Salud Mental 2014;37:127-138
ISSN: 0185-3325
DOI: 10.17711/SM.0185-3325.2014.016

Critical review of the sources of variability in measuring the prevalence of schizophrenia

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Original article

SUMMARY

Epidemiological research plays a very relevant role in knowing the prevalence of schizophrenia. However, sometimes data from different studies is compared without taking into account some methodological questions that influence the results. This paper reviews different methodological factors that influence the variability of rates in the prevalence of schizophrenia. We also provide some general recommendations for measuring prevalence. We have revised 52 studies which offer prevalence rates of schizophrenia. A significant difference appears in the prevalence rates of schizophrenia which range between 1 and 45 per 1000 people. The factors found can be summarized as follows: 1) type of measure of prevalence; 2) upper and lower age limit of the denominator population; 3) scope of case detection; 4) classification of illnesses; 5) diagnostic groups and 6) method of diagnostic assessment. In conclusion, in epidemiological studies about schizophrenia prevalence we have to take into account the methodological factors involved in order to interpret and compare results from different studies.

Key words: Schizophrenia, prevalence studies, epidemiology.

RESUMEN

Conocer la prevalencia de la esquizofrenia y trastornos afines tiene una importancia relevante en la investigación epidemiológica y en la planificación de servicios. Sin embargo, existe una gran variabilidad en los resultados obtenidos en las diferentes investigaciones. El objetivo de este artículo es hacer una revisión crítica de los aspectos metodológicos de los estudios epidemiológicos que pueden influir en la medición de la prevalencia de esquizofrenia y trastornos afines y ofrecer una serie de recomendaciones generales para su medición. Se revisan 53 estudios epidemiológicos que relatan 76 tasas de prevalencia que oscilan entre 1 y 45 por 1000 habitantes. Se han encontrado seis factores metodológicos que creemos que están influyendo en la variabilidad de la medida de prevalencia de la esquizofrenia: 1. el tipo de prevalencia según el periodo de tiempo, siendo la más utilizada la prevalencia puntual; 2. el rango de edad de la población de estudio, siendo lo más frecuente incluir a personas mayores de 18 años; 3. el ámbito de detección de los casos más frecuentemente utilizado es la población general; 4. las clasificaciones de enfermedades utilizadas son la CIE y la DSM en similar proporción; 5. la categoría diagnóstica incluida frecuentemente en los estudios es el grupo de psicosis no afectivas; 6. el método de valoración diagnóstica más utilizado es la entrevista CIDI.

Conclusión

Consideramos que llegar a un consenso internacional para homogeneizar los aspectos metodológicos en los estudios epidemiológicos para calcular cifras de prevalencia de esquizofrenia nos facilitará la comparación de sus resultados.

Palabras clave: Esquizofrenia, estudios de prevalencia, epidemiología.

Translation of the original version published in spanish in: Salud Mental 2014, Vol. 37 Issue No. 2.

INTRODUCTION

There is no doubt that schizophrenia is a chronic and serious illness with a high load worldwide.[1,2] Despite its long history, epidemiological research into the prevalence of schizophrenia is still of great interest. There are numerous studies in various regions worldwide and their results differ greatly. The theory on a lower variability in the rates is backed up by the results of the *International Study of Schizophrenia* (*ISoS*) sponsored by the OMS,[3] which found

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Received first version: May 1, 2013. Second version: November 25, 2013. Accepted: December 2, 2013.

figures with between two and three times' variability through a standardized method. One review of studies published on prevalence of schizophrenia shows that the magnitude of said variability could oscillate between two and five times.[4] An extensive review carried out by Saha et al.[5] included 46 countries and 188 studies, and the prevalence of schizophrenia ranged between four and seven per 1,000 people. In this sense, the now classic review by Torrey[6] reports a variation of 10 times in the prevalence of schizophrenia in accordance with the different areas of the study; a finding shared by Eaton.[7,8] Indeed, the question to be addressed is whether schizophrenia can be considered a disorder that is distributed similarly in different parts of the world.[9]

One vital requirement for epidemiological research is the possibility of valid and consistent methods to carry out studies and investigation.[10] Further to etiological and environmental causes, there is increasing consensus that variability in the prevalence of schizophrenia is also influenced by the methodological aspects of studies.[11]

The aim of this article is to conduct a critical review of the methodological aspects that could influence the measurement of the prevalence of schizophrenia and related disorders, as well as to offer a series of general recommendations to standardize the measurement methods.

METHOD

This review has included studies published after 1990 in English or Spanish, which give figures for the prevalence of schizophrenia and related disorders. In order to identify the studies suitable for review, a bibliographic search was carried out using the electronic resources MEDLINE, PsychINFO, Web of Science, and Scopus. The bibliographies of the primary articles were also reviewed, as well as the systematic reviews published on the subject. This process was carried out by the authors BMK and CMG.

Studies carried out in populations considered to be at-risk were excluded (homeless people, prison inmates, etc.), as well as studies developed in fixed population groups according to age (young people, senior citizens), gender (men, women), and populations admitted to psychiatric institutions. Studies centered on psychotic disorders induced by substances were also excluded, as well as affective disorders with psychotic characteristics and psychotic disorders due to a medical condition, which could present more variability between different countries.

RESULTS

Some 52 articles have been analyzed, corresponding to 53 studies (one study was included twice as it was carried out in two different populations), which communicate a total of 75 figures for the prevalence of schizophrenia and related disorders. The articles included in this review have been carried out in 23 countries all over the world: 28 studies in Europe, 11 in America, seven in Asia, five in Oceania, and two in Africa.

Appendix 1 includes the references for all articles covered in this review. Table 1 shows the methodological aspects of each one of the studies. Finally, the articles have been classified in accordance with each of the methodological characteristics used (table 2).

From this critical review, the aspects we have found which most influenced the variability of the results are the following: 1) type of measure of prevalence, according to the period of study; 2) upper and lower age limit of the denominator population; 3) scope of case detection; 4) classification of illnesses; 5) diagnostic groups and 6) method of diagnostic assessment.

What follows is a presentation of the frequency with which each factor is used in the different studies reviewed, and a description of each one of these aspects.

1. Type of measure of prevalence, according to the period of study

In the 53 studies reviewed (appendix 1), 76 figures for prevalence were presented (some studies calculated more than one type of measurement) which range between one and 45 per 1,000 people. Point prevalence has been calculated in 40% of the studies, annual prevalence is presented in 26%, and life prevalence in 34% (tables 1 and 2).

Prevalence in an important measure of morbidity which is calculated as a proportion, dividing the total number of individuals who have the illness by the reference population. Various types of prevalence can be distinguished according to the period of study: point prevalence and period prevalence which can be annual or life, and which we will define as follows.[12-14]

Point prevalence

This is defined as the proportion of existing cases (previous and new) in a population at a unique point in time. It represents individuals who are ill at that determined moment. It is obtained through a study with a transversal, not longitudinal, design. Reference should be made to the cut-off date for obtaining the information. The measurements carried out in a brief interval of time, for example a week or a month, are usually also denominated point prevalences.

$$p = \frac{\text{N° of existing cases in a population defined in a moment or point in time } (t)}{\text{Total N° of people in the defined population at that moment } (t)}$$

Table 1. Description of studies reviewed according to methodological characteristics

Author and year (Ref. no.)	Place	Prevalence 1000 people	2 lower	2 upper	3	4	5	6
Arajärvi et al., 2005 (1)	Finland	Life: 15,0	40	69	Targeted	DSM-IV	1	Clinic - SCID
Almeida et al., 1997 (2)	Brazil	Point: 9,3 Life: 12, 0	15	SL	Census	DSM-III	3	SCID DSM-III
Andrade et al., 2002 (3)	Brazil	Point: 7,0 Annual: 8,0 Life: 19,0	18	SL	Census	CIE-10	3	CIDI
Andrews et al., 2001 (4)	Australia	Point: 4,0 Annual: 4,0	18	SL	Census	CIE-10 + DSM-IV	3	CIDI
Awas et al., 1999 (5)	Ethiopia	Point: 6,0 Point: 8,0	15	85	Census	CIE-10	1	CIDI
Bamrah et al., 1991 (6)	UK	Point: 6,3 Annual: 7,0	15	SL	Targeted	CIE-9	3	PSE
Bijl et al., 1998 (7)	Holland	Point: 2,0 Annual: 2,0 Life: 4,0	18	64	Census	DSM-III-R	1	CIDI
Bourdon et al., 1992 (8)	USA	Point: 7,0 Annual: 10,0 Life: 15,0	18	SL	Census	DSM-III	2	DIS
Chen et al., 1993 (9)	Hong-Kong	Life: 1,3	18	64	Census	DSM-III	1	DIS-III
Chien et al., 2004 (10)	Taiwan	Annual: 4,4	18	SL	Targeted	CIE-9	2	Clinic
Cho et al., 2007 (11)	Korea	Annual: 5,0 Life: 12,0	18	64	Census	DSM-IV	3	CIDI
Cohidon et al., 2009 (12)	France	Life: 27,0	18	SL	Census	CIE-10	4	MINI
Díaz-Martínez et al., 2003(13)	Mexico	Point: 20,0	15	65	Census	CIE-10	3	CIDI
Harvey et al., 1996 (14)	UK	Point: 5,3	18	SL	Targeted	DSM-III-R	3	MSP
Herrera et al., 1990 (15)	Spain	Point: 10,7	18	SL	Census	CIE-8	3	PSE
Hosain et al., 2007 (16)	Bangladesh	Point: 11,7	18	60	Census	DSM-IV	3	Clinic
Hovatta et al., 1997 (17 a)	Finland b	Life: 12,1	35	54	Targeted	DSM-III, CIE-8,CIE-9	4	OPCRIT, CHECK LIST DSM III-R
Hovatta et al., 1997 (17 b)	Finland a	Life: 22,1	35	54	Targeted	DSM-III, CIE-8,CIE-9	4	OPCRIT, CHECK LIST DSM III-R
Jablensky et al., 2000 (18)	Australia	Point: 4,7	18	64	Targeted	CIE-10	4	OPCRIT (DIP)
Jacobi et al., 2004 (19)	Germany	Point: 15 Annual: 26,0 Life: 45,0	18	65	Census	DSM-IV	4	CIDI-M
Jay et al., 1997 (20)	France	Annual: 14,9	15	SL	Targeted	DSM-III-R	3	Clinic
Jeffreys et al., 1997 (21)	UK	Point: 5,1	15	54	Targeted	DSM-III-R	3	Clinic
Jenkins et al., 1997 (22)	UK	Annual: 4,0	16	65	Census	CIE-10	3	SCAN
Jorgensen et al., 2013 (23)	Switzerland	Annual: 6,7	18	64	Targeted	CIE-10	2	Clinic
Kebede et al., 1999 (24)	Ethiopia	Point: 3,0 Life: 9,0	15	SL	Census	CIE-10	2	CIDI
Kendler et al., 1996 (25)	USA	Life:13,0 Life: 22,0	15	54	Census	DSM-III-R	2 4	CIDI
Kessler et al., 1994 (26)	USA	Annual: 5,0 Life: 7,0	15	54	Census	DSM-III-R	3	SCID-DSM III
Kessler et al., 2005 (27)	USA	Annual: 3,0	18	SL	Census	DSM-IV	3	SCID
Kringlen et al., 2001 (28)	Norway	Annual: 2,0 Life: 4,0	18	65	Census	DSM-III-R	3	CIDI
Lehtinen et al., 1990 (29)	Finland	Point: 13,0	30	SL	Census	CIE-9	1	PSE
Lora et al., 2007 (30)	Italy	Point: 2,4	14	SL	Targeted	CIE-10	2	Clinic
McConnell et al., 2002 (31)	Ireland	Annual: 4,3	18	65	Census	CIE-10 + DSM-IV	1	SCAN
McCreadie et al., 1997 (32)	UK Nithsdale Nunhead Norwood	Point: 2,4 Point: 3,3 Point: 1,9	18	SL	Targeted	CIE-10	1	OPCRIT

Table 1. Continued

Myles-Worsley et al., 1999 (33)	Micronesia	Life: 19,9	15	SL	Targeted	DSM-III-R	2	SADS-L and clinic
Ortega et al., 1995 (34)	Spain	Point: 1,3	15	65	Census	DSM-III-R	1	CIS
Perala et al., 2000 (35)	Finland	Life: 8,7	30	SL	Census + targeted	DSM-IV	1	SCID DSM-IV
Phillips et al., 2009 (36)	China	Point: 7,8	18	SL	Census	DSM-IV	1	SCID DSM-IV
Ran et al., 2003 (37)	China	Point: 4,1	15	SL	Census	CIE-10	3	PSE, SDSS
Regier et al., 1993 (38)	USA	Point: 6,0 Annual: 8,0 Life: 13,0	18	SL	Census	DSM-III	1	DIS
Roca et al., 1999 (39)	Spain	Point: 5,0	15	SL	Census	CIE-10	2	SCAN
Ruggieri et al., 2000 (40)	Italy	Annual: 3,4	18	SL	Targeted	CIE-10	3	Clinic
Scully et al., 1996 (41)	Ireland	Life: 3,9	18	SL	Targeted	DSM-III-R	1	SCID DSM-III-R
Seva A et al., 1992 (42)	Spain	Point: 2,5	15	SL	Census	DSM-III	1	CIS
Shrout et al., 1992 (43)	Puerto Rico	Life: 9,5 Life: 21,0	18	65	Census	DSM-III	2	DIS
Thornicroft et al., 1998 (44)	UK	Annual: 5,2	15	85	Targeted	CIE-10	3	SCAN
Tizon et al., 2006 (45)	Spain	Annual: 5,5	15	SL	Targeted	DSM-IV	1	Clinic
Van Os et al., 2001 (46)	Holland	Life: 3,7	18	64	Census	DSM-III-R	3	CIDI
Vicente et al., 2004 (47)	Chile	Point: 1,0	15	SL	Census	DSM-III-R	3	CIDI
Villaverde et al., 1993 (48)	Spain	Point: 6,5	15	SL	Census	DSM-III-R	3	CIS
Waldo et al., 1999 (49)	Micronesia	Point: 6,8	15	SL	Targeted	DSM-IV	3	SCIDP
Widerlov et al., 1997 (50)	Switzerland	Annual: 4,2	18	SL	Targeted	DSM-III-R	1	Clinic
Wittchen et al., 1992 (51)	Germany	Life: 7,2	18	55	Census	CIE-9	1	DIS
Xiang et al., 2008 (52)	China	Life: 4,9	15	SL	Census	CIE-10	2	CIDI
Youssef et al., 1991 (53)	Ireland	Annual: 3,3	15	SL	Targeted	DSM-III-R	1	Clinic

Legend for methodological characteristics: 2: Denominator population age limit; 3: Scope of case detection; 4: Classification of illnesses; 5: Diagnostic category; 6: Diagnostic assessment method

Legend for diagnostic categories: 1: Schizophrenia only; 2: Schizophrenic disorder, schizo-affective disorder, schizophreniform disorder, delirium ideas disorder, brief psychotic disorder in different combinations; 3: Psychotic disorders or non-organic psychosis; 4: Probable psychosis

Legend for diagnostic method: CIDI: Composite International Diagnostic Interview; DIS: Diagnostic Interview Schedule; CIS: Clinical Interview Schedule; OPCRIT: Operational Criteria Checklist for Psychosis; SCID: Structure Clinical Interview for DSM-IV; SCAN: Schedules for Clinical Assessment in Neuropsychiatry; DIP: Diagnostic Interview for Psychoses; MSP: Manchester Scale Psychiatry; PSE: Present State Examination; SADS-L: Schedule for Affective Disorders and Schizophrenia; MINI: Mini-International Neuropsychiatric Interview.

On some occasions the denominator is defined as the *population at risk* of illness. These are situations where the reference population is a subset of the total population.

We can give the following expression to estimate prevalence:[15]

$$P = \frac{C_t}{N_t},$$

where $C_t = N_t - N_t'$ is the number of cases prevalent at time t.

As such, if at a determined moment t, we have 2 271 cases of schizophrenia in an area (C_t) and the population census for the area is 225 255 inhabitants (N_t), the prevalence is given by:

$$P = \frac{2271}{2271 + 222984} = 0.01\ (1\%)$$

Supposing that the prevalence was obtained through a random simple, we can calculate the corresponding confidence interval. Given that the prevalence is a proportion, the confidence interval (*CI*) is given by:[16]

$$CI_{1-\alpha}(\pi) = \left(p \pm z_{\alpha/2}\sqrt{\frac{p(1-p)}{n}}\right)$$

where π represents the population prevalence, p is the prevalence calculated for the sample, and n is the size of the sample.

Calculating the confidence interval

Supposing that the prevalence was obtained through a random sample, we can calculate the corresponding confidence interval. Given that the prevalence is a proportion, the confidence interval (*CI*) can be given by:[15]

$$CI_{1-\alpha}(\pi) = \left(p \pm z_{\alpha/2}\sqrt{\frac{p(1-p)}{n}}\right)$$

where π represents the population prevalence, p is the prevalence calculated for the sample, and n is the size of the sample.

Table 2. Distribution of articles in accordance with methodological aspects

Methodological aspects	Categories	Bibliography reference number
1. Types of prevalence*	Point	2-8,13-16,18,19,21,24,29,30-32,34,36-39,42,47-50
	Annual	3,4,6-8,10,11,19,20,22,23,26-28,31,38,40,44,45,51,54
	Life	1-3,7-9,11,12,17,19,23-26,28,33,35,38,41,43,46,52,53
2. Study population age limits	Lower age	
	14	30
	15	2,5,6,13,20,21,24-26,33,34,37,39,42,44,45,47,48,49,52,53
	16	22
	18	3,4,7,8,9,10,11,12,14,15,16,18,19,23,27,28,31,32,36,38,40,41,43, 46,50,51
	30	29,35
	35	17
	40	1
	Upper age	
	54	17,21,25,26
	55	52
	60	16
	64	7,9,11,18,23,46
	65	13,19,22,28,31,34,43
	69	1
	85	5,44
	Unlimited	2,3,4,6,8,10,12,14,15,20,24,27,29,30,32,33,35-42,45,47-52,53
3. Scope of case detection	General population	2-5,7-9,11-13,15,16,19,22,24-29,31,34-39,42,43,46-48,52
	Targeted population	1,6,10,14,17,18,20,21,23,30,32,33,40,41,44,45,49,50,53
4. Classification of illnesses	CIE	
	8	15
	9	6,10,51,29
	10	3,4,5,12,13,18,22,23,24,30,31,32,33,39,40,44,52
	DSM	
	III	2,8,9,17,38,42,43
	III-R	7,14,20,21,25,26,28,33,34,41,46,47,48,50,53
	IV	1,11,16,19,27,35,36,45,49
5. Diagnostic criteria	1	1,5,7,9,29,31,32,34,35,36,38,41,42,45,50,51,53
	2	8,10,23,24,30,33,39,43,52
	3	2,3,4,6,11,13,14,15,16,20,21,22,26,27,28,37,40,44,46,47,48,49
	4	12,17,18,19,25
6. Diagnostic assessment method	CIDI	3,4,5,7,11,13,19,24,25,26,46,47,52
	PSE/SCAN	6,15,22,29,31,37,39,44
	DIS	8,38,43,51,9
	Clinic	10,16,20,21,23,30,40,45,50,53,1
	CIS	34,42,48
	OPCRIT	17,18,32
	SCID	2,26,27,35,36,41,49
	Others	12,14,33

*More than one type of prevalence may present itself in each study, in which case the reference number is repeated.
Legend for diagnostic categories: 1: Schizophrenia only; 2: Schizophrenic disorder, schizo-affective disorder, schizophreniform disorder, delirium ideas disorder, brief psychotic disorder in different combinations; 3: Psychotic disorders or non-organic psychosis; 4: Probable psychosis.

Period prevalence (annual)

The measures most derived from point prevalence have been defined:[15,17] period prevalence and *lifetime prevalence*.

Period prevalence is defined as the ratio of existing cases (previous and new) in a population in a period of time. It usually refers to a year, when it is called annual prevalence.

$$pp = \frac{\text{N° of existing cases in a population defined at one moment } t_0 + \text{new cases between } t_0 \text{ y } t}{\text{Total n° of people in the population at mid-range } t_0 : t}$$

We can estimate the period prevalence through the following equation:

$$P_{(t_0:t)} = \frac{C_{t_0:t}}{N_{t_0:t}}$$

where $C_{(t0,t)}$ includes both the prevalent cases (C_0) in t_0 as well as the incidents (I) detected in the defined period (t_0:t). If the study is carried out on a fixed cohort, the denominator of the expression can be replaced by (N_0) the size of the cohort in time t_0.

With the definition that we have given of period prevalence, the previous equation can be expressed in terms of a measure of incidence I, in such a way that:

$$P_{(t_0:t)} = \frac{C_{t_0:t}}{N_{t_0:t}} = \frac{C_0 + I}{N_0}$$

Period prevalence (life)

If the study period is broadened to the entire life of the subject it is known as life prevalence, which is defined as the proportion of individuals in a population that have manifested the disorder at any time during their life. This includes not only those individuals who present symptoms when being surveyed, but also those who have suffered from the condition previously.

To calculate life prevalence, we use the same expression as that to estimate point prevalence P, where C_t now includes the people who have the illness at the time t, those who were previously cured of the illness, and those who are in a state of remission from the same.

The figure of life prevalence for a mental illness of long-term development such as schizophrenia is assimilated into that of life risk, while in illnesses that can develop towards an improvement, the notion of risk cannot be equated with life prevalence. Life risk is the probability that a particular disorder or phenomenon will appear if all individuals live to a certain age. As a form of estimating it, certain authors calculate the proportion of subjects in the general population that have presented with the disorder once. This is life prevalence.

What follows is a summary of some characteristics of prevalence: *i*) it is a proportion, which is not necessarily a percentage, given that it be multiplied by a base value other than 100 (1,000, 10,000…); *ii*) it correctly reflects the magnitude of an illness; *iii*) it is useful for healthcare management; *iv*) it depends on the frequency of new cases appearing and the median duration of the illness; *v*) it has little use in etiological studies.

2. Age range of the population studied

The majority of the studies reviewed in this work set the minimum age limit for inclusion in studies at 18 years (49%), followed in second place (37%) by studies that determined a minimum age of 15 years. Furthermore, the majority of the studies (64%) did not indicate an upper age limit for the population to be analyzed.

3. Scope of case detection: general or targeted population

In the articles reviewed, the majority of the studies (64%) were carried out on the general population, whereas 36% were carried out on people cared for by mental health, primary care, or social services.

If the study is carried out on the general population, it obtains figures of real prevalence, whereas if cases are chosen from the services, in the particular case of mental health, they will be treated, assisted, or administrative prevalence rates.

General population.
Community studies (census method)

Community studies can be divided into two types: intensive census studies, which are usually carried out in very reduced geographical areas (in this case the study is very exhaustive and the entire population is interviewed), and sample studies that include, among others, bi-phasal studies in which a screening phase is introduced before carrying out the psychiatric interview[18] (second phase).

Targeted population (key informant method and records of psychiatric cases)

Studies on populations cared for by healthcare (primary care and mental health) and social services usually use the key informant method. This procedure consists of preparing a list of services and institutions of a certain area –normally small communities– which can be places that possible cases will likely attend. People who know what is going on around them should be selected as key informants.

Another possibility is to only include those cases that come to require care from the mental health services in a certain area (record of psychiatric cases). However, the number of cases is very much affected by the level of developed care in the place where the study is carried out, and furthermore, cases that do not require care will be lost.

Translation of the original version published in spanish in: Salud Mental 2014, Vol. 37 Issue No. 2.

Diagnostic questions: classification of illnesses, diagnostic groups, and method of diagnostic assessment

The difficulty in knowing the exact cause of schizophrenia and related disorders, as well as the lack of pathognomonic care or reliable diagnostic tests mean working with a construct that is difficult to define, which complicates its epidemiological study. Bearing in mind the problems that surround the definition of schizophrenia, epidemiological studies must be interpreted under this premise.[19] Decades behind the introduction of the concept of schizophrenia, research is still in need of a conceptual validation of this construct; fundamentally of its psychopathological characteristics and its phenotypic limits.[20] Epidemiological studies have recently been carried out in which psychosis is analyzed from a dimensional perspective.[21]

4. Classification of illnesses

In terms of the classification of illnesses used in the 53 studies reviewed, the majority (58.5%) utilized the DSM (Diagnostic and Statistical Manual of Mental Disorders), and the rest used the ICD (International Classification of Diseases) (table 2). It should also be noted that some studies used both.

The system for classification of illnesses is extremely important in epidemiological research, given that the application of one or the other can considerably affect the prevalence data obtained in research studies, especially in the case of schizophrenia.[22]

With the development of the different classifications of illnesses, both by the World Health Organization with the ICD,[23] and the American Psychiatric Association with the DSM,[24] great efforts have been made to base the classification of mental illnesses on operative criteria and to use these routinely in clinical practice and in research. If the 9th edition of the ICD was considered by Kulhara et al.[25] as a useful and reliable system to diagnose schizophrenia, the development of the tenth version of the ICD and the inclusion of multiaxial criteria in the DSM-IV has increased the possibility of comparing these systems. The criteria for the diagnosis of schizophrenia and related disorders have not changed substantially with the recent publication of the DSM-5.[26] In particular, types of schizophrenia have been removed, with the aim of creating greater diagnostic stability. As this classification was published in 2013, it is still early to quantify how it has influenced the calculation of prevalence figures.

5. Diagnostic groups

In the majority (42%) of the epidemiological studies reviewed, an analysis was made of the group of non-affective psychoses (schizophrenia, schizophreniform disorders, delirium idea disorders, and atypical psychoses) (code 3, tables 1 and 2). The next most analyzed diagnosis (32%) is schizophrenia –in this case we are referring exclusively to this disorder– (code 1, tables 1 and 2).

The different diagnostic categories used by researchers at various times and in various parts of the world have been another source of variability for prevalence rates of schizophrenia and related disorders. The first comparisons between rates given by European and North American studies showed such important differences that this could only be explained by the presence of different diagnostic cultures on the two sides of the Atlantic.[22]

6. Method of diagnostic assessment

There is great diversity between the diagnostic assessment methods in epidemiological studies on schizophrenia and related disorders. Our review found that the studies analyzed most frequently used the CIDI (*Composite International Diagnostic Interview*) (24.5%), followed by the clinical interview (20.7%). Other instruments used were the PSE/SCAN (*Present State Examination-Schedules for Clinical Assessment in Neuropsychiatry*) (15.1%), the SCID (*Structure Clinical Interview for DSM-IV*) (13.2%), and the DIS (*Diagnostic Interview Schedule*) (9.4%).

The so-called third generation epidemiological studies seek to reduce the burden of this source of variability, making a qualitative and quantitative leap, fundamentally with the introduction of structured diagnostic instruments. These normalized methods represent an important step in reaching greater reliability in epidemiological research. Furthermore, the majority of these instruments have been translated and validated in numerous languages, which allows them to be used in international studies.

The first instrument developed to determine a systematic and structured diagnosis was the PSE,[27] which was developed and improved upon until the production of the PSE-9 and the PSE-10, which allow classification criteria to be used from the CIE-9 or the CIE-10, respectively. The latest version of this instrument is the semi-structured clinical interview SCAN.[28] This is designed to be used in the clinical environment and experience and specific training in this area are necessary for its application.

In 1980, the Diagnostic Interview Schedule-DIS[29] was developed for use in epidemiological studies on the general population. The later-developed Composite International Diagnostic Interview – CIDI[30] is based on the DIS. It is a very structured and user-friendly interview which does not require clinical experience, although it does require regulated training.

Another appropriate instrument for the detection of serious disorders such as schizophrenia is the Structured Clinical Interview for DSM-IV-II – SCID-II,[31] which should be applied by lay persons trained in handling the interview.

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DISCUSSION

Limitations

The authors should first point out that we are mindful of the limitations of this study, which are as follows. Even if the use of systematic revisions has offered a new perspective on the landscape of the epidemiology of schizophrenia,[32] this article does not pretend to be a meta-analysis, and the necessary methodology for the same has not been followed. Nor has every published article on the subject been included. Another limitation of this work is that it is based solely on certain methodological aspects, although there are other factors that can also influence the figures for prevalence and which we have not included in this review, for example, the size of the study sample, the type of sampling used to select cases, and the calculation of standard error. Despite these limitations, we consider that this work is a critical review that provides relevant information in the sphere of psychiatric epidemiology.

Resulting principles and recommendations

The primary contribution of this review is the analysis we made of the most widely-used methodological aspects in 53 epidemiological studies covering a broad representation of recent epidemiological research into schizophrenia (appendix 1, table 1).

We have found six methodological factors that we believe are influencing the variability of measuring the prevalence of schizophrenia: 1) the type of prevalence according to time (point, annual, and life), with point prevalence being the most used; 2) the age range of the study population, most frequently including people older than 18 years and with no upper age limit; 3) the scope for case detection (general population and those cared for by healthcare –primary care and mental health– and social services, studies on the general population being most frequent; 4) the classification of diseases used, the CIE and the DSM being used in similar proportions; 5) the diagnostic category, the group of non-affective psychoses being the most frequently used in the studies, and 6) the method of diagnostic assessment, the most widely used being the CIDI interview, although we have found more than eight methods of diagnostic assessment (table 2).

What follows is a set of recommendations that we consider would be useful in carrying out epidemiological studies into the prevalence of schizophrenia, as well as biases that could be present in the different factors analyzed.

1. Type of prevalence measure according to period studied: point and period (annual and life)

In studies on schizophrenia, point prevalence is a more conceptual than real term, given than in practice, it is difficult to gather information from the cases at a determined moment. When referring to diseases of long-term development, especially when these present themselves insidiously, as is the case with schizophrenia, it is advisable for the period covered to span at least six months or a year.

2. Age range of the population studied

Due to schizophrenic disorders not usually starting in childhood, a population over the age of 15 or 18 is normally used as the denominator, as including people under this age would reduce the rates artificially. In some cases, an upper age limit is established; for example, a maximum of 55 years. This is a circumstance that is appropriate to take into account when comparing prevalence between schizophrenia and related disorders.

3. Scope of case detection: general and targeted population

In epidemiological studies, case detection is usually carried out in the general population. However, the low frequency of schizophrenia means that these types of study are not very appropriate for calculating prevalence rates, because it would be necessary to interview a very broad population in order to be able to gather a statistically representative number of cases. Furthermore, these studies can present a selection bias, as a significant group of people with serious mental disorders could be based in protected accommodation or institutions, and it is difficult to access this section of the population.[33] The NEMESIS[34] study calculated a loss of 0.05% of cases for this reason. Another possible selection bias is presented by the difficulty of including homeless people.34 Finally, those with schizophrenia and related disorders are often not inclined to answer extensive surveys,[11] which could give an information bias.

When the aim is to obtain figures for the prevalence of schizophrenia, it is most effective to carry out studies in the population cared for within the scope of social/health care (mental health and primary care services). In the case of schizophrenia this is a good design, given that those who have the illness usually attend some type of health or social care service throughout their lives. It would not currently be pertinent to carry out epidemiological studies on schizophrenia solely within the hospital environment due to Berkson's bias, and furthermore because after the psychiatric reform, patients with schizophrenia attend a wide variety of health and social services to receive care. It should not be forgotten that these figures always refer to people who have been treated or received care.[35-37] As concluded by Përalä et al.,[11] in order to determine the true dimension of this illness, the greatest possible number of information sources should be used.

Diagnostic questions

4. Classification of illnesses,
5. Diagnostic groups, and
6. method of diagnostic assessment

The problems specifically derived from the lack of normalization of diagnostic criteria significantly impede the com-

parison between results produced by researchers and those obtained in other cultures. The differences and disagreements that affect the diagnostic standards are based on the use of narrow criteria before wide criteria;[38] that is, on the dichotomy between specificity (level of detection of true negatives) and sensitivity (level of detection of true positives).

To diagnose cases of schizophrenia, it is most appropriate to use structured clinical interviews, although it is not always possible to use these in epidemiological studies due to their training requirements.

As demonstrated in the ECA –*Epidemiologic Catchment Area*–[39] study, the value of the DIS interview in quantifying schizophrenia in general population samples is small, due to the detection of many false positives. Also, the model for schizophrenia in the CIDI interview, one of the most widely used instruments in population studies, generates false positives in census studies.[40] A selection bias could be present in both cases due to the inappropriate use of diagnostic tests that could lead to including patients with different diagnostic criteria. An information bias could also be given in epidemiological studies on schizophrenia, given that in order to carry out the diagnosis, it is necessary to gather information from the subject themselves, and in some cases they may not be inclined to give this information. The improvement in the reliability of diagnoses has influenced the figures for prevalence in epidemiological studies.[41]

CONCLUSION

The primary conclusion drawn from this work is that there is great heterogeneity in the methodological aspects of the studies analyzed, and that this is influencing the figures obtained.

We believe that it would be extremely useful to arrive at an international consensus to use standard criteria that allow for the results of epidemiological studies in general, and of schizophrenia and related disorders in particular, to be reliably shared.

The approval and standardization of these procedures would conclusively determine whether there truly are differences in different areas of the world in the prevalence of schizophrenia, or whether these differences are due to purely methodological factors. If we apply these methodological aspects homogenously, we can contribute more reliable information to the complex journey of the epidemiology of schizophrenia.

ACKNOWLEDGEMENTS

To the Junta de Andalucía for financing the following research projects of the Consejería de Sanidad (PI338/2008 and PI332/2008) and of the Consejería de Innovación, Ciencia y Empresa (P10-CTS-5862) and for financing the GAP group (CTS-945). To the PSICOST Scientific Association.

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Declaration of conflict interest: None

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Salud Mental 2014, Vol. 37 Issue No. 2.

APPENDIX 1. Epidemiological studies published since 1990 that give figures for the prevalence of schizophrenia. Studies included in our review,

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