

MEDICINE AND SOCIETY

Ethical and Epidemiological Dimensions of Labeling Psychosis Risk

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Abstract

The past two decades have marked an increase in research on the prodromal stages of schizophrenia that precede a first episode of psychosis. Criteria for a clinical high risk (CHR) state for psychosis have been validated and included in the *DSM-5* as the attenuated psychosis syndrome and as requiring further study. This was hotly debated, given the concern of stigmatizing young people who would receive this psychosis risk label. In this article, I review ethical issues related to the psychosis risk label, including the potential harm of stigma and paternalism if risk labels are withheld in the context of the observed low predictive power of the psychosis risk designation. I review data that supports that the psychosis risk label need not be harmful, and could even confer benefit, and set out strategies for reducing stigma through individualized risk assessment and public health education.

Introduction

[Schizophrenia](#) is a neurodevelopmental disorder with antecedents in childhood and adolescence. Eighty percent of all persons with schizophrenia have had a prodromal period preceding their first episode of psychosis, which has been estimated to last from months to years [1]. This prodromal period is characterized by functional decline; decreased motivation; nonspecific symptoms such as anxiety, dysthymia, and poor concentration; and the *forme fruste* of psychosis, e.g., [attenuated or subthreshold psychotic symptoms](#) [2]. These subthreshold psychotic symptoms include overvalued odd ideas and suspiciousness (subthreshold delusions), perceptual disturbances (subthreshold hallucinations), and subtle disturbances in speech and language (subthreshold thought disorder). What distinguishes psychotic symptoms as *subthreshold* is that insight and reality testing are retained.

This putative prodromal period has formed the basis for early identification of and preventative interventions for schizophrenia and related psychotic disorders. Young people who have these subthreshold psychotic symptoms and who are help-seeking have been identified as at ultra-high risk or clinical high risk (CHR) for psychosis, labels that have been employed in this field of “prodromal” schizophrenia research for the past 15 to 20 years [3]. The subthreshold psychotic symptoms must have begun or worsened

for the patient in the year prior to having been identified as CHR and cannot be accounted for by another psychiatric disorder, criteria adopted in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders (DSM)* [4]. Among teens and young adults who meet these CHR criteria, roughly a third will develop psychosis in the ensuing one to three years [5-7]. Although this [positive predictive value](#) (PPV) is more than tenfold the prevalence of psychosis onset among young people in the general population [8], CHR still yields a high “false positive” rate (i.e., diagnostic instruments have high sensitivity but low specificity) [9], such that nearly two-thirds of those with CHR will not develop psychosis within three years [6, 7]. The CHR designation has fairly good validity and reliability [10], meaning that the psychosis risk syndrome can be differentiated from the norm and from psychosis itself, and that different clinicians tend to reach the same conclusion about whether the risk syndrome is present or not. But beyond the aforementioned subthreshold psychotic symptoms, with measures of auditory processing being among the most replicated of potential risk biomarkers thus far [11, 12], no biological assay is available yet for predicting psychosis onset among persons with CHR. Moreover, there is no established evidence base of treatment yet for CHR syndrome: antipsychotics lead to significant side effects, such as weight gain, although psychological treatments such as cognitive behavioral therapy (CBT) might have efficacy [13].

In 2011, it was proposed that the constellation of symptoms consistent with increased psychosis risk be considered for inclusion in the *DSM-5* as attenuated psychosis syndrome [14]. This proposal was hotly debated among investigators [4, 15, 16] in large part because of the concern about stigmatizing young people with the label of “psychosis risk” and subsequent risks of discrimination [4, 17]. Based on [concerns about stigma](#) (and unnecessary exposure to antipsychotics), especially in the context of a high false positive rate, the syndrome was placed in *DSM-5*'s appendix as requiring further study [4]. In this paper, I briefly review the ethical issues that were raised at the time [17], when no empirical data were available yet on the actual stigma perceived by the young people who themselves have subthreshold psychotic symptoms, and who, by virtue of such symptoms, receive a label of “psychosis risk.” I then present the data on self-stigma related to CHR that have been reported within the past five years and set out a proposal for reducing potential harm from labeling.

Ethical Concerns

Stigma (threat to nonmaleficence). In 2011, when attenuated psychosis syndrome was proposed for inclusion in the *DSM-5*, there was a scarcity of research on the stigma associated with CHR syndrome symptoms and labeling. Many psychiatrists and family advocacy organizations were concerned that the stigma of schizophrenia—with its associations of otherness, dangerousness, and hopelessness [18, 19]—would attach itself also to the label of psychosis risk [17]. Potential harmful consequences for young people could include internalized stigma (youths see themselves as bad, defective, or unworthy); identity engulfment (youths see illness as defining who they are, rather than

as something they have); shame (the label is kept secret and concealed); and, finally, discrimination from others, expressed as devaluation or unfair treatment [20]. Clinicians and researchers were concerned that the label of psychosis risk could threaten a young person's sense of self (by incurring subsequent identity labeling, such as fragile, damaged, sick, or crazy) and curtail his or her aspirations in terms of education, employment, or romantic attachments [4]. Family members might not encourage healthy risk-taking necessary for growth and achievement, fearing that stress could trigger psychosis or, worse, that risk-taking is a doomed enterprise in the face of impending major mental illness [4]. Schools might become wary of students with the psychosis risk label, as might peers [4]. Even if clinicians and researchers maintained confidentiality, young people and their families might disclose the label—which could be easily misperceived as a label of actual psychosis—to others in their community [4]. And if psychosis risk syndrome treatment was reimbursable through insurance, then a young person could be labeled with a pre-existing condition that influences insurability and employability [4], a concern that has since been reduced significantly with the passing of health care reform legislation.

Paternalism (threat to autonomy). Whether a young person who receives a diagnosis of psychosis risk ultimately develops psychosis or not, all young people with attenuated psychotic symptoms who seek help are primarily doing so from a sense of distress and require our attention [16]. However, their distress often is not focused on their subthreshold psychotic symptoms but instead on trouble with concentration, loneliness, anxiety, fear, or lack of motivation, among other problems [21]. One approach, then, has been to consider limiting information given to patients and families and to avoid mentioning psychosis or schizophrenia risk in an effort to avoid “labeling” and its possible harms. However, this approach raises concerns about paternalism. Across medicine, physicians tend not to censor or greatly filter information they provide to patients and their families, even if the goal is to protect them, as this behavior is not consistent with the ethical principle of [patient autonomy](#) and [patients' right to informed consent](#). It has also long been argued that avoidance of words like psychosis and schizophrenia actually reifies their stigmatizing effects by promoting secrecy and shame [22]. Generally, such linguistic avoidance is not effective, as smart young people tend to look up their symptoms online; they also might look up a clinical research program they are considering attending, or even the publications and curricula vitae of researchers they meet. Then, if young people obtain from other sources information that their clinicians had withheld from them, they might not trust their clinicians. Also, if someone—a teacher, physician, family member—has referred young people with the psychosis risk label to a program for evaluation and treatment of attenuated psychotic symptoms, these young people might already think that they are at risk for psychosis.

Epidemiological Questions and Prognostic Uncertainty

The potential harmful effects of stigma are especially worrisome, considering the high false positive rate of the psychosis risk designation, which is nearly two-thirds after

three years, according to a meta-analysis [7]. Moreover, in one study [23], the false positive rate was estimated to be as high as 84 percent after two years among those referred for intervention, which means that more than 8 of 10 young people who were referred for mental health or community intervention after being given this label turned out not to have been at real risk for psychosis at all, at least in the short term; this high false positive rate has been interpreted as untenable from an ethical perspective by researchers in the field [4]. The high false positive rate results from a number of factors: (1) not everyone at risk develops psychosis; (2) clinicians have high rates of misdiagnosis of risk (only about half of community clinicians' diagnoses are confirmable by experts [23]); and (3) the base rate of psychosis risk in the general population is low—only 1-3 percent.

It is unclear how many of these false positives could in fact be *false* false positives—persons with the psychosis risk label who *would* have eventually developed psychosis had they not received treatment that prevented its onset. Although there is not a sizable evidence base for treatment of attenuated psychosis syndrome yet, data support that both antipsychotic medications and psychological treatments might be efficacious in preventing psychosis onset [13]. One could also argue about the nature and scope of the benefit that an early risk label has on the “true positives”—those who do in fact develop psychosis, sometimes even despite preventative treatment [24]. What, for example, is the benefit of learning you are at risk for something that might not have been preventable?

The Role of Data in Determining Harm

Some earlier studies that my colleagues and I conducted suggested that stigma associated with a label of psychosis risk might be less than that associated with the label of schizophrenia. For instance, we found that family members of young people identified as at risk for psychosis had low “associative” family stigma; they reported that at-risk youths should vote and work, and they denied any sense of shame about their family members or need to conceal their symptoms [25]. Further, we found that, among college students, public stigma elicited by a clinical vignette describing attenuated psychotic symptoms was similar regardless of whether the diagnosis was psychosis risk or schizophrenia, unless the psychosis risk label also had a few brief informational sentences attached to it stating that the real risk of psychosis was 35 percent in 2.5 years, in which case public stigma, expressed as a desire for social distance, was greatly reduced [26].

It is only in the past few years that data have become available on stigma experienced by young persons with attenuated psychotic symptoms. More specifically, studies of young people with attenuated psychotic symptoms, or with a history of hypomanic symptoms (consistent with an increased risk for bipolar disorder), have focused on the relationship between self-labeling as mentally ill and stigma stress, defined as perceived harm of

mental health stigma in excess of perceived resources to cope with it. These studies found that, after adjusting for age, gender, symptoms, and functioning, [self-labeling as mentally ill](#) was associated with greater stigma stress and reduced well-being [27, 28], more suicidal ideation (mediated by social isolation) [29], and higher rates of developing schizophrenia [30], although self-labeling also was associated with more positive attitudes toward treatment [31]. Thus, these studies suggest that self-labeling as mentally ill is harmful overall for youths at risk for mental illness, although they do not provide any data as to the specific effects of clinicians' use of diagnostic labels.

Although these studies on self-labeling are informative and advance our understanding of the harms of self-labeling, questions remain. It is plausible that self-labeling and its attendant stigma stress derive from the very symptoms that place persons at risk for psychosis rather than from an external label of psychosis risk given by a clinician or researcher. For example, "perceived negative attitude of others"—which is correlated with symptoms such as ideas of reference and suspiciousness [32]—like stigma stress, predicts psychosis onset [33]. But "perceived negative attitude of others" might have some basis in reality; others might be responding negatively or in a stigmatizing way to symptomatic behavior or speech. Also, this sort of self- and other-labeling as mentally ill can occur in a community long before persons seek help or receive any official labels of psychosis risk, which can take years, if in fact help is sought at all. Analysis of the Collaborative Psychiatric Epidemiology Surveys found that more than two-thirds of persons with psychotic-like experiences do not seek help [34]. In fact, in a large Chinese study of 524 persons who had no lifetime history of psychiatric disorder, perceived public stigma was associated with the degree of psychotic-like experiences, specifically delusion proneness [35]. Thus, stigma was experienced by people with psychotic-like experiences who had never met a psychiatrist, much less been given a label by one.

In an effort to study the degree to which "official" labels of psychosis risk might be harmful and stigmatizing, our group specifically queried at-risk youths in New York about stigma associated with coming to our psychosis risk program, while accounting for stigma related to symptoms [36]. Upon enrollment in our program, youths were informed that they met criteria for being at risk for psychosis and that psychosis was like the experiences and symptoms that they already had, only more severe. They were told that about two-thirds of the people in the program would *not* develop psychosis, and that if they were in fact among the third who did, they would immediately receive treatment for it. To study stigma, we used the "labeling processes" heuristic developed by the sociologist Bruce Link, which describes how patients, upon receiving a psychiatric diagnosis, begin to identify with and internalize negative stereotypes associated with mental illness, in particular schizophrenia, such that they feel discouraged and ashamed and withdraw from others [20]. Using Link's measures adapted for an at-risk group, we assessed participants' awareness of and agreement with stereotypes related to the psychosis risk label we conferred, controlling for symptom severity; and we also queried

participants about negative emotions (e.g., shame) and positive emotions (e.g., relief) they experienced with respect to both the psychosis risk label and the symptoms that they had [36]. Overall, we found that these youths were aware of stereotypes associated with “emotional problems” (such as impaired, dangerous, less trustworthy), even more so than youths with nonpsychotic mental health disorders. However, they largely did not agree with or endorse these stereotypes. Participants also reported significantly more shame and discrimination related to their symptoms rather than to the label itself, which instead evoked more positive emotions, such as feeling understood, hopeful, and relieved [36].

Altogether, these data support that the psychosis risk label need *not* be harmful and might even confer considerable benefit, as it offers an explanatory framework for symptoms experienced that could then be treated, a quantification of risk for psychosis, and potential strategies for minimizing risk.

Future Directions

Efforts at early intervention in schizophrenia are based on the premise that identification of youths at risk for psychosis will facilitate earlier and better intervention that addresses current morbidity and delays or even prevents psychosis and its consequent functional disability. A number of interventions hold promise, in particular psychological interventions and pharmacological approaches that, unlike antipsychotics, target abnormal glutamatergic function [37] or oxidative stress [38], as these may be more relevant to the pathophysiology of the early stages of schizophrenia than the abnormal dopaminergic function that underlies later full-blown psychosis. In the coming years, individualized risk assessment for psychosis might follow the lead of personalized medicine, such that risk could be stratified by severity or quantified, especially with the emergence of biomarkers and greater understanding of underlying neural mechanisms. This development should lead to both a reduction in the false positive rate and the development of more effective intervention strategies.

But the emotional risks of stigma and discrimination associated with the label of psychosis risk are real, especially if the label occurs without information about what it means. Autonomy—including the right to be informed of one’s diagnosis—is a relevant ethical concept, but so is nonmaleficence, specifically the Hippocratic Oath and the promise “to do no harm” (i.e., *primum non nocere*). In a thoughtful review of these complexities in disclosing psychosis risk, Mittal and colleagues [39] argue that the conveying of diagnostic or prognostic labeling information should be tailored to each individual, particularly when working with minors. They also argue that legal standards and the promotion of autonomy support full disclosure of at-risk status to adults and parents of minors in order to facilitate informed treatment decisions. The provision of information to minors themselves, however, must take into account age and developmental sensitivities, such as social context, identity formation, cognitive capacity,

and comorbidities [24]. Moreover, clinicians must remain cognizant that the interests of the minor (and his or her feelings) might not be entirely isomorphic to those of his parents (which shape how he behaves) [24]. Overall, it is important to take time to speak with young people and their families, provide clear and easy-to-understand information, solicit and answer questions, and to do these things on an ongoing basis, not as a one-time discussion [39]. It is also important to recognize the personal strengths each person has and to promote hope and recovery.

Finally, the potential stigma of a psychosis risk label can be addressed at the structural or public health level. This strategy has worked in Australia, where ultra-high risk clinical research programs were first located in community centers instead of hospitals or universities [22] and then embedded entirely in nationwide strategies to promote teen mental health and well-being support [40]. Furthermore, being considered as at risk for psychosis is not inherently pejorative, and stigma can be tackled head on by those who have attenuated psychotic experiences. For example, there are now movements afoot, such as Intervoice, that conceptualize hearing voices as not necessarily pathological but as a variant, such as being left-handed [41].

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