Identifying the young person at risk of psychosis

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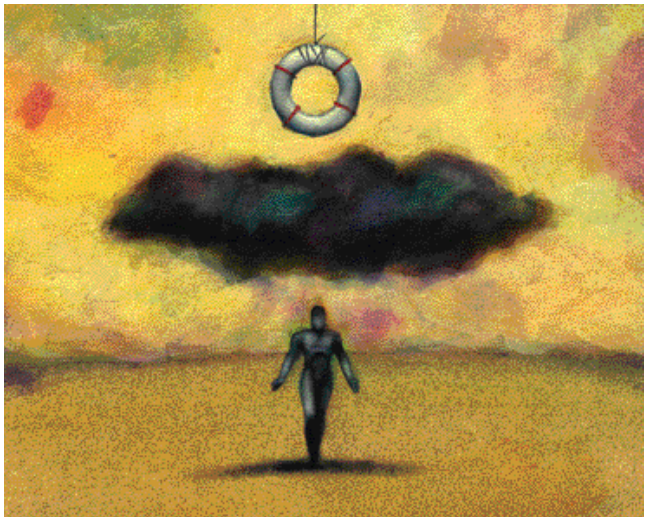

A fundamental shift in the approach to early identification of psychosis is urgently needed. Recognising treatment-resistant symptoms of anxiety and depression in young people is the most effective way of identifying those at risk of psychosis.

At least 10% of the population experience chronic psychiatric disorders, and these generally first manifest in adolescence.[1,2] More than 3% of the general population develop a psychotic disorder such as schizophrenia or bipolar disorder at some time in their lives.[3] The World Bank predicts that by 2020 mental health will become the most costly healthcare sector and the global burden of disease attributable to neuropsychiatric disorder will increase by 50%. When this occurs, neuropsychiatric disorders will represent 15% of the global human disease burden.[4] Given these projections, preventative measures are urgently needed.

The value of early intervention

There is evidence that the neurobiological processes underlying some chronic and relapsing psychiatric disorders are progressive, at least in the early course of these diseases. Hippocampal changes associated with major depressive disorder increase as a function of the total number and duration of depressive episodes.[5]

In schizophrenia, course severity and treatment resistance, indexed by the higher doses of antipsychotic medications needed and the reduced likelihood of full recovery, are proportionate to the length of delay to first treatment[6] and the number of relapses subsequently experienced.[7,8] It is the early course of schizophrenia that is the most active stage of the illness overall,[9] producing the bulk of the mostly permanent consequences of this illness.[10-13]

With the possible exception of strategies to reduce substance use, there are no established cost-effective approaches for the primary and universal prevention of serious psychiatric disorders. Although the focus has been on what is known as indicated prevention (where 'at risk' individuals are identified before the onset of psychiatric illnesses), only early recognition[14] and intervention[15] approaches (in which people are identified early in the course of their disease) have been demonstrated to be feasible.

Targeting young people

The main target group for the identification of individuals at risk of psychiatric disorders is young people because the onset of most of these conditions occurs in childhood and adolescence. Half of all lifetime cases of mental disorders start by the age of 14 years, and three-quarters of cases occur by 24 years of age.[16] Psychotic disorders rarely occur before the age of 14, but there is a marked increase in prevalence between the ages of 15 and 17 years. Most lifetime cases of mental disorders have occurred before the patient is 35 years old.[17]

Importantly, 18% of Australian school students report regular use of cannabis by the age of 15 years.[18] This fact is significant because the use of cannabis in this age group is highly predictive of adult psychiatric comorbidity. Hence, reduction of cannabis use in young people represents one of the few currently feasible primary preventative measures in mental health.

Challenges with early identification

Although adolescents are the target population for early identification of psychotic disorders, they are the age group least likely to access health services[19] and for whom healthcare providers feel least well equipped to manage.[20] This combination of factors results in major delays in the recognition and treatment of adolescent-onset psychiatric disorders.[21,22]

Approximately 40% of patients with anxiety disorders and mood disorders report that they had sought treatment in the same year as the onset of their disorder; the median delay in help-seeking was eight years for the remaining 60%.[23]

One-third of patients with bipolar

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disorder experience a delay before treatment of at least 10 years and 69% of patients with this condition report being repeatedly misdiagnosed initially.[24]

For patients with schizophrenia, the mean time from onset of the first signs of illness until treatment is commenced exceeds five years (median greater than three years).[25]

Although many adolescent-onset disorders are self-limiting, 10% of adolescents and young adults progress to chronic psychiatric disability[1] that might have been reduced by earlier treatment.

Identifying risk factors

Considerable effort has been made to investigate the predictive values of risk factors for psychosis that are remote from the disease itself. These so-called 'distal' risk factors include family history, childhood developmental issues, social anomalies[26] and changes in cognitive function.[13,27] The main conclusion of this work is that these risk factors alone do not provide sufficient predictive value of future psychotic disorder in individual cases.[28]

The limited predictive value of 'distal' factors has turned attention to the recognition of 'proximal' factors, specifically the early but nonspecific symptoms of these disorders that appear before permanent psychosocial disability occurs. Detection of these proximal factors represents the most feasible approach to early detection.

The early disease course

The ability to recognise people at risk of a psychotic disorder is based on a sound knowledge of the early disease course of schizophrenia, major depressive disorder and bipolar disorder, which are often indistinguishable.

Schizophrenia

The early course of schizophrenia is usually insidious and fewer than 20% of patients have an acute onset.[29] The pretreatment period is divided into two stages: the prepsychotic prodrome and the psychotic stage.[30,31] The prepsychotic stage lasts from the appearance of the first symptom until appearance of the first psychotic symptom, and usually has a mean duration of more than four years.[25,29] The psychotic stage covers the period from the appearance of the first psychotic symptom until first effective antipsychotic treatment. Also known as the Duration of (initially) Untreated Psychosis (DUP), this phase has a mean duration of more than 12 months.

The prepsychotic prodrome can be divided into an extended early prodrome phase, lasting three years on average, and a late prodrome phase lasting about 12 months.[29] The first symptoms to appear in the early prodromal phase are persistent or recurrent depressive symptoms. Within 12 to 18 months of disease onset, negative symptoms (such as difficulty thinking and concentrating, loss of motivation and energy) and social disability (reflected in poor work/school performance and social withdrawal) are added to the depressive symptoms that were already evident.[29,30]

In the late prodromal phase, increasing levels of dysphoric and hyperarousal symptoms (e.g. insomnia) herald the breakthrough of attenuated positive symptoms (ideas of reference, odd beliefs, unusual perceptual experiences, suspiciousness or paranoid ideation).[10,31] Alternatively, patients may experience brief bursts of psychotic symptoms that resolve spontaneously within hours or days. In fewer than 10% of onsets of psychotic illnesses, psychotic symptoms are the first recognisable symptoms.

Major depressive disorder

The early course of depressive disorder, from the appearance of the first symptoms until diagnosis and first effective antidepressant treatment, is usually protracted. Depressive disorder cannot be distinguished from schizophrenia until the emergence of obvious psychotic symptoms in the latter.[29,30]

Treatment delays in excess of seven years are typical with depressive disorder because of the insidious onset of the persistent or recurrent depressive symptoms.[29]

Bipolar disorder

The early features of bipolar disorder also overlap with the early symptoms of unipolar depression and schizophrenia. Young people with a past diagnosis of depressive disorder followed by ongoing mood instability or 'frequent ups and downs' are at high risk of a future diagnosis of bipolar disorder,[32,33] especially bipolar type II.[34] In this context, mood instability diagnostically represents sub-threshold bouts of depressive and manic symptoms.

Therapeutic implications

Strategies for early detection of psychotic disorders should use a broad net to capture patients at risk of developing major depression or bipolar disorder as well as those at risk of developing schizophrenia. An important therapeutic reason for early identification is that disease progression, in all three disorders, appears to damage brain systems and cognitive function,[9] both of which are associated with increased treatment resistance. The causes and consequences of delays in treatment for these disorders are similar and include:

- increased secondary risks of suicide
- disrupted development in young people
- chronic psychosocial disability, including relationship breakdown
- vocational failure
- substance abuse
- itinerancy.

Early detection efforts must focus on young people, and any young person presenting with symptoms of depression and anxiety that do not spontaneously resolve within a month or two should be the target of effective assessment and intervention.

The subgroup of patients that develop additional signs of social role impairment or negative symptoms are at heightened risk of major psychiatric disorder, including

schizophrenia. By the time bouts of attenuated or obvious psychotic symptoms appear in the early course of schizophrenia, serious permanent disability will have already occurred, and the role of early psychosis intervention at this stage is restricted to mainly tertiary prevention. Although there is accumulating evidence that early detection is the most feasible approach to reducing morbidity, there is little research data on how best to achieve timely intervention in the real world.

Assessment and management

Healthcare systems and clinical practice are both important in identifying persons at a high enough risk of psychosis to enable diagnostic discrimination and justify early intervention. In the absence of diagnostic tests, the results of assessments and treatment trials over time iteratively provide information to progressively refine the final diagnosis.

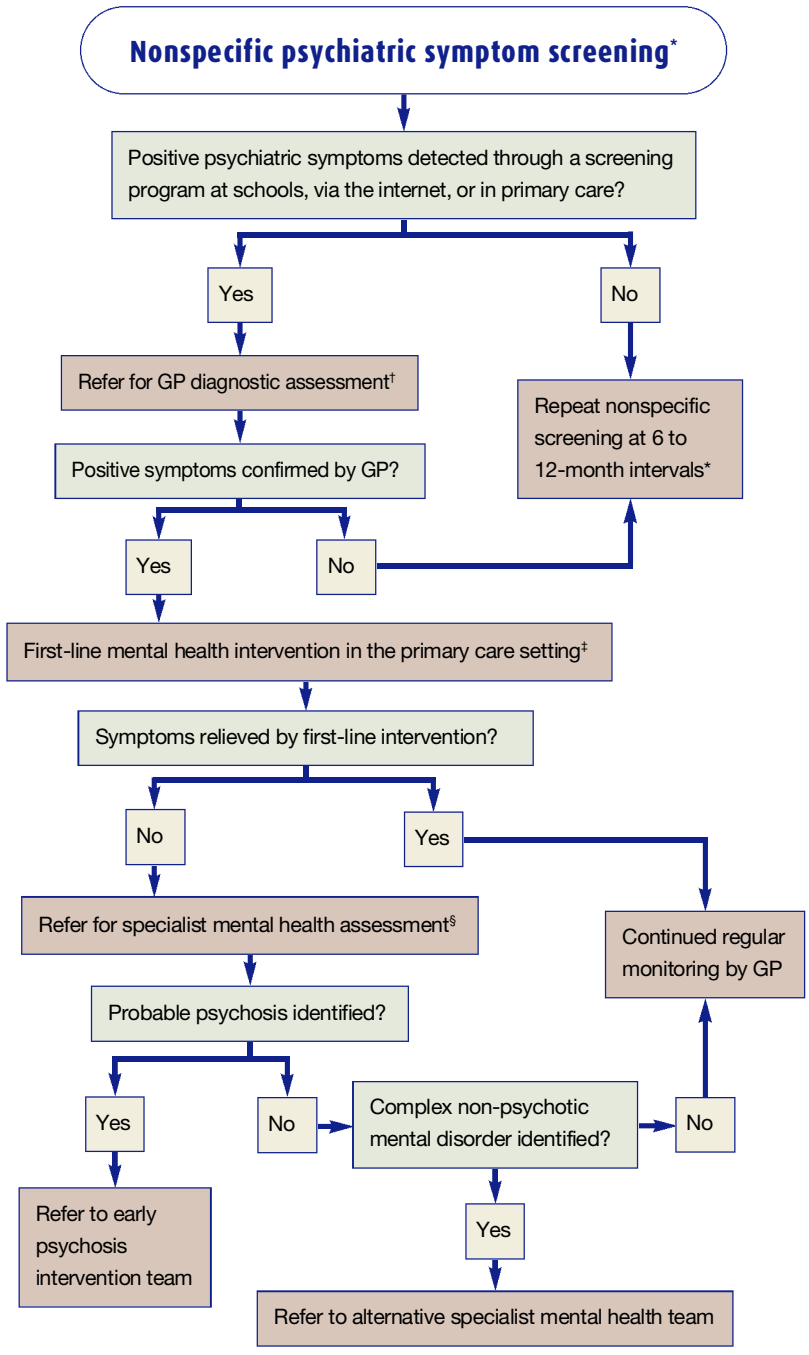
Healthcare systems

A dilemma in the identification of young people at risk of psychosis is that diagnosis and predictive accuracy can only be obtained at the cost of delayed intervention.[30] One strategy has been to assess help-seeking patients in the late prodromal phase of incipient psychosis. This research method was pioneered at the PACE Clinic in Melbourne and produces up to a 40% conversion rate to frank psychosis within 12 months.[35] Although this approach identifies a higher rate of definitive cases, its limitations are that the early prodrome phase produces the bulk of most permanent consequences of schizophrenia,[10,31] and only a small number of individuals at risk seek help. The design of better systems for routine early detection must incorporate aspects of disease screening theory.

A staged approach to detection

The predictive accuracy of a screening test improves as the prevalence of the disease of interest increases in the pretested population.[36] Therefore, early recognition is

A staged approach to the detection of young people at risk of psychosis



* Symptom screens are prompts that elicit reports of experiences that could possibly be symptoms. An example is the questions listed in Table 1.
† GP diagnostic assessments refer to interviews that help confirm the presence of symptoms or disorders, and include the PHQ-QA[47] or the CIDI-Auto.[48]
‡ Examples of a brief mental health intervention in primary care include GP supportive counselling, a trial of antidepressants and/or cognitive behaviour therapy and GP-arranged family intervention by allied health staff.
§ A specialist mental health assessment involves thorough assessment of psychosocial disability, neurocognitive function and the patient's family; developmental, educational and dietary history taking; and a diagnostic assessment by a psychiatrist. Multiple appointments are usually required.

improved by designing healthcare systems that operate as a series of filters, enriching the tested population with disease cases by filtering out low risk members.[37] The flowchart on page 63 outlines such an approach to the detection of young people at risk of psychosis.

The first filter in such a hierarchy might be regular routine screening of young people for the nonspecific symptoms of depression and anxiety at school,[38] either by student questionnaire or by parent or teacher reports. Most young people without significant symptoms and at low risk of psychosis would be filtered out by such a procedure. The remainder could be encouraged to see their general practitioner for a general health check and diagnostic assessment, which would filter out patients with self-limiting or treatable conditions.

The next filter could operate by offering young people with persistent or recurrent symptoms first-line brief mental health interventions in the primary care setting delivered in conjunction with allied health clinicians. Nonresponders to these interventions would then progress to the final filter, referral to a specialist mental health service. Irrespective of whether psychotic symptoms were present, all members of this psychosis-enriched group would be at high risk of a broad range of major psychiatric disorders and warrant specialist observation and treatment. Once this group was defined it is assumed approximately one-quarter of these people would be likely to convert to a psychotic disorder in the subsequent five years based on age-adjusted prevalence estimates noted above.

Our healthcare systems only occasionally operate according to this description, which is one of the main reasons for the extensive delays seen in the routine treatment of serious psychiatric disorders. If young people at risk of psychosis and other major mental disorders are to be identified earlier than they currently are, there must be a greater emphasis on the health needs of adolescents[39-41] and the provision of preventative mental healthcare.[42] Barriers to adolescents attending general practitioners,[39,40,43] including fears about confidentiality breaches, must also be addressed. More accessible and responsive specialist mental health services are essential to support the early detection efforts of general practitioners.[44] Improved

Table 1. Screening questions

The following screening questions can be adapted in the light of knowledge about the individual patient. Parents can be asked about their teenage children using the same questions modified appropriately.

Introductory comment

I want to ask you a few questions about how you are getting on with life.

Depression and anxiety

Have you been feeling depressed or sad lately, or are you unhappy about everything?
Have you been feeling nervous or tense lately or are you worried about everything?

Negative symptoms

Do you have trouble concentrating or remembering things or making decisions?
Have you lost motivation or do you feel you cannot be bothered doing things you used to do?
Have you withdrawn from your friends or do you prefer to spend your time by yourself?
Have you lost interest in dating?

Psychosocial role impairment

Are you having trouble keeping up with your (school) work or is keeping up stressing you out?
Are you having trouble getting along with your school mates (work mates) or teachers (work supervisors) lately? [Follow up on reasons why, especially if related to neglect of duties or responsibilities in relationships.]
How are you getting on with your parents? [Follow up on reasons why, especially if related to neglect of duties, responsibilities in relationships, or antisocial/risk taking behaviour.]
Have you stopped doing things you are supposed to do, like exercising or playing sport?
Have you stopped doing your chores at home, because you just want to sit down or lie on your bed?
Do you neglect your personal hygiene sometimes?

Psychotic symptoms

Has anything very unusual or strange happened to you recently?
Have you recently felt that people are talking about you or watching you in an odd manner?
Have you noticed anything suspicious going on around you lately?
Have you heard unusual noises or voices when no one is around?

Risk assessment

Are there times when you feel despair or complete hopelessness, like there is no future for you?
Have you ever had thoughts of deliberately harming yourself, or even killing yourself?
Are there times when you feel so angry that you want to smash things or hit other people?
Have you felt like doing something impulsive or antisocial lately, like wanting to steal things, take street drugs, run away from home, or have unprotected sex with total strangers?

community mental health literacy will also play a positive role in improving the current system.[45]

Implications for clinical practice

Until there is strong evidence for how to improve adolescent access to healthcare, general practitioners may be guided by youth preferences for the following:[43,46]

- flexible hours
- drop-in long appointments
- minimum out-of-pocket expenses
- management of confidentiality in relation to family
- nonjudgemental advice
- across-agency linkage
- access to multidisciplinary support
- competency in adolescent health issues.

All adolescent patients should be asked probe questions about depression, anxiety, substance use and psychosocial function; this action should be routine in the same way blood pressure measurement is with older patients (Table 1). Alternatively, parents can provide information from indirect observation. Confirmatory diagnostic assessment may require the general practitioner to upgrade their psychiatric diagnostic skills or use support tools such as the Patient Health Questionnaire for Adolescents (PHQ-QA)[47] or the computerised Composite International Diagnostic Interview (CIDI-Auto).[48]

The subgroup of adolescents most at risk of major psychiatric disability is those with persistent symptoms.[49] These young patients justify timely and energetic intervention, starting with brief mental health interventions applied by the general practitioner and undertaken with the assistance of allied health staff where possible.

Evidence for effective treatment

Unfortunately the effectiveness of first-line mental health intervention in adolescents is limited.[50] The largest trial in adolescents with major depressive disorder showed that after 12 weeks of treatment only 37% of cases achieved full remission with antidepressant medication and cognitive behavioural therapy (CBT) combined.[51] This outcome was superior to either intervention alone, although the rate of partial response was much higher,[52] especially if treatment continued for six to nine months.[53] At 12 weeks, more than 50% of the responders continued to suffer residual symptoms[51] or functional impairment.[54] Importantly, the rate of suicidal thinking was highest in the group that only received antidepressant medication, a finding that emphasises the need for frequent supportive contact with adolescents in the early stages of treatment.[52,53]

For the young person who does not respond to a brief mental health intervention, it is important to review:

- the diagnosis
- adherence with prescribed medication
- co-existing substance abuse
- personality issues – especially borderline or antisocial traits that may complicate diagnosis and treatment
- family factors – such as parental psychopathology, marital conflict or a physically or emotionally abusive home environment.

Specialist referral

A one-off second opinion from a specialist may be useful in considering whether continuation of primary care treatment or referral to a specialist mental health service might be the most beneficial. Ultimately if these actions do not achieve substantial relief of symptoms, then the young patient should be referred for a comprehensive assessment at a specialist mental health service.

Although adolescents with difficult to treat psychiatric symptoms are at heightened long-term risk of a psychotic disorder, it is more likely that they have a nonpsychotic illness. Decisions, however, about ongoing assessment and treatment are probably best made by a specialist child and adolescent psychiatric service or an adult mental health service with a dedicated early detection and intervention team for psychotic disorders. In these services, thorough risk assessments, which can be repeated over time, should lead to an accurate diagnosis.

Specialised treatment trials, including augmentation with antipsychotic agents and specialised CBT for high-risk patients,[55] can also be carried out through dedicated services following contact with specialist intervention teams. Additionally, multidisciplinary rehabilitation and disability support strategies can be introduced earlier if negative symptoms are present or psychosocial impairment has already become apparent.

A number of novel low-risk dietary/pharmacological treatments, including the use of glycine, omega-3 fatty acid or pregnenolone dietary supplementation or antidepressants, might also be considered in this context.[56-60]

Conclusions

The earliest feasible point in time at which a young person at risk of psychosis can be identified is during the early prodrome of psychosis, before the onset of the first psychotic symptoms. Even achieving this will require a fundamental shift in our health systems towards an emphasis on youth mental health and the importance of prevention. Routine screening of young people and competent diagnostic evaluation in primary care settings is essential for the success of this endeavour.

A focus on the recognition of young people with persistent or recurrent symptoms of anxiety and depression is the most effective way of identifying those at risk of psychosis and screening alone will not improve outcomes.[61] Only a new standard of primary and specialist mental health care will substantially reduce the massive burden of disability associated with these diseases.[62,63] MT

A list of references is available on request to the editorial office.

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