Differential diagnosis of first-episode psychosis: importance of an optimal approach in psychiatric emergency

Diagnóstico diferencial de primeiro episódio psicótico: importância da abordagem otimizada nas emergências psiquiátricas

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Abstract

Objective: To review the literature regarding the diagnosis of first-episode psychosis in the context of psychiatric emergency. Method: Review of empirical and review articles selected by electronic search in the PubMed database. Results: Specific features of emergency care - single, brief, and cross-sectional assessments with little information - may jeopardize the diagnostic process. These limitations can be circumvented by the application of operational diagnostic criteria, by the use of scales and structured interviews, and by short observation periods (24-72 hours). Diagnoses of bipolar disorder, schizophrenia, psychotic depression, and delusional disorder performed in the context of emergency have good stability, but the same does not apply to the diagnoses of brief psychotic disorder, schizophreniform disorder, and schizoaffective disorder. Firstepisode psychosis can occur in the course of the use of psychoactive substances and the persistence of psychotic symptoms even after cessation of the use of the substance is relatively frequent. The rational use of subsidiary tests may be of help in establishing the differential diagnosis of psychotic episodes due to general medical conditions. Conclusion: The diagnosis of first-episode psychosis can be adequately performed by psychiatric emergency services if evidence-based routines are implemented.

Descriptors: Emergency services, psychiatric; Diagnosis, differential; Reproducibility of results; Interview; Evidence-based medicine

Resumo

Objetivo: Revisar dados da literatura relativos ao diagnóstico de primeiro episódio psicótico no contexto das emergências psiquiátricas. Método: Revisão de artigos empíricos e de revisão selecionados por meio de busca eletrônica no indexador PubMed. Resultados: Características específicas de atendimento de emergência – avaliação única e breve, em corte transversal e com poucas informações disponíveis – podem dificultar o processo diagnóstico. Essas limitações podem ser contornadas por meio da aplicação adequada de critérios diagnósticos operacionais, do uso de escalas e entrevistas diagnósticas padronizadas e de um tempo mínimo de observação de 24 a 72 horas. Diagnósticos de transtorno bipolar, esquizofrenia, depressão psicótica e transtorno delirante elaborados em contexto de emergência apresentam boa estabilidade temporal, não ocorrendo o mesmo com diagnósticos de transtorno psicótico breve, transtorno esquizofreniforme e transtorno esquizoafetivo. Primeiro episódio psicótico pode ocorrer na vigência do uso de substâncias psicoativas, sendo relativamente frequente a manutenção do quadro psicótico mesmo após cessação do uso. A utilização racional de exames complementares pode ajudar no diagnóstico diferencial com episódios psicóticos devido a condições médicas gerais. Conclusão: Diagnósticos de primeiro episódio psicótico podem ser adequadamente realizados durante emergências psiquiátricas, desde que sejam implementadas rotinas baseadas em evidências científicas.

Descritores: Serviços de emergência psiquiátrica; Diagnóstico diferencial; Reprodutibilidade dos testes; Entrevista; Medicina baseada em evidências

Introduction

The diagnosis performed in the first episodes of mental disorders has important therapeutic and prognostic implications. Based on this first diagnostic impression, decisions are taken concerning the treatment to be implemented and the service that the patient is to be referred to, and parameters are set to define the expected evolution of each case.

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The early recognition and intervention offer a unique opportunity to implement measures to prevent occasional impairments and complications that are inherent to chronic disorders. These measures include the definition of the most adequate drug treatment and the implementation of psychosocial interventions which might significantly contribute to the reduction of later morbidity, thus offering greater chances of recovery.¹

In many countries psychiatric emergency services are frequently the first contact patients have with the health system or the main source of referral for the treatment of first-episode psychosis.² In Brazil, a study performed in the city of São Paulo showed that emergency services were the first contact of the patient with the health system in around 70% of the cases of first-episode psychosis,³ and in around 50% of the cases this contact is made within up to four weeks of the onset of psychotic symptoms.⁴

Some characteristics inherent to psychiatric emergency care may affect diagnostic accuracy. Usually, psychiatric diagnoses in emergency contexts are performed in a single assessment, based on a cross-sectional evaluation and with no additional information that could be provided by caretakers. Moreover, the opportunity to follow up the patient is normally lost, together with the possibility of observing the evolution of the case. The high demand, added to the great rotation commonly seen in emergency services, restrains the time available for the consultation,⁵ as well as the duration of the observation period that could enable a more adequate symptom evaluation.⁶

With the expansion of the role of emergency services in the mental health network, the diagnosis performed in these conditions came to have additional therapeutic and prognostic implications, as commented previously. Furthermore, it is known that the diagnosis established at the time of admission in the mental health network tends to be maintained throughout the treatment of the patient.⁷

The systematic application of operational diagnostic criteria and the use of standardized assessment instruments have proved useful to improve the diagnosis of first-episode psychosis performed in the context of psychiatric emergency. In this article we review literature concepts and data that might contribute to enhance psychiatric diagnoses performed in emergency contexts.

Definition of first-episode psychosis

Historically, the term 'psychosis' has received several definitions. In older diagnostic classifications, the definition of 'psychosis' was excessively broad, focusing the severity of functional impairment, and a given mental disorder was termed 'psychotic' if it resulted in relevant interference with the individual's capacity to conform to the demands of daily life. In the current diagnostic classifications, the use of the term is basically restricted to the prominent presence of delusions and/or hallucinations and/or disorganized speech and/

or disorganized behavior (including catatonia) with no insight concerning the nature of these symptoms, denoting a broad impairment in one's capacity to perform critical judgments of reality.

The establishment of criteria for the definition of first-episode psychosis is even more complex. The literature on this topic is controversial in regard to the limits of the duration of symptoms and the inclusion of prodromal symptoms, together with the symptoms of the acute phase, for the definition of first-episode psychosis. 9-12 The prodromal phase is characterized by reported or observed alterations in mental state or behavior that appear before the onset of the full-blown psychotic symptoms described above, including changes in mood, thought, behavior, perception, and global functioning. For these prodromal symptoms to be considered part of a psychotic episode they cannot be fully remitted, with return to the pre-morbid functional level, before the onset of psychotic symptoms. 13

Not all patients presenting with symptoms that are typical of the prodromal phase will develop a psychotic disorder and the predictive validity of these symptoms has great variation across studies. Prodromal phase symptoms alone, regardless of the increased risk for psychosis that they represent, may be enough to fulfill the criteria for the diagnosis of a mental disorder (defined as a syndrome or behavioral or psychological pattern associated with clinically significant suffering and impaired global functioning), which could also justify the need and the right of the patient to receive assistance (not necessarily pharmacological). Nevertheless, there is still great controversy in respect to the identification and management of prodromal symptoms because studies on the effectiveness and efficacy of interventions in this phase are scarce.

The samples enrolled in different studies on first-episode psychosis can be fairly heterogeneous. Some studies, for instance, are based on the first admission or on the first contact with the health system to define recent-onset psychosis.^{3,15} Even so, these studies are of great relevance for a better comprehension of the incidence, clinical characterization, and prognosis of mental disorders, given that the diagnosis established in the early stages of the disorder has the advantage of suffering minimal impact from psychotropic medications and institutionalization.

1. Accuracy of the diagnosis of first-episode psychosis

Reliability refers to the agreement between multiple measures of one same phenomenon. Two methods are most frequently used to assess the reliability of diagnoses, namely, test-retest reliability, in which the presence or absence of a given condition is assessed with the same diagnostic instrument in two different moments; and inter-rater reliability, where the same cases are assessed

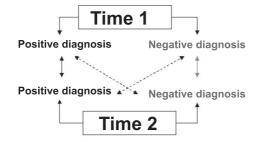
with the same instrument by two or more observers. Normally, statistical measures such as the Kappa coefficient and the Intraclass Correlation Coefficient (ICC) are considered as the most adequate to evaluate reliability because they take into account the proportion of agreement excluding the influence of chance. ¹⁶ Figure 1 illustrates methods used in the assessment of reliability.

Since the 1970s, great effort has been dedicated to enhance the reliability of psychiatric diagnoses. Among these efforts are the creation of operational diagnostic systems like the Diagnostic and Statistical Manual of Mental Disorders (DSM), currently in its fourth edition,⁸ and the development of standardized interviews for the application of these classification systems, such as the Structured Clinical Interview for DSM-IV Disorders (SCID).¹⁷ The improvement of nosological classifications and the development of interviews and assessment instruments have greatly contributed to increase the reliability of psychiatric diagnoses. The enhancement of the psychometric qualities of diagnoses, initially motivated by the necessity to enroll homogeneous samples in research studies, fostered a significant improvement in the quality of psychiatric assistance.

In general, the reliability indicators of psychiatric diagnoses performed in emergency settings are lower than those obtained in other clinical settings. 18 Some results show adequate reliability indices for the diagnostic categories proposed in the revised third edition of the DSM (DSM-III-R) based on diagnoses performed at the moment of admission in emergency services and the diagnoses at discharge performed after multiple evaluations, including the participation of professionals experienced in the diagnostic process and long observation periods.¹⁹ There is evidence, however, that diagnoses performed in emergency contexts are poorly reliable as a result of the great variability in the concepts and information used in the diagnostic process.²⁰ In addition to this variability, other aspects that are not directly related to the diagnostic process itself also seem to affect the reliability of the diagnosis of first-episode psychosis in emergency settings. For example, the diagnoses of non-white patients were shown to have lower agreement levels when compared to the diagnoses of white patients. The reasons underlying this disagreement were information variability (58%) and variations in diagnostic criteria (42%).21

The systematic use of diagnostic taxonomies and of guidelines, scales, and structured interviews for the evaluation of patients has been proposed as a possible solution to improve diagnoses performed in emergency settings.²⁰ Along these lines, we have observed that the use of operational diagnostic criteria and

Test-retest reliability



Inter-rater reliability

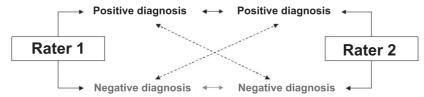


Figure 1 – Methods used to assess the reliability (test-retest and inter-rater) of psychiatric diagnoses

the training in the application of the SCID have increased the reliability of diagnoses performed in psychiatric emergency assessments.²²

2. Validity of the psychiatric diagnosis

The validity of an assessment instrument can be defined as its capacity to measure what it is intended to measure. Predictive validity can be statistically assessed through measures such as sensitivity (proportion of correctly identified positive cases), specificity (proportion of correctly identified negative cases), positive predictive value (probability that cases identified as positive are indeed positive), and negative predictive value (probability that cases identified as negative are indeed negative). The diagnosis considered as true or more reliable is established as the "gold standard". Figure 2 describes the assessment of predictive validity.

The stability of the diagnosis has been proposed as a criterion contributing to its validity, given that the more stable a diagnosis is, the more it will consistently reflect an underlying psychopathological or physiopathological process.^{10,23}

Stability refers to the proportion of diagnoses that remain unchanged over time according to multiple, successive evaluations. For a diagnosis to be stable, it has to be reliable in the first place. However, stability is not simply a function of diagnosis reliability, but it is also dependent on many other factors. The first of these factors refers to those characteristics that are inherent to the mental disorder itself, which might have symptom variations along its course. Additionally, novel information may appear

over the longitudinal follow-up leading to a reformulation of the initial diagnosis. ^{10,11} Conversely, methodological artifacts in the diagnostic process, such as variability in information sources, poor or absent use of reliable diagnostic classification systems and standardized diagnostic instruments, and lack of professional experience all might lead to mistakes in the initial diagnosis. ²³

Current diagnostic classification systems in psychiatry, consisting of the DSM, published by the American Psychiatric Association, and of Section 5 of the International Classification of Diseases (ICD-10), published by the World Health Organization, have significantly contributed to enhance the stability of the psychiatric diagnosis performed during a first psychotic episode or in the first psychiatric hospitalization. In general, the diagnoses of schizophrenia and mood disorders - especially bipolar disorder - performed in accordance with the two classification systems for patients in a first psychotic episode proved to have adequate positive predictive values. 10,11,25-28 Conversely, the diagnoses of brief psychotic disorder, schizophreniform disorder (included only in the DSM), and schizoaffective disorder seem to have low predictive values. 11,26,28

A recently published study²⁹ assessed the stability of diagnoses performed over two years with use of the SCID by experienced professionals in a sample of 500 patients in their first psychotic episode. The diagnosis of bipolar disorder was the most robust, maintained in 96.5% of the cases, followed by the diagnosis of schizophrenia (75%), delusional disorder (72.7%), major depression with psychotic symptoms (70.1%), and brief psychotic disorder (61.1%). Diagnoses of schizophreniform disorder had a

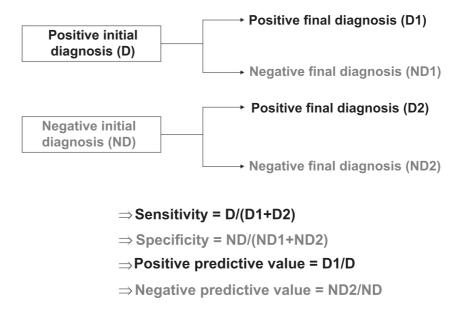


Figure 2 - Methods used to assess the predictive validity of psychiatric diagnoses

low positive predictive value, maintained in only 10.5% of the patients.

Schizophreniform disorder is a diagnostic category proposed only in the DSM-IV and characterized by the presence of delusions, hallucinations, negative symptoms, important thought disorganization, and disorganized or catatonic behavior, similar to the criteria proposed for the diagnosis of schizophrenia except for the duration, which must lie between one and six months.⁸ Earlier results have questioned the clinical usefulness of the diagnosis of schizophreniform disorder because of its high migration to a diagnosis of schizophrenia.³⁰ Only one-fourth of cases diagnosed with schizophreniform disorder in the initial assessment had their diagnosis maintained after six months,³¹ and around one-third had their diagnosis changed to mood disorders after six years of follow up.³² Other studies indicate that the relapse rate in patients with a diagnosis of schizophreniform disorder is high, leading to the relocation of patients to the schizophrenia diagnostic group.^{33,34}

Brief psychotic disorder is defined by the presence of the symptoms previously described for the diagnosis of schizophrenia or schizophreniform disorder, but lasting for no more than one month and with full remission and return to pre-morbid functioning levels.⁸ The validity of this diagnostic category is also limited. After one year of follow-up, the initial diagnosis was changed in half of the cases, most frequently to mood disorders (28%) and schizophrenia (15%).³⁵ The diagnosis of acute polymorphic psychotic disorder, proposed in the ICD-10, is also characterized by the sudden onset of psychotic symptoms lasting between 2 and 30 days and presented somewhat better stability levels, with around 75% of patients maintaining the same diagnosis after a three-year follow-up period. Most cases relocated to a new category received a diagnosis of mood disorder.³⁶

In our service we found that out of 31 patients receiving a diagnosis of brief psychotic disorder at discharge from the emergency service, only 22.6% maintained the same diagnosis after a mean follow-up of 19.5 months. A significant portion of these patients (41.9%) evolved to schizophrenia or schizophreniform disorder over the follow-up period, which could even be considered as diagnostic concordance according to DSM-IV criteria, given that the differential diagnosis in these three diagnostic classifications is dependent on the time of the evolution of symptoms. Nonetheless, 35.5% of the cases had their diagnoses changed to mood disorders. In this context, the diagnosis of brief psychotic disorder had good sensitivity (87.5%) but low specificity (52.9%) indicators.³⁷

The diagnoses of schizophreniform disorder and brief psychotic disorder in patients presenting with psychotic symptoms for the first time are, by definition, provisional diagnoses, since there is a time limit for the remission of symptoms and consequent diagnostic confirmation. Accordingly, the migration to other diagnostic categories is to be expected in a portion of first-episode

psychosis patients. The same applies for the diagnosis of major depression in these patients, since this index episode may be the first manifestation of bipolar disorder, whose presence will only be confirmed with the later occurrence of a manic episode.

Schizoaffective disorder encompasses a combination of symptoms that fulfill criteria for the diagnosis of schizophrenia and of a mood episode occurring simultaneously, successively, or preceded by a period where only schizophrenia symptoms are present. The validity of the diagnosis of schizoaffective disorder is maybe one of the most controversial topics in psychiatry, probably due to the difficulties involved in distinguishing this condition from schizophrenia, on the one hand, and from mood disorders, on the other. The controversies are centered on the question of what schizoaffective disorder would actually refer to: (1) a subtype of schizophrenia; (2) a subtype of mood disorders; (3) a fully separate condition; or (4) a compromise between schizophrenia and mood disorders. Between schizophrenia and mood disorders.

Generally, studies report low stability indicators for the diagnosis of schizoaffective disorder in first-episode psychosis. For instance, only 36% of the patients initially diagnosed with schizoaffective disorder had the same diagnosis after a two-year follow-up, with diagnosis changed to schizophrenia in 42% of the cases. ^{11,39} In a study performed in Brazil, 60.6% of the patients diagnosed with schizoaffective disorder, manic subtype, had their diagnoses changed by their attending physicians to bipolar disorder at some point during follow-up. ³⁹ Conversely, there is evidence suggesting good stability levels for the diagnosis of schizoaffective disorder in first-episode psychosis patients. ^{40,41} The latter results are probably related to the fact that these diagnoses were performed in research contexts, in large cohorts of cases with first-episode psychosis, and using scales and diagnostic interviews administered by experienced professionals.

In an extensive review on the validity of the schizoaffective disorder construct, Malhi et al. concluded that the existence of this disorder as a distinct diagnostic category is unlikely, considering the lack of evidence supporting this distinction. ⁴² In an attempt to improve the current diagnostic classifications, two possible models to approach schizoaffective disorder have been proposed: (1) as an intermediate point in a continuum between schizophrenia and mood disorders; or (2) as a set of comorbid symptoms occurring as a byproduct of those two conditions. With this evidence in mind, the diagnosis of schizoaffective disorder should be considered as an exclusion diagnosis in the clinical practice and especially in first-episode psychosis, since its confirmation depends on careful longitudinal observation.

Disorders related to the use of psychoactive substances are among the main diagnoses attended at psychiatric emergency services, 43 and substance-induced first-episode psychosis is not infrequently observed. According to the current diagnostic classifications, 8 psychotic symptoms in these cases are remitted

in a short period of time (up to one month) after withdrawal of the substance. Nonetheless, a significant portion of first-episode psychosis patients with a diagnosis of psychotic disorder induced by the use of substances, especially *cannabis*, will present signs and symptoms fulfilling the diagnostic criteria for disorders in the schizophrenia spectrum during follow-up.⁴⁴ A survey of psychiatric emergency records in Denmark⁴⁵ revealed that most patients admitted in the health system with a diagnosis of *cannabis*-induced psychosis had additional psychotic episodes during a minimum follow-up of three years. Furthermore, almost half of these patients were diagnosed with schizophrenia spectrum disorders during follow-up, and these diagnoses were performed more than one year after the initial contact, which suggests that substance-induced symptoms were the first step in the onset of schizophrenia spectrum disorders.

As mentioned above, time restraints and little availability of information sources cause the psychiatric diagnosis performed in emergency services to present only moderate agreement with diagnoses formulated in other clinical settings¹⁸ where longer observation periods and multiple evaluations enable the establishment of more consistent diagnostic processes. We have observed³⁷ that, in fact, the emergency admission diagnosis in first-episode psychosis performed within the clinical routine of the service had a low agreement with the diagnosis performed in accordance with conditions considered to be the gold-standard: assessments performed by experienced psychiatrists using longitudinal observation, all sources of information available, and application of operational diagnostic criteria by means of standardized diagnostic instruments. 46 However, the observation consisting of only two days in emergency services, with multiple assessments performed by different professionals, has had a considerable impact on diagnostic stability,³⁷ highlighting the importance of a minimum observation period for the conclusion of the diagnostic process.

Diagnosis of first-episode psychosis in the emergency context

The translation of scientific concepts into practice is generally a complex task that demands constant renovation and effort. The challenge becomes even greater in the case of clinical settings characterized by high demand and rotation and whose clientele consists mostly of patients at risk for aggressive behavior against self and others, as seen in emergency situations. An evidence-based possibility to systematize the performance of psychiatric diagnoses in the emergency practice is discussed below. Attachment 1 (available online at www.scielo.br/rbp) proposes a script to assess first-episode psychosis patients designed from available evidence concerning the reliability and validity of the diagnosis performed in the context of psychiatric emergency.

One fundamental aspect to be considered in the differential diagnosis of first-episode psychosis is the fact that psychiatric signs and symptoms can be manifestations of conditions other than primary mental disorders, such as clinical and neurological disorders. Although such conditions are relatively rare, their non-recognition has serious implications for the proper management of the case. Therefore, the emergency psychiatrist must be aware of this possibility and actively seek information that is relevant for the differential diagnosis. Since the general medical conditions liable to provoke psychiatric symptoms are many and diverse, the psychiatrist should ideally establish a hierarchy for his clinical reasoning so as to ensure that relevant information for the differential diagnosis is systematically obtained.

The first step for an adequate assessment and differential diagnosis of first-episode psychosis is, obviously, a thorough psychiatric evaluation, with data concerning the current illness and an emphasis on the detailed characterization of signs and symptoms, disease onset, severity, and evolution. Information should also be gathered regarding the patient's personal history, with an emphasis on pre-morbid functioning and on the occurrence of life events and stressors that might be related to the onset of symptoms.

The process of raising diagnostic hypotheses must be based on operational diagnostic criteria with demonstrated validity and reliability parameters. This skill of the psychiatrist depends on specific training, since the currently available diagnostic classifications are not simple checklists, depending fundamentally on the clinical judgment of the observer to perform the assessment. Ideally, the presence and severity of symptoms should be recorded using standardized instruments.

This initial assessment should be faced as a syndromic diagnosis whose confirmation is dependent on the exclusion of general medical conditions, including neurological disorders and the use of psychoactive substances (legal and illegal drugs and medicines). The exclusion of a general medical condition can be performed through the collection of a detailed clinical history that encompasses the active search for information concerning clinical and neurological complaints and the interrogation on the different systems, in addition to the performance of a complete physical examination and a brief neurological examination. The emergency psychiatrist, when facing a first psychotic episode, must always investigate the possibility of a general medical condition, but there are some clues that might increase the necessity to make this investigation deeper. Among these, some are worth mentioning: (1) the report by the patient or family of the occurrence of physical signs and symptoms immediately before or concomitant with the psychiatric manifestations; (2) atypical psychiatric manifestations; (3) later age at onset; and (4) poor response to the initial treatment.

The comorbidity of substance abuse or dependence with other mental disorders is common and frequently, in a cross-sectional cut as the emergency assessment, the establishment of a temporal relation between the beginning of the use of the substance and the onset of psychiatric manifestations is compromised. Regardless of the history of substance use and with the agreement of the patient and his caretaker, it might be useful to request drug screening tests, especially for marijuana and cocaine. This routine is suggested because in some situations the disorganized thought of patients in an acute psychotic episode can affect the quality of the information provided. In addition, the patient and family may have difficulties to openly acknowledge the use of illicit substances in their first contacts with the examiner.

Besides the clinical anamnesis and the interrogation on the different systems, additional laboratory tests, also performed with the consent of the patient and family, may be useful in the process of excluding a general medical condition. These tests include: complete blood count, fasting glycemic level, eletrolites, assessment of kidney, liver, and thyroid functions, screening for autoimmune diseases (ANF), serology for HIV and syphilis, and computed tomography of the skull. Attachment 1 presents a list of screening tests that can be requested in an initial approach. In the case that alterations are found in these screening tests, the evaluation should be deepened in accordance with formulated hypotheses and together with the relevant medical specialist.

Despite the recommendation to perform imaging exams (computed tomography and magnetic resonance of the skull) by some specialist guidelines and consensuses, their practical usefulness is questionable because most exams performed in first-episode psychosis patients are normal or present accidental anomalies with no clinical significance.⁴⁷ In fact, the currently available evidence is insufficient to define the real clinical necessity and the cost-benefit profile of the performance of neuroimaging exams in first-episode psychosis, and further clinical controlled trials involving representative samples are needed to answer this question.⁴⁸ In cases in which neuroimaging exams are to be requested, the first option is magnetic resonance, and computed tomography of the skull is only indicated when magnetic resonance is not available or when there is suspected brain injury. Neuroimaging exams are particularly recommended in the presence of neurological signs and symptoms, atypical presentations of psychosis, symptoms suggestive of delirium, and in patients over 50 years of age.⁴⁷

According to the initial diagnostic hypotheses, the most appropriate treatment in the short-to-medium term should be implemented and the patient should remain under observation for a period of 24-72 hours. This minimum observation period is proposed to permit successive evaluations for the confirmation of the initial diagnostic hypotheses, in addition to the investigation on the initial therapeutic response and on the occurrence of occasional side-effects. Next, the patient should be forwarded

for adequate follow-up. The decision on the type of referral to be performed must take into account the severity of symptoms, risk for aggressive behavior, clinical response to the initial therapeutics, presence of comorbidities, availability of social support, and characteristics of the service available in the mental health network. The patients and their families must be given clear information concerning the therapeutic and follow-up proposal. All information collected, as well as the results of exams, evolution of the condition, and implemented conducts must be recorded in detail in medical records.

Conclusion

Taken together, the data presented here show that relatively simple measures like training and continuing education of emergency psychiatrists, the systematic application of diagnostic criteria and guidelines and the use of standardized diagnostic instruments, the rational use of complementary tests, and a minimum observation period can be useful to circumvent the limitations inherent to psychiatric emergency services and contribute to significantly improve the quality of the diagnosis of first-episode psychosis performed in emergency contexts,

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^{*} Modest

Note: FMRP-USP = Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo; UFSC = Universidade Federal de Santa Catarina; FMUSP = Faculdade de Medicina, Universidade de São Paulo; FAPESP = Fundação de Amparo à Pesquisa do Estado de São Paulo; CAPES = Coordenação de Aperfeiçoamento de Pessoal de Nível Superior; CNPq = Conselho Nacional de Desenvolvimento Científico e Tecnológico. For more information, see Instructions for Authors.

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^{**} Significant

^{***} Significant. Amounts given to the author's institution or to a colleague for research in which the author has participation, not directly to the author.

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Attachment 1 – First-episode psychosis assessment protocol¹

Name	Record				
Date and time of admission	Rater				
Anamnesis and tests					
Main complaint: Onset of symptoms:					
History of current illness (record positive data)					
Interrogation on the different systems					
Positive data? Yes	No				
If yes, describe:					
Current use of psychoactive substances/medications					
Positive data? Yes	No				
If yes: substance type, age at onset, weekly frequency of use, dose, duration of	f use, clinical response.				
Mental Status Examination (Record positive data)					
Physical and neurological examination					
Positive data? Yes	No				
If yes, describe:					
Personal history					
Problems during pregnancy or delivery					
Maternal infection	Gestational age <				
Maternal diabetes Low weight at birth Maternal malnutrition Neonatal hypoxia					
	Neonatal hypoxia				
Other. Describe:					
Type of delivery Regular - hospital	Regular - home				
Forceps	Cesarean surgery				
_ тогооро					
Problems during childhood and adolescence					
Impaired neuropsychomotor development	Traumatic	brain injury			
Physical abuse		Sexual abuse			
Derelict behavior	Low acade	emic performance			
Disruptive behavior	Language	disorders			
Difficulties in sexual development	Negligenc	e			
Socialization difficulties / Social isolation					
Other. Describe:					
Past use of psychoactive substances/medications					
Positive data? Yes	No				
If yes: type of substance, life period, weekly frequency of use, dose, duration of	f use, clinical response.				
Family history					
History of mental disorders in the family Yes	No				
If yes:					
Degree of relatedness: Probable diagnosis:					
Degree of relatedness: Probable diagnosis:					
Degree of relatedness: Probable diagnosis:					
Environmental factors (describe if positive)					
Migration		Date			
Changes in socioeconomic status		Date			
Life events		_ Date			

¹ Protocol developed by the medical staff of the psychiatry division of the Ribeirão Preto Medical School University Hospital Emergency Unit of the University of São Paulo.

Distressing events	Distressing events							
Other	Other							
Social support (describe)								
Lives with								
Family				Friends				
Alone				Institution				
Other. Describe:								
Does the patient have personal income?	Yes		No					
If yes, describe:								
If not. Where does the patient get support	rt from?							
Initial diagnosis and conduct								
Probable diagnosis(es) (at admission):								
Frobable diagnosis(es) (at admission).								
Initial conduct:								
Poculte of complementary toots								
Results of complementary tests Hb	 Na ⁺		A	 ST/ΔΙ Τ				
Ht	<u> </u>			AST/ALT INR				
	 │ Ca ⁺⁺		TSH/ free T4					
Leukocytes Bands	Urea							
Segs	Creatinine							
Eosinophils	Fasting glyce	mic level	olites					
Lymphocytes	ANF	THIC IEVE	ites					
Other	ANI		iies					
Imaging exam (MRI or CT scan of the sk								
imaging exam (with or or scan or the sk	uii)							
Final diagnosis (discharge):								
Prescription at discharge:								
Frescription at discharge.								
		Attending physiciar	n					
Referral (describe)		Attending physician	n					
Referral (describe) Full-time hospitalization:		Attending physiciar	n					
Full-time hospitalization: Public network:		Attending physiciar	n					
Referral (describe) Full-time hospitalization:		Attending physician	n					

Severity of symptoms

BPRS ²			Hamilton ³				YMRS⁴				
Item Score		Item Score		Item		Score					
		adm	disch	ĺ		adm	disch			adm	disch
1.	Somatic concern			1.	Depressed mood			1.	Elevated mood		
2.	Anxiety			2.	Feelings of guilt			2.	Increased motor activity - energy		
3.	Emotional withdrawal			3.	Suicide			3.	Sexual interest		
4.	Conceptual disorganization			4.	Insomnia - early			4.	Sleep		
5.	Guilty feelings			5.	Insomnia - middle			5.	Irritability		
6.	Tension			6.	Insomnia - late			6.	Speech (rate and amount)		
7.	Mannerisms and posturing			7.	Work and activities			7.	Language – thought disorder		
8.	Grandiosity			8.	Retardation			8.	Content		
9.	Depressive mood			9.	Agitation			9.	Disruptive- aggressive behavior		
10.	Hostility			10.	Anxiety - psychic			10.	Appearance		
11.	Suspiciousness			11.	Anxiety - somatic			11.	Insight		
12.	Hallucinatory behaviors			12.	Somatic symptoms - gastrointestinal						
13.	Motor retardation			13.	Somatic symptoms - general						
14.	Uncooperativeness			14.	Genital symptoms						
15.	Unusual thought content			15.	Hypochondriasis						
16.	Blunted affect			16.	Loss of weight						
17.	Excitement			17.	Insight						
18.	Disorientation			18.	Diurnal variation						
19.				19.	Depersonalization and derealization						
20.				20.	Paranoid symptoms						
21.				21.	Obsessional and compulsive symptoms						
Tot	al score - BPRS		_	Tot	al score - Hamilton			Tot	al score - YMRS		_

adm = admission; disch = discharge

 ² Zuardi et al. Rev ABP-APAL 1994;16:63–8
 ³ Carvalho et al. J Bras Psiquiatr 1993;42:255–60
 ⁴ Vilela et al. Braz J Med Biol Res. 2005 38(9):1429-39