Schizophrenia Research 204 (2019) 458–459

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Letter to the Editor

Incidence of psychotic disorders and its association with methodological issues. A systematic review and meta-analyses

Keywords:
Incidence
Psychosis
Schizophrenia
Epidemiology
Methodological factor
Method

In the last few years, several systematic reviews on the epidemiology of schizophrenia and related disorders (SRD) have been carried out, all of them finding great variability of the incidence rates among studies (McGrath et al., 2004; Saha et al., 2005a, 2005b; Kirkbride et al., 2012; Moreno-Küstner et al., 2018), and that is, when we perform a systematic review on a question, we cannot forget the methodology diversity that it comes with each study included in it, which may differ in the design and how it was conducted, participants, interventions, exposures or results (Higgins and Thompson, 2002). Therefore, the different methodology used in the studies to calculate incidence rates influences part of this variability, so it must be taken into account at the time of the subsequent analysis (McGrath et al., 2004).

We previously performed a meta-analysis on the incidence of psychosis worldwide between 2000 and 2015 (Castillejos et al., 2018) and we found a great variability in the methodology across studies. Therefore, in the current study, we aimed to determine if the variability of the incidence rates of psychosis found was associated with methodological aspect of the studies such as: study type, case ascertainment, diagnosis, diagnostic instrument to confirm cases, diagnostic classification system, duration of the case ascertainment, lower and upper age included in the studies and quality of the study (Table S1).

A meta-analysis of these factors was performed for all incidence rates as a whole. For the analysis of subgroups we used a mixed effects model. For each subgroup, heterogeneity was calculated using the Q statistic and its corresponding *p*-value. In addition, a multivariate regression was performed. To detect publication bias, a funnel plot was used, performing a visual inspection of the graph and the Egger test to detect asymmetry. All incidence rates are expressed per 100,000 persons with 95% CI and differences were considered significant for *p*-value ≤ 0.05. For all analyses, the metafor package (Viechtbauer, 2010) was used in the open source software environment R 2.12.0 (R Development Core Team, 2010).

We analysed 92 estimates of incidence of psychosis corresponding to 30 citations from our previous meta-analysis (Castillejos et al., 2018). The pooled incidence rates of psychosis (mean effect: 18.30 per 100,000 [14.19–22.42]) revealed that heterogeneity between studies was very high ($I^2 = 96.85\%$). The final model explains 63.53% of the variability in the incidence rates reported by the different studies (Table 1).

Based on the subgroup analysis, we found statistically significant differences in incidence rates associated with diagnosis ($p < 0.001$), diagnostic instruments used ($p = 0.020$), duration of case ascertainment period ($p = 0.026$) and ages of both lower ($p = 0.017$) and upper ($p = 0.051$) cutoff. Finally, study type ($p = 0.148$) and quality of the studies ($p = 0.094$) had a weak association (Table S2).

Regarding meta-regression, studies that collected patients in the first contact with mental health units presented higher incidences rated, but with a weak association ($p = 0.071$), more cases are detected in the studies in which the cases are included at the first contact, since there is not always an admission in the first episode. Studies that recruited patients in mental health units and primary care services ($p = 0.004$), or in both and in social services ($p = 0.001$) had significantly higher incidence rates than only in primary care. The more services we take into account at the time of recruitment, the higher the number of patients recruited and, therefore, the higher incidence. Taking as a diagnosis reference all psychoses (Non-Affective Psychosis + Affective Psychosis + Substance-Induced Psychosis), the rest of categories (except for Non-Affective Psychosis + Affective Psychosis) presented incidence rates significantly lower. It seems logical to think that the more diagnoses of the spectrum of schizophrenia and associated disorders included, the greater the incidence rate, according to Moreno-Küstner et al. (2018) and in Simeone et al. (2015) in term of prevalence. Studies based on clinical diagnosis had significantly higher incidence ($p < 0.001$). This could be due to the fact that the criteria used by the clinical professional to make the diagnosis are more lax and less restrictive than those used in a standardized diagnostic instrument. According to McGrath et al. (2004), Simeone et al. (2015), and Moreno-Küstner et al. (2018), we found no differences in incidence estimates associates with any of the international classifications used. The lower duration of the case ascertainment the higher incidence rate reported ($p = 0.006$). From the statistical point of view the most plausible explanation is that duration is a confusing variable, but this would be a question to examine in future studies. Higher lower age of cut showed higher incidence rates ($p < 0.001$). By decreasing the lower age, we are increasing the denominator population and, nevertheless, we do not increase the number of new cases of psychosis in the same proportion, since it includes a period of age in that the onset of a psychosis is rare. Finally, incidence rates were higher in studies with higher methodological quality ($p = 0.037$). This result is similar to Saha et al. (2008), who found that studies with higher quality scores tended to identify more cases. However, Simeone et al. (2015) and Moreno-Küstner et al. (2018) states that prevalence estimates were higher for studies with low quality scores (Table 1).

Forest plot for all incidence rates and by subgroup are shown in Figs. S1 and S2. In Fig. S3, a funnel plot is shown for the mean effect. Visually there was no bias publication, and the Egger test to detect asymmetry was not significant ($z = -0.3279$, $p = 0.7430$).

When clinical systematic reviews are carried out properly and data analysed in a rigorous manner, they are very useful for planning sanitary services in an appropriate way. Thus, we believe that, in order to

https://doi.org/10.1016/j.schres.2018.07.031

Table 1
Multivariate meta-regression. Random effects model.

	Coefficient	CI[a]	SE	*p*-Value
Study type				
First admission	1			
First contact	0.00361	−0.0003–0.0075	0.0020	0.0707
Case ascertainment				
PHS[b]	1			
PHS + PC[c]	0.00362	0.0012–0.0061	0.0012	0.0037
PHS + PC + SS[d]	0.00645	0.0025–0.0104	0.0020	0.0013
Diagnosis				
NAP + AP + SIP[e]	1			
S[f]	−0.00734	−0.0110–0.0037	0.0019	0.0001
NAP[g]	−0.00391	−0.0069–0.0010	0.0015	0.0091
AP[h]	−0.00977	−0.0126–0.0069	0.0015	0.0000
NAP + AP	0.00233	−0.0014–0.006	0.0019	0.2143
SIP	−0.0126	−0.0165–0.0088	0.0020	0.0000
Diagnostic instrument				
Clinical diagnosis	1			
Standardized instrument	−0.01088	−0.0157–0.0061	0.0024	0.0000
Duration	−0.00035	−0.0006–0.0001	0.0001	0.0060
Lower cutoff age	0.0006	0.0003–0.0009	0.0002	0.0002
Quality rank	0.00086	0.0001–0.0017	0.0004	0.0371

$N = 92$; $I^2 = 96.85$; $Q = 157.96$; $p = 0.000$; $R^2 = 63.53$.
[a] 95% confidence interval.
[b] Treated in psychiatric health services.
[c] Treated in psychiatric health services and primary care.
[d] Treated in psychiatric health services, primary care and social services.
[e] Substance-induced psychosis.
[f] Schizophrenia.
[g] Non-affective psychosis.
[h] Affective psychosis.

increase the quality of systematic reviews, appropriate methods have to be developed to avoid this variability in the results found. The present review provides a complete general comparison of the methodologies used in the incidence studies of psychosis, which is important to generate revealing information for future epidemiological studies in adopting the appropriate methodological approach.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.schres.2018.07.031.

Funding body agreements and policies

Does not apply.

Conflicts of interest

None.

Acknowledgements

Does not apply.

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12 July 2018