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Review article

Diagnostic stability of schizophrenia: A systematic review

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ABSTRACT

The objective is to systematically review previous literature on the diagnostic stability of schizophrenia, particularly to investigate prospective and retrospective consistency. We carried out a systematic literature search in PubMed and other minor sources from 1980 to July 2017. Specifically, prospective and retrospective consistency were examined. Thirty-nine studies were included, 5 focused on schizophrenia, 23 on psychotic episodes and 11 on psychiatric disorders in general. Samples sizes range from 60 to 10 058 subjects (total $N = 39\,965$). The majority of studies ($n = 26$, 66.67%) were performed in Europe and North America and they had a prospective design ($n = 27$, 69.23%), with a median follow-up of 3 years. Prospective and retrospective consistency means were 84.29% and 67.15% respectively. Diagnostic change was also frequently measured ($n = 12$, mean 31.28%). The factors more commonly associated with diagnostic stability were: male sex, older age at the study inception, older age at onset, late stages of illness, family history of mental illness, poorer functioning and longer length of stay. Schizophrenia was found to have high diagnostic stability over time, although research on this topic is mainly focused in first psychotic episodes. More standardized methods are needed to further research diagnostic stability of schizophrenia over time and its determinants.

1. Introduction

Schizophrenia is characterized by chronic or recurrent symptoms of psychosis and impairments in social and occupational functioning (Fischer et al., 2017a). Schizophrenia has thus become a major cause of disability and economical burden due to direct and indirect costs according to the World Health Organization (Mathers et al., 2008; Murray and Lopez, 1996). However, its course and prognosis are considerably heterogeneous (from full symptomatic remission with positive outcome to presentations with continuous symptoms and poor outcome). Schizophrenia affects individuals across the world with a widely accepted prevalence of 1% internationally and an estimated cost more than \$60 billion per year, including direct healthcare costs and indirect costs due to loss of productivity (Chong et al., 2016; Daradkeh, 1996; Fischer et al., 2017b; Insel, 2010; Nicholl et al., 2010; Owen et al., 2016; Simon

et al., 2018; Vetter and Köller, 1993).

The diagnosis of schizophrenia is commonly made by exclusion since there are no pathognomonic symptoms and it is based on picking up features of psychosis from the diagnostic interview and collateral information (Fischer et al., 2017b). The psychiatric diagnoses in general, including that of schizophrenia, are therefore operationalized in the international taxonomies, in contrast to other areas of medicine (Fusar-Poli et al., 2016). In psychiatry, diagnoses are still based on the identification of the clinical syndrome (Chang et al., 2009) and the diagnostic criteria continue to rely on clinical features, outcomes and family history (Robins and Guze, 1970). Given the absence of biological markers, clinicians need to further verify clinical information for longer periods of observation over time (Chang et al., 2009; Ponizovsky et al., 2006). In 1938, Masserman and Carmichael (1938) followed-up a series of patients with schizophrenia and found that at twelve months a major

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revision of diagnosis was necessary in over 40% of them (Masserman and Carmichael, 1938). Concordance between clinicians, which is usually measured by the kappa index, has improved since the categorization of diagnostic criteria and so has improved the reliability of most diagnostic categories of mental disorders, although not as fully (Bousoño-García and Bousoño-Serrano, 2005; Ponizovsky et al., 2006). The utility of these diagnostic categories depend both on the inter-rater reliability and the temporal stability (Kendell, 2005; 1974). Diagnostic stability has been defined as the degree to which the original diagnosis is not changed at follow-up (Kendell, 1989), although diagnostic uncertainty and temporal instability are the rule rather than the exception in early psychosis (Chang et al., 2009). Diagnostic stability is therefore a measure of predictive validity for psychiatric syndromes, although an under-studied area despite its clinical and research implications (Bromet et al., 2005; Chang et al., 2009; Forrester et al., 2001). On the other hand, several studies addressing diagnostic stability of first episode of psychosis diagnoses have been published, although the results were highly heterogeneous and diagnosis frequently changed to schizophrenia as shows a recent meta-analysis (Fusar-Poli et al., 2016). The method proposed by Robins and Guze (1970) was an outstanding initiative, although it is yet to be incorporated into routine clinical practice.

Within schizophrenia, evidence of diagnostic stability is fundamental to guide accurate early interventions. Its stability has been found very high in comparison to other clinical diagnoses in the medical field (Fusar-Poli et al., 2016). Moreover, schizophrenia appears to be a stable diagnosis from early phases of the illness (Pope et al., 2013), with higher stability over time than other psychosis spectrum disorders (Addington et al., 2006; Babigian et al., 1965; Forrester et al., 2001; Rice and Todorov, 1994), particularly higher than affective psychosis (Stanton and Joyce, 1993). These assertions have been confirmed by a recent meta-analysis on stability of first psychosis episodes (Fusar-Poli et al., 2016).

Schizophrenia is a very common and highly disabling mental disorder; however, early intervention can result in better outcomes. Hence, making an early diagnosis of schizophrenia (Nicholl et al., 2010) to be followed by a proper intervention (Flaum et al., 1992) is matter of major clinical relevance. Thus, the subject of diagnostic stability of schizophrenia merits further investigations in order to have a deeper understanding of this disorder, especially in the early stages of the illness, which could help clinicians to make more accurate diagnoses from the onset of the illness. Better understanding of diagnostic stability of this disorder will also improve the classification of first psychotic episodes, with the subsequent benefits to patients and their families. With this in mind, we aimed to conduct an up-to-date systematic review of the diagnostic stability of schizophrenia. Specifically, we hypothesized that while overall schizophrenia will have high levels of stability and some factors, namely being male, longer duration of untreated psychosis and more severe symptoms at first presentation will be associated with a more stable diagnosis whilst shorter studies will increase the likelihood of a diagnosis switch.

2. Material and methods

The methodology used in this review was similar to a previous work from our group on diagnostic stability of mental disorders and Bipolar Disorder (Baca-Garcia et al., 2007; Cegla-Schwartzman et al., 2018).

2.1. Search strategy

A systematic MedLine bibliography search was conducted using the following key-words: (“schizophrenia” OR “psychosis” OR “psychotic episode”) AND (“diagnostic stability” OR “diagnostic consistency” OR “diagnostic shift” OR “diagnostic change” OR “diagnostic progression” OR “diagnostic conversion” OR “diagnostic concordance”), which was restricted to the last 35 years (from 1980 to July 2017) and language

(English or Spanish). Other sources were searched (MEDES and Google Scholar). References within identified articles were also included if they met the selection criteria below. Book chapters were excluded. The review complied with the PRISMA guidelines (Beller et al., 2013; Liberati et al., 2009; Moher et al., 2009; Urrútia and Bonfill, 2010). The statistical analysis was carried out using the R programming language (version 3.5.0) (“R: The R Project for Statistical Computing,” 2019).

2.2. Selection criteria

Articles were included if they fulfilled the following selection criteria: 1) information on diagnostic stability of schizophrenia had to be available; 2) age: 15 years or older; 3) diagnosis: schizophrenia, psychotic episodes and other psychoses according to the ICD-9 (295.0–4, 295.8 and 295.9), ICD-10 (F20, F23, F29 and F22), DSM-III (295.10–35, 298.90 and 295.91–95), DSM-IV (295.9–40, 298.8) and DSM-V (295.40, 295.90, 298.8 and 298.9); 4) sample size larger than 10; 5) and only publications in peer-reviewed journals were considered.

2.3. Operative definitions

Diagnostic stability measures the extent to which a diagnosis remains unchanged over the follow-up, hence validating the baseline diagnosis and it is based on the concordance of diagnoses over time irrespective of potential further cross-sectional diagnoses over follow-up (Fennig et al., 1994). In 1970, Robins and Guze proposed diagnostic stability as one of the necessary criteria to confirm the presence of a psychiatric syndrome, which was also linked with the predictive value of psychiatric diagnoses, thus becoming a major innovation in psychiatry (Robins and Guze, 1970). Diagnostic stability is mainly assessed by Prospective and Retrospective Consistency.

Prospective consistency (PC) is the proportion of subjects in a category that maintain the same diagnosis at follow-up as at baseline, hence similar to Positive Predictive Value.

Retrospective consistency (RC, which is similar to Sensitivity) is the proportion of subjects in a category at follow-up who were in the same category at baseline (Addington et al., 2006).

3. Results

The initial search yielded 8121 references and 39 papers met the above predetermined selection criteria (Fig. 1 and Table 1). Seven studies (19.94%) included adolescents (age 15–17). The total sample of this review was $n = 39\,965$. As shown in Table 1, out of the thirty-nine selected papers, 5 of them focused on schizophrenia (Chen et al., 1996; Dhossche and Ghani, 1998; Hwu et al., 1988; Munk-Jørgensen, 1985; Parnas et al., 2011), 23 works focused on psychotic episodes (or psychosis in general) (Addington et al., 2006; Amin et al., 1999; Amini et al., 2005; Baldwin et al., 2005; Bromet et al., 2011; Chang et al., 2009; Chinchilla et al., 1992; Crebbin et al., 2009; Fennig et al., 1994; Forrester et al., 2001; Haahr et al., 2008; Heslin et al., 2015; Jakobsen et al., 2007; Jørgensen and Mortensen, 1988; Kim et al., 2011; Kingston et al., 2013; Pope et al., 2013; Rahm and Cullberg, 2007; Salvatore et al., 2009; Schimmelmann et al., 2005; Schwartz et al., 2000; Subramaniam et al., 2007; Whitty et al., 2005) and 11 studies focused on psychiatric disorders in general (Atwoli et al., 2012; Baca-Garcia et al., 2007; Daradkeh et al., 1997; Daradkeh, 1996; Kim et al., 2011; Ponizovsky et al., 2006; Rabinowitz et al., 1994; Stanton and Joyce, 1993; Tsuang et al., 1981; Vetter and Köller, 1993; Woo et al., 2006).

The sample sizes of these studies ranged from 60 to 10 058 patients, with a total population of $n = 39\,965$ (mean = 974.76, SD = 1774.24, media = 278). The vast majority of them ($n = 26$, 66.67%) were performed in Europe and North America, although there were also studies from Asia ($n = 10$, 25.6%) and Oceania ($n = 2$, 5.12%). Only one was performed in Africa (2.56%). The follow-up periods ranged from 5 months to 40 years (median = 3 years).

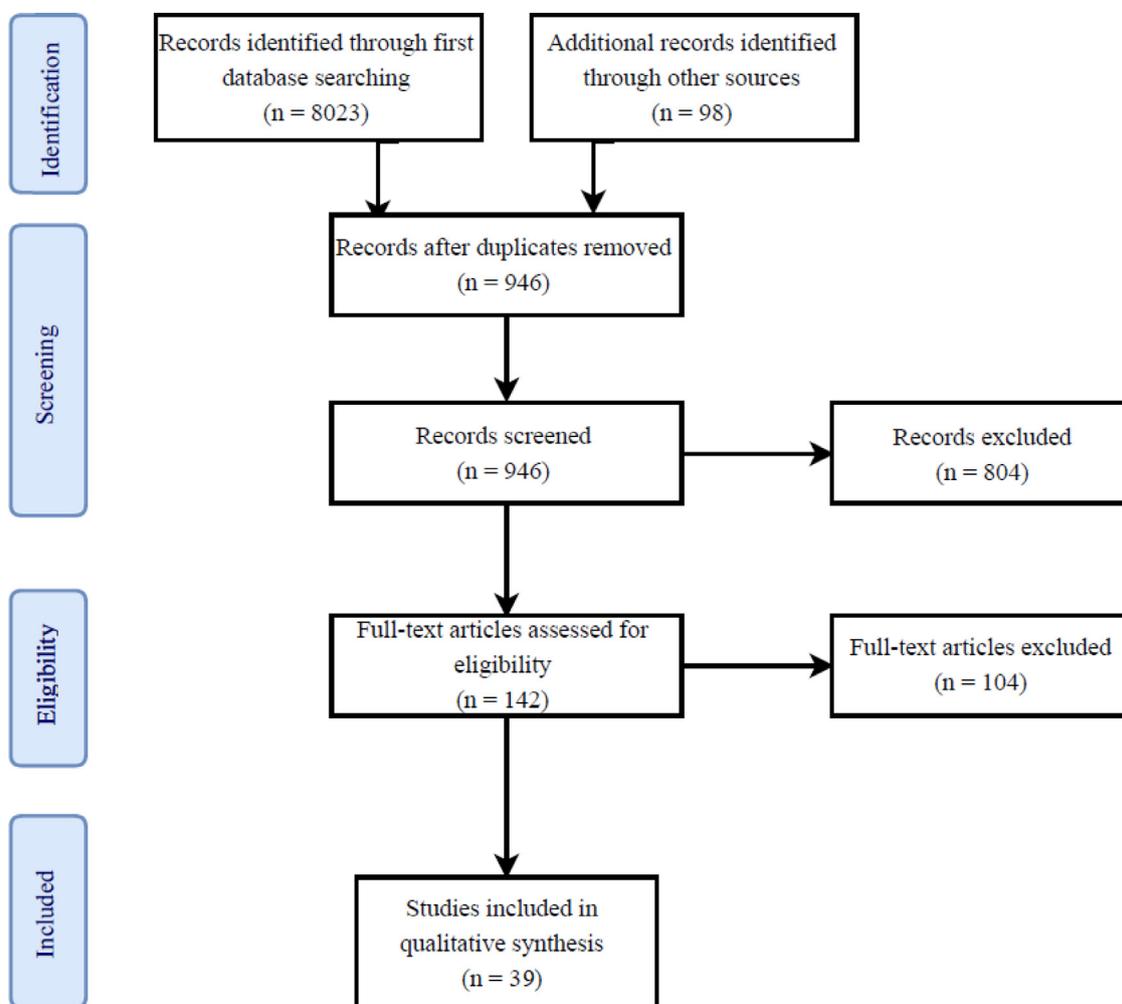


Fig. 1. Flow chart describing study selection during literature search.

Most of studies had a prospective design ($n = 27$, 69.23%) and used DSM-IV/DSM-IV-TR diagnostic criteria ($n = 18$, 46.15%).

In order to measure diagnostic stability PC was used in 32 studies (82.05%), while 15 of them also used RC (38.46%) (see Fig. 2). The proportion of diagnostic change to schizophrenia was used in 12 studies (30.76%), and in 5 of them it was the only measure of diagnostic stability. The Cohen's kappa inter-rater reliability ($n = 1$, 2.56%) and the number of diagnostic changes ($n = 1$, 2.56%) were also taken as diagnostic stability measures by one study each. We based the description of the results on the prospective and retrospective consistency, which were the most common measures of diagnostic stability. We calculated simple means and SD. Furthermore, we completed the weighted means controlled for sample size given the high variation of samples sizes across studies and within each diagnostic group (Table 2). For PC, mean, SD and weighted mean are 84.29%, 11.21% and 76.81%; for RC, 67.15%, 13.05% and 54.09%. The mean proportion of diagnostic change was 31.28% (SD 19.34). These measures were not normally distributed.

3.1. Studies focused on schizophrenia

Five studies with schizophrenia samples were selected. Results in terms of diagnostic stability are shown in Table 2. Only one of these studies used RC, whilst the majority of them used the proportion of diagnostic change to schizophrenia, being the mean, SD and weighted mean 30.5%, 20.74 and 43.48% respectively. Three of them were prospective studies, while two of them had a retrospective design.

In the study of Parnas et al. (2011), changes of diagnosis were not related with baseline socio-demographic or psychopathological variables, other studies failed to replicate this. In Dhossche and Ghani (1998) diagnostic change to schizophrenia was associated with being female sex (i.e., women were more likely to be diagnosed with schizophrenia at the second visit). Furthermore, these two authors pointed out that the consensus in the diagnosis of schizophrenia was greater for males than for females, who tended to receive an affective disorder diagnosis prior to being diagnosed with schizophrenia, which also tended to occur later (Munk-Jørgensen, 1985). On the other hand, Chen et al. (1996) observed that more subjects had a diagnostic change to schizophrenia rather than schizophrenia being ruled out, which was more likely to occur in males and those from African or American origin.

The diagnostic stability of schizophrenia was moderate in the emergency room since it was an uncommon diagnosis at first admission (Dhossche and Ghani, 1998; Munk-Jørgensen, 1985), although most of the diagnostic changes were made in the early stages (Hwu et al., 1988).

3.2. Studies focused on psychosis and psychotic episodes

The majority of the selected studies fell under this group. Most of them assessed diagnostic stability using PC ($n = 20$, 86.95%), or RC ($n = 10$, 43.47%), as shown in Table 2. The mean diagnostic change to schizophrenia was 31.9%.

Several of these studies found schizophrenia to have high diagnostic stability levels (Addington et al., 2006; Amini et al., 2005; Baldwin

Table 1
Literature review of studies examining diagnostic stability in schizophrenia.

Authors & year Studies focused in schizophrenia	N Country	Study design & Follow up Time	Inclusion criteria	Instruments	Results (%)
Munk-Jørgensen (1985)	587 Denmark	Retrospective 10.7–11.7 years	At least one diagnosis of schizophrenia	ICD-8	PC: - Men: 51.6 - Women: 54.1 RC: - Men: 71.4 - Women: 64.4
Hwu et al. (1988)	127 Taiwan	Prospective 7 years	Hospitalized Functional psychosis	IDC-9 DSM-III	Diagnostic change to schizophrenia: -ICD-9: 9.4 -DSM-III: 8
Chen et al. (1996)	936 USA	Retrospective 7 years	Diagnosis of schizophrenia Inpatients	DSM-III	Diagnostic change to schizophrenia: 32.8
Dhossche and Ghani (1998)	2212 USA	Prospective 7 months	Emergency assessments of schizophrenia	DSM-III	Diagnostic change to schizophrenia: 50
Parnas et al. (2011)	155 Denmark	Prospective 5 years	Patients diagnosed with schizophrenia in the first admission < 40 years	ICD-10	PC: 93
Studies focused in psychosis and psychotic episodes					
Chinchilla et al. (1992)	79 Spain	Prospective 46.4 months (mean)	Psychosis	ICD-9 DSM-III	Diagnostic change to schizophrenia: - ICD-9: 7.5 - DSM-III: 24
Fennig et al. (1994)	278 USA	Prospective 6 months	Hospitalized first admission patients	DSM-III-R	PC: 75.4 Diagnostic change to schizophrenia: 50
Jørgensen and Mortensen (1988)	2294 Denmark	Prospective 2 years	First admitted to a psychiatric hospital as in-patients Diagnosis of functional psychosis > 15 years	ICD-8	PC: 74.6
Amin et al. (1999)	168 United Kingdom	Prospective 3 years	Population based cohort, first contact with psychiatric services	ICD-10 DSM-III-R	PPV: - ICD-10: 83 -DSM-III-R: 82
Schwartz et al. (2000)	547 USA	Prospective 2 years	First admissions initially diagnosed with psychosis	DSM-IV	PC: 91.7 RC: 73.1
Forrester et al. (2001)	204 UK	Retrospective 1 year	> / = 2 admissions 18–55 years	ICD-9 ICD-10 DSM-III-R RDC Feighner Criteria	PC: 56.6–97.9
Amini et al. (2005)	60 Iran	Prospective 1 year	First psychostic episode inpatients 15–60 years old	ICD-10 DSM-IV	PC: - ICD-10: 100 - DSM-IV: - RC: - ICD-10: 100 - DSM-IV: 16.6
Baldwin et al. (2005)	194 Ireland	Prospective 6 months	First episode of psychosis	DSM-IV	PC: 100
Schimmelmann et al. (2005)	492 Australia	Prospective 18 months	First psychotic episode	DSM-IV	PC: 97.3 RC: 50.2
Whitty et al. (2005)	147 Ireland	Prospective 4 years	First psychotic episode	DSM-IV	PC: 96 RC: 71
Addington et al. (2006)	228 Canada	Prospective 1 year	Individuals 16–50 years old Non-affective, non-organic, first psychotic episode	DSM-IV	PC: 95 RC: 63 Diagnostic change to schizophrenia: 26
Jakobsen et al. (2007)	100 Denmark	Retrospective 1 year	Functional psychosis	ICD-10	Number of diagnostic shifts: 3
Rahm and Cullberg (2007)	146 Sweden	Prospective and retrospective 3 years	First psychotic episode 18–45 years	DSM-IV	PC: 83
Salvatore et al. (2009)	517 USA	Prospective 2 years	First psychotic episode	DSM-IV	PC: 75 Diagnosis change to schizophrenia: 12.5
Subramaniam et al. (2007)	154 Singapore	Prospective 2 years	Early psychosis diagnoses	DSM-IV	PC: 87 RC: 63.2
Haahr et al. (2008)	301 Norway and Denmark	Prospective 3 years	First psychotic episode 18–65 years	DSM-IV	PC: 85–99 Diagnostic change to schizophrenia: 72
Chang et al. (2009)	166 China	Prospective 5 years	First psychotic episode Consensus diagnosis	ICD-10	PC: 95.8 RC: 82.9
Crebbin et al. (2009)				IDC-10	

(continued on next page)

Table 1 (continued)

Authors & year Studies focused in schizophrenia	N Country	Study design & Follow up Time	Inclusion criteria	Instruments	Results (%)
Bromet et al. (2011)	62 UK	Prospective 8 years	> 16 years First episode of psychosis	DSM-III-TR DSM-IV	Diagnostic change to schizophrenia: 20 PC: 89.2 RC: 53.0
	470 USA	Prospective 10 years	Consensus diagnosis First admissions		
Kim et al. (2011)	150 Korea	Prospective 15 years	Readmissions for psychotic episodes after first hospitalization for psychotic episode	DSM-IV	Diagnostic change to schizophrenia: 32 PC: 91.3 RC: 90.3
Kingston et al. (2013)	202 Ireland	Prospective 6 years	First psychiatric episode > / = 16 years	DSM-IV	PC: 88 RC: 62
Pope et al. (2013)	214 Canada	Prospective 1 year	First psychotic episode 14–30 years	DSM-IV-TR	PC: 92.1 Diagnosis change to schizophrenia: 43.1
Heslin et al. (2015)	557 UK	Prospective 10 years	First psychotic episode	ICD-10 DSM-IV-TR	ICD-10: -PC: 75.1 -RC: 68.6 DSM-IV-TR: -PC: 72.9 -RC: 59.8
Studies focused in psychiatric disorders in general					
Tsuang et al. (1981)	525 USA	Prospective 30–40 years	Admissions to hospital after first diagnosis	Feighner criteria	PC: 92.5
Stanton and Joyce (1993)	3184 New Zealand	Retrospective 5 years	First admission 15–65 years	ICD-9	PC: 67 Diagnosis change to schizophrenia: 10–15% PC: 93
Vetter and Köller (1993)	267 Germany	Prospective 12.5 years (mean)	Inpatients Consensus diagnosis	ICD-9	PC: 73
Rabinowitz et al. (1994)	2220 Israel	Prospective 9 years	Random first admissions	ICD-9	PC: 74
Daradkeh (1996)	312 United Arab Emirates	Retrospective 4 years	In-patients > 1 admission	ICD-10	PC: 87
Daradkeh et al. (1997)	107 United Arab Emirates	Retrospective 2 years	In-patients	ICD-10	PC:
Ponizovsky et al. (2006)	10 058 (3 cohorts of 2996, 3021, 4041) Israel	Cross-sectional 14 years	Psychiatric admissions Diagnosis after discharge	ICD-9 ICD-10	- Cohort 1: 68.0 - Cohort 2: 81.6 - Cohort 3: 94.2
Woo et al. (2006)	934 USA	Retrospective 1 year	Attended in emergency service and then hospitalized	DSM-IV	k:0.5
Baca-Garcia et al. (2007)	10 025 Spain	Prospective 12 years	> 18 years Assessed at least 10 times in multiple psychiatric settings	ICD-10	PC: 69.6 RC: 45.9
Kim et al. (2011)	472 Korea	Retrospective 2 years	Admitted to psychiatric ward Diagnosis after discharge	DSM-IV	PC: 86.9 RC: 75
Atwoli et al. (2012)	114 Kenya	Cross-sectional descriptive Turnaround time during 5 months	In-patients (at least one previous hospital stay)	DSM-IV-TR	PC: 75.9 RC: 87.2

SCZ: Schizophrenia. DSM-IV-TR: Diagnostic and Statistical Manual of Mental Disorders Text Revision. ICD-10: The International Classification of Diseases. PC: Prospective Consistency. RC: Retrospective Consistency. PPV: Positive Predictive Value. RDC: The Research Diagnostic Criteria.

et al., 2005; Bromet et al., 2011; Chang et al., 2009; Chinchilla et al., 1992; Fennig et al., 1994; Haahr et al., 2008; Heslin et al., 2015; Kim et al., 2011; Pope et al., 2013; Rahm and Cullberg, 2007; Salvatore et al., 2009; Schimmelmänn et al., 2005; Schwartz et al., 2000; Subramaniam et al., 2007; Whitty et al., 2005), concluding that schizophrenia was a generally stable diagnosis (Kingston et al., 2013).

Those less likely to change a diagnosis of schizophrenia were women (Salvatore et al., 2009) and were significantly older than those with a diagnosis change (Addington et al., 2006); they had a longer duration of untreated psychosis (DUP) (Addington et al., 2006), and they were older age at study inception when there was a gradual onset (Addington et al., 2006; Salvatore et al., 2009). Also, these subjects had the longest length of hospitalization (Subramaniam et al., 2007).

The relationships between diagnostic stability and family history of mental illness and global assessment of functioning (GAF) were not significant, although they showed a trend (Jakobsen et al., 2007).

Lower GAF disability scores were associated with diagnostic stability in another study (Subramaniam et al., 2007). Diagnostic instability was associated with an initial unconfirmed diagnosis, initial non-affective disorders and auditory hallucinations at first presentation (Salvatore et al., 2009).

Also, the majority of diagnostic shifts resulted in a diagnosis of schizophrenia (Addington et al., 2006; Bromet et al., 2011; Chang et al., 2009; Chinchilla et al., 1992; Crebbin et al., 2009; Fennig et al., 1994; Forrester et al., 2001; Heslin et al., 2015; Pope et al., 2013; Salvatore et al., 2009; Schimmelmänn et al., 2005; Schwartz et al., 2000; Subramaniam et al., 2007). Moreover, Jørgensen and Mortensen pointed out that the number of patients diagnosed with schizophrenia increased at readmissions (Jørgensen and Mortensen, 1988). Other studies failed to find associations between stability and socio-demographic characteristics (Amin et al., 1999; Chang et al., 2009). Nevertheless, males (Haahr et al., 2008; Heslin et al., 2015), young age, black

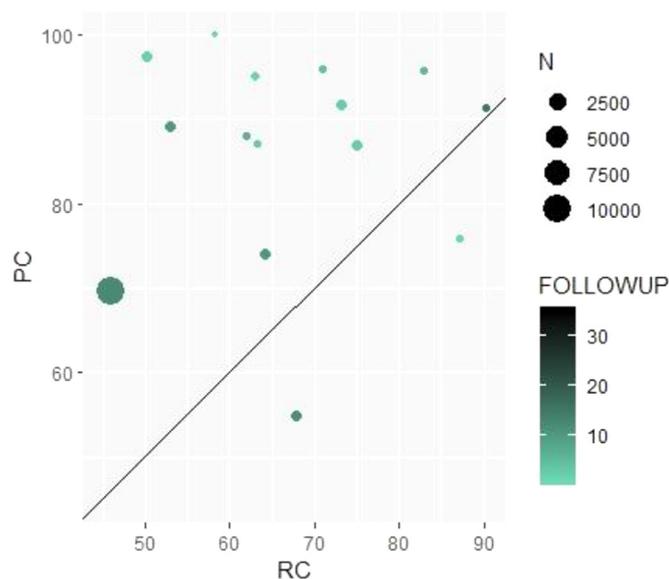


Fig. 2. Correlations between RC and PC in studies that calculated both variables. The oblique line corresponds with PC=RC, that is, if a point is above, then the study has PC>RC (stable and accumulating diagnosis), and the farther from the line the bigger the difference (PC-RC). We can see that the most common scenario corresponds with PC close to 90% and much bigger than RC (these are the points in the upper left corner. Low RC suggests that a significant number of patients may be diagnosed at baseline). Notice that the exceptions can be explained because the follow-up is particularly big (both PC and RC are close to 90%) (Kim et al., 2011) or the size is specially big (size approx. 10 000) (Baca-Garcia et al., 2007).

Table 2
Main results for diagnostic stability by group of studies and in global.

Studies focused in	Schizophrenia	Psychotic Episodes	General Psychiatric disorders	Global
PC				
Mean (%)	72.93	87.86	80.22	84.29
SD	28.38	8.83	10.22	11.21
Weighed mean (%)	61.25	83.20	75.48	76.81
RC				
Mean (%)	–	66.47	69.37	67.15
SD	–	12.09	21.22	13.05
Weighed mean (%)	–	64.04	47.64	52.09

SCZ: Schizophrenia. PC: Prospective Consistency. RC: Retrospective Consistency. SD: Standard Deviation.

Africans, being single (Heslin et al., 2015) and more academically and socially impaired at baseline (Bromet et al., 2011; Haahr et al., 2008; Heslin et al., 2015; Schimmelmann et al., 2005; Schwartz et al., 2000; Whitty et al., 2005) predicted a change of diagnosis to schizophrenia.

Longer duration of the initial episode and longer hospital stay were also associated with a change of diagnosis (Amin et al., 1999; Crebbin et al., 2009; Schwartz et al., 2000). However, mixed results were reported regarding DUP, which was the only predictor of a diagnosis shift in one study (Subramaniam et al., 2007). A diagnostic change towards schizophrenia was linked with longer DUP (Haahr et al., 2008; Heslin et al., 2015; Schwartz et al., 2000), although one study failed to replicate this (Chang et al., 2009). With regard to the effects of early substance abuse on diagnostic stability overall findings were inconclusive (Schwartz et al., 2000; Whitty et al., 2005).

Other factors associated with diagnostic shift towards schizophrenia

were family history of psychotic illness (Chang et al., 2009); use of antipsychotics (Bromet et al., 2011; Schwartz et al., 2000); more negative symptoms and reality distortion (Bromet et al., 2011; Heslin et al., 2015; Schwartz et al., 2000) and psychopathological severity (Haahr et al., 2008; Schimmelmann et al., 2005; Whitty et al., 2005).

However, being diagnosed with bipolar disorder and having manic (Heslin et al., 2015) or depressive symptoms (Bromet et al., 2011) were associated with an unchanged diagnosis.

3.3. Studies focused on psychiatric disorders in general

Eleven selected studies reported on psychiatric disorders and diagnosis change towards schizophrenia, which was measured by PC except in one study, which used the Cohen’s Kappa inter-rater reliability (Woo et al., 2006).

Schizophrenia was found to be one of the most stable diagnosis (Daradkeh, 1996; Ponizovsky et al., 2006; Rabinowitz et al., 1994; Stanton and Joyce, 1993; Tsuang et al., 1981; Vetter and Köller, 1993; Woo et al., 2006), and stability tended to increase over time (Atwoli et al., 2012; Daradkeh et al., 1997).

In this group, the clinical setting predicted diagnostic stability, which was greater in in-patient settings (Baca-Garcia et al., 2007; Woo et al., 2006) and in those subject to legal restrictions, while it was lower in those with medical comorbidities (Woo et al., 2006). A baseline diagnosis of “schizophrenic” psychosis and prior hospitalization (Vetter and Köller, 1993) but not the number of previous admissions (Kim et al., 2011) increased the diagnostic stability of schizophrenia.

Although older age was associated with a less likely diagnostic change (Rabinowitz et al., 1994; Stanton and Joyce, 1993), there were no differences in age of onset (Kim et al., 2011). Sex had little effect on stability (Kim et al., 2011; Stanton and Joyce, 1993) and it was not related to diagnostic subtype, symptom severity or family history of psychiatric illness (Kim et al., 2011). Even though duration of course is a diagnostic criteria in schizophrenia (Vetter and Köller, 1993), stability was not affected by the duration of the illness (Kim et al., 2011).

On the other hand, instability was linked with a “first” diagnosis of schizophrenia within 1–2 months following a readmission (Stanton and Joyce, 1993); and a transfer of care during the inpatient episode (Stanton and Joyce, 1993).

The diagnostic change to schizophrenia was more common from affective psychosis (10–15%) (Stanton and Joyce, 1993) or delusional psychosis (Ponizovsky et al., 2006) than from all other diagnoses.

4. Discussion

We investigated diagnostic stability of schizophrenia on previous literature by conducting a systematic review, which included 39 studies and 39 965 participants. Overall, diagnostic stability of schizophrenia was found to be high (approximately 70–90%), although first presentation with psychosis was linked with increase diagnostic instability, as expected. These considerations suggest the need for better monitoring of these patients upon initial diagnosis (Nicholl et al., 2010), which may have implications on clinical management plans (Flaum et al., 1992), patient outcomes and service provision (Whitty et al., 2005).

Compared to other psychotic and non-psychotic psychiatric diagnostic categories, schizophrenia shows the highest rate of diagnostic stability in the majority of studies, or at least it is among the most stable diagnoses (Daradkeh, 1996; Ponizovsky et al., 2006; Rabinowitz et al., 1994; Salvatore et al., 2009; Stanton and Joyce, 1993; Tsuang et al., 1981; Vetter and Köller, 1993; Woo et al., 2006), which replicate the results of a recent meta-analysis on this topic (Fusar-Poli et al., 2016). This may have reflected some over-diagnosis of schizophrenia (Atwoli et al., 2012) and the schizophrenia diagnosis criteria themselves, though it could rather show that diagnosis criteria for schizophrenia are accurate, well known and established.

Interestingly, diagnostic stability is not commonly researched in other areas of medicine, although diagnostic stability of dementia was estimated at approximately 90% (Koepsell et al., 2013), with a 26.6% of diagnostic change for dementia (De Moraes and Bertolucci, 2017), which increased up to 45–67% for cognitive impairment (Anstey et al., 2013; Brodaty et al., 2012; Loewenstein et al., 2009), hence comparable with the diagnostic stability of schizophrenia.

4.1. Diagnostic stability in terms of PC and RC

There are no established criteria for diagnostic stability. The majority of the selected studies used PC and RC, and the proportion of diagnostic change, and more rarely the Cohen's Kappa inter-rater reliability. Although there was heterogeneity, most of the selected studies showed schizophrenia to have high diagnostic stability, in the line with our hypotheses (Addington et al., 2006; Amini et al., 2005; Daradkeh, 1996; Fennig et al., 1994; Kim et al., 2011; Pope et al., 2013; Schimmelmann et al., 2005; Schwartz et al., 2000; Stanton and Joyce, 1993; Woo et al., 2006).

The mean PC and RC were 84.29% (SD 11.21) and 67.15% (SD 13.05), respectively, with weighted means 76.81% and 54.09%, which shows that schizophrenia diagnoses tend to remain stable over the follow-up and that initial diagnoses of schizophrenia were relatively accurate (see Fig. 2). In the frame of clinical staging models (McGorry et al., 2006; Wood et al., 2011), lower RC may indicate that in early stages, symptomatology is mainly unspecific, and so it is expected to evolve as the illness does (Fusar-Poli et al., 2017; Millan et al., 2016). Thus, the change in diagnosis might be a part of the disorder rather than a flaw in diagnostic criteria and current taxonomies.

Diagnostic stability was found to be associated with: male sex (Dhossche and Ghani, 1998), older age (Addington et al., 2006; Rabinowitz et al., 1994), older age at onset (Addington et al., 2006), late stages of illness (Hwu et al., 1988), a family history of mental illness (Chang et al., 2009; Hwu et al., 1988), lower GAF (Jakobsen et al., 2007; Subramaniam et al., 2007) and longer hospitalization (Subramaniam et al., 2007). Also, the in-patient setting was linked with higher diagnostic stability (Baca-Garcia et al., 2007). However, the above relationships may be due to tautological issues since the diagnosis of schizophrenia in the clinical setting is commonly based on the presence of such factors. Regarding DUP, overall results were mixed, with both longer (Addington et al., 2006; Haahr et al., 2008) and shorter DUP (Chang et al., 2009; Subramaniam et al., 2007) being associated with increased diagnostic stability, which also increased over time (Daradkeh, 1996). In terms of sex, women tended to receive diagnosis of schizophrenia later (Munk-Jørgensen, 1985). In addition, at longer duration of the initial episode (Amin et al., 1999) and the presence of medical comorbidities (Woo et al., 2006) were related to diagnostic instability.

With regard to a diagnostic change to schizophrenia, being male (Chen et al., 1996; Haahr et al., 2008; Heslin et al., 2015; Salvatore et al., 2009), younger age (Salvatore et al., 2009), an African or American origin (Chen et al., 1996; Heslin et al., 2015), number of hospitalizations (Crebbin et al., 2009; Jakobsen et al., 2007), and days in hospital (Crebbin et al., 2009; Schwartz et al., 2000), poorer functioning as measured by the GAF (Bromet et al., 2005), less severe depressive symptoms (Bromet et al., 2005) and more significant negative symptoms (Bromet et al., 2005; Heslin et al., 2015; Schwartz et al., 2000), receiving antipsychotic treatment (Bromet et al., 2005; Schwartz et al., 2000), the first years of the illness (Haahr et al., 2008), poorer baseline functioning (Haahr et al., 2008; Heslin et al., 2015; Schwartz et al., 2000; Whitty et al., 2005) and symptomatic severity (Haahr et al., 2008; Whitty et al., 2005) made such change more likely. Two studies reported on the relationship between early substance abuse and diagnostic stability of schizophrenia, with conflicting findings (Schwartz et al., 2000; Whitty et al., 2005).

4.2. Study limitations

Although the results of the study do not differ from those found on previous literature, they reflect the relevant between-studies methodological differences, namely study design, sample size and population of origin, number of assessments over the study period, duration of follow-up, scales and instruments used, diagnosis criteria and statistical analysis, which hinder for direct comparisons. In addition, the cultural differences of the populations of the studies need to be considered when interpreting the results.

Measures of diagnostic change to or from schizophrenia is neglected in most of the studies. Factors associated with diagnostic shift, specially towards schizophrenia should be examined as it could be of real interest in the assessment of first psychotic episodes.

It is also remarkable that the number of studies focused on schizophrenia ($n = 5$, 12.8%) is limited, being less numerous than in the other groups.

4.3. Conclusion

Schizophrenia was found to be one of the most stable diagnosis (Daradkeh, 1996; Fusar-Poli et al., 2016; Rabinowitz et al., 1994; Stanton and Joyce, 1993; Tsuang et al., 1981; Vetter and Köller, 1993; Woo et al., 2006), and stability tended to increase over time (Daradkeh et al., 1997). On the other hand, factors related to longer and better assessment of patients (such as in-patient setting, longer duration of stay, number of hospitalizations, later stages of illness) led to a more accurate and stable diagnosis from early stages of the illness. Consequently, making an early precise diagnosis remains a goal yet to be achieved in the clinical practice.

Diagnostic stability of schizophrenia was found to be very high (Addington et al., 2006; Amini et al., 2005; Baldwin et al., 2005; Bromet et al., 2011; Chang et al., 2009; Chinchilla et al., 1992; Daradkeh, 1996; Fennig et al., 1994; Fusar-Poli et al., 2016; Haahr et al., 2008; Heslin et al., 2015; Kim et al., 2011; Pope et al., 2013; Rabinowitz et al., 1994; Rahm and Cullberg, 2007; Stanton and Joyce, 1993; Subramaniam et al., 2007; Tsuang et al., 1981; Vetter and Köller, 1993; Woo et al., 2006), particularly when compared to other psychiatric disorders. However, consensus criteria for diagnostic stability and validated tools for its measurement are needed, which may lead to further research on this topic. Specifically, longitudinal first-episode psychosis studies are warranted to better understand diagnostic changes from early stages of the psychotic illness and their contributing factors, thus improving patient clinical outcomes via preventing adverse effects of misdiagnosis.

Conflict of interest

The authors declare there are no conflict of interest in the making of this work.

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