoaffective disorder were excluded.

Search Strategy

The initial searches were carried out using PsychINFO, MEDLINE and EMBASE from inception to 2 October 2014. The following keywords were used for these searches: *schizophrenia, schizophrenia

(disorganised type), or undifferentiated schizophrenia, or fragmentation schizophrenia or process schizophrenia or paranoid schizophrenia, or childhood schizophrenia or catatonic schizophrenia or acute schizophrenia and learning disability, learning difficulty, learning disorder, intellectual disability, intellectual difficulty, intellectual disorder, developmental disability, developmental difficulty, developmental disorder, mental retardation, mental handicap, mental disability, learning disabled, LD, learning impairment, developmental impairment, intellectual impairment, developmental delay, developmental disability. The full search strategy is available on request.

We included studies that examined the prevalence of psychosis among individuals with an ID aged 14 years or older. We used an inclusive definition of schizophrenia and learning disability as described below. We included studies that reported data both for children and for adults only when the data for populations of patients 14 years of age and older could be obtained separately. The population had to be representative of the ID population. Studies that described the prevalence of schizophrenia in a normal population and those with organic psychosis or brain injury were excluded.

We used a two-stage process of exclusion; in the first stage, we looked at the title and abstracts and in the second stage we looked at full-text articles. We carried out a manual search of the references of the articles included to identify any additional relevant articles. Two authors (H.A. and M.A.) independently assessed the articles for inclusion and any disagreement was resolved through a face-to-face discussion or additional advice from other authors (F.N. and S.F.). We contacted authors for additional information (Fig. 1).

Description of intellectual disability

We included all the studies of the prevalence of psychosis in which authors reported on populations with mental retardation, mental handicap, learning disability or ID. These studies cover the period from the mid-20th century onwards. Different methodologies were used to define these populations, which are further described in the Results section.

Description of schizophrenia and psychosis

We included all studies that reported schizophrenia or nonaffective psychoses. We looked at the description provided in the text for schizophrenia and nonaffective psychosis and used an inclusive approach. In our quality assessment, we reported the method used for the diagnosis of ID as well as psychosis.

Data extraction and analysis

Once the study was included, we identified the total sample size and the number of affected individuals with psychosis. We also extracted information on the setting, year of publication and instruments used for the diagnosis of ID and psychosis. When studies only reported percentages, we calculated the numbers by utilizing the sample size and the percentage of affected individuals.

We used the program Metafor implemented in R to calculate the effect size (Viechtbauer, 2010) and SE. We reported the effect size with a 95% confidence interval (CI). If the same data were reported in more than one publication, we selected the publication that had the most complete data. For assessment of the quality of the study, we examined a number of factors. In terms of the settings of the studies, we differentiated between the studies carried out in institutions and in a community.

We expected many sources of heterogeneity in the studies because the methodology of assessment of ID and psychosis has evolved over the period covered by the studies. We used a random-effect model for meta-analysis because of heterogeneity. We examined the CIs in the forest plot for variability in the studies and we are reporting an I2 statistic as an indicator of heterogeneity. To explore systematic sources of heterogeneity, we carried out several sensitivity analyses. We investigated the effect of a number of factors: setting of the studies: community versus institutional studies, clinical diagnoses versus diagnoses on the basis of structured instruments and administrative samples versus samples where assessments were performed for the study. In each case, we carried out an analysis with one group of studies and noted the overlap in CIs in the effect

size. In a second step, we investigated the effects of these factors as moderators in a mixed-effect model. To investigate the publication bias, we used a funnel plot.

For assessment of quality, we did not use any summary measure; instead, we provide qualitative information on each study in the Supplementary Table S1 (Supplemental digital content 1, http://links.lww.com/PG/A154).

Results

We initially identified 1313 titles and abstracts. After excluding duplicates, 833 papers were examined. We identified 54 additional studies through a manual search. Of the total of 887 articles, we excluded 827 articles. We examined the full text of 60 articles and excluded 35 further articles.

We contacted authors of five studies (Reiss, 1990; Rojahn et al., 1993; Cooper, 1997; Deb et al., 2001; Morgan et al.,2008) for additional information. We could not obtain any additional information except for one study (Morgan et al., 2008). We used the email address supplied for one study, but the email message was not delivered (White et al., 2005). For eight older publications, it was not possible to contact the authors for a number of reasons, as either the contact information had changed or the authors had died or were not traceable (Wright, 1982; Day, 1985; Lund, 1985; Jacobson, 1990; Farmer et al., 1993; Patel et al., 1993; Sansom et al., 1994; Heaton-Ward, 1977). We used 25 articles with 27 datasets for this systematic review.

Description of studies

We could identify 25 studies with 27 datasets that fulfilled the inclusion criteria. All except one study (Al-Mutairi and Al-Mutairi, 2010) were from western industrialized nations. The study from Kuwait (Al-Mutairi and Al-Mutairi, 2010) was based on data from clients living in the community and attending day service. Twelve studies were carried out in the UK, two in Norway and three in Sweden. None of the studies were from low-income or middle-income countries.

European Studies

Five studies from the UK were carried out in Intellectual Disability Institutions (Reid, 1972; Heaton-Ward, 1977; Wright, 1982; Day, 1985; Sansom et al., 1994). Two British studies were based on information from case registers (Farmer et al., 1993; Bhaumik et al., 2008). One study from the UK was based on a mixed hospital and a community sample for individuals from one geographical area (Corbett, 1979). Four studies from the UK were based on the data from community samples in the UK (Patel et al., 1993; Cooper, 1997; Deb et al., 2001; Cooper et al., 2007; Bhaumik et al., 2008).

Two Swedish studies were based on data from community residents (Göstason, 1985; Nettelbladt et al., 2009) and the third one was based on a mixed sample of individuals residing in institutions and the community in a geographical area. This study was carried out at the time when the institutions were closing (Gustafsson and Sonnander, 2004). Two studies from Norway (Holden and Gitlesen, 2004; Bakken et al., 2010) and one study from Denmark (Lund, 1985) were based on community samples. The study by Holden and Gitlesen (2004) did not include individuals with mild ID.

Studies from the United States

Three studies from the USA were based on administrative data of the community samples of individuals registered with the state-run services for disability (Jacobson, 1990; Rojahn et al., 1993; Clay and Thomas, 2005) and one study was based on individuals attending day programs (Reiss, 1990).

Australian studies

One Australian study was based on state-run disability services administrative data (Morgan et al., 2008). Another study from Australia was a subanalysis of National Psychiatric Morbidity surveys (White et al. 2005).

Description of the sample

There was a wide variation in the size of the samples. Twenty studies provide complete information on population and samples, which are described in Supplementary Table S1 (Supplemental digital

content 1, http://links.lww.com/PG/A154). The study by White et al. (2005) was a sub-analysis of national survey and the total sample was not clearly provided; we estimated the sample from the total sample size and the percentage of ID information. In Morgan et al.'s (2008) study, we could separate and exclude the schizophrenia cases in the borderline ID range.

The prevalence estimates

The total sample in all studies providing information on the sample and population size was 140 189 and 4292 individuals were affected. The estimated prevalence for all psychotic disorders in this population was 3.46% (95% CI: 2.51–4.42). Figure 2 shows the Forest plot of all the studies. Estimated heterogeneity was $\tau 2=0.0002$ (SE=0.001), τ was 0.0152, I2 was 97.87%, and Q (d.f.=26) was 2444.36, with P-value of less than 0.0001. This plot provides the diagnoses used by the authors. In 17 studies, the diagnosis was schizophrenia; in one study, the diagnosis was schizophrenia and delusional disorder. In three studies, the label used was psychosis, but from the description, it was clear that affective disorders were not included. In two studies, the diagnosis was schizophrenia and other psychotic disorders. These studies did not include affective disorders. One study was based on schizophrenia and schizoaffective disorder.

Supplementary Table S2 (Supplemental digital content 1, http://links.lww.com/PG/A154) provides the different estimates of prevalence provided by the studies. There is a subanalysis of point prevalence and undefined prevalence. Eleven studies provided undefined prevalence rates (Reid, 1972; Heaton-Ward, 1977; Day, 1985; Jacobson, 1990; Farmer et al., 1993; Rojahn et al., 1993; Clay and Thomas, 2005; Bhaumik et al., 2008; Morgan et al., 2008; Al-Mutairi and Al-Mutairi, 2010). The prevalence in these studies is estimated to be 3.30% (95% CI: 2.02–4.59). Eleven studies provided point prevalence and the cumulative prevalence in these studies is 3.75% (95% CI: 2.63–4.87) (Göstason, 1985; Lund, 1985; Reiss, 1990; Patel et al., 1993; Sansom et al., 1994; Cooper, 1997; Deb et al., 2001; Gustafsson and Sonnander, 2004; Holden and Gitlesen, 2004; Cooper et al., 2007; Bakken et al., 2010). One study provided cumulative lifetime incidence (Nettelbladt et al., 2009), one

study provided the 6-month prevalence (White et al., 2005) and one study provided point as well as lifetime prevalence (Corbett, 1979).

Prevalence in five high-quality studies

Five studies were carried out in representative community samples using standardized instruments for diagnostic assessments (Göstason, 1985; Lund, 1985; Patel et al., 1993; Deb et al., 2001; Cooper et al., 2007). The prevalence estimate was 2.91 (95% CI: 1.38–4.44), I2 was 61.82% and Q (d.f. =4) was 12.3166, with P-value of 0.0151 (Fig. 3).

Estimate of the prevalence of schizophrenia

The meta-analysis in the general population was based on schizophrenia studies (Saha et al., 2005). We carried out a subanalysis of studies that had used schizophrenia as a diagnosis. Seventeen studies were included in this analysis. The prevalence estimate was 3.55% (95% CI: 2.66–4.44) (Fig. 4).

Prevalence in subpopulations

Sex, intellectual disability and psychosis

Supplementary Table S2 (Supplemental digital content 1, http://links.lww.com/PG/A154) provides information on the sex-wise distribution of psychosis. In nine studies, a separate distribution of men and women was available (Wright, 1982; Göstason, 1985; Lund, 1985; Jacobson, 1990; Sansom et al., 1994; Cooper et al., 2007; Bhaumik et. al., 2008; Morgan et al., 2008; Al-Mutairi and Al-Mutairi, 2010). The total sample of men was 28 830 and 1596 individuals were affected; the prevalence was estimated to be 3.78 (95% CI: 2.56–5.00). The sample size for women was 22 907, with 1208 of the participants being affected. The prevalence estimate in the female population was 4.10 (95% CI: 2.86–5.35).

Prevalence on the basis of the severity of intellectual disability

The subanalysis on the basis of the level of ID is shown in Table 1. The degree of ID was not available in all studies. Information was available for mild ID in seven studies (Göstason, 1985; Lund, 1985; Sansom et al., 1994; Cooper et al., 2007; Bhaumik et al., 2008; Morgan et al., 2008; Al-Mutairi and Al-Mutairi, 2010), moderate ID for seven studies (Lund, 1985; Sansom et al., 1994; Cooper et al., 2007; Bhaumik et al., 2008; Morgan et al., 2008; Al-Mutairi and Al-Mutairi, 2010) and severe ID for seven studies (Göstason, 1985; Lund, 1985; Sansom et al., 1994; Holden and Gitlesen, 2004; Cooper et al., 2007; Bhaumik et al., 2008; Morgan et al., 2008). The prevalence rates were as follows: mild ID: 514/7160, 5.55% (95% CI: 3.86–7.25); moderate ID: 179/4231, 4.21% (95% CI: 2.56–5.86) and severe ID: 53/3274, 0.89% (95% CI: 0.15–1.62).

Quality assessments

The validity of prevalence studies is a function of sampling and measurement methods (Boyle, 1998). We examined the measurement for the diagnosis of ID and schizophrenia, the expertise of the assessor in making a diagnosis, description of the method and the setting and year of publication. We describe the characteristics of the studies in Supplementary Table S3 (Supplemental digital content 1, http://links.lww.com/PG/A154), which provides indicators of the quality. The older studies were carried out in the hospitals. A number of studies have used administrative data from organizations providing services to ID population. There is a wide variation in the method of diagnosis of ID as well as psychosis. Because of these reasons, it is not possible to devise a quantitative score to summarize the quality of the studies.

The studies used widely different methods for the diagnosis of ID and psychosis, and were carried out in a variety of different settings.

Instruments/measures used for the diagnosis of intellectual disability

The method is not described in four publications in any detail (Heaton-Ward, 1977; Wright, 1982; Sansom et al., 1994; Al-Mutairi and Al-Mutairi, 2010). Some studies utilized a standardized

intelligence test or evaluation of adaptive functions and International Classification of Diseases, 10th revision (ICD-10) criteria (WHO, 1992) for diagnosis (Cooper et al., 2007; Bakken et al., 2011). Bhaumik et al. (2008) used diagnoses on the basis of a case register that uses the Disability Assessment Schedule (Holmes et al., 1982) to estimate the developmental age and WHO's ICD-10 criteria (WHO, 1992) for diagnosis. Clay and Thomas (2005) gathered information from patient records in an administrative database. In the database, the diagnosis of ID was established after cognitive and adaptive testing performed by a licensed psychologist for eligibility to receive the service. Few studies based their diagnoses on utilization of ID services (Corbett, 1979; Jacobson, 1990; Reiss, 1990; Farmer et al., 1993; Cooper, 1997; Deb et al., 2001). Day used the ICD-9 (WHO, 1975, p. 9) criteria for diagnoses using information in the patients' records, including IQ (Day, 1985).

In one study, psychological assessments were performed for the study (Göstason, 1985). Other methods were Diagnostic and statistical manual of mental disorders, 4th ed. (DSM-IV) (American Psychiatric Association, 1994) criteria (Holden and Gitlesen, 2004), American Association on Mental Retardation criteria (Morgan et al., 2008), IQ assessment or a clinical evaluation using DSM-IV (American Psychiatric Association, 1994) criteria (Nettelbladt et al., 2009), multiple instruments (Patel et al., 1993) and information on IQ from patient records (Reid, 1972).

In studies based on administrative data, information on ID was drawn from the records of the patients and in some studies, patients were assumed to have ID because they were receiving services. In some studies, it was supplemented by further assessments. In a small number of studies, new assessments were performed. We provide details in the Table S3 (Supplemental digital content 1, http://links.lww.com/PG/A154), for each study.

Instruments/measures used for the diagnosis of schizophrenia

Usually establishment of a psychiatric diagnosis involves two steps: information gathering about the symptoms and use of a classification system for interpretation of that information to assign a

diagnosis. In six studies, the clinical information was gathered through already available records (Jacobson, 1990; Farmer et al., 1993; Rojahn et al., 1993; Clay and Thomas, 2005; Bhaumik et al., 2008; Morgan et al., 2008), whereas in nineteen studies, other assessments were completed for the purpose of the study. There was a variation in the information provided on the assessment methods in both the groups. We provide these details in the Table S3 (Supplemental digital content 1, http://links.lww.com/PG/A154), for each study. Some of the instruments used for information gathering were as follows: the Mini Psychiatric Assessment Schedule for Adults with Developmental Disability (Deb et al., 2001; Holden and Gitlesen, 2004) and the Psychiatric Assessment Schedule for adults with Developmental Disability (Patel et al., 1993; Deb et al., 2001), Psychiatric Present State – Learning Disability, a semistructure interview (Cooper et al., 2007), Diagnostic Assessment for the Severely Handicapped (Deb et al., 2001), Comprehensive Psychopathological Rating Scale (Göstason, 1985), Psychopathology in Autism Checklist (Bakken et al., 2011), the Reiss Screen for Maladaptive Behaviour (Reiss, 1990; Gustafsson and Sonnander, 2004) and the MRC Schedule for Handicap, Behaviour and Skills (Lund, 1985). The classification system for diagnoses used included ICD-8 (Corbett, 1979), ICD-10 (WHO, 1992) criteria (Deb et al., 2001; Bhaumik et al., 2008), ICD-9 (WHO, 1975, p. 9) criteria (Reid, 1972; Morgan et al., 2008), DSMII (American Psychiatric Association, 1968; Jacobson, 1990), DSM-III (American Psychiatric Association, 1980; Göstason, 1985), DSM-III-R (American Psychiatric Association, 1987; Rojahn et al., 1993; Sansom et al., 1994; Gustafsson and Sonnander, 2004); and DSM-IV (American Psychiatric Association, 1994) diagnoses (Gustafsson and Sonnander, 2004 Al-Mutairi and Al-Mutairi, 2010). Cooper et al. 2007 used multiple criteria including ICD-10, DSMIV and DC-LD (Cooper et al., 2007).

Sensitivity analysis

Because of variations in the methodology, we carried out a series of sensitivity analyses to identify the effect of these variations on the results. Table 2 presents these results. There was a consistency in results and there was no systematic difference between community and institutional studies,

clinical diagnoses versus diagnoses on the basis of structured instruments and administrative samples versus samples where assessments were performed for the study. Five hospital studies were all from the UK (Reid, 1972; Heaton-Ward, 1977; Wright, 1982; Day, 1985; Sansom et al., 1994). Seven studies used diagnoses made by clinicians (Heaton-Ward, 1977; Wright, 1982; Day, 1985; Farmer et al., 1993; Holden and Gitlesen, 2004; Clay and Thomas, 2005; Nettelbladt et al., 2009). Six studies used administrative data or register data for diagnoses (Jacobson, 1990; Farmer et al., 1993; Rojahn et al., 1993; Clay and Thomas, 2005; Bhaumik et al., 2008; Morgan et al., 2008); in the rest of the studies, diagnoses were made for the purpose of the study.

In categorical analysis of moderators, institutional versus community samples [QM (d.f.=1)=0.0781, P=0.7799], clinical diagnosis versus diagnosis on the basis of structured instruments [QM (d.f.=1)=0.1183, P=0.7309] and administrative samples versus samples where assessments were performed for the study [QM (d.f.=1)=0.4678, P=0.4940] were not significant. The factors that we investigated as possible causes of heterogeneity were not found to be significant contributors toward heterogeneity.

Publication bias

Funnel plot did not show the bias one would expect from the file-drawer problem. Publication bias is identified by a skew in the distribution toward higher effect sizes at the bottom of the funnel plot. The presence of this type of bias is not visually shown in our plot (Fig. 5).

Discussion

This is the first systematic review and meta-analysis of the prevalence of schizophrenia in populations with ID. Meta-analysis in the general population found a median lifetime morbid risk of 0.72% (95% CI: 0.31–2.71). The point, period and lifetime prevalence figures were 0.6% (95% CI: 0.19–1.0), 0.33% (95% CI: 0.13–0.82) and 0.40% (95% CI: 0.16–1.21), respectively (Saha et al., 2005).

This indicates that prevalence rates of schizophrenia in the ID population are almost three times higher than those in the general population. The majority of the studies included in this review reported rates higher than those in the general population. Individuals with ID generally have problems in understanding their own symptoms and reporting those symptoms. The distress caused by the psychiatric symptoms may result in changes in behaviour, which is dismissed as

an integral component of ID. These factors result in difficulties in the diagnosis of psychiatric disorders in this population. Reports from caregivers and observations on changes in behaviour are important tools for diagnostic assessment. Structured and semistructured instruments were developed later than those for the general population for the assessment of psychiatric syndromes in this population. Some of these instruments rely on reports from caregivers for severe and profound ID (Bamburg et al., 2001). There is evidence that some of the instruments developed for non-ID population can be used for this population (Hatton et al., 2005). Many instruments for populations with ID are now available (Melville, 2003) and more recent studies have used these instruments, but most of the older studies have used clinicians' judgment as the main measure of diagnosis. Despite all these difficulties, most of the studies reported a prevalence higher than that in the general population. Administrative prevalence rates were in the same range as other studies and were generally based on a larger sample size. All these factors indicate that the higher rate of prevalence is a true finding. In line with the general population, prevalence estimates in the male and female populations were broadly similar. An interesting finding is a lower estimate in severe ID. We found that the mean prevalence rate was 5.55 (95% CI: 3.86–7.25) for mild ID, 4.21 (95% CI: 2.56–5.86) for moderate ID, and 0.88 (95% CI: 0.15–1.62) for severe ID. The prevalence is similar in individuals with mild and moderate ID. The rate decreases for individuals with severe ID. There is more than one possible explanation for this difference. One possibility is that the lower rates are because of the difficulty in making a diagnosis of schizophrenia in individuals with a severe

level of disability. This can also be linked to the nature of the underlying mechanism of association between the two disorders. For example, it is possible that if there is a common underlying genetic aetiology, this only affects individuals with mild/moderate ID and schizophrenia. Further research can help to unravel this issue.

The higher prevalence of schizophrenia has implications for the practice and organization of services for individuals with ID and psychiatric disorders. Diagnostic overshadowing, where disturbed behaviours are assumed to be caused by ID and additional psychiatric diagnoses are missed, is a well-known phenomenon in this population (Reiss and Szyszko, 1983). Schizophrenia is a potentially treatable, although not curable disorder and effective treatments can help to prevent significant distress in a population that already has significant disability.

It would be important to detect and treat the schizophrenia in this population. There is only one study outside the western industrialized nations. Considering that LAMI countries have more than three quarters of those affected with schizophrenia, there is a significant gap in this knowledge in the published literature. In most developing countries, there is a higher prevalence of ID because of increased prevalence of neurodevelopment disorders; thus, it is even more cause for concern. A few different mechanisms have been postulated as possible explanations for the association between ID and psychosis: common underling aetiology, deficits related to ID increase the risk of psychosis and a combination of ID and schizophrenia is a severe form of schizophrenia (Doody et al., 1998). These possibilities are not mutually exclusive.

The strongest evidence is for a common aetiology both genetic and environmental in nature. A number of studies show considerable familiality across the two disorders. There are reports of increased rates of schizophrenia in families of probands with ID (Penrose, 1938; Gustavson et al., 1986; Greenwood et al., 2004); ID in families of probands with schizophrenia (Heston, 1966; Modrzewska, 1980; Alaghband-Rad et al., 1998) and multiply affected families with co-occurring ID and schizophrenia (Penrose, 1938; O'Dwyer, 1997; Doody et al., 1998). A number of genetic

syndromes with ID also have associated schizophrenia. Examples in this group are velocardiofacial syndrome 22q11.2 microdeletions (Bassett and Chow, 1999; Schneider et al., 2014), fragile X syndrome (Gustavson et al., 1986), Klinefelter's syndrome (Jablensky et al., 1970; DeLisi et al., 2005; Boks et al., 2007) and Dandy–Walker variant (Papazisis et al., 2007); copy number variants in many regions of the genome have been associated with both disorders (van Den Bossche et al., 2012; Derks et al., 2013). Evidence from epidemiological studies also supports a shared genetic risk for lower IQ and schizophrenia. In this respect, a recent study reported a dose–response relationship between low IQ and schizophrenia, and the strength of genetic effect increased with a decrease in IQ. It was absent in the high IQ range. This strongly points to a shared genetic aetiology (Kendler et al., 2015).

In terms of environmental risk factors, obstetric complications have been reported to cause both schizophrenia and ID (Rosanoff et al., 1934; Cannon et al., 2002; Leonard and Wen, 2002). Changes in the intrauterine environment such as increased maternal cytokines resulting from hypoxia or infections can cause adverse neuropsychiatric outcomes that can involve both ID and schizophrenia (Brown, 2006; Meyer et al., 2007; Tsukimori et al., 2007). Similarly, increased levels of corticosteroids because of stress can result in the disruption of neurodevelopment (Goodyer et al., 2001). The mechanisms by which these environmental insults effect the brain development are not well understood. Individuals with ID have difficulty in processing information and sometimes their disability involves emotional and social deficits. This increases their vulnerability to misperceive and misinterpret others (Crick and Dodge, 1994). They have fewer positive and rewarding relationships in life (Rosen and Burchard, 1990). They experience a variety of stresses (Bramston et al., 1999)

and stigma and discrimination as a result of their ID (Pratt, 2009; Jahoda et al., 2010). The studies included in the review were carried out over the last 50 years. Many of the participants in these studies would have experienced institutional life. Increased vulnerability in terms of cognitive and

emotional resources combined with increased levels of stressors can be another likely explanation for the association between ID and schizophrenia.

There is some evidence from neuroimaging studies that the combination of schizophrenia and ID is a severe form of schizophrenia (Sanderson et al., 1999). The main strength of this systematic review is the historical depth of the datasets and the broadly similar prevalence across the majority of the studies, irrespective of the period, setting and methodology. There are a number of limitations in this study. Most of the studies have not reported separate prevalences in men and women and for different levels of disability. Populations from low-income and middle-income countries are not represented. There is a wide variation in the diagnostic methods used and also the settings of the studies. There is a variation in the sampling frame and methods because of changes in the way services are provided to the ID population and the living arrangement of individuals with ID (deinstitutionalization). There is a significant geographical variation in the delivery of service and this is also reflected in the sampling method. On balance, we believed that it would be more useful to include all the studies and report the reason for the variation.

References

Alaghband-Rad J, Kumra S, Lenane MC, Jacobsen LK, Brown AS, Susser E, Rapoport JL (1998). Early-onset schizophrenia: mental retardation in siblings. J Am Acad Child Adolesc Psychiatry 37:137–138.

Al-Mutairi H, Al-Mutairi S (2010). Psychiatric disorders among mentally retarded adults in Kuwait. Alex J Med 45:691–696.

American Psychiatric Association (1968). Diagnostic and statistical manual of mental disorders II, 2nd ed. Washington, DC: American Psychiatric Association.

American Psychiatric Association (1980). Diagnostic and statistical manual of mental disorders III. 3rd ed. Washington, DC: American Psychiatric Association.

American Psychiatric Association (1987). Diagnostic and statistical manual of mental disorders III-R, III-R ed. Washington, DC: American Psychiatric Association.

American Psychiatric Association (1994). Diagnostic and statistical manual of mental disorders IV, 4th ed. Washington, DC: American Psychiatric Association.

Aylward E,Walker E, Bettes B (1984). Intelligence in schizophrenia: meta-analysis of the research. Schizophr Bull 10:430–459.

Bakken TL, Helverschou SB, Eilertsen DE, Heggelund T, Myrbakk E, Martinsen H (2010). Psychiatric disorders in adolescents and adults with autism and intellectual disability: a representative study in one county in Norway. Res Dev Disabil 31:1669–1677.

Bakken TL, Martinsen H, Friis S, Lovoll S, Eilertsen DE (2011). FC02-04 –Assessment of schizophrenia in adults with intellectual disability and autism –an empirical study. Eur Psychiatry 26:1818.

Bamburg JW, Cherry KE, Matson JL, Penn D (2001). Assessment of schizophrenia in persons with severe and profound mental retardation using the Diagnostic Assessment for the Severely Handicapped-II (DASH-II). J Dev Phys Disabil 13:319–331.

Bassett AS, Chow EW (1999). 22q11 deletion syndrome: a genetic subtype of schizophrenia. Biol Psychiatry 46:882–891.

Bhaumik S, Tyrer FC, McGrother C, Ganghadaran SK (2008). Psychiatric service use and psychiatric disorders in adults with intellectual disability. J Intellectual Disabil Res 52:986–995.

Bilder RM, Reiter G, Bates J, Lencz T, Szeszko P, Goldman RS, et al. (2006). Cognitive development in schizophrenia: follow-back from the first episode. J Clin Exp Neuropsychol 28:270–282.

Boks MPM, de Vette MHT, Sommer IE, van Rijn S, Giltay JC, Swaab H, Kahn RS (2007). Psychiatric morbidity and X-chromosomal origin in a Klinefelter sample. Schizophr Res 93:399–402.

Boyle MH (1998). Guidelines for evaluating prevalence studies. Evid Based Mental Health 1:37–39.

Bramston P, Fogarty G, Cummins RA (1999). The nature of stressors reported by people with an intellectual disability. J Appl Res Intellect Disabil 12:1–10.

Brown AS (2006). Prenatal infection as a risk factor for schizophrenia. Schizophr Bull 32:200–202.

Cannon TD, Bearden CE, Hollister JM, Rosso IM, Sanchez LE, Hadley T (2000). Childhood cognitive functioning in schizophrenia patients and their unaffected siblings: a prospective cohort study. Schizophr Bull 26:379–393.

Cannon M, Jones PB, Murray RM (2002). Obstetric complications and schizophrenia: historical and meta-analytic review. Am J Psychiatry 159: 1080–1092.

Caspi A, Reichenberg A, Weiser M, Rabinowitz J, Kaplan Z, Knobler H, et al. (2003). Cognitive performance in schizophrenia patients assessed before and following the first psychotic episode. Schizophr Res 65:87–94.

Clay J, Thomas JC (2005). Prevalence of axis I psychopathology in an intellectually disabled population: type of pathology and residential supports. J Dev Phys Disabil 17:75–84.

Cooper SA (1997). Epidemiology of psychiatric disorders in elderly compared with younger adults with learning disabilities. Br J Psychiatry 170:375–380.

Cooper SA, Smiley E, Morrison J, Allan L, Williamson A, Finlayson J, et al. (2007). Psychosis and adults with intellectual disabilities. Prevalence, incidence, and related factors. Soc Psychiatry Psychiatr Epidemiol 42:530–536.

Corbett J (1979). Psychiatric morbidity and mental retardation. In: James FE, Snaith RP, editors. Psychiatric illness and mental handicap. London: Gaskell. pp. 11–25.

Cosway R, Byrne M, Clafferty R, Hodges A, Grant E, Abukmeil SS, et al. (2000). Neuropsychological change in young people at high risk for schizophrenia: results from the first two neuropsychological assessments of the Edinburgh High Risk Study. Psychol Med 30:1111–1121.

Crick NR, Dodge KA (1994). A review and reformulation of social information processing mechanisms in children's social adjustment. Psychol Bull 115:74–101.

David AS, Malmberg A, Brandt L, Allebeck P, Lewis G (1997). IQ and risk for schizophrenia: a population-based cohort study. Psychol Med 27:1311–1323.

Davidson M, Reichenberg A, Rabinowitz J, Weiser M, Kaplan Z, Mark M (1999). Behavioral and intellectual markers for schizophrenia in apparently healthy male adolescents. Am J Psychiatry 156:1328–1335.

Day K (1985). Psychiatric disorder in the middle-aged and elderly mentally handicapped. Br J Psychiatry 147:660–667.

Deb S, Thomas M, Bright C (2001). Mental disorder in adults with intellectual disability. 1: Prevalence of functional psychiatric illness among a community based population aged between 16 and 64 years. J Intellectual Disabil Res 45:495–505.

DeLisi LE, Maurizio AM, Svetina C, Ardekani B, Szulc K, Nierenberg J, et al. (2005). Klinefelter's syndrome (XXY) as a genetic model for psychotic disorders. Am J Med Genet B Neuropsychiatr Genet 135B:15–23.

Derks EM, Ayub M, Chambert K, Del Favero J, Johnstone M, MacGregor S, et al. (2013). A genome wide survey supports the involvement of large copy number variants in schizophrenia with and without intellectual disability. Am J Med Genet B Neuropsychiatr Genet 162B:847–854.

Doody GA, Johnstone EC, Sanderson TL, Owens DG, Muir WJ (1998). 'Pfropfschizophrenie' revisited. Schizophrenia in people with mild learning disability. Br J Psychiatry 173:145–153.

Farmer RDT, Rhode JR, Sacks B (1993). Changing services for people with learning disabilities. London: Chapman and Hall.

Fuller R, Nopoulos P, Arndt S, O'Leary D, Ho B-C, Andreasen NC (2002). Longitudinal assessment of premorbid cognitive functioning in patients with schizophrenia through examination of standardized scholastic test performance. Am J Psychiatry 159:1183–1189.

Goodyer IM, Park RJ, Netherton CM, Herbert J (2001). Possible role of cortisol and dehydroepiandrosterone in human development and psychopathology. Br J Psychiatry 179:243–249.

Göstason R (1985). Psychiatric illness among the mentally retarded: a Swedish population study. Acta Psychiatr Scand 71:1–119.

Greenwood CMT, Husted J, Bomba MD, Hodgkinson KA, Bassett AS (2004). Elevated rates of schizophrenia in a familial sample with mental illness and intellectual disability. J Intellectual Disabil Res 48:531–539.

Gunnell D, Harrison G, Rasmussen F, Fouskakis D, Tynelius P (2002). Associations between premorbid intellectual performance, early-life exposures and early-onset schizophrenia. Cohort study. Br J Psychiatry 181:298–305.

Gustafsson C, Sonnander K (2004). Occurrence of mental health problems in Swedish samples of adults with intellectual disabilities. Soc Psychiatry Psychiatr Epidemiol 39:448–456.

Gustavson KH, Modrzewska K, Wetterberg L (1986). Mental retardation in a North Swedish isolate. Clin Genet 30:374–380.

Hatton C, Haddock G, Taylor JL, Coldwell J, Crossley R, Peckham N (2005). The reliability and validity of general psychotic rating scales with people with mild and moderate intellectual disabilities: an empirical investigation. J Intellectual Disabil Res 49:490–500.

Heaton-Ward A (1977). Psychosis in mental handicap. The tenth Blake Marsh lecture delivered before the Royal College of Psychiatrists, February 2, 1976. Br J Psychiatry 130:525–533.

Heston LL (1966). Psychiatric disorders in foster home reared children of schizophrenic mothers. Br J Psychiatry 112:819–825.

Holden B, Gitlesen JP (2004). The association between severity of intellectual disability and psychiatric symptomatology. J Intellectual Disabil Res 48:556–562.

Holmes N, Shah A, Wing L (1982). The Disability Assessment Schedule: a brief screening device for use with the mentally retarded. Psychol Med 12:879–890.

Jablensky A, Janota I, Shepherd M (1970). Neuropsychiatric illness and neuropathological findings in a case of Klinefelter's syndrome. Psychol Med 1:18–29.

Jacobson JW (1990). Do some mental disorders occur less frequently among persons with mental retardation? Am J Mental Retard 94:596–602.

Jahoda A, Wilson A, Stalker K, Cairney A (2010). Living with stigma and the selfperceptions of people with mild intellectual disabilities. J Soc Issues 66:521–534.

Johnstone EC, Ebmeier KP, Miller P, Owens DGC, Lawrie SM (2005). Predicting schizophrenia: findings from the Edinburgh High-Risk Study. Br J Psychiatry 186:18–25.

Jones P, Rodgers B, Murray R, Marmot M (1994). Child development risk factors for adult schizophrenia in the British 1946 birth cohort. Lancet 344:1398–1402.

Kendler KS, Ohlsson H, Sundquist J, Sundquist K (2015). IQ and schizophrenia in a Swedish national sample: their causal relationship and the interaction of IQ with genetic risk. Am J Psychiatry 172:259–265.

Keshavan MS, Diwadkar VA, Montrose DM, Stanley JA, Pettegrew JW (2004). Premorbid characterization in schizophrenia: the Pittsburgh High Risk Study.World Psychiatry 3:163–168.

Keshavan MS, Diwadkar VA, Montrose DM, Rajarethinam R, Sweeney JA (2005). Premorbid indicators and risk for schizophrenia: a selective review and update. Schizophr Res 79:45–57.

Kremen WS, Buka SL, Seidman LJ, Goldstein JM, Koren D, Tsuang MT (1998). IQ decline during childhood and adult psychotic symptoms in a community sample: a 19-year longitudinal study. Am J Psychiatry 155:672–677.

Lencz T, Smith CW, McLaughlin D, Auther A, Nakayama E, Hovey L, Cornblatt BA (2006). Generalized and specific neurocognitive deficits in prodromal schizophrenia. Biol Psychiatry 59:863–871.

Leonard H, Wen X (2002). The epidemiology of mental retardation: challenges and opportunities in the new millennium. Ment Retard Dev Disabil Res Rev 8:117–134.

Lund J (1985). The prevalence of psychiatric morbidity in mentally retarded adults. Acta Psychiatr Scand 72:563–570.

Melville CA (2003). A critique of the diagnostic criteria for psychiatric disorders for use with adults with learning disabilities/mental retardation (DC-LD) chapter on non-affective psychotic disorders. J Intellectual Disabil Res 47:16–25.

Meyer U, Yee BK, Feldon J (2007). The neurodevelopmental impact of prenatal infections at different times of pregnancy: the earlier the worse? Neuroscientist 13:241–256.

Modrzewska K (1980). The offspring of schizophrenic parents in a North Swedish isolate. Clin Genet 17:191–201.

Morgan VA, Leonard H, Bourke J, Jablensky A (2008). Intellectual disability co-occurring with schizophrenia and other psychiatric illness: population based study. Br J Psychiatry 193:364–372.

Nettelbladt P, Göth M, Bogren M, Mattisson C (2009). Risk of mental disorders in subjects with intellectual disability in the Lundby cohort 1947–97. Nord J Psychiatry 63:316–321.

O'Dwyer JM (1997). Schizophrenia in people with intellectual disability: the role of pregnancy and birth complications. J Intellectual Disabil Res 41:238–251.

Papazisis G, Mastrogianni A, Karastergiou A (2007). Early-onset schizophrenia and obsessive-compulsive disorder in a young man with Dandy-Walker variant. Schizophr Res 93:403–405.

Patel P, Goldberg D, Moss S (1993). Psychiatric morbidity in older people with moderate and severe learning disability. II: The prevalence study. Br J Psychiatry 163:481–491.

Penrose LS (1938). A clinical and genetic study of 1280 cases of mental defect. London: H M Stationery Office.

Pratt HD (2009). Psychological issues in chronically ill adolescents. Adolescence and chronic illness. A public health concern. New York, NY: Nova Science. pp. 151–163.

Rabinowitz J, Reichenberg A, Weiser M, Mark M, Kaplan Z, Davidson M (2000). Cognitive and behavioural functioning in men with schizophrenia both before and shortly after first admission to hospital. Cross-sectional analysis. Br J Psychiatry 177:26–32.

Reichenberg A, Weiser M, Rapp MA, Rabinowitz J, Caspi A, Schmeidler J, et al. (2005). Elaboration on premorbid intellectual performance in schizophrenia: premorbid intellectual decline and risk for schizophrenia. Arch Gen Psychiatry 62:1297–1304.

Reichenberg A, Caspi A, Harrington H, Houts R, Keefe RSE, Murray RM, et al. (2010). Static and dynamic cognitive deficits in childhood preceding adult schizophrenia: a 30-year study. Am J Psychiatry 167:160–169.

Reid AH (1972). Psychoses in adult mental defectives: II. Schizophrenic and paranoid psychoses. Br J Psychiatry 120:213–218.

Reiss S (1990). Prevalence of dual diagnosis in community-based day programs in the Chicago metropolitan area. Am J Mental Retard 94:578–585.

Reiss S, Szyszko J (1983). Diagnostic overshadowing and professional experience with mentally retarded persons. Am J Ment Defic 87:396–402.

Rojahn J, Borthwick-Duffy SA, Jacobson JW (1993). The association between psychiatric diagnoses and severe behavior problems in mental retardation. Ann Clin Psychiatry 5:163–170.

Rosanoff AJ, Handy LM, Plesset IR, Brush S (1934). The etiology of so-called schizophrenic psychoses. Am J Psychiatry 91:247–286.

Rosen JW, Burchard SN (1990). Community Activities and Social Support Networks: a social comparison of adults with and adults without mental retardation. Educ Train Ment Retard 25:193–204.

Saha S, Chant D, Welham J, McGrath J (2005). A systematic review of the prevalence of schizophrenia. PLoS Med 2:e141.

Sanderson TL, Best JJ, Doody GA, Owens DG, Johnstone EC (1999). Neuroanatomy of comorbid schizophrenia and learning disability: a controlled study. Lancet 354:1867–1871.

Sansom DT, Singh I, Jawed SH, Mukherjee T (1994). Elderly people with learning disabilities in hospital: a psychiatric study. J Intellectual Disabil Res 38:45–52.

Schneider M, Debbané M, Bassett AS, Chow EWC, Fung WLA, van den Bree M, et al., International Consortium on Brain and Behavior in 22q11.2 Deletion Syndrome (2014). Psychiatric disorders from childhood to adulthood in 22q11.2 deletion syndrome: results from the International Consortium on Brain and Behavior in 22q11.2 Deletion Syndrome. Am J Psychiatry 171:627–639.

Shprintzen RJ (2008). Velo-cardio-facial syndrome: 30 years of study. Dev Disabil Res Rev 14:3–10.

Tsukimori K, Nakano H, Wake N (2007). Difference in neutrophil superoxide generation during pregnancy between preeclampsia and essential. Hypertension 49:1436–1441.

van Den Bossche MJ, Johnstone M, Strazisar M, Pickard BS, Goossens D, Lenaerts A-S, et al. (2012). Rare copy number variants in neuropsychiatric disorders: Specific phenotype or not? Am J Med Genet B Neuropsychiatr Genet 159B:812–822.

Viechtbauer W (2010). Conducting meta-analyses in R with the Metafor package. J Stat Softw 36:1–48.

White P, Chant D, Edwards N, Townsend C, Waghorn G (2005). Prevalence of intellectual disability and comorbid mental illness in an Australian community sample. Aust N Z J Psychiatry 39:395–400.

Woodberry KA, Giuliano AJ, Seidman LJ (2008). Premorbid IQ in schizophrenia: a meta-analytic review. Am J Psychiatry 165:579–587.

WHO (1975). ICD-9 – International classification of diseases, ninth revision, 9th ed. Geneva: World Health Organization.

WHO (1992). The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. Geneva: World Health Organization.

Wright EC (1982). The presentation of mental illness in mentally retarded adults. Br J Psychiatry 141:496–502.

Zammit S, Allebeck P, David AS, Dalman C, Hemmingsson T, Lundberg I, Lewis G (2004). A longitudinal study of premorbid IQ Score and risk of developing schizophrenia, bipolar disorder, severe depression, and other nonaffective psychoses. Arch Gen Psychiatry 61:354–360.

Figures/Tables

Fig 1

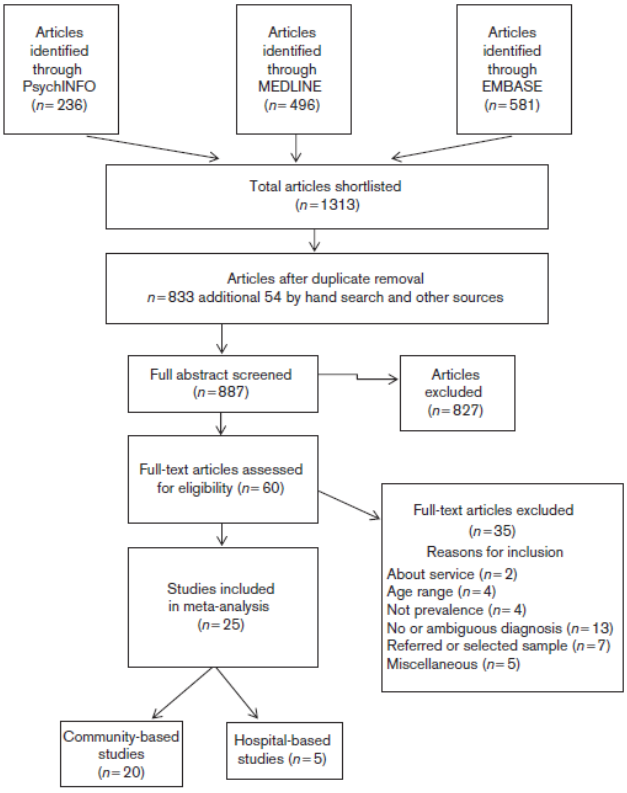
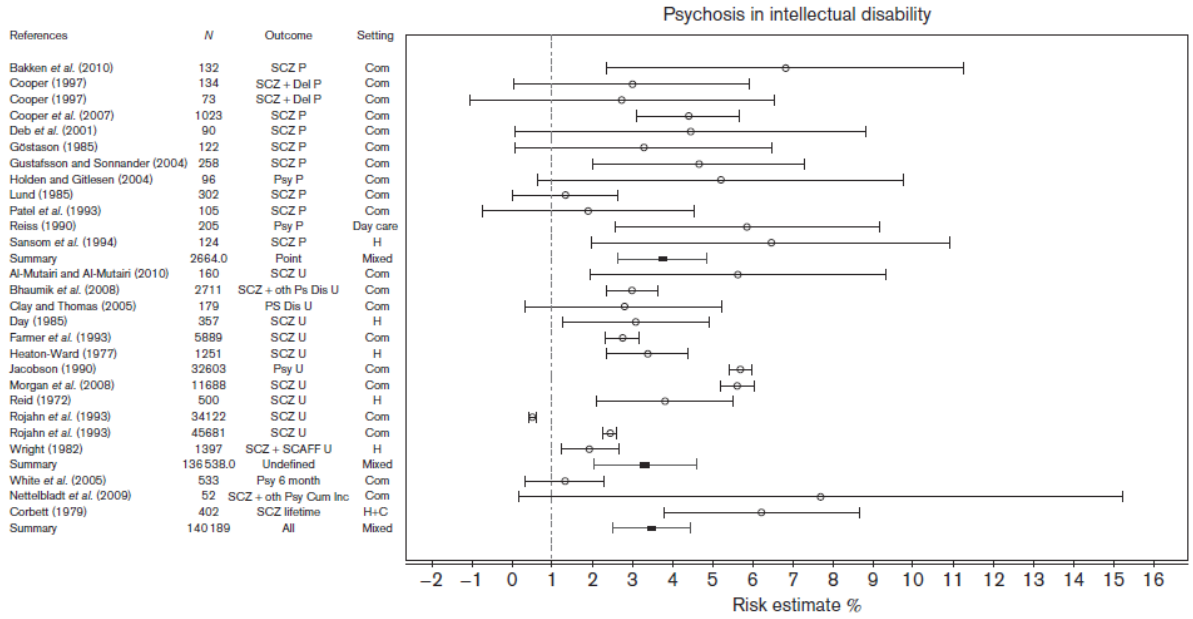
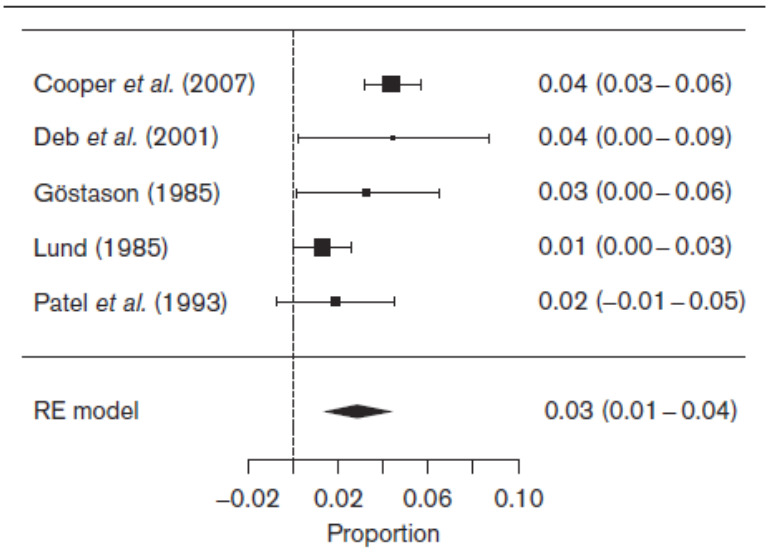


Fig 2



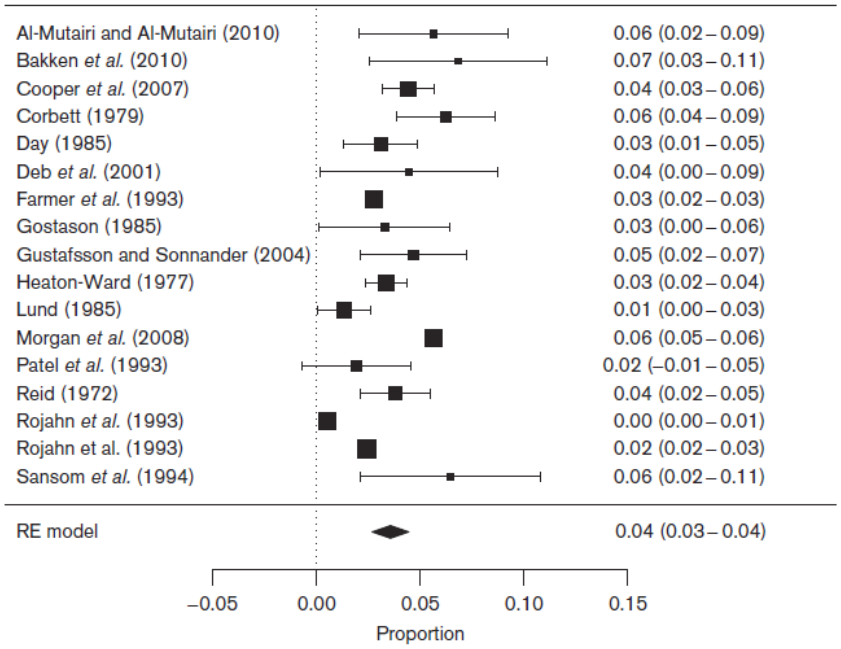
Forest plot of all the studies. Com, community; Cum Inc, cumulative incidence; Del, delusional; H, hospital; Oth, other; P, point prevalence; Ps Dis, psychotic disorder; Psy, psychosis; SCAFF, schizoaffective; SCZ, schizophrenia; U, undefined prevalence.

Fig 3



Forest Plot for High Quality Studies. The unit is fraction of 1.

Fig 4



Forest plot of schizophrenia-only studies. The unit is fraction of 1.

Table 1

Table 1 Level of intellectual disability and psychosis prevalence

References	Mildly affected/total (N) prevalence (%) (95% CI)	Moderately affected/total (N) prevalence (%) (95% CI)	Severely affected/ total (N) prevalence (%) (95% CI)
Al-Mutairi and Al-Mutairi (2010)	4/75 5.33 (0.11–10.56)	5/85 5.88 (0.72–11.03)	–
Bhaumik *et al.* (2008)	30/537 5.59 (3.64–7.53)	32/555 5.77 (3.83–7.71)	39/880 4.43 (3.07–5.79)
Cooper *et al.* (2007)	23/398 5.78 (3.49–8.07)	11/248 4.44 (1.87–7.00)	8/193 4.15 (1.33–6.96)
Göstason (1985)	2/68 2.94 (−1.07–6.96)	–	2/54 3.70 (−1.33–8.74)
Holden and Gitlesen (2004)	–	5/34 14.71 (2.80–26.61)	0/31
Lund (1985)	IQ 52–67 2/77 2.60 (−0.96–6.15)	IQ 36–55 1/85 1.18 (− 1.12–3.47)	IQ 20–35 0/34
Morgan *et al.* (2008)	451/5973 7.55 (6.88–8.22)	119/3168 3.76 (3.10–4.43)	Severe/profound 34/2046 1.66 (1.11–2.22)
Sansom *et al.* (1994)	2/32 6.25 (−2.14–14.64)	6/56 10.71 (2.61–18.82)	0/36
Total	514/7160 5.55 (3.86–7.25)	179/4231 4.21(2.56–5.86)	53/3274 0.88 (0.15–1.62)

CI, confidence interval; IQ, Intelligence Quotient.

Fig 5

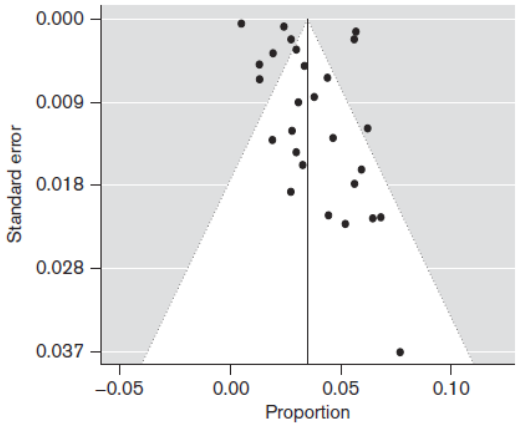


Table 2 Sensitivity Analysis

Types of studies	Number of datasets	Affected total	Prevalence estimate
Community	22	4185/136 560	3.48 (2.39–4.56)
Institutions	5	107/3629	3.08 (2.05–4.12)
Clinician's diagnosis	7	255/9132	2.77 (2.17–3.37)
Structured instruments diagnosis	20	4036/130 968	3.56 (2.41–4.71)
Admin samples	7	4037/132 883	3.31 (1.50–5.12)
Nonadmin samples	20	250/7316	3.30 (2.50–4.09)