Diagnostic Stability of Functional Psychosis: a Systematic Review

功能性精神病診斷穩定性分析的系統評價

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Abstract

Objective: Stability of diagnosis is one measure of predictive validity for psychiatric syndromes. It is an under-studied area despite its clinical and research implications. This report aimed to critically review the literature concerning diagnostic stability in functional psychosis.
Methods: Articles concerned with evaluating the diagnostic stability of functional psychosis and factors associated with diagnostic change were reviewed.
Results: Despite methodological variation, schizophrenia was found to be the most stable diagnosis followed by affective psychosis. Other psychotic disorders were diagnostically unstable over time. Around one-fifth of patients with first-onset psychosis had their diagnoses revised at follow-up. Diagnostic change occurred early in the course of the psychotic illness. The major pattern of diagnostic shift was towards schizophrenia spectrum disorders, particularly schizophrenia. Few variables were identified as predictors of such diagnostic conversion and the evidence established thus far is inconclusive.
Conclusions: The present analysis indicates that diagnostic uncertainty and temporal instability is common in the early phase of psychosis especially in less prevalent diagnostic categories. It also highlights the limitations of the contemporary nosological classification in functional psychosis. In the absence of biological markers, a diagnostic process taking into account longitudinal observations across consecutive episodes should be a major requirement for making a definitive diagnosis.

Key words: *Diagnosis, differential; Early diagnosis; Follow-up studies; Psychotic disorders*

摘要

目的：診斷穩定性可量度精神病綜合症的預測效度。雖然有著臨床應用和研究的重要性，診斷穩定性這範疇卻很少被探討。本文回顧有關功能性精神病診斷穩定性的文獻。
方法：搜集並回顧關於功能性精神病診斷穩定性的分析，及與診斷改變的因素有關的文獻。
結果：撇除方法學上的差異，診斷穩定性最高的仍是精神分裂症，其次為情感性精神病。至於其他精神病，診斷會隨著時間改變。約有五份之一的首發精神病患者在隨訪時會有診斷上的改變。而診斷的改變只會在精神病的初期進化過程中出現。診斷改變主要朝向精神分裂症譜系障礙，尤其是精神分裂症。很少能夠確認診斷改變的預測因素，而可見的實證亦缺乏結論性。
結論：本分析顯示早期精神病普遍會出現不確定和隨時間不穩定的診斷，尤其發生在一些較少見的精神病中。本分析亦顯示功能性精神病現代等級分類的不足。在缺乏生物學指標的情況下作出肯定的診斷，必須要對連續發作的精神病作一個長期的觀察研究。

關鍵詞：*鑒別診斷、早期診斷、隨訪研究、精神病*

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Introduction

Diagnosis is regarded as a sine qua non for clinical practice and research.[1] It provides information about patients' symptom profiles, prognosis, treatment outcomes and sets the boundaries for research through delineating homogeneous patient groups.[2] Unlike other branches in medicine where there is better understanding of the underlying biological processes, in psychiatry the diagnoses are still based on identification of clinical syndromes. The introduction of

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explicit operational criteria and rule-based classifications significantly improved diagnostic agreement.[3] Nevertheless, adequate diagnostic reliability does not necessarily provide information about the construct of disorders.[4] Owing to the lack of objective measurements for making definitive diagnoses, operationalised diagnoses should therefore be regarded as provisional and the validity of the diagnoses of psychotic disorders incorporated by the contemporary classifications cannot be taken for granted.[3,5]

It is stated that a valid diagnostic category should be defined by more fundamental characteristics such as physiological, pathological, or genetic abnormalities.[3] In the absence of clinicopathological correlates, it is difficult to verify psychiatric syndromes.[6] Outcome has been regarded as the most important and the most widely applicable criterion of validity in the context of clinical psychiatry.[7] Stability of diagnosis over time, being an outcome measure, has been postulated as one criterion for diagnostic validity[8,9] as it is the measure of the degree to which a diagnosis remains the same at subsequent evaluations.[10] It is assumed that the more stable the diagnosis, the more likely it is to reflect a basic and consistent psychopathological or pathophysiological process and is hence more valid.[11]

Diagnostic revision can be attributable to a change in the clinical picture and methodological artifacts such as information variance, unreliable assessment, inconsistent application of diagnostic criteria, and low inter-rater reliability.[12] In most epidemiological studies, a subject's lifetime diagnosis for longitudinal outcome analysis is usually based on the cross-sectional diagnosis derived from a baseline assessment.[13] Yet it is known that any given patient's diagnosis can change over time.[14,15] Longitudinal diagnostic instability thus raises concerns regarding the validity of research into aetiology, genetics, prognosis, and treatment efficacy.[16] Clinically, diagnostic misclassification can lead to iatrogenic effects through inappropriate treatment recommendations.[17]

Given the clinical and research significance of diagnostic instability, along with its relevance to the nosological framework of functional psychosis, we performed a systematic review of the literature with an aim to evaluate: (1) the diagnostic stability of functional psychotic disorders; (2) patterns of diagnostic shift among various categories of functional psychosis; and (3) factors associated with diagnostic instability. We will also discuss methodological variations in current research on diagnostic stability and suggest strategies for future research.

Methods

A literature search was conducted using the Medline computerised database to identify relevant English-language articles published from 1 January 1980 to 31 October 2008. Keywords used as search terms included: diagnostic stability, temporal stability, diagnostic consistency, AND psychotic disorder, functional psychosis, first-episode psychosis. Citations within identified papers were included as additional sources. Earlier studies conducted before the introduction of operational diagnostic criteria were excluded from the review as the results of these studies were confounded by inconsistent diagnostic formulation with low reliability.[11] Studies that only focused on child and adolescent samples were also excluded.[18-21] We also excluded two other studies which measured diagnostic agreement between those assigned in an emergency setting and structured interview-derived diagnoses[22] or inpatient discharge diagnoses.[23] These studies evaluated the reliability of diagnostic procedures conducted in emergency settings rather than diagnostic stability per se.

A total of 35 publications were selected for review. Tables 1 and 2 summarise their key features.

Results

Methodological Considerations

Methodological heterogeneity was observed with respect to subject collection, diagnostic scope, sample size, diagnostic assignment, and time intervals studied (Table 3). Sample selection and diagnostic ascertainment are the two fundamental issues affecting evaluation of the results of diagnostic stability. Methodologies affecting these two aspects varied widely and are discussed in detail below.

Sample Selection

Re-admission Versus First-episode Sample

Many studies recruited subjects from re-admission samples, making such studies limited by the bias inherent in sampling rehospitalised patients. These patients were much more likely to have established chronic illnesses, causing an overestimation of diagnostic stability.[24] It is postulated that the first few years following the onset of psychosis are the critical period in illness evolution.[25] Studying first-episode cohorts allows researchers to capture the true diversity in the course of functional psychosis from the onset. It also ensures relative homogeneity within the sample with respect to illness chronicity and treatment exposure.[26] Nevertheless, it should be noted that a "first-admission" sample is not synonymous with a "first-episode" sample. The former excludes subjects with less severe first psychotic episodes that did not require hospitalisation. Using a cohort of first presentation for treatment, i.e. "first contact to treatment" sample is less biased and thus more representative of patients with first-onset psychosis.[27]

Diagnostic Scope

Some studies only focused on non-affective psychosis.[28] As there is significant overlap between affective and psychotic symptoms in the early phase of illness,[11] exclusion of affective psychosis can introduce bias by automatically removing from the study analysing those who might have their baseline diagnosis of affective disorder reclassified at follow-up. Another sampling bias arises from the exclusion of patients with comorbid substance abuse. Concomitant substance use is frequently observed among patients presenting for treatment with psychosis.[29] It has

Table 1. Studies on diagnostic stability of functional psychosis: non–first episode studies.[10,14-16,32,35-45]

Study	Diagnostic criteria	Design	Source of subjects	Age range (years)	Duration of follow-up
Tsuang et al,[32] 1981; Iowa, US	Feighner criteria	Historical prospective cohort	Re-admission sample	Not reported	30 to 40 years
Munk-Jorgensen,[35] 1985; Denmark	ICD-8	Retrospective cohort	Re-admission sample	Not reported	Within 11-year period
Jorgensen & Mortensen,[36] 1988	ICD-8	Retrospective cohort	Re-admission sample	Not reported	2 years
Marneros et al, 1988,[37] 1991[14]; Cologne, Germany	DSM-III (slightly modified)	Historical prospective cohort	Inpatient sample with subsequent outpatient follow-up data	Not reported	Mean follow-up: 25.2 years
Hollister,[38] 1992; Houston, US	DSM-IIIR	Retrospective cohort	Re-admission sample; at least 4 admissions	16-73	Within 3-year period
Vetter & Köller,[39] 1992; Kiel, Germany	ICD-9	Historical prospective cohort	Re-admission sample	Not reported	Mean follow-up: 12.5 years
Stanton & Joyce,[10] 1993; New Zealand	ICD-9	Retrospective cohort	Re-admission sample	15-65	5 years
Rabinowitz et al,[40] 1994; Israel	ICD-9	Retrospective cohort	Re-admission sample	Not reported	Mean follow-up: 2.2 years
Chen et al,[15] 1996; Houston	DSM-IIIR	Retrospective cohort	Re-admission sample; at least 4 admissions	Not reported	Within 7-year period
Daradkeh et al,[41] 1997; United Arab Emirates	ICD-10	Retrospective cohort	Re-admission sample	Not reported	Within 2-year period
Huguelet et al,[42] 2001; Geneva, Switzerland	DSM-IIIR	Retrospective cohort	Re-admission sample	Not reported	Within 45-month period
Forrester et al,[43] 2001; Edinburgh	DSM-IIIR ICD-10 RDC Feighner criteria	Retrospective cohort	Re-admission sample	18-55	In 2-year period
Marneros et al,[45] 2003; Halle, Germany	ICD-10	Prospective cohort	Inpatient sample incorporating subsequent outpatient follow-up data	Not reported	Mean follow-up: 4.7 years
Baca-Garcia et al,[16] 2007; Madrid, Spain	ICD-10	Retrospective cohort	Inpatient, outpatient, and emergency settings	18 or above	Inpatient and emergency setting sample: within 4-year period Outpatient sample: within 12-year period
Craig et al,[44] 2007; WHO study 4 Independent cohorts involving 18 regions: IPSS (3) DOSMeD (9) RAPyD (3) Invited cohort (3)	ICD-10	Mixture of prospective and historical prospective cohorts	Both prevalence and incidence samples IPSS included psychosis at various stages of illness; RAPyD excluded affective psychosis; Iivited cohort included SCZ only	Varied among cohorts	12 - 26 years

Abbreviations: *ATPD = acute and transient psychotic disorders; BPD = bipolar affective disorder; DEP = depressive disorder; DOSMeD = Determinants to Outcome of Severe Mental Disorders; DSM = Diagnostic and Statistical Manual of Mental Disorders; ICD = International Classification of Disease; IPSS = International Pilot Study of Schizophrenia; NOS = not otherwise specified; PSE = Present State Examination; RAPyD = Reduction and Assessment of Psychiatric Disability; RDC = Research Diagnostic Criteria; SAD = schizoaffective disorder; SCAN = Schedules for Clinical Assessment in Neuropsychiatry; SCZ = schizophrenia.*

Sample size	Methods of diagnostic assignment	Results
445	Initial diagnosis: based on medical notes Lifetime diagnosis: based on medical notes +/- single follow-up structured interview (Iowa structured interview) Consensus diagnosis was determined involving at least two psychiatrists who assigned a diagnosis to each subject independently and were blind to the initial diagnosis	Prospective consistency* (with interview) SCZ 92.5%, BPD 56%, DEP 62.9% Prospective consistency (medical notes only) SCZ 96.3%, BPD 80.4%, DEP 84.3%
587	Case register	Prospective consistency SCZ (male) 73.6%, SCZ (female) 71.2%
1136	Case register	Prospective consistency SCZ 74.6%, BPD 72.9%, paranoia 48.3%
355	Initial diagnosis: based on medical notes Lifetime diagnosis: based on medical notes and single follow-up structured interview (PSE) Consensus diagnosis was determined by two psychiatrists including one interviewer	Prospective consistency SCZ 90%, SAD 54%, BPD 62%, DEP 79%
162	Case register	Prospective consistency SCZ 45.8%, BPD 52.2%
267	Initial diagnosis: based on medical notes Lifetime diagnosis: based on medical notes +/- single follow-up personal interview Both initial and lifetime diagnoses were made by single psychiatrist	Prospective consistency SCZ 93%, affective psychosis 58%
3184	Case register	Prospective consistency SCZ 67%, affective psychosis 53%, other psychosis 22%
2200	Case register	Prospective consistency SCZ 73%, affective disorder 66.2%, paranoid disorder 43.6%, other psychosis 30.3%
934	Case register	Prospective / retrospective† consistency SCZ 78.1% / 47.3%
107	Case register	Prospective consistency SCZ 87%, BPD 87%, DEP 73%, paranoid disorder 50%
1443	Case register	Prospective consistency SCZ 72.7%, SAD 57.4%, delusional disorder 75.7%, brief reactive psychosis 60.9%, psychosis NOS 49.2%, BPD 75.5%, DEP 60.3%
204	Initial diagnosis: based on structured interview (SCAN) Final diagnosis: based on medical notes and 2 follow-up structured interviews (2.2 and 4.7 years after initial assessment) Consensus diagnosis was determined	Prospective consistency (consecutive admissions) SCZ 58-98%, SAD 5-39%, affective psychosis 24-83%
39		Prospective consistency ATPD 53.9%
10025	Case register	Prospective consistency (overall / inpatient) SCZ 69.9% / 90.9%, BPD 49.9% / 91.5%, DEP 40.3% / 66.7% Retrospective consistency (overall / inpatient) SCZ 45.9% / 91.5%, BPD 38.1% / 89.3%, DEP 40.4% / 100%
1043	Initial diagnosis (invited cohort): based on medical notes and past PSE data Initial diagnosis (3 other cohorts): based on PSE Final diagnosis: based on PSE at follow-up +/- medical notes Invited cohort: 1 follow-up assessment at 15th year Other cohorts: 3 follow-up assessments at 1st, 2nd and final year (longest interval up to 26 years) Consensus diagnostic procedure was not applied in all cohorts	Prospective consistency (total sample) SCZ 86.6%, SAD 33.9%, acute schizophrenia 20%, affective psychosis 76.1%

* *Prospective consistency: the proportion of subjects in a category at baseline assessment who retained the same diagnosis at the end of follow-up (positive predictive value).*

† *Retrospective consistency: the proportion of subjects with a given diagnosis at the end of follow-up who had received the same diagnosis at baseline assessment (sensitivity).*

Table 2. Studies on diagnostic stability of functional psychosis: first-episode studies.[6,11-13,17,28,46-58]

Study	Diagnostic criteria	Design	Source of subjects	Age range (years)	Duration of follow-up	Sample size
Beiser et al,[12] 1989; Vancouver, Canada	DSM-III ICD-9 RDC Feighner criteria	Prospective cohort	First contact to treatment sample	15-54	18 months	129
Lenz et al,[46] 1991; Vienna	DSM-IIIR ICD-9 RDC	Prospective cohort	First-admission sample	Not reported	7 years	186
Fennig et al,[11] 1994; New York, US	DSM-IIIR	Prospective cohort	First-admission sample	15-60	6 months	278
Mason et al,[6] 1997 Nottingham, UK	DSM-IIIR ICD-10	Historical prospective cohort	First contact to treatment sample	15-54	13 years	86
Jorgensen et al,[56] 1997; Risskov, Denmark	ICD-10	Prospective cohort	First-admission sample	18-65	1 year	51
Goater et al,[47] 1999; North London	ICD-9	Prospective cohort	First contact to treatment sample	16-54	5 years	85
Amin et al,[48] 1999; Nottingham, UK	DSM-IIIR ICD-10	Prospective cohort	First contact to treatment sample	16-64	3 years	166
Schwartz et al,[13] 2000; New York, US	DSM-IV	Prospective cohort	First-admission sample	15-60	2 years	547
Zarate Jr. et al,[55] 2000; Boston, US	DSM-IV	Prospective cohort	First-admission sample	18 or above	2 years	30
Sajith et al,[57] 2002; Pondicherry, India	ICD-10	Prospective cohort	First contact to treatment sample	15-60	3 years	45
Veen et al,[49] 2004; Hague, Netherlands	DSM-IV	Prospective cohort	First contact to treatment sample	15-54	30 months	168
Baldwin et al,[50] 2005; Cavan-Monaghan, Ireland	DSM-IV	Prospective cohort	First contact to treatment sample	16 or above	6 months	194
Whitty et al,[51] 2005; Dublin, Ireland	DSM-IV	Prospective cohort	First contact to treatment sample	Not reported	4 years	147
Schimmelmann et al,[17] 2005; Melbourne, Australia	DSM-IV	Retrospective cohort	First contact to treatment sample	15-29	18 months	492
Amini et al,[52] 2005; Tehran, Iran	DSM-IV ICD-10	Prospective cohort	First-admission sample	15-60	1 year	48
Addington et al,[28] 2006; Toronto, Canada	DSM-IV	Prospective cohort	First contact to treatment sample	16-50	1 year	228

Methods of diagnostic assignment	Results
Diagnoses were based on medical notes +/- structured interview (PSE) Consensus diagnosis was determined No independent diagnostic assignment 2 Follow-up assessments at 9th and 18th month	Diagnostic consistency* SCZ 30-80%, SAD (RDC) 10%, ScF (DSM-III) 22.6%, BPD 20%, DEP 5-10%
Diagnoses were based on medical notes +/- structured interview (PSE) Not consensus diagnosis 1 Follow-up assessment at 7th year	Prospective consistency† SCZ 77-86.4%, SAD 16.7-84.4%, ScF (DSM-III) 3.4%, affective psychosis 67.1-76%, paranoid disorder 31.6-57.1%
Diagnoses were based on medical notes +/- structured interview (SCID) Consensus diagnosis was determined Independent diagnostic assignment by 2 psychiatrists 1 Follow-up assessment at 6th month	Prospective / retrospective‡ consistency SCZ 75.4% / 75%, SAD 61.5% / 38.1%, ScF 63.6% / 87.5%, BPD 85.7% / 81.9%, DEP 80% / 75.5%, delusional disorder 50% / 100%
Initial diagnosis: retrospectively diagnosed based on medical notes and past PSE data (13 years before index assessment) Lifetime diagnosis: based on medical notes and structured interview (PSE) Both initial and lifetime diagnoses were determined by same rater Not consensus diagnosis 1 Assessment was conducted (13-year interval)	DSM-IIIR prospective / retrospective consistency SCZ 100% / 60.8% ICD-10 prospective / retrospective consistency SCZ 88.6% / 92.7%
Diagnoses were based on medical notes +/- interview according to Operational Criteria System Not consensus diagnosis	Prospective consistency ATPD 52%
Diagnoses were based on medical notes +/- structured interview (PSE) Consensus diagnosis was determined No independent diagnostic assignment 2 Follow-up assessments at 1st and 5th year	Prospective / retrospective consistency SCZ 97.1% / 61.8%
Diagnoses were based on medical notes +/- structured interview (SCAN) Consensus diagnosis was determined No independent diagnostic assignment 1 Follow-up assessment at 3rd year	Prospective consistency (DSM-IIIR / ICD-10) SCZ 83% / 82%, SAD 33% / 20%, ScF 10% (DSM-IIIR only), BPD 78% / 91%, DEP 70% / 65%, delusional disorder 39% / 39%, brief psychosis disorder / ATPD 8% / 37%
Diagnoses were based on medical notes and structured interview (SCID) Consensus diagnosis was determined Independent diagnostic assignment by 2 psychiatrists 2 Follow-up assessments at 6th & 24th month	Prospective / retrospective consistency SCZ 91.7% / 73.1%, SAD 36.4% / 44.4%, ScF 54.6% / 85.7%, BPD 83% / 84.8%, DEP 73.8% / 81.7%, delusional disorder 66.7% / 50%, brief psychosis disorder 27.3% / 50%, psychosis NOS 44% / 47.8%
Diagnoses were based on structured interview (SCID) Not consensus diagnosis 1 Follow-up assessment at 24th month	Prospective consistency SCZ 100%, ScF 0%
Diagnoses were based on medical notes and personal interview Consensus diagnosis was determined No independent diagnostic assignment 4 Follow-up assessments at 1st, 3rd, 6th, and 36th month	Prospective consistency APPD 73.3%
Diagnoses were based on medical notes +/- structured interview (CASH) Consensus diagnosis was determined No independent diagnostic assignment 1 Follow-up assessment at around 30th month	Prospective consistency SCZ 91%, ScF 17%, affective psychosis 67%, brief psychosis disorder 38%
Initial diagnosis: based on structured interview (SCID) Final diagnosis: based on medical notes and intake SCID data Consensus diagnosis was ascertained only when diagnostic uncertainty arose after review by single rater No follow-up structured interview conducted	Prospective consistenc SCZ 100%, SAD 100%, ScF 50%, BPD 97%, DEP 95%, delusional disorder 75%, brief psychosis disorder 76.9%, psychosis NOS 87.5%
Initial diagnosis: based on structured interview (SCID) Final diagnosis: based on SCID +/- medical notes Not consensus diagnosis 1 follow-up assessment at 4th year	Prospective / retrospective† consistency SCZ 96% / 71%, ScF 33% / 100%, affective psychosis 81% / 83%, delusional disorder 41.7% / 83%
Diagnoses were based on medical notes Consensus diagnosis was determined by 2 psychiatrists No independent diagnostic assignment Not blind to facility clinical diagnosis	Prospective /retrospective consistency SCZ 97.3% / 50.2%, SAD 94.1% / 57.1%, ScF 40% / 95%, BPD 83.2% / 89.2%, DEP 100% / 100%, delusional disorder 86.7% / 86.7%, brief psychosis disorder 72.7% / 100%, psychosis NOS 51.7% / 100%
Diagnoses were based on personal interview (not structured interview) and medical notes Consensus diagnosis was determined Independent diagnostic assignment by 2 psychiatrists 3 Follow-up assessments at 3rd, 6th & 12th month	DSM-IV prospective / retrospective consistency SCZ - / 16.6%, ScF 50% / 100%, BPD 100% / 94.4%, DEP 87.5% / 100%, brief psychosis disorder 100% /88.8% ICD-10 prospective / retrospective consistency SCZ 100% / 100%, BPD 82.3% / 100%, DEP 75% / 100%, ATPD 100% / 83.3%
Diagnoses were based on structured interview (SCID) Not consensus diagnosis 1 Follow-up assessment at 12th month	Prospective / retrospective consistency SCZ Spectrum 95% / 93%, ScF 36% / 100%, delusional disorder 100% / 100%, brief psychosis disorder 80% / 80%, psychosis NOS 44% / 100%

Subramaniam et al,[53] 2007; Singapore	DSM-IV	Prospective cohort	first contact to treatment sample	18-40	2 years	154
Rahm & Cullberg,[54] 2007; Sweden	DSM-IV	Retrospective cohort	First contact to treatment sample	18-45	3 years	146
Castagnini et al,[58] 2008; Denmark	ICD-10	Retrospective cohort	First admission sample	Not reported	Withinn 6-year period	503

Abbreviations: *APPD = acute polymorphic psychotic disorders; APTD = acute and transient psychotic disorders; BPD = bipolar affective disorder; CASH = Comprehensive Assessment of Symptoms & History; DEP = depressive disorder; DSM = Diagnostic and Statistical Manual of Mental Disorders; ICD = International Classification of Disease; NOS = not otherwise specified; PSE = Present State Examination; RDC = Research Diagnostic Criteria; SAD = schizoaffective disorder; SCAN = Schedules for Clinical Assessment in Neuropsychiatry; ScF = schizophreniform disorder; SCID = Structured Clinical Interview for DSM-IIIR; SCZ = schizophrenia.*

Table 3. Methodological variations in studies examining diagnostic stability

Methodological variations
Sample
Re-admission versus first-episode sample
First contact to treatment versus first-admission sample
Diagnostic scope (broad spectrum of functional psychosis or single diagnostic category)
Inclusion of comorbid substance abuse
Age distribution criteria
Single hospital or academic centre or multiple treatment settings
Diagnostic ascertainment
Diagnostic criteria (e.g. ICD-10, DSM-IV)
Longitudinal versus cross-sectional
Case register or medical record reviews or structured interviews
Consensus diagnosis versus individual psychiatrist's diagnosis
Follow-up issues
Length of follow-up
Number of interim follow-up assessments
Inclusion of face-to-face interviews during assessment
Assessment scales and tools
Attrition rate

Abbreviations: *DSM = Diagnostic and Statistical Manual of Mental Disorders; ICD = International Classification of Disease*.

been reported that approximately one-third of those with first-episode psychosis had a co-existing substance use disorder.[30] Because of the pervasiveness of substance abuse problems in patients with psychosis, the generalisability of findings from studies using this exclusion criterion would be severely compromised.

Diagnostic Ascertainment

Diagnostic Criteria

Various diagnostic schemes have been used in studies investigating diagnostic stability but there is little consensus on the validity of any particular diagnostic system over the others and a lack of objective indicators for definitive diagnoses.[31] Different diagnostic criteria denoting the same disorder will certainly identify patient groups with overlapping but non-identical characteristics. These discrepancies in diagnostic definitions need to be considered when interpreting the findings.

Methods of Diagnostic Assignment

Misclassification of diagnoses could also be attributed to diagnostic evaluation procedures per se, i.e. procedural validity.[31] Case registers, structured interviews, and medical record reviews were methods applied either alone or in combination for diagnostic assignment. Studies deriving diagnoses from case registers were limited by the variation in information and variability in application of diagnostic criteria.[12] Retrospective application of diagnostic criteria to case notes was adopted in numerous studies and was shown to be reliable for diagnostic ascertainment.[24] Nonetheless, the validity of results is limited by the documentary quality of medical notes. Structured interviews provide a systematic way of formulating differential diagnoses. However, denial of symptoms and recall bias are common in patients with psychosis and affective disorders, so relying on structured interviews to make a diagnosis or verify previous episodes without incorporating other sources of information impairs the reliability and validity of generating a longitudinal diagnosis.[32,33] Although there is no gold standard method for formulating psychotic disorder diagnoses, employing "best-estimate" consensus diagnostic procedures by using all available information from multiple sources incorporated with longitudinal assessments has been considered a reliable and is the currently accepted standard method for diagnostic assignment.[34]

Measures of Diagnostic Stability

Diagnostic stability was most commonly measured and presented as prospective and retrospective consistencies. Prospective consistency is defined as the proportion of subjects in a category at baseline assessment who retained the same diagnosis at the end of the follow-up period.

Diagnoses were based on structured interview (SCID) Not consensus diagnosis 1 Follow-up assessment at 2nd year	Prospective / retrospective consistency SCZ 87% / 63.2%, SAD 37.5% / 37.5%, ScF 12.1% / 40%, affective psychosis 54.5% / 42.8%, delusional disorder 50% / 100%, brief psychosis disorder 30.7% / 57.1%, psychosis NOS 25% / 28.6%
Clinical diagnosis of first-episode service program Not consensus diagnosis No review of medical notes Structured interview (SCID) might be applied to individual subjects during follow-up period	Prospective consistency SCZ 83%, SAD 30%, ScF 10%, affective psychosis 9%, delusional disorder 33%, psychosis NOS 18%
Case register (readmission) Non-readmission cases were assumed to be diagnostically stable	Prospective consistency ATPD 38.9%

* *Diagnostic consistency defined in this study: diagnosis was considered stable only if confirmatory criterion symptoms were active at the time of follow-up assessment, i.e. patients in remission at follow-up were considered to have "no diagnosis".*

† *Prospective consistency: the proportion of subjects in a category at baseline assessment who retained the same diagnosis at the end of follow-up (positive predictive value).*

‡ *Retrospective consistency: the proportion of subjects with a given diagnosis at the end of follow-up who had received the same diagnosis at baseline assessment (sensitivity).*

Retrospective consistency is the proportion of subjects whose diagnosis at the end of follow-up is the same as that made at the baseline assessment.[13] Diagnostic stability is considered present if the information within the follow-up period confirms the original baseline diagnosis, irrespective of whether the symptoms of the original diagnosis were actively present during follow-up assessments.[12]

Review of Study Findings

Non–first Episode Psychosis Study

Methodology

Most of these studies selected patients from re-admission samples.[10,14,15,32,35-43] One recent study included subjects from outpatient and emergency settings apart from rehospitalised patients.[16] A study initiated by the World Health Organization recruited a mixture of both prevalence and incidence samples from 4 independent cohorts with different inclusion criteria for analysis.[44] There was a wide variation in the follow-up period ranging from 40 years to 2 years with the majority using a follow-up period of less than 5 years.

Most studies were retrospective in design, using case registers as the only source of information for diagnostic ascertainment.[10,15,16,35,36,38,40-42] Forrester et al[43] applied the operational criteria checklist to case notes of re-admitted subjects to generate diagnoses. Other researchers utilised a combination of either case register[9] or medical note reviews[14,32,37] and follow-up interviews for diagnostic assignment. The baseline diagnosis was determined retrospectively while the final diagnosis was formulated using information obtained from both interviews and medical records. Only one follow-up interview was conducted, however, and the time interval between the initial episode and the follow-up assessment ranged from 12.5 years to 40 years.

Findings of Diagnostic Stability

Schizophrenia had the highest diagnostic stability (mostly above 70%), followed by affective disorder (mostly below 70%).[15,32,35-42] Many studies did not differentiate affective disorder into bipolar affective disorder and depressive disorder. Most studies did not discriminate between psychotic and non-psychotic affective disorders. Relatively few studies examined the diagnostic stability of other psychotic disorders such as delusional disorder, schizoaffective disorder and acute psychoses, which have been reported to be diagnostically unstable over time.[10,14,40-43,45]

Findings of Diagnostic Shift

Few studies assessed the pattern of diagnostic change. Conflicting results regarding the diagnostic shift between schizophrenia and bipolar affective disorder were noted. Some studies demonstrated a minimal diagnostic switch[10,32] while others found considerable conversions between schizophrenia, bipolar affective disorder, and schizoaffective disorder.[14,15,37] Findings regarding factors associated with diagnostic change were also inconsistent. Some researchers revealed no variables associated with diagnostic shift apart from diagnostic group memberships.[42] Others reported that gender, ethnicity,[15] age and hospital changes[10] were associated with a shift in the schizophrenia diagnosis. Diagnostic consistency also correlated with treatment settings; a diagnosis made for an inpatient was more stable than that derived in outpatient and emergency settings.[16]

First-episode Psychosis Study

Methodology

Most of these studies examined a wider spectrum of psychotic disorders,[11-13,17,28,46-54] though some reports focused solely on single diagnostic categories such as schizophrenia,[6] schizophreniform disorder[55] and acute and transient psychotic disorders (ATPD).[56-58] Affective psychosis[28] and comorbid substance abuse[11,53] were excluded by some studies.

Most studies had short follow-up intervals, with the majority following up for less than 2 years (6 months - 13 years). Three studies had follow-up durations of 5 years or above[6,46,47] but one such study assessed schizophrenia only[6] and another one was limited by its small sample size (n = 85).[47]

Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV)[59] was the most common diagnostic criteria adopted by these studies, followed by DSM-IIIR[60] and International Classification of Disease–10 (ICD-10).[61] Most studies recruited a "first contact to treatment" sample rather than a "first-admission" sample.[6,11,17,28,47-51,53-54,57] The majority used a prospective design, [6,11-13,28,46-53,55-57] however, many had only one follow-up assessment conducted after

a long time interval from the onset diagnostic evaluation. Some studies ascertained the diagnosis via structured interviews without a case notes review covering the interval between the 2 assessment time points.[28,53-55] Information on the subject's diagnostic status and clinical changes within this interval might be missed and thereby misjudged as diagnostic stability.[12]

Some studies relied on a single rater to make either the initial or final diagnosis or even the same researcher to determine both diagnoses in individual subjects.[6,28,46,51] Even though a more reliable consensus procedure was adopted, large variation still remained. Very few studies conducted independent diagnostic assignments by at least 2 psychiatrists blinded to the facility diagnosis.[12,13,52] Some studies involved 2 diagnosticians for the consensus procedure but one of them was responsible for compiling all the necessary information and presented the data to the other to generate the consensus diagnosis.[11,47-50] In this context, bias might be introduced when formulating the consensus diagnosis as it is likely to depend on the judgement of the diagnostician who prepared the clinical information.

Findings of Diagnostic Stability

Overall diagnostic consistency was around 70%. Schizophrenia was the most stable initial diagnosis (mostly above 90%), followed by bipolar affective disorder (mostly above 80%) and depressive disorder (about 70%). Inconsistent results were observed in delusional disorder (33-100%) and acute and brief psychoses (27-100%).[11-13,17,28,46-54,56-58] Diagnostic categories like schizophreniform disorder, schizoaffective disorder and unspecified psychosis were the least stable. For patients initially diagnosed as having schizophreniform disorder, 50 to 100% had their diagnoses switched to schizophrenia or rarely schizoaffective disorder later on.[17,28,49,51,55] With few exceptions, schizoaffective disorder was found to have low temporal stability (below 40%) with subsequent transition mainly to schizophrenia and bipolar affective disorder at follow-up.[11,13,46,48]

Findings of Diagnostic Shift

The diagnostic category receiving the largest influx of cases at follow-up was schizophrenia spectrum disorder, with most switching to schizophrenia.[13,17,28,49,51,53] The category with the most frequent diagnostic transition to the latter was schizophreniform disorder. There were more shifts from affective disorder to schizophrenia spectrum than vice versa. Substantial diagnostic movement to affective disorder and schizophrenia from acute psychosis was also demonstrated by certain studies.[48,56,57] Few studies examined predictors of diagnostic instability and results thus far are inconclusive. A longer duration of untreated psychosis (DUP) and poorer premorbid adjustment were found to be predictive of a diagnostic shift to schizophrenia spectrum or schizophrenia.[13,17,28,51] Conflicting results regarding comorbid substance abuse and baseline symptom severity as predictors of diagnostic change towards schizophrenia spectrum were observed.[13,17,51]

Discussion

Despite the wide disparity in methodological design, relatively uniform results have been observed across studies, especially those recruiting first-episode cohorts. The overall diagnostic consistency for first-onset psychosis was around 70%. Both schizophrenia and bipolar affective disorder displayed high levels of diagnostic stability, supporting the distinct nature of these disorders.[62] Other psychotic disorders including schizoaffective disorder, schizophreniform disorder, acute and brief psychoses, delusional disorder and unspecified psychosis were found to be diagnostically unstable over time with a prospective consistency usually below 50%. A diagnosis of schizophrenia showed a relatively lower retrospective consistency compared with its prospective consistency, indicating that more subjects changed their diagnoses towards rather than away from schizophrenia. Schizophrenia was also shown to have a high level of specificity; patients diagnosed as not having schizophrenia at follow-up rarely received a schizophrenia diagnosis at baseline.[13,17,28,48,50]

Diagnostic change in functional psychosis was found to be a relatively early phenomenon. Diagnostic revision tended to occur within the first few years after the onset of psychotic illness.[14,17,44,46,51] Around 30% of patients with a first psychotic episode were re-diagnosed at follow-up and a diagnostic shift to schizophrenia spectrum occurred most frequently. Within this group the majority changed to a diagnosis of schizophrenia.[13,17,28,44,48,51,53]

Contrary to studies using re-admission samples which demonstrated that patients presenting with manic episodes at a younger age of onset were frequently misdiagnosed as schizophrenia,[10] results of first-episode studies suggested that this misclassification bias was no longer a major reason for diagnostic inaccuracy in bipolar affective disorder.[13,63] Nonetheless, a high frequency of mood-incongruent or Schneiderian first-rank psychotic symptoms in bipolar affective disorder, particularly in first-episode mania might be attributable to diagnostic ambiguity in the early phase of a psychotic illness.[64,65]

Virtually all studies reported that schizophreniform disorder was diagnostically unstable and the majority with this baseline diagnosis switched to schizophrenia over time.[17,28,48,49,51,55] It was therefore suggested that such high temporal instability was in part due to an arbitrary separation between these 2 diagnoses and the subsequent conversion merely reflected the natural illness evolution rather than diagnostic change per se.[48,51]

Acute and brief psychoses were consistently shown to be diagnostically unstable and frequently changed to schizophrenia and affective disorder at follow-up.[45,56-58] Some researchers suggested that subdividing ICD-10 acute polymorphic psychotic disorder into the groups with and without schizophrenic symptoms might be unwarranted since such differentiation has no bearing on outcome and diagnostic shift.[66] As well, being a subcategory under the rubric of ATPD, acute schizophrenia-like psychotic

disorder was found to have low diagnostic stability and a large proportion of subjects with this diagnosis at baseline changed to schizophrenia later on.[44,66] On the other hand, the temporal instability of unspecified psychosis was to a large extent expected due to its non-specific nature inherent in the diagnostic definition. Most of these patients were reclassified as schizophrenia at follow-up.[13,17,28] Overall, the pattern of diagnostic shift echoed the concept of differentiation, which hypothesises that an initial atypical and non-specific clinical picture of functional psychosis might become clearer over time and evolve into prototypical categories such as schizophrenia and bipolar affective disorder.[67]

There was a lack of research into the factors associated with a change in diagnosis, in particular the diagnostic conversion towards schizophrenia spectrum. Owing to the paucity of relevant data, correlates of the diagnostic shift such as DUP and poorer premorbid adjustment were far from conclusive. Replication in future studies is required to confirm their predictive value.

With intensive and comprehensive assessments provided by a specialist team, schizophrenia and bipolar affective disorder can be reliably diagnosed in patients presenting with a first episode of psychosis. The findings of temporal instability in less common diagnostic entities, such as acute and brief psychoses and unspecified psychotic disorders, highlight the greater phenomenological fluidity in the early phase of psychotic illness and the difficulty with ascertaining an accurate diagnosis at the initial assessment. Since provision of particular treatment modalities is partly dependent on specific diagnostic categories, misdiagnosis may therefore expose patients and their families to inappropriate treatment and adverse psychological impacts.[17] Additionally, information and education about their diagnosis has been shown to improve patients' treatment adherence, illness outcomes, and their sense of well-being.[68] As predictors of a diagnostic shift towards the more severe form of functional psychosis, i.e. schizophrenia, are yet to be established, it is therefore recommended that patients suffering from early psychosis should be kept under close scrutiny with thorough assessment and regular diagnostic reviews to minimise misclassification.

Diagnostic instability has implications for research. Schizophrenia is considered a lifetime diagnosis[15] but previous studies have consistently demonstrated a diagnostic flux towards schizophrenia. A proportion of patients with this final longitudinal diagnosis were misclassified as having other psychotic disorders during the intake assessment. This underscores the need to recruit a broad spectrum of patients with functional psychosis instead of restricting the sample to those subjects who fulfill the diagnostic criteria for schizophrenia at baseline. Otherwise, a significant proportion of patients with a lifetime schizophrenia diagnosis, i.e. false-negative cases, will be missed at study entry and the validity of the research findings will be undermined by this misclassification bias.[26,27]

Several studies found that use of the ICD-10 definition for schizophrenia had comparable diagnostic stability, specificity and predictive validity to but higher sensitivity than the DSM-IIIR / DSM-IV schizophrenia diagnosis.[6,48] Some researchers stated that the DSM-IV definition with its 6-month duration criterion was overly restrictive and led to underdiagnosis of schizophrenia in the first-episode sample.[13,49] The DSM-IV criteria for schizophrenia has also been criticised for only identifying a subgroup of patients with a more chronic illness and poorer prognosis.[69] Thus it is suggested that the broader concept of schizophrenia as defined by the ICD-10 criteria might represent a clinically more useful definition for first-episode psychosis studies.[6,48]

From a nosological point of view, heterogeneity within and a lack of clear boundaries between certain psychotic disorders, as evidenced by frequent diagnostic shifts between them, reflected the insufficiency of current taxonomy for classifying functional psychosis,[16] such as ATPD and schizoaffective disorder. The subdivision of ATPD into 6 categories has been criticised by some researchers[70,71] and recognised by ICD-10[61] as lacking empirical evidence. Simplifying this subclassification on the basis of the presence of polymorphic symptoms and reassigning acute schizophrenia-like psychotic disorder into schizophrenia spectrum might improve its applicability and validity.[44,66,72] As well, the diagnostic instability, low inter-rater and clinical reliability of schizoaffective disorder[73,74] indicates that the present diagnostic criteria are insufficient for defining this group of patients.[75] It has been demonstrated that schizoaffective disorder is polymorphous in nature, showing frequent syndrome shifts among schizoaffective, pure mood and pure schizophrenic episodes along the illness course.[14,37] Focusing on cross-sectional presentation, as adopted in current diagnostic systems, without taking into account the chronological perspective, makes it difficult to assign a diagnosis of schizoaffective disorder. Delineating the disorder into concurrent and sequential subtypes by incorporating the longitudinal course might help resolve the diagnostic dilemma and difficulty differentiating between subgroups of patients presenting with overlapping affective and schizophrenic symptoms both cross-sectionally and longitudinally.[75]

The main limitation of using temporal stability as an indicator for validating psychiatric diagnoses is that it is based on an implicit assumption of the existence of discrete entities associated with relatively unique clinical syndromes reflecting underlying biological dysfunction.[3,76] As the reigning nosological paradigm in clinical and research psychiatry, the categorical approach has been criticised for the lack of evidence supporting its assumption of distinct entities in functional psychosis.[3,44,76] Owing to the failure to identify zones of rarity[77] and the presence of overlapping psychopathology,[4] genetic susceptibility[78] and neuroimaging findings[79] in schizophrenia and bipolar affective disorder, a dimensional or continuum model has been proposed as a substitute for categorical classification across the psychotic spectrum.[80] On the other hand, it has been recognised that discrete diagnostic entities and continuous variables are not mutually exclusive means of conceptualising psychiatric disorders.[81] Depending on the focus of research questions, the choice and the use of a combination of categorical and dimensional representations may offer additional advantages and serve as complementary means of hypothesis testing.[82]

It is suggested that an accurate delineation of syndromes by minimising clinical heterogeneity, though not a prerequisite, paves the way for, and increases the likelihood of, aetiological discovery.[7,82] In this context, although diagnostic stability is not the ultimate criterion for validity, in combination with other parameters, such as course of illness, treatment outcome,[83] genetics and neurobiological deficits,[84] it might assist with the establishment of more distinctive diagnostic categories in functional psychosis and facilitate investigation of underlying pathophysiological abnormalities.

Contemporary diagnostic systems have been shown to be relatively consistent for reconfirming the prototypical diagnostic entities, i.e. schizophrenia and bipolar affective disorder.[13,15] Nevertheless, the diagnostic stability and patterns of diagnostic shift in less common psychotic disorders such as ATPD and delusional disorder are far from clear. Future studies focusing on these specific diagnostic subgroups with larger sample sizes will better elucidate their illness trajectories and the boundaries between the major psychotic disorders, schizophrenia and affective disorder. More research is also needed for evaluation of the longitudinal course of substance-induced psychosis and its diagnostic change to functional psychosis as the distinction between these two conditions has important implications in treatment strategies.[29] Studies of this nature may also shed light on the potential aetiological links and neurobiological substrates of functional psychosis.[85]

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