

A SYSTEMATIC REVIEW OF THE INCIDENCE OF PSYCHOTIC DISORDERS: THE DISTRIBUTION OF RATES AND THE INFLUENCE OF GENDER, URBANICITY, IMMIGRATION AND SOCIO-ECONOMIC LEVEL.

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ABSTRACT

Background. Considering existing knowledge on the relationship between certain environmental factors and incidence rates of psychosis, we carried out a systematic review to provide a broad and updated picture of the incidences of different psychotic disorder subgroups worldwide and how some environmental factors influence these rates.

Methods. Studies with original data related to the incidence of psychosis (published between 2000 and 2015) were identified via searching electronic databases (CINAHL, MEDLINE, PSYCINFO, PUBMED and SCOPUS) and reviewing manual citations. Title, abstract and full-text were reviewed by two independent reviewers to identify suitable citations. Data on the following risk factors were extracted to a standardized extraction form: gender, urbanicity, immigration and socio-economic level. Descriptive appraisals of variation in incidence rates (IR) and incidence rate ratios (IRR), with a 95% confidence interval were calculated. In addition, a meta-analysis was performed to calculate IR pooled by diagnosis group and IRR pooled by diagnosis and gender, urbanity, immigration and socio-economic level, using a random effects model.

Results. We identified 33 reports to analyse. Overall IR per 100,000 persons for non-affective psychoses (IR pooled = 22.53 (16.51 – 28.54) per 100,000) were higher than affective psychoses (IR pooled = 7.12 (5.03 – 9.22) per 100,000). When we compared rates of psychosis for men and women, generally, IR were higher in men (IRR pooled = 1.54 (1.37 – 1.72)). There was a clear increase in rates of psychosis in urban versus rural areas (IRR pooled = 1.64 (1.38 – 1.95)). Despite the great variability in the immigrant groups included in the studies, we observed that IR for immigrants were higher than for natives, mainly among black immigrants (IRR pooled = 3.09 (2.74 – 3.49)). Finally, in studies assessing socio-economic levels, rates were higher for a lower socio-economic level (IRR pooled = 1.78 (1.43 – 2.22)).

Conclusions. IR among different psychotic disorders were found to vary depending on gender, urbanicity and immigration (as most of previous literature focuses on non-affective psychosis or schizophrenia).

Key words: Psychosis, incidence, epidemiology, environmental factors, gender, socio-economic level, urbanicity, immigration.

INTRODUCTION

As one of the most devastating illnesses, schizophrenia entails serious social and health implications, and presents demographic and geographic differences. Recent systematic reviews found that incidence rates of schizophrenia vary widely from 7.7 to 43.0 per 100,000 persons (McGrath et al., 2004; Saha et al., 2008). Moreover, this incidence was significantly higher in men than in women (Aleman et al., 2003) with a male/female incidence rate ratio (95% C.I.) of 1.4 (0.9-2.4) (McGrath, 2006).

Several studies argue that people who live in cities had approximately double the risk of developing schizophrenia compared to those who live in rural areas (Pedersen et al., 2001; Harrison et al., 2003; Moreno-Küstner et al., 2014; Vassos et al., 2016). Recently, a meta-analysis also reported that people living in urban areas had significantly higher rates of incidence of schizophrenia compared to those living rural-mixed places (Vassos et al., 2012).

Cantor-Graae et al. (2005) in a systematic review and meta-analysis showed that immigration is a risk factor for schizophrenia. Two subsequent studies showed that this risk continued in the second generation of immigrants (Cantor-Graae et al., 2007; Cantor-Graae et al., 2013). Studies with African-Caribbean immigrants in the UK, people from Surinam and Moroccans in the Netherlands, plus several groups of immigrants in Denmark have presented higher incidence rates compared with the native population (McGrath et al., 2004; Bourque et al., 2011; Tortelli et al., 2015).

Burns et al. (2014) found a significant association between increased income inequality in the country and increased incidence rates of schizophrenia. However, Saha et al. (2006) did not find these results, arguing that there is no evidence to suggest that the incidence of schizophrenia differs between nations when we adjust rates according to the economic situation.

As we are interested in the epidemiological aspects of the incidence of psychotic disorders, we have included in our study the same variables that McGrath et al. (2004) and Kirkbride et al. (2012) included in their systematic review, in order to update their studies. Therefore, we have considered it appropriate to conduct a systematic review to encompass the variability of all psychotic disorders worldwide and to be able to give an up-to-date assessment of recent trends in this area.

We think that systematising this information is very important in order to advance our understanding of the above-mentioned issues and to provide valuable clues as to the aetiology of this disorder.

Taking into account the previous scientific literature, our hypotheses about the epidemiology of psychotic disorders are as follows: 1) Incidence rates of non-affective psychoses will be higher than the affective ones; 2) Incidence rates of psychosis will be higher in men than in women; 3) Incidence rates of psychosis will be higher in the population living in urban settings compared to those living in rural ones; 4) Incidence rates of psychosis will be higher in the immigrant population than in the native population; 5) Incidence rates of psychosis will be higher in the population living in environments with a lower socio-economic level.

Therefore, our principle objective was to give a broad and updated picture of the incidences among different psychotic disorder subgroups worldwide from 2000 to 2015. Specifically, we report the variation of these incidence rates depending on:

1. Gender
2. Urbanicity
3. Immigration
4. Socio-economic level

METHODOLOGY

A. Identification of the studies

We conducted a systematic search of electronic bibliographic indexes of published research. The broad search string *"schizophreni* OR psychosis" AND "incidence OR epidemiolog*"* was used to search within the abstract section of articles found in CINAHL, MEDLINE, PSYCINFO, PUBMED and SCOPUS, during the period 2000-2015.

Studies had to meet the following inclusion criteria to be included in the review: a) Population-based incidence studies of any psychotic disorder. We refer to population-based studies as any study carried out on the general population residing within a defined catchment area and include people who made first contact or first admission with health or social services, thus excluding people living in institutions or prisons; b) Age range: there must be at least a 30-year difference between the lower and upper age included in each study, in order to obtain a wide age range; c) With original data; d) Published during the period from 2000 to 2015. We chose this range because we found a systematic review with similar characteristics as ours carried out with studies prior to 2001 (McGrath et al., 2004); e) Setting: all over the world; f) Any language included.

With the electronic search in the five databases we found a total of 13,418 articles. After removing 8,412 duplicate reports, we obtained 5,006 articles to review. Two independent reviewers (BM, MC) applied inclusion criteria to the titles and abstract, resulting in 71 articles for full text review. We were not able to locate 5 articles (Hickling et al., 2001; Rivera Martinez et al., 2002; Hamada et al., 2006; Toshitani et al., 2006; Hart et al., 2007). Finally, we read the full text of 66 papers.

We excluded articles: a) Which included duplicated data (N=12). When several publications presented overlapping data in time frame and setting, the most informative version (which contains the most extended information) of the study was included and the others were discarded; b) With insufficient data to analyse incidence rates (N= 11). The papers did not show incidence rates data and they did not present sufficient data to calculate it; c) Which were carried out with a subgroup of the population (N=10) (Children, adolescents, soldiers, persons in prisons or institutions).

We identified a final sample of 33 reports for data extraction (Figure 1).

In this review, we refer to a “citation” as any unique article from the published literature included in our analyses. We distinguish this from a “study”, which refers to any of the studies described in an article. Thus, it is important to highlight that one citation may generate many items of information on the incidence of psychosis.

B. Data extraction

Detailed data were independently abstracted by 2 reviewers using a data collection sheet.

After consensus, the information extracted was stored and managed with Microsoft Excel.

Studies with original data collected from the population living within a certain area of influence were divided into four categories: 1) Core studies: studies which provided an overall incidence rate and different rates for men and for women (Man/Woman); 2) Urbanicity studies: studies which provided incidence rates in urban and in rural settings, depending on population density (Urban/Rural); 3) Immigration studies: studies which provided incidence rates for immigrants and natives (Immigrant/Native). Studies classified immigrant/native according to their place of birth and parental place of birth; 4) Socio-economic level studies: studies which provided incidence rates for different socio-economic levels (Deprivation/Non Deprivation area).

Three different types of variables were gathered: a) Citation-level variables: author, published year, title, country, setting, age range, last year of case ascertainment period and duration in years, study type, case ascertainment, diagnostic instrument, classification system, diagnosis, and quality ranking of the study; b) Rate-level variables: number of cases, population at risk, IR per 100,000 persons and IRR for different risk factors (gender, urbanicity, immigration and socio-economic level). c) Meta-variables: variation of rates depending on gender, urbanicity, immigration and socio-economic level.

Given the limited space, presenting all details of these studies in tabulated form is not possible. All variables drawn from each study are available in the dataset of the incidence studies (Dataset S1). Variables used to characterise incidence studies are presented in Table S1.

The quality of the studies was assessed using the quality criteria scale proposed by Saha et al. for epidemiological studies (2005). Each study was allocated a quality score depending on the following indicators: rate type, case ascertainment, diagnostic system, method of diagnostic assignment, information on rates (raw data, age and/or sex standardised (If age/sex standardised, method provided), confidence intervals, numerator/denominator match in time and numerator/denominator match in space) and additional 'merits' (text on inter-rater reliability and leakage study). This quality index can range from 1 to 16 points. Details about this information are provided in Table S2.

C. Diagnostic outcomes

A variety of diagnostic classification systems was used to estimate incidence rates of psychotic disorders (RDC (Research Diagnostic Criteria); DSM-III-R (Diagnostic and Statistical Manual of Mental Disorders-III-R), DSM-IV (Diagnostic and Statistical Manual of Mental Disorders-IV); ICD-9 (International Classification of Diseases-9), ICD-10 (International Classification of Diseases-10)).

Original studies presented their diagnostic outcome as follows: a) Affective and non-affective psychoses (which can also include substance-induced and/or organic psychosis); b) Non-affective psychoses; c) Non-affective psychosis, substance-induced psychosis, organic psychosis, psychotic disorder in childhood; d) Schizophrenia, schizophreniform disorder and schizoaffective disorder; e) Schizophrenia, schizophreniform disorder, schizoaffective disorder and delusion disorder; f) Schizophrenia and schizophreniform disorder; g) Schizophrenia; h) Affective psychoses; i) Bipolar disorder with psychotic features; j) Depressive disorder with psychotic features; k) Substance-induced and organic psychosis; l) Substance-induced psychosis.

To facilitate the subsequent analysis, we grouped the diagnoses into the following categories: NAP, AP - Non-affective and Affective psychoses (a); NAP - Non-affective psychoses (b,c,d,e,f,g); S – Schizophrenia (f); AP - Affective psychoses (h,i,j); SIP - Substance-induced psychosis (k,l).

D. Data analysis

We created a dataset with the Microsoft Excel programme to classify the studies into core studies, urbanicity studies, immigration studies and socioeconomic level studies. In this chart, we added data on the number of total cases found in the studies, the total population at risk, raw or standardised IR (for persons, male and female according to diagnoses, and for urban and rural population if applicable) and the IRR for different risk factors (male/female, urban/rural area, immigrant versus native and deprivation/non- deprivation area). If the studies did not provide them, such data were calculated from the data shown. These data were presented with confidence intervals of 95%. If they were not offered, they were calculated (Table S3). Most of the studies

did not provide standardised rates, therefore, in studies where both rates were presented, we chose raw rates. In studies only providing the standardised rate (indicated in the chart), it was treated as a raw rate, assuming minimal distortion for results (Kirkbride et al., 2012).

In addition, a meta-analysis was performed in R with the package metaphor open-source software environment R 2.12.0 (Rothman et al., 2008; Stijnen et al., 2010; Viechtbauer, 2010). To calculate mean effect (mean incidence) by group of diagnosis, a random effects model was used and the results were weighted by the size of each study. To calculate the mean effect (mean incidence) by diagnosis and gender, urbanity, immigration and socio-economic level, a random effects model was used and the results were weighted according to the size of the study. In order to estimate if the differences between the IR by gender, urbanicity, immigration and socio-economic level were statistically significant, the Mantel-Haenszel method for statistical incidence was used for the incidence rate ratio. We used I^2 statistics to estimate variation in rates between citations.

This systematic review was based on the criteria guideline of the PRISMA statement (Annex 1). This review has been entered in PROSPERO, with registration number 42016050902.

RESULTS

We identified 33 articles which provided original data on the incidence of psychotic disorders worldwide during the period 2000 to 2015 [1-33]. All of studies were conducted in 13 different countries (Brazil, Canada, China, England, Ireland, France, Italy, Norway, Scotland, Spain, Sweden, The Netherlands and Surinam).

This systematic review identified 30 citations that provided overall incidence rates of psychotic disorders (core studies) [1,2,3,4,6-23,25,27-33], 8 compared incidence rates between urban and rural populations [1,6,11,14,18,19,25,26], 14 did so between incidence rates in immigrants and in natives or whites, mainly [3,5,6,7,11,13,14,15,21,22,23,24,27,29], and 4 between incidence rates in socio-economic-depressed areas and rates in higher status areas [3,14,18,32].

The majority of the studies were first contact type [1-7,9-16,18-21,23,26-28,30,32,33], while only 7 were first admission type [8,17,22,24,25,29,31]. In 23 studies, case ascertainment was carried out in Mental Health Services [1,4,5,7,8,10-17,20,22,24-26,29-31], 9 in Mental Health Services and in Primary Care [3,9,19,21,23,27,28,32] and 4 in Mental Health Services, Primary Care and in Social Services [2,9,18,33]. Sixteen studies used face-to-face diagnostic interviews such as a diagnostic tool [2,7,9,11-13,15,16,18,19,21,23,32,33], 6 studies used standardised case note review [1,3-5,14,27] and, finally, 14 used clinical diagnosis (recorded in hospital notes or registries) [6,8-10,17,20,22,24-26,28-31]. The quality indexes of the 36 studies ranged from 7 [10] to 14 [7,11-13,15]; the mean was 11.19. Estimated variation in rates between citations was very high, $I^2=1$ in all cases, showing great variability between studies.

The main characteristics of the citations are shown in Table 1.

Incidence rates of psychotic disorders

The incidence rates of different psychotic disorders are plotted in Figure 2. We can observe how the incidence rates were higher in non-affective psychoses than in affective ones. We also show forest plots for incidence rates for non-affective psychosis and affective (Figure S1), for non-affective psychosis (Figure S2), for affective psychosis (Figure S3), for schizophrenia (Figure S4) and for substance-induced psychosis (Figure S5). We next detail the incidence rates by diagnostic groups:

There were 16 citations that showed incidence rates for non-affective and affective psychoses [1,2,3,4,7,11,12,14,16,18,20,21,25,27,29,32] (Table 2). We are referring to any rate that considered affective and non-affective psychoses, although some also included substance-induced and/or organic psychosis. Incidence rates ranged from 15.8 [16] to 58.42 [7] per 100,000 persons; the latter rate was found in a study carried out in East London. The mean effect was 27.42 (22.37 – 32.46) per 100,000 (Table S7).

We found 20 citations which reported incidence rates for only non-affective psychosis (Table 2) [2,7,8,9,10,12,14,16,18,19,20,21,23,25,27,28,29,30,31,32], which varied from 10.0 [16] to 69.0 [9] per 100,000 persons. The latter was identified in a study conducted in The Hague. The mean effect was 22.53 (16.51 – 28.54) per 100,000 (Table S7).

Regarding incidence rates for only schizophrenia, 7 citations were found [2,6,11,12,14,17,20]. Incidence rates varied from 3.93 [14] to 61.6 [6] per 100,000 persons, which was found in a study in China. The mean effect was 14.55 (2.81 – 26.3) per 100,000 (Table S7).

Incidence rates for affective psychoses were usually lower than for non-affective ones (table 2). The former were obtained from 12 citations [2,7,11,12,14,16,18,20,25,27,29,32]. Rates ranged from 1.35 [29] to 14.72 [7] per 100,000 persons. This last rate was found in the aforementioned study carried out in East London. The mean effect was 7.12 (5.03 – 9.22) per 100,000 (Table S7). (For calculations we have discarded rates that include only bipolar disorder or only depressive disorder with psychotic features).

Finally, 5 citations [12,14,20,27,33] (Table 2) reported incidence for substance-induced psychosis separately, which ranged from 0.19 [14] to 6.5 [33] per 100,000 persons. The mean effect was 3.03 (1.26 – 4.8) per 100,000 (Table S7).

Gender

IRR by gender were found in 20 citations (when not provided, we calculated it) [1,4,6,7,9,10,11,13,14,15,18,19,21,23,25,27,29,30,31,32] (Table 3).

Examining IRR by diagnoses, firstly, we identified 11 citation that reported IRR for affective and non-affective psychoses [2,4,7,11,13,14,18,21,27,29,32]. The mean effect for men and for women was 41.99 (29.69 – 54.30) and 25.83 (19.40 – 32.26) per 100,000, respectively (Table S8). IRR mean men/women was 1.54 (1.37 – 1.72) (Table S8).

Secondly, we found 13 citations that showed IRR for non-affective psychosis [2,9,10,11,14,18,19,21,23,25,27,30,31]. The mean effect for men and for women was 32.86 (18.06 – 47.67) and 20.01 (10.7 – 29.31) per 100,000, respectively (Table S8). IRR mean men/women was 1.08 (1.01 – 1.16) (Table S8).

Thirdly, we identified 4 citations that reported IRR for schizophrenia [2,6,11,14]. The mean effect for men and for women was 9.05 (5.03 – 13.07) and 1.69 (-0.21 – 3.59) per 100,000, respectively (Table S8). IRR mean men/women was 8.52 (3.25 – 22.32) (Table S8). Fourthly, IRR for affective psychosis were obtained from 7 citations [2,11,14,15,18,22,27]. Contrary to non-affective psychosis, incidence for men was lower than for women in virtually all cases. The mean effect for men and for women was 5.28 (3.22 – 7.34) and 7.71 (4.46 – 10.96) per 100,000, respectively (Table S8). IRR mean men/women was 0.53 (0.49 – 0.57) (Table S8). Finally, 2 citations conducted gender incidence studies on substance-induced psychosis [14,27]. The mean effect for men and for women was 1.91 (-1.21 – 5.03) and 0.48 (-0.34 – 1.3) per 100,000, respectively (table S8). IRR mean men/women was 4.33 (0.36 – 51.76) (Table S8).

Urbanicity

We identified 8 citations which provided IRR by urbanicity level (when not provided, we calculated it) [1,6,11,14,18,19,25,26] (Table S4). In the studies which provided several incidence rates according to urbanicity level, we included the lowest and the highest urbanicity level.

Examining IRR by diagnoses, firstly, we identified 5 citations that reported IRR for affective and non-affective psychoses [1,11,14,18,26]. The mean effect for urban and for rural setting was 30.46 (17.20 – 43.72) and 17.80 (14.95 – 20.65) per 100,000, respectively (Table S9). IRR mean urban/rural setting was 1.64 (1.38 – 1.95) (Table S9).

Secondly, we found 5 citations that reported IRR for non-affective psychoses [11,14,19,25,26]. The mean effect for urban and for rural setting was 34.57 (10.77 – 58.36) and 16.46 (9.15 – 23.78) per 100,000, respectively (Table S9). IRR mean urban/rural setting was 2.25 (2.00 – 2.52) (Table S9).

Thirdly, we identified 3 citations that reported IRR for schizophrenia [6,11,14]. The mean effect for urban and for rural setting was 13.8 (-1.49 – 29.09) and 6.65 (3.61 – 9.69) per 100,000, respectively (Table S9). IRR mean urban/rural setting was 1.64 (1.38 – 1.95) (Table S9).

Finally, we found 3 citations that reported IRR for affective psychosis [11,14,26]. The mean effect for urban and for rural setting was 7.33 (1.84 – 12.82) and 3.79 (2.04 – 5.54) per 100,000, respectively (Table S9). IRR mean urban/rural setting was 1.64 (1.21 – 2.25) (Table S9).

Immigration

In our review, due to the great variability of immigrant groups included when analysing the incidence studies carried out on immigrants, we collected the most homogeneous estimates of IRR according to place of birth (or parental place of birth) in terms of the immigrant groups analysed from 14 citations (when not provided, we calculated it) [3,5,6,7,11,13,14,15,21,22,23,24,27,29] (Table S5).

Most migrant group rates were compared with rates in the native population. When comparing different categories of immigrants (black immigrants, Moroccans, Surinamese, non-white immigrants or all immigrants treated as a block) with the native population, incidence rates were higher for the former regardless of the disorder studied. There were two studies that considered other comparisons. In a study conducted in the Netherlands and Surinam [23], they investigated incidence for non-affective psychotic disorders in the Surinamese population residing in the Netherlands with the Surinamese population living in Surinam, finding a higher incidence rate for the former with a statistically significant difference. In the second study [6] in Taiwan, incidence of schizophrenia was compared between aboriginal and non-aboriginal populations, with a higher incidence for schizophrenia in the former, although the difference in this case was not statistically significant.

Examining IRR by diagnoses, we found 9 citations that reported IRR for affective and non-affective psychoses [3,5,7,11,13,14,21,27,29]. The mean effect for migrant and for native was 52.60 (35.47 – 69.73) and 16.58 (12.04 – 21.11) per 100,000, respectively (Table S10). IRR mean migrant/native was 3.09 (2.74 – 3.49) (Table S10).

Secondly, we identified 6 citations that reported IRR for non-affective psychoses [7,11,14,23,24,27]. The mean effect for migrant and for native was 39.41 (20.52 – 58.30) and 12.13 (7.93 – 16.32) per 100,000, respectively (Table S10). IRR mean migrant/native was 3.08 (2.62 – 3.63) (Table S10).

Thirdly, we found 4 citations that reported IRR for schizophrenia [6,11,13,14]. The mean effect for migrant and for native was 36.91 (-11.22 – 85.04) and 15.32 (-6.89 – 37.52) per 100,000, respectively (Table S10). IRR mean migrant/native was 2.74 (2.04 – 3.67) (Table S10).

Finally, we identified 6 citations that reported IRR for affective psychoses [7,11,13,14,15,22]. The mean effect for migrant and for native was 20.20 (10.34 – 30.07) and 11.03 (1.26 – 20.80) per 100,000, respectively (Table S10). IRR mean migrant/native was 1.28 (1.23 – 1.34) (Table S10).

Socioeconomic level

We identified 4 citations which reported IRR of psychosis depending on socioeconomic status (when not provided, we calculated it) [3,14,18,32] (Table S6). As in the case of urbanicity, when a study provided several incidence rates according to socioeconomic level of the area, we included the lowest and the highest socioeconomic level.

Examining IRR by diagnoses, we found 4 citations that reported IRR for affective and non-affective psychoses [3,14,18,32]. The mean effect for deprivation and for non-deprivation areas was 34.40 (20.89 – 47.90) and 24.74 (10.03 – 39.46) per 100,000, respectively (Table S11). IRR mean migrant/native was 1.78 (1.43 – 2.22) (Table S11).

For the remaining diagnoses, we only found one study [14]. In this study, carried out by Lasalvia et al. in Italy, differences were statistically significant only when they considered affective and non-affective psychosis as a whole and non-affective psychosis separately, while the opposite occurred for schizophrenia separately and affective psychoses (both separately and as a whole).

DISCUSSION

This systematic review updates existing knowledge regarding the incidence of psychotic disorders worldwide. To best of our knowledge, it is the only one that does so by analysing the different diagnostic groups separately. We also provide valuable data on how these incidence rates are influenced by certain factors, such as gender, urbanicity, immigration and socioeconomic level.

Overall incidence rates of psychosis

As in the recent systematic review carried out by Kirkbride et al. (2012), we found that incidence rates were higher for all psychoses as a whole, followed by incidence rates for non-affective psychoses and schizophrenia. Regarding affective psychoses, incidence rates were lower than for non-affective ones. When incidence rates were analysed for substance-induced psychosis, it was found that these psychoses were generally rare.

Gender

In our review we found similar results to previous systematic reviews (Aleman et al., 2003; McGrath et al., 2004). Analysing the incidence of psychosis for all disorders, we found that the incidence was higher for men than for women (IRR = 1.54 [1.37 – 1.72])

Overall, a higher risk for psychosis in males than in females was found in most studies included in this review. However, an important fact found is that incidence rates may vary if we study each type of psychosis separately. For example, rates were higher for men than for women in case of non-affective psychoses, whereas for affective psychoses, rates were higher for women than for men. This result agrees with those

found in the meta-analysis of Jääskeläinen et al. (2017), finding a higher proportion of women who presented psychotic depression versus schizophrenia.

These differences could be explained given the gender difference in age at onset in schizophrenia and related disorders, with an earlier age at onset in males (Bogren et al., 2010; Eranti et al., 2013). A previous systematic review found strong evidence in favour of men and women having different susceptibility to schizophrenia in different stages of life, being higher in men than in women in all cases, and finding that this difference was higher at the age of 20-29 than at the age of 30-39 (van der Werf et al., 2017). However, in the studies included in this review, the lowest upper cut age was 54 years old. In addition, this effect of later onset in women than in men continues to occur for affective psychoses and yet in our review we found a higher incidence of affective psychosis in women (Bogren et al., 2010).

Finally, Petkary et al. (2016) showed that the role of gender in schizophrenia has become a very important matter for designing effective psychosocial services to focus on patient needs.

Urbanicity

In our review, evidence indicates that there was an association between psychotic disorders and urbanicity, with increased rates in urban areas. We found only three studies which did not show statistically significant differences between urban and rural environments. In two of them (Lasalvia et al., 2014; Omer et al., 2014), the differences in the degree of urbanity of the locations studied were very small; thus explaining the results found. In the first study (Lasalvia et al., 2014), recruitment was carried out in the Italy's Veneto region, which presented few urban-rural differences in key social variables, such as social disintegration, emigration and level of social network. The second study was conducted in Cavan and Monaghan (Ireland), a predominantly rural region, consisting of widely dispersed farms with a scattering of villages and small towns, in the absence of any major urban areas (Omer et al., 2014).

In line with other systematic reviews carried out on this subject (McGrath et al., 2004; Kirkbride et al., 2012; Vassos et al., 2012), we found that incidence of schizophrenia and other psychotic disorders increased with the level of urbanicity. Although the literature shows that the association between affective psychoses and urbanicity are both contradictory and limited (Kelly et al., 2010), our results were stable regardless of the disorder studied.

These results are only applicable to developed countries. The few studies found in the literature on urbanicity and schizophrenia from the developing world reported no excess of cases of schizophrenia in urban compared to rural India or in semi-urban compared to rural Kenya (Kelly et al., 2010). Further information is needed to confirm this.

Despite the initial debates about whether living in large cities constituted a risk factor for developing the disorder or it was the disorder that led one to live in dense population settings, recent literature supports the former position. There is considerable evidence showing an increase in the risk for schizophrenia and other non-affective psychoses as the level of urbanisation in the moment of birth increases (March, 2008; Heinz, 2013).

Van Os (2004) reviewed possible causes of this association, concluding that individuals with a genetic liability to schizophrenia are more vulnerable to the negative effects of urban areas, such as social fragmentation, poor cohesion, isolation, lack of perceived safety or social stress.

Finally, we consider that our results could be very useful in order to ensure early prevention and improve mental health services planning.

Immigration

According to previous reviews (McGrath et al., 2004; Cantor-Graae et al., 2005; Kirkbride et al., 2012), in our study we also found increased incidence rates of psychosis for immigrants compared to natives.

Due to the wide variability found in the groups of immigrants analysed, an analysis of the studies as a whole became difficult, so we tried to homogenise the data by extracting the most commonly studied groups, in this case, black immigrants. In other cases, the incidence rate took into account all races of local immigrants. Incidence rates were especially high among black immigrants compared to Asian or other immigrants from Eastern countries (Coid et al., 2008; Kirkbride et al., 2008). In some studies, incidence rates among black immigrants are up to 8-fold higher than in white natives (Boydell et al., 2001).

Previous studies have shown that the increased risk of psychosis among immigrants clearly persists in the second generation (Cantor-Graae et al., 2007, Cantor-Graae et al., 2013), suggesting that post-migration factors play a more important role than pre-migration factors or migration itself. The observed ethnic variability suggests that the risk could be mediated by the social context rather than a biological basis (Bourque et al., 2011). Recent studies have shown that in healthy people, factors such as lower education level and belonging to minority groups are associated with increased activity in the brain circuits involved in the regulation of emotions during the process of social interaction (Zink et al., 2008; Hooker et al., 2010; van Harmelen et al., 2010; Kishida et al., 2012; Servaas et al., 2013). These findings support the hypothesis that changes in the ability to regulate social stress contribute to the risk mechanism (Krabbendam et al., 2014). This evidence supports the rates in the black race being higher than the other races due to the high levels of social exclusion and racist discrimination to which they are potentially exposed (Lanier et al., 2016; Taylor et al., 2017). Moreover, high incidence found in immigrants could be influenced by the fact that they tend to settle in inner cities, where they are often exposed to social exclusion and discrimination (Heinz et al., 2013).

It was also demonstrated that the association between schizophrenia and migrant status in London varies according to the level of the size of the migrant group (Kelly et al. 2010). Minority ethnic groups are at an increased risk of psychosis in areas with low ethnic density (Heinz et al., 2013).

The high rates in these groups could be related to urbanicity. Allardyce et al. suggested that non-white individuals living in an urban area of London account for a large proportion of the increased urban incidence that they found (Allardyce et al., 2001).

Socio-economic level

Living in a lower socio-economic level environment has been consistently associated with an increased risk of developing schizophrenia for decades (Dean et al., 2005; Ahmed El-Missiry et al., 2011; O'Donoghue et al., 2016).

The main obstacle that we found when analysing the relationship between the socio-economic level and the incidence of psychotic disorders is the different indexes used in each of the studies included in the review for the analysis of this risk factor. In each of the indexes, different variables have been included, such as unemployment, overcrowding, child poverty, lack of amenities, low earnings, no car and low level of education (Boydell et al., 2001); married individuals, separated or divorced or widowed, single-parent families, elementary school-level education, university qualification, living in rented accommodation, employment in the industrial sector, civil servants or people employed in the tertiary sector, and unemployed (Lasalvia et al., 2014); material deprivation (unemployment, social class, type of house tenure and car ownership) and social fragmentation (non-married adults, single person households, population turnover and private renting) (Omer et al., 2014); and mean income, housing quality, proportion of residents who are long-term unemployed, and mean educational level (Veling et al., 2015).

Due to this variability and the small sample analysed (only 4 studies), we can not conclude that there was a clear increase of psychosis in lower socio-economic environments.

LIMITATIONS

It should be borne in mind that the incidence rates found reflect attended incidence, that is, incidence rates were based on the population which was attending any of the services mentioned above and not based on a community survey, thus the actual incidence may be underestimated.

Grey literature was not included and, despite a wide-ranging search carried out in the electronic databases, we are aware that we have not been able to assess all the published articles.

The major limitation of our study is the great methodological variability found in the original studies. This entailed some difficulties for later analysis, but we believe that the approach we have used to homogenise them, considering the variables that they

had in common, helped ameliorate these problems. In any case, it would be necessary to analyse how such variability influences the results obtained.

Another related question is the significant variety of immigrant groups studied, as they were, in themselves, very heterogeneous. In this case, we selected for our analysis those immigrant groups most commonly studied among our citations. In addition to this, we have detected differences in the definition of immigrant throughout the included studies. Some speak of ethnicity, while others speak of migrant status. Most of them define immigrants according to their country of birth or that of their parents, and therefore, this is the definition we have adopted in our review. However, we are aware that in the studies analysed it is not clear that the assignment of black or white to individuals is at the individual level or at the ecological level (i.e., based on the majority race of their country of birth).

Given the marked difference between the age-specific incidence of most mental disorders for the two sexes, one limitation of our review is that by not taking into account age we inherently assumed a fixed sex-effect independent of age.

We have also analysed the studies taking into account only gender, urbanity, immigration and socio-economic level, and may have included other factors such as the country where each study was carried out, the differences in incidence rates over time, etc.

In addition, we are aware that our review contains a relatively small sample size, due to the comparatively short period of time we have restricted the search to. We consider that this sample is sufficient to show an updated view of the subject.

Finally, most of the incidence studies were carried out in Western Europe. We found few studies conducted in developing countries because, unlike prevalence studies, they are expensive and time-consuming, and sometimes complicated by the loss of cases. This would be a goal for the future, to get to know these incidence rates better and compare them with those of developed countries.

CONCLUSION

In this review we have demonstrated the significant variability presented in the incidence rates of psychotic disorders during the last 15 years worldwide. Part of this apparent heterogeneity could be explained by the different diagnoses analysed in each study. Generally, incidence rates were higher for non-affective versus affective psychosis. In addition, we have presented data on how some risk factors intervene in this variability. Incidence rates were higher for men than for women in non-affective psychoses and lower than women in affective psychoses. They were also higher in urban versus rural areas and higher in immigrants (especially among black immigrant communities) compared to native populations.

We believe that this data can be potentially useful for generating new hypotheses on the aetiology of these disorders. A recent systematic review like this could also have important implications when it comes to health planning. We recommend that all these findings be taken into account for the planning of health services, in order to ensure that they are more effective (and efficient) when caring for such patients.

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