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Review of the operational definition for first-episode psychosiseip

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Abstract

Aim—Given the growing interest in the study of first-episode psychosis, clinical and research programmes would benefit from a conceptual clarification of how to operationalize 'first-episode psychosis'. We review the variety of definitions in use and discuss their relative merits with respect to both clinical (e.g. early treatment) and research (e.g. obtaining meaningfully homogeneous populations) agendas.

Methods—We completed a selective review of the literature to investigate how first-episode psychosis was operationally defined.

Results—Operational definitions for 'first-episode psychosis' fall largely into three categories: (i) first treatment contact; (ii) duration of antipsychotic medication use; and (iii) duration of psychosis. Each definitional category contains a number of underlying assumptions that contribute to the strengths and weaknesses of the definition.

Conclusions—The term 'first-episode psychosis' as used within clinical and research settings is misleading regardless of which operational definition is used. This term is typically used to refer to individuals early in the course of a psychotic illness or treatment rather than individuals who are truly in the midst of a first 'episode' of illness. The alternative of 'recent-onset psychosis' with related definitions based on 'duration of psychosis' is proposed. Based on this review, we provide suggestions with regard to the overarching pragmatic consideration of setting up a clinical service that can attract and assemble a population of early psychosis patients for the related purposes of treatment and research.

Keywords

definition; first-episode psychosis; review

The beginning of wisdom is the definition of terms – Socrates

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INTRODUCTION

Within psychiatric research, there is growing interest in early psychosis. From a clinical perspective, the provision of treatment early in the course of illness raises the possibility that one may be able to prevent or reduce the morbidity that rapidly occurs during the first few years of a psychotic disorder.[1] From a research perspective, the study of early illness course provides an opportunity to identify the various biopsychosocial variables that accompany, cause or result from this decline in functioning.

However, the establishment of multiple successful clinical and research programmes has not removed an important conceptual difficulty. Specifically, there is no consensus operational definition for what is commonly referred to as 'firstepisode psychosis', and existing diagnostic systems (i.e. DSM-IV[2] and ICD-10[3]) provide little guidance with regard to defining this construct. The significant variability in definition and application across different clinical and research programmes threatens meaningful integration of findings from these populations[4,5] and may ultimately hinder our progress in identifying key elements of the early course and treatment of psychotic disorders.

OPERATIONAL DEFINITIONS FOR FIRST-EPISODE PSYCHOSIS

We completed a selective review of exemplar first-episode psychosis research and clinical programmes to investigate how these programmes define their target population (Table 1).

Definitions for 'first-episode' fall largely into three categories: (i) first treatment contact; (ii) duration of antipsychotic medication use; and (iii) duration of psychosis. Although some programmes may cross definitional boundaries,[34–39] these three categories typically distinguish current first-episode treatment and research programmes. Each definitional category contains a number of underlying assumptions that are useful to examine and reveal particular strengths and weaknesses with regard to the specific definition.

Early studies of first-episode psychosis relied primarily on a 'first treatment contact' operational definition (e.g.[6–15]) – although several more recent studies (i.e. published since 2000) have also used this definition.[16–21] According to this operational definition, an individual who presents at a clinical setting with psychosis and who has never previously presented at a clinical setting with psychosis is identified as experiencing their 'first-episode'. Although little has been written with regard to an explicit rationale for using this approach, we see two major strengths: (i) it is relatively simple to comprehend and apply reliably and (ii) it reflects an intuitively appealing way to organize clinical care around a naturally occurring service need.

Emerging data with regard to the pathways to care taken by individuals with psychotic disorders reveal key limitations of this approach. The first treatment contact for individuals with psychotic disorders often occurs well after the initial onset of symptoms.[40,41] A recent multi-study review of the duration of untreated psychosis (DUP), or the time between the onset of psychosis and receipt of adequate treatment, found a mean DUP of almost 2 years.[42] Also, an individual's 'first contact' (i.e. when psychotic symptoms are first identified) is often not the first attempt to seek treatment. Individuals can make up to five

unsuccessful attempts at obtaining treatment prior to successfully engaging with a first-episode psychosis programme.[34,43] Finally, available evidence suggests that the 'first treatment contact' operationalization may be an overly conservative proxy for identifying people early in the course of a psychotic illness. For instance, among the studies included in this review as well as studies included in two recent meta-analyses of DUP and first-episode psychosis,[42,44] we found that the median DUP for participants in studies using the 'first treatment contact' definition ranged from 6 weeks[13] to 6 months.[16] This suggests that, in practice, this definition may overly exclude individuals who are still early in the course of a psychotic disorder but who have experienced psychotic symptoms for 1 year or more. Thus on examination, the 'first treatment contact' definition appears neither simple nor necessarily able to collect individuals who meaningfully share service needs or research characteristics.

The second common operationalization is based on duration of antipsychotic medication use. Drawing on research finding a negative association between DUP and treatment response,[42,44] reducing DUP has been identified as one of the primary goals in the treatment of first-episode psychosis.[13] Consequently, many first-episode psychosis programmes[22–30] limit enrolment to individuals who have yet to receive adequate treatment for their psychosis (i.e. individuals for whom the DUP has yet to stop), with adequate treatment defined as the receipt of antipsychotic medication for a specific duration of time.

The 'duration of antipsychotic medication use' definition is attractive in that it provides a clear, objective criterion for clinicians and researchers. This definition has demonstrated feasibility in several studies testing clinical interventions for first-episode psychosis,[23,25–30] including the largest randomized controlled trial of intensive treatment to date (i.e. OPUS[25]).

However, this definition is not without its faults. Similar to 'first treatment contact', the 'duration of antipsychotic medication use' definition can be an unsatisfactory proxy for the first episode of a psychotic illness. For example, this definition would identify an individual who has not received adequate treatment with antipsychotic medication as experiencing his or her first episode of psychosis even if he or she had experienced psychotic symptoms for many years. Additionally, the growing use of antipsychotic medications for non-psychotic disorders, especially among children and adolescents,[45,46] raises additional questions with regard to the utility of the duration of antipsychotic medication use in demarcating the first episode of a psychotic disorder. Moreover, within studies using a 'duration of antipsychotic medication use' operational definition, there is considerable variation in the acceptable duration of medication use. Although many studies[25–28] use a duration of less than 3 months of continuous use as suggested by Wyatt[47] and Larsen and colleagues,[48] other studies use durations ranging from no more than 3 days[23] to less than 6 months[30] with little explanation as to why these values were selected. Thus, although the duration of antipsychotic medication use may be a frequently used operational definition for firstepisode psychosis, the variability in the definition of acceptable duration of medication use and the variable populations recruited even within a single duration criterion hinder our ability to accurately integrate findings across studies for clinical or research purposes. Finally, available evidence suggests that the duration of antipsychotic medication use may be an overly conservative

proxy for identifying people early in the course of a psychotic illness. Among the studies included in this review as well as studies included in two recent meta-analyses of DUP and first-episode psychosis,[42,44] the median DUP for participants in studies using the 'duration of antipsychotic medication use' definition ranged from 5 weeks[27] to 28 weeks.[49] Thus, similar to the 'first treatment contact' definition, in practice, the duration of antipsychotic medication use definition may overly exclude individuals who are still early in the course of a psychotic disorder but who have experienced psychotic symptoms for 1 year or more.

The third approach identifies individuals as experiencing their 'first episode' of psychosis if they have experienced psychotic symptoms for less than a pre-specified amount of time.[31–33] Although the least used, this operational definition possesses the most construct validity. Whereas the first two definitions prove to be inaccurate proxies, the 'duration of psychosis' definition attempts to most directly address the goal of identifying individuals early in the course of illness. From a research perspective, this limits inappropriate inclusion of latecomers or 'chronic' patients who are experiencing their 'first treatment contact' or exclusion of those who happen to have been exposed to antipsychotic medication for too long but are better conceptualized as early in illness course. From a clinical or service provider perspective, this would challenge programmes to track how early after illness onset patients are able to enter the pathway to care (rather than to be falsely reassured by a first treatment contact or several prior weeks or months of antipsychotic treatment) and also to understand which subgroups of individuals within a broader early course perspective cluster together in terms of service needs.

Utilizing a'duration of psychosis' operational definition does present the clinician or researcher with several challenges. The accurate retrospective assessment of the onset of psychotic symptoms is fraught with methodological difficulties. However, there is promising evidence suggesting that individuals experiencing their first episode of psychosis can provide relatively precise estimates of the onset of psychotic symptoms.[50–52] Moreover, programmes now have access to several reliable measures that facilitate the collection of these estimates.[53] These include the Interview for the Retrospective Assessment of Schizophrenia,[41] Royal Park Multidiagnostic Instrument for Psychosis[54] and the Symptom Onset in Schizophrenia inventory[55] which incorporate information from multiple sources (e.g. caregiving relatives and medical records) to maximize accuracy.

Yet, the most significant problem with regard to the 'duration of psychosis' operational definition is that we lack a validated durational criterion for demarcating the end of the first episode of a psychotic disorder. Given that most of the deterioration in functioning that accompanies psychotic disorders occurs within the first 2–5 years following the onset of psychotic symptoms,[56] one may wish to demarcate the first episode as ending at some point 2–5 years later. However, the speed at which this functional deterioration occurs varies across individuals,[57] and we lack strong scientific evidence to inform an appropriate cut-off point for the end of the first episode within this 2- to 5-year period.

DISCUSSION

At present, each of the three commonly used operational definitions for first-episode psychosis suffers significant limitations. Moreover, it is clear that the term ‘first-episode psychosis’ as currently used within clinical and research settings may be misleading regardless of which operational definition is used. Specifically, it appears as if the term is typically used to refer to individuals who have experienced a short duration of illness (e.g. 2–5 years)[58] or treatment for a psychotic illness rather than individuals in the midst of a first ‘episode’ of mental illness. The term ‘recent-onset psychosis’ more accurately describes the populations actually studied so far and, conceptually, may be more accurate than the term ‘first-episode psychosis’ given that psychotic disorders do not always follow an episodic course.[11]

How then should research and clinical endeavours proceed with regard to developing knowledge of psychotic illnesses and effective early interventions? We suggest a pragmatic solution that can address the varying needs of specific clinical and research settings as well as the need to produce data that can be combined across settings for aggregate analysis. First, we suggest that the operational definitions for first-episode psychosis used within clinical and research settings include a ‘duration of psychosis’ criterion while simultaneously tracking specific measures that would allow for comparison with data from other populations (e.g. date of first contact with treatment setting, duration of antipsychotic medication use, etc.). Although ‘first treatment contact’ and ‘duration of antipsychotic medication’ criteria may be more reliably assessed, systematic evaluations of the accuracy of these operational definitions as proxies for identifying people early in the course of a psychotic disorder are lacking, and available evidence suggests that they may be too conservative. Although there are situations in which the use of these proxy measures as additional inclusion criteria may be appropriate (e.g. requiring subjects to be drug naïve in certain neuroanatomical studies), justification should be provided for the inclusion of these additional criteria as well as an acknowledgement that the study sample may not be representative of all individuals early in the course of a psychotic illness.

Noting that (i) the initial needs and challenges experienced by individuals with psychosis[58] and their family members (see[59] vs.[60]) appear not to change dramatically during the first 5 years post-onset and (ii) the use of narrower, ‘research-friendly’ operational definitions of first-episode psychosis is only practicable within the context of a larger clinical service where these individuals can be offered comprehensive care, we suggest that it may be appropriate for clinical settings to be liberal in determining the duration of psychosis cut-off to use when identifying individuals experiencing their first episode of psychosis (e.g. less than 5 years since the onset of psychotic symptoms). This arrangement would allow programmes to organize themselves around providing a specific set of clinical services – despite providing these services to what may be a relatively heterogeneous group of patients and families – while simultaneously allowing for the accumulation of a sufficient subject pool from which research protocols can recruit more selected populations. Programmes with limited resources may choose to use a shorter duration of illness criterion (e.g. less than 2 years after the onset of psychotic symptoms) as patients who are still highly symptomatic

after 4 to 5 years of illness may have more in common with chronic patients than with patients who are in the first or second year of their illness.

Accumulating a large pool of participants within a clinical setting through the use of a liberal duration of psychosis criterion may have an additional benefit – it may assist in the development of a staging model for psychotic disorders. As psychotic illnesses progress at different rates in different individuals,[57] duration of psychosis might not be a meaningful classification from a clinical or pathophysiological perspective among individuals early in the course of a psychotic illness. Rather, stage of illness might be a more useful classification system (e.g. grouping individuals who initially present with severe negative symptoms and cognitive compromise within 1 month of onset along with those who have deteriorated to this stage after 1 year as opposed to differentiating these two groups based on duration of psychosis). McGorry and colleagues[61] have proposed a tentative framework for a staging model for psychotic and severe mood disorders but have noted that future research is necessary to evaluate and refine this framework. Ultimately, the accumulation of large, heterogeneous pools of individuals early in the course of a psychotic disorder will facilitate the continued exploration and refinement of staging models for psychotic disorders.

Thus, we propose a tentative 3-point solution with regard to devising an appropriate operational definition of first-episode psychosis. First, until validated staging models for psychosis are available, ‘first episode’ target populations should be recruited in both clinical and research settings based on duration of illness criteria. Second, clinical programmes should consider a liberal durational criterion (e.g. 5 years) as the clinical needs of individuals with psychosis and their caregiving relatives appear not to vary significantly during the first 5 years post-onset of psychotic symptoms. Determination of the appropriate durational criterion should be done based on the resources available in the specific clinical setting. Third, research programmes may choose to add additional operational criteria for first-episode psychosis in situations in which their research question requires the examination of a specific sub-type of individuals early in the course of a psychotic illness. Explicit acknowledgement and justification for the addition of these additional operational criteria will aid in the integration and interpretation of findings.

In his seminal paper on operational definitions, SS Stevens[62] noted that ‘no concept can be defined once and for all: every concept of science requires constant purging to keep it operationally healthy’. The study of first-episode psychosis is no exception. Continued evaluation and revision of the operational definition for ‘first-episode psychosis’ (or as we would suggest, ‘recent-onset psychosis’) will likely improve our efforts to better understand and treat psychotic disorders.

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TABLE 1

Studies included in selective review and operational definition category for first-episode psychosis

Study	Operational definition category
Kane and colleagues[6]	First treatment contact
Scottish First Episode Schizophrenia Study[7]	First treatment contact
Stony Brook First-Episode Schizophrenia Longitudinal Study of Brain Morphology[8]	First treatment contact
WHO Determinants of Outcome of Severe Mental Disorder (DOSMD)[9]	First treatment contact
Suffolk County Mental Health Project[10]	First treatment contact
The Iowa Prospective Longitudinal Study of Recent-Onset-Psychosis[11]	First treatment contact
Hass and Sweeney[12]	First treatment contact
EPPIC13	First treatment contact
Hutton and colleagues[14]	First treatment contact
Madsen and colleagues[15]	First treatment contact
Browne and colleagues[16]	First treatment contact
SOCRATES[17]	First treatment contact
Parachute Project[18]	First treatment contact
LEO[19]	First treatment contact
Cavan-Monaghan Study[20]	First treatment contact
AESOP[21]	First treatment contact
Prospective study of psychobiology in first-episode schizophrenia at Hillside Hospital[22]	Duration of antipsychotic medication use (<12 weeks lifetime use)
Emsely[23]	Duration of antipsychotic medication use (≤3 days)
Fannon and colleagues[24]	Duration of antipsychotic medication use (≤12 weeks)
OPUS[25]	Duration of antipsychotic medication use (<12 weeks continuous use)
EPP[26]	Duration of antipsychotic medication use (<12 weeks continuous use)
TIPS[27]	Duration of antipsychotic medication use (<12 weeks continuous use)
PEPP[28]	Duration of antipsychotic medication use (≤1 month)
STEP[29]	Duration of antipsychotic medication use (<8 weeks lifetime use)
CAMEO[30]	Duration of antipsychotic medication use (<6 months)
WHO Collaborative Study on Impairments and Disabilities Associated with Schizophrenic Disorders[31]	Duration of psychosis
Developmental Processes in Schizophrenic Disorders Project[32]	Duration of psychosis
CAFEPS[33]	Duration of psychosis

AESOP, Aetiology and Ethnicity in Schizophrenia and Other Psychoses; CAMEO, Cambridge Early Psychosis Service; CAFEPS, Child and Adolescent First-Episode Psychosis Study; EPP, Calgary Early Psychosis Program; EPPIC, Early Psychosis Prevention and Intervention Centre; LEO, Lambeth Early Onset; PEPP, Prevention and Early Intervention Programme for Psychoses; SOCRATES, Study of Cognitive Reality Alignment Therapy in Early Schizophrenia; STEP, Specialized Treatment Early in Psychosis; TIPS, Early Treatment and Intervention in Psychosis.