The incidence of psychotic disorders: only the tip of the iceberg?

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The incidence of psychotic disorders such as schizophrenia varies across person and place. We've known this since at least the 1930s, when Faris and Dunham demonstrated that rates were higher in inner-city areas in Chicago compared with the suburbs, and in African-Americans compared with their white American counterparts[1]. This certainty was lost as the twentieth century wore on. The WHO ten-country study, published in 1992, demonstrated a 2.5 times differences in 'broad schizophrenia' (non-affective disorders)[2] but this study was widely interpreted to indicate that schizophrenia was one of those disorders that is uniquely invariant across cultures.

It is important to understand if incidence varies or not: substantial variance points to a role for the environment in aetiology, whereas a lack thereof might indicate a genetic basis. Since the WHO ten-country study, an accumulating evidence base demonstrates that not only does incidence vary widely, but certain characteristics of the environment, such as being more urban and living at a higher latitude, are associated with a higher incidence of psychotic disorders. Incidence is also shown to be higher in young people, and in men. It is also widely demonstrated that ethnic minorities in Western countries face an increased risk of developing a psychotic disorder, although exactly which minority group is most severely affected appears to differ by country[3].

However, the evidence comes from a wide variety of studies using different methods, each with strengths and weaknesses that may contribute to some of the patterns observed. Fortunately, a recent international incidence study (the EU-GEI study[4]) was carried out. Here, we attempted to use similar methods across multiple settings in six countries. The study demonstrated an eightfold variation in incidence rates across the seventeen catchment areas included, adding nuance to the received wisdom that psychosis incidence is higher in men and in young people. There appeared to be an interaction: incidence peaks up until approximately age 35 for both men and women, after which it declines. For men, this decline appears to be particularly steep, whereas for women it is a more gradual with a secondary peak in middle-age. Before age 35, men seem to be at increased risk of all psychotic disorders compared with women, whereas after age 35 risk appears to be evenly distributed[4] (see Figure 1 below). We also found that incidence was higher in ethnic minorities, but not in more densely populated (as a more detailed measure of urbanicity) areas or in areas at higher latitude. We did demonstrate that incidence was higher in areas with lower owner-occupancy of houses, which we understood to be a measure of social fragmentation.

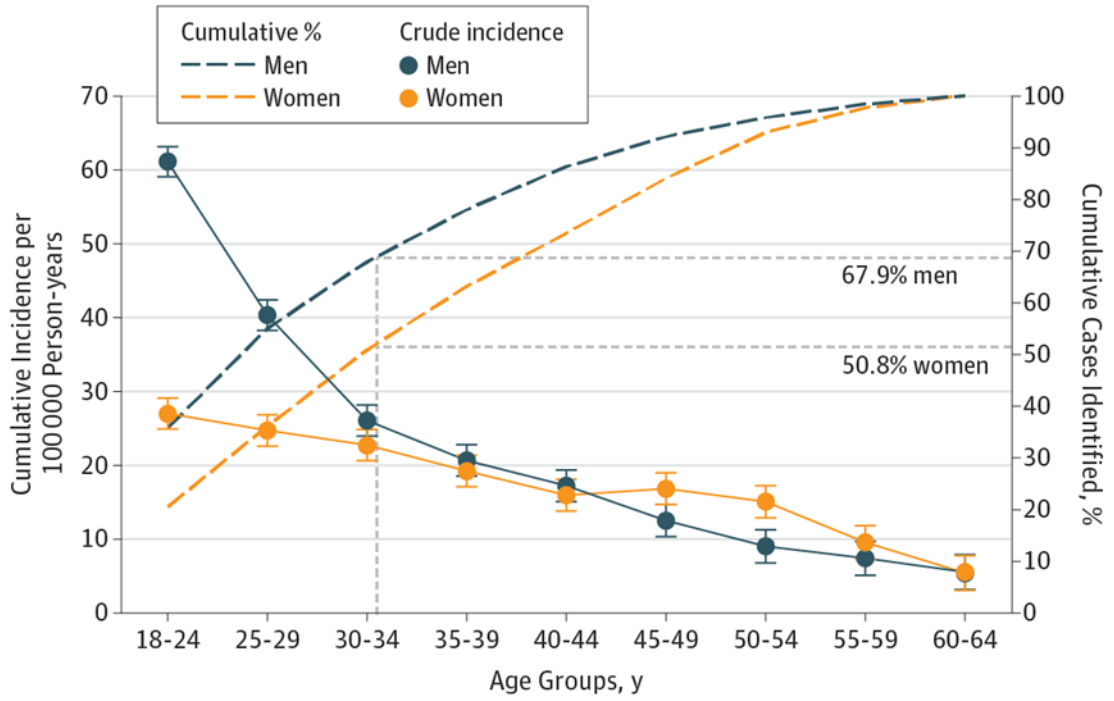

Figure 1: Crude incidence and cumulative percentage of psychotic disorders, by age and sex (reproduced from Jongsma et al, 2018).

A systematic review and meta-analysis of all incidence studies gives an even broader perspective. Ultimately including 177 studies this review showed that incidence varied across studies, and was higher in ethnic minorities compared with the majority population. This meta-analysis also suggested that any excess risk in men is specific to non-affective disorders and was not observed for affective disorders including bipolar disorder[5]. However, incidence did not only vary across the studies that we included, but did so systematically by study type. Studies that were based on national or regional health service registers observed higher rates of disorder than first-contact studies.

This leaves us with a slightly puzzling picture: we've demonstrated substantial variation in a single study where methodology was broadly comparable, but also substantial variation by study methodology. Does this mean that variance is explained by socio-demographic and –economic covariates, or by study methodology?

To answer that, we need to take a step back and look at what we mean by incidence. What is captured in first-contact studies is what is called treated incidence: the people who presented to the appropriate services with their first episode of psychosis. It would be a mistake to think that these are all the people in the community experiencing a first episode of psychosis. So-called leakage studies (where researchers actively try to find participants that might not have presented to service via for instance the police or social work) commonly find around 10% more cases than were picked-up in the primary survey, but recent studies from Canada and The Netherlands suggest that only about 50% of first episode cases present to the designated early intervention services[6,7].

It seems therefore that first contact studies focusing on particular health services might measure only the tip of the iceberg when it comes to psychosis incidence. Registry-based studies often count any healthcare contact, including for instance in general practice, and can accumulate cases over a longer period of time than the year or two period commonly used by other approaches. Thus, it is not surprising they record higher rates. The downside of registry-based studies might be that they record too much. First-contact studies often have quite stringent diagnostic criteria, whereas population

registers often rely on clinical diagnoses. There may be more false-positives included in these registers, though this is likely to vary country by country, too; registers in Finland, for instance, have been shown to be highly specific attributing schizophrenia diagnoses relatively sparingly[8].

The variation we observe in studies of the incidence of psychotic disorders appears to depend on a number of things, illustrated in Figure 2. There are methodological differences (in green) which have no aetiological basis, and there are certain socio-economic, demographic and geographic characteristics associated with increased incidence which probably do have an aetiological basis. Finally, there are some factors that are harder to capture, and include properties of healthcare systems (such as universal health insurance) and behavioural factors such as willingness to seek help and GP's referral behaviour.

Figure 2: Factors influencing the reported incidence of psychotic disorders.

The evidence for the variation by person is quite robust and widely replicated across a number of study designs, and the evidence of socio-economic factors to a lesser extent. The delineation of methodological and geographic characteristics is less clear. In the EU-GEI study for instance, we found no latitude effect. Combined with the finding that incidence tends to be higher in population registers (which are more commonly used in Scandinavian countries), this might lead us to wonder if this latitude effect isn't partially a methodological artefact.

An important limitation of the body of evidence of psychotic disorders is its Western bias. Only around 10% of studies included in our meta-analysis yielded from outside Europe, Australia and North America. The relevance of this becomes clear when we look at the association between urbanicity and psychosis. Even though this is well-replicated in a Western context, it is rarely studied outside of it. A

recent study that did investigate this in low-and middle-income countries, did not find such an association[9]. Whilst this is only one study, it should serve as a warning that what we think we know about psychotic disorders might be more specific than we realise. Socio-economic factors have been studied in both registry-based and first contact studies, but again only in a Western context.

Whereas we have gained a good understanding of the distribution of psychotic disorders in a Western context, there is substantial work to be done to understand this in the vast majority of the world. This will be crucial to our understanding of the determinants of this distribution.

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