Monitoring and Care of Young People at Incipient Risk of Psychosis

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Abstract

This article describes the theoretical background, origins, and development of a new clinical service for intervention in the putatively prodromal phase of schizophrenia and other psychotic disorders. Establishing such a service required examination of conceptual issues such as the meaning of the prodrome in psychosis and its association with risk of subsequent psychosis, and of practical issues related to identifying prodromal patients in the community and engaging them in monitoring and treatment. Patients' needs, timing, and mode of treatment had to be considered. Preliminary data from the service's 20-month pilot phase are presented to help inform these issues.

Schizophrenia Bulletin, **22(2): 283–303, 1996.**

The possibility of preventing psychosis by intervening in the prodromal phase of schizophrenia and other psychotic disorders has been acknowledged for decades. In 1927, Harry Stack Sullivan said of schizophrenia, "I feel certain that many incipient cases might be arrested before the efficient contact with reality is completely suspended, and a long stay in institutions made necessary" (Sullivan 1927/1994, p. 135). Likewise, in 1959 the Australian psychiatrist Ainslie Meares stated, "What is needed is not the early diagnosis of schizophrenia, but the diagnosis of prepsychotic schizophrenia. We must learn to recognize that state of mind which will develop into schizophrenia unless appropriate measures are taken to prevent deterioration" (Meares 1959, p. 55). The idea of early detection and treatment to prevent or minimize psychosocial (Johnstone et al. 1986; Loebel et al. 1992) and possibly biological disruption (Wyatt 1991) is tantalizing but elusive. This article describes our attempt to intervene in the prodromal phase of psychosis by establishing a clinic for monitoring and care of young people at putatively high risk of impending psychosis. A parallel research agenda was to investigate the predictive power and relative risk for psychosis of a number of neurobiological, neuropsychological, and psychopathological markers.

We had to address several key issues in developing this service. First was the concept of the prodrome in psychosis and its relationship to the actual risk of developing a psychotic disorder. Second was the problem of defining onset and deciding when to commence treatment. Next, we had to define the characteristic clinical features preceding a first psychotic episode and to consider their significance and the difficulties in recognizing them. Further issues were related to detecting prodromal patients in the community, determining their needs, and considering what types of interventions to use and how to provide them. In this article, we discuss each of these issues and present data from the first 20 months of our clinic's operation.

We refer throughout to preventing, modifying the course of, and

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determining the onset of *psychosis*. Historically, this term has been defined a number of different ways. Current definitions tend to be symptom based. For example, the *DSM–IV* (American Psychiatric Association 1994) glossary suggests that psychosis is defined by the presence of "delusions or prominent hallucinations" but recognizes that the definition can be widened to include disorganized speech and grossly disorganized or catatonic behavior. The relationship between the syndromes of psychosis, schizophrenia, and other psychotic disorders needs to be briefly discussed. Like psychosis, schizophrenia has been defined several different ways. The current dominant paradigm, encapsulated in the *DSM–IV* definition, combines a symptom-based approach requiring the presence of certain positive features and a prognostic approach requiring a decline in psychosocial functioning and a prolonged course. Another issue is the instability of the clinical picture in early psychosis such that psychotic mood disorders and schizophrenia are sometimes indistinguishable (McGorry 1994), making it difficult to diagnose schizophrenia at the time of first onset of psychosis.

Conceptual Issues

Prodromes, Precursors, and At-Risk Mental States. It has long been recognized that the onset of the first episode of psychosis may be gradual and preceded by low-grade symptoms and signs retrospectively labeled the "prodrome" (Keith and Matthews 1991). The term "prodrome" is derived from clinical medicine and refers to the early symptoms and signs of a disease that occur before the obvious characteristic features become manifest (Yung and Stanley 1989). Measles has previously been used to illustrate this concept (Yung and McGorry 1996, this issue). In this disease, a nonspecific prodrome of cough and coryza usually precedes the characteristic measles rash by 3 or 4 days. During this prodromal period, a definitive diagnosis of measles cannot be made because the features are not specific to the disease. The symptoms could result from an upper respiratory infection or another disease. However, with the advent of the rash, measles is diagnosed, and the cough and coryza of the previous few days are then retrospectively recognized as the measles prodrome. This example illustrates how the prodrome, a retrospective concept, cannot be defined with certainty prospectively (Eaton et al. 1995; Yung and McGorry et al. 1996, this issue).

How then, can we conceptualize the mental state of a person who displays features suggesting an impending disorder, that is, who seems to be in the "prodromal period"? Eaton and colleagues (1995) have suggested the term "precursor signs and symptoms" and defined as "signs and symptoms from a diagnostic cluster that precede disorder but do not predict onset with certainty" (p. 968). Our group has suggested an alternative term, "at-risk mental state," which implies that the clinical picture will not invariably be followed by full disorder (McGorry and Singh 1995). The advantage of this term is that it emphasizes that the syndrome represents a *state* risk factor for the disorder. That is, at the point when a person has a particular mental state, he or she is at increased risk of onset of the actual disorder. This concept of a state risk factor is to be distinguished from *trait* risk factors such as family history and certain biological markers, which confer heightened probability of onset at all times, regardless of the patient's current mental state (Wolf and Cornblatt, in press).

The idea of state risk factors has analogies in clinical medicine. It is recognized, for instance, that people who experience the characteristic chest pain "angina pectoris" are at increased risk for later acute myocardial infarction (AMI). Angina pain is not as severe as the pain of an infarct and is accompanied by fewer of the features generally associated with infarcts, such as sweating, nausea, vomiting, pallor, and breathlessness. Thus, angina could be seen as an attenuated or subthreshold version of the full-blown AMI, with both conditions having the same underlying pathology of ischemic heart disease and atherosclerosis. The syndrome of "crescendo angina," which is angina of increasing frequency and severity, is described as a "preinfarction syndrome" indicating high risk of imminent AMI.

This model can be applied to psychotic disorders. Symptoms such as overvalued ideas or vague perceptual abnormalities can be thought of as attenuated forms of psychotic symptoms, indicating increased risk for subsequent psychosis as angina indicates increased risk for subsequent AMI. Likewise, delusional mood can be seen as the equivalent of the preinfarction syndrome. Note that these mental state features must be new phenomena and must be distinguished from schizotypal personality features, which are long-

standing and represent a trait risk factor for psychosis (analogous to hypertension's relationship to AMI). This kind of attenuated or subthreshold model has been used in relation to depressive disorders. Subthreshold depressive symptoms, for example, have been viewed as risk factors for major depressive disorder in children (Jaycox et al. 1994) and as precursors with a degree of relative risk for major depression in adults (Eaton et al. 1995).

Another example is transient ischemic attacks (TIAs). These consist of sudden focal neurological abnormalities that settle rapidly within 24 hours with full clinical recovery (Kistler et al. 1991). They resemble a full-blown stroke but are distinguished from stroke in that they spontaneously resolve. TIA's are known to confer an increased risk of stroke, with an estimated 40 percent of patients with some types of TIA progressing to a complete stroke within 3 years (Rubenstein and Wayne 1980). As in the above example, the underlying pathology, that of thromboembolic cerebrovascular disease, is the same in TIA and stroke. Again, this model can be used in psychotic disorders. Histories of brief transient episodes of psychotic symptoms that spontaneously resolve have been described occasionally by patients presenting with psychotic disorders (Faergman 1963; Jauch and Carpenter 1988). Such transient psychotic symptoms are also known to occur in some people under the influence of certain psychoactive substances such as amphetamines and hallucinogens (Tsuang et al. 1982; Vardy and Kay 1983) and cannabis (McGuire et al. 1994). They have also been noted in patients with some personality disorders such as borderline personality, particularly when the patients are under stress (Gunderson and Singer 1975; Vaillant and Perry 1980), and in a proportion of normal individuals who, when subjected to sensory deprivation, temporarily suffer from visual and auditory hallucinations (Slade 1984). These transient psychotic episodes may indicate increased risk of subsequent psychosis and can be thought of as the "psychosis equivalent" of TIAs.

Defining Onset. Identifying symptoms or signs that reliably predict onset would obviously aid attempts to prevent mental disorders. Such specific predictors do not currently exist (Eaton et al. 1995). In fact, one could argue that if any such risk factors were identified they would be best conceptualized as early phenomena of the disorder itself. For example, a feature that is invariably followed by onset of psychosis might be thought of as part of schizophrenia itself. Researchers would then call the syndrome "prepsychotic schizophrenia" rather than label the feature a "specific prodromal feature," "specific precursor feature," or "specific feature in the at-risk mental state." Identifying the feature should therefore lead to initiation of treatment.

This perspective is of course partly true but not so simple in practice. Again using the model of measles, an early sign of the disease is the presence of Koplik spots, small, white lesions inside the mouth that represent the mucosal manifestation of the skin rash but that precede the rash (Yung and Stanley 1989). Koplik spots can be thought of as an early feature of the measles disease itself, or a "specific precursor feature." Skilled clinicians would note their presence in an ailing child and correctly predict the inevitable development of the measles rash. However, clinicians not so knowledgeable or experienced in managing measles patients could easily fail to look for Koplik spots, not detect the spots even if they sought them, or misdiagnose them as, for example, oral candidiasis. Conversely, another patient presenting with cough and coryza might be labeled as having Koplik spots and therefore measles, but not actually have them because of misdiagnosis of another oral lesion such as candidiasis. Hence, false negatives and false positives could occur. For this reason, *clinically detected* Koplik spots can be thought of as a measles precursor with high specificity.

The idea of false positive and false negative precursor features can be further illustrated by the TIA example. A migraine might resemble a TIA clinically but have a different underlying pathophysiology and not confer increased risk of stroke; that is, it would be a false positive. Conversely, a TIA might be wrongly labeled as a migraine; hence, this warning sign for impending stroke would be missed.

The Koplik spot equivalent for psychosis generally or for a subtype such as schizophrenia (if defined disorders are in fact biologically meaningful subtypes) would be a very useful entity to identify. A feature that predicted subsequent psychosis in the near future with a high degree of probability could be used to indicate the timing of specific antipsychotic treatment such as neuroleptic medi-

cation. Several authors have suggested that certain clinical phenomena have some specificity for subsequent development of psychosis. For example, Chapman (1966) theorized that a disorder of selective attention and perceptual abnormalities may predict psychosis and called such phenomena "the early symptoms of schizophrenia," thus conceptualizing these subthreshold symptoms as part of the schizophrenic disorder itself. Others have suggested that a change in the sense of self and the world (Bowers and Freedman 1966) and suspiciousness (Cameron 1938; Conrad 1958) may predict subsequent psychosis. Huber and colleagues (1980) have suggested that coenaesthesic symptoms and certain cognitive abnormalities (some similar to Chapman's disorder of selective attention) represent "transition states" preceding psychotic schizophrenia (Ebel et al. 1989; Gross 1989) and claim that such "basic symptoms" are primary experiences of psychotic symptoms. If any of these clinical features can be found to be strong predictors of subsequent psychosis, then the prospect of intervention before onset of frank psychosis in schizophrenia and other psychotic disorders may be possible. Such hypotheses therefore need to be tested rigorously.

The onset and course of psychotic disorders are more complex than in measles, which is an "all or nothing" phenomenon; that is, either the full disorder develops or it does not. In psychosis, defining the onset of disorder involves a degree of judgment. One important underlying conceptual consideration is whether psychotic symptoms represent qualitatively different phenomena from normal mental experiences or occur on a continuum with normal experiences, representing quantitative deviations only. Traditionally, schizophrenia and psychotic symptoms have been viewed as discontinuous, qualitatively distinct from normal experiences, and "ultimately un-understandable" (Jaspers 1923/1963). "These are true illnesses in which a sharp break in the personality occurs, probably the result of a neurophysiological disorder which so far has escaped detection" (Fish 1985, p. 15). Schizophrenia and psychosis are contrasted with neurotic disorders such as anxiety and depression, in which the definition of "caseness" is made arbitrarily because of a quantitative variation from normal. For example, Falloon states, "the task of identifying schizophrenia is facilitated by the usual presentation of clearly specified florid symptoms that represent a qualitative departure from normal mental phenomena" (Falloon 1992, p. 6).

Others, however, conceptualize psychotic symptoms such as delusions and hallucinations as part of a continuum with normal and neurotic experiences (Strauss 1969). Several researchers have investigated subthreshold variants of psychotic symptoms as indicators of "psychosis proneness" or "schizotypy" and found them to occur on a dimension in the general population (Chapman and Chapman 1980, 1987; Claridge and Broks 1984). There is also considerable evidence from family members of schizophrenia probands (Kety et al. 1975) and high-risk followup studies of children of psychotic parents (Mednick et al. 1987) that certain neurological and psychological abnormalities occur on a spectrum. These factors can be seen as vulnerability markers for schizophrenia or partial expressions of the disorder.

A further possibility is that psychotic symptoms represent quantitative differences at onset but at a later point undergo a qualitative change. Claridge (1985), drawing an analogy between psychosis and systemic physical disease, noted that hypertension is arbitrarily defined initially as a quantitative change from normal, but that a point is reached when qualitative structural changes occur in various tissues in response to chronic raised blood pressure. Like physical systemic disorders, mental disorders probably require environmental stress and an underlying susceptibility (Zubin and Spring 1977). Claridge has suggested that as both of these factors are continuous variables then manifestations of disorder occur on a dimension also, from mild or incomplete through severe (Claridge 1985). Claridge concludes that "a continuity view of psychotic behavior becomes not just feasible but the most probable explanation of currently available evidence" (p. 109) and speculates that there may be a point in the course of the disorder when a qualitative change occurs, as happens in hypertensive disease. The timing and clinical indicators of this point beyond which psychosis will invariably occur are not yet known. Ongoing prospective investigation is needed.

To further complicate matters, attention is increasingly being drawn to the multidimensionality of florid positive symptoms, that is, the degree of preoccupation with delusional beliefs, the intensity and frequency of such delusions, the affects they generate, and so on (Chadwick and Birch-

wood 1994; Chadwick et al. 1994). There is no reason why this conceptualization cannot, or should not, be extended to prodromal phenomena. In fact, it may be that the various dimensions of a particular prodromal symptom have different onsets and developments and are loosely correlated with one another. It may also be that particular aspects of a prodromal symptom are more important for different persons.

The definition of actual timing of onset of schizophrenia and other psychotic disorders has received little attention in the literature. One reason for this is that prospective studies mapping the onset of psychosis are difficult to achieve, and onset features of psychosis are usually described retrospectively. The date of onset of psychosis is usually decided arbitrarily based on a combination of patient and informant data, for example, the time of the first noted auditory hallucination (Häfner et al. 1992*a*; Loebel et al. 1992). Such arbitrary decisions do not address the issues of how long a symptom needs to be present, how often, and to what degree of intensity or impact on functioning. Should the label of psychosis be applied to someone who experiences 1 day of auditory hallucinations several times during that day for a few minutes at a time? Or to someone who has had such symptoms for 1 hour, or 1 week, or 2 weeks? Do hallucinatory phenomena occur on a spectrum, and if so, when are they considered frankly psychotic? The same questions could be asked of overvalued ideas and delusions. The significance of combinations of symptoms, such as perceptual abnormalities and disorders of thought content, also needs to be clarified. This issue is important in considering when to treat.

It is also likely that the transition from the premorbid state through the prodromal phase to psychosis is not smooth. Fluctuations should be expected to occur, depending on the person's coping resources, life circumstances, and stress level at the time. As Sullivan stated, "It is never easy to say just when the schizophrenic patient has crossed the line into actual psychosis. In several cases we have found that there had occurred a brief phase of marked psychotic condition some considerable time before the final break" (Sullivan 1927/1994, p. 137).

The definition of onset of disorder is also relevant to considerations of whether intervention during the putative prodromal phase constitutes primary or secondary prevention. If the prodromal period is considered to be part of the disorder itself, then intervention at this stage would be seen as secondary—albeit early secondary—prevention. If, however, the prodrome is viewed as a separate syndrome conferring heightened but not inevitable risk for psychosis, then intervention would be viewed as primary prevention. The perspective may also depend on the stage of the prodrome. Intervention in an early nonspecific prodrome may be thought of as more likely to be primary prevention, whereas later intervention into a prodrome that has possibly passed the point of a qualitative change may be seen as secondary prevention. Eaton et al. (1995) addressed this point, stating, "At some point during development, the onset of full-blown disorder becomes inevitable and the prevention efforts are conceptually shifted from primary to secondary" (p. 971). Thus, the "Koplik spot" of psychosis, if it could be found, would indicate the onset of disorder, and intervention at this time would constitute secondary prevention.

Clinical Issues

Characteristic Features Preceding a First Psychotic Episode. Research into the nature of symptoms and signs preceding the first episode in schizophrenia and other psychotic disorders has necessarily been retrospective in nature, involving reconstructing the prodromal changes in patients who have become psychotic (Cameron 1938; Chapman 1966; Beiser et al. 1993). These studies have found a range of prodromal phenomena and have noted prodrome lengths ranging from a few days to years. The most methodologically sound studies are those of Varsamis and Adamson (1971) and Häfner and colleagues (1992*b*, 1994). The symptoms found most often are, in descending order of frequency, reduced concentration and attention, reduced drive and motivation, anergia, depressed mood, sleep disturbance, anxiety, social withdrawal, suspiciousness, deterioration in role functioning, and irritability. The nonspecific nature of these common features is notable. As mentioned previously, some researchers have suggested that certain symptoms such as disturbance of selective attention, perceptual abnormalities, and other attenuated forms of psychotic symptoms have some specificity for psychosis (Cameron 1938; Conrad 1958; Bowers and Freedman 1966; Chapman 1966).

A more recent and operationalized description of schizophrenic prodrome can be found in *DSM–III–R* (American Psychiatric Association 1987). According to this manual, the criteria for schizophrenic prodrome require the presence of two or more of the following features: marked social isolation or withdrawal; marked impairment in role functioning; markedly peculiar behavior; marked impairment in personal hygiene and grooming; blunted or inappropriate affect; digressive, vague, overelaborate, or circumstantial speech, or poverty of speech or speech content; odd beliefs or magical thinking; unusual perceptual experiences; and marked lack of initiative, interest, or energy. The first six items are based on observable behavioral changes. Item 7, odd beliefs, requires the unusual thought content to influence behavior; thus, an observable element is again necessary. This requirement is problematic, as the behaviors listed may result from a number of different underlying mental states, including frank psychosis itself. The inclusion of mainly observable phenomena is intended to increase the reliability of the diagnosis. The reliability of some items, such as "odd or bizarre ideation" or "markedly peculiar behavior," appears to vary according to the measuring instrument used (Jackson et al. 1994). Additionally, in a first-episode psychotic population, prodromal symptoms do not appear to be particularly specific to schizophrenia but are also found in other psychotic disorders (Jackson et al. 1995). It is also apparent that the *DSM–III–R* list omits many of the features, particularly the experiential phenomena, frequently noted in other studies (Yung and McGorry 1996, this issue). Because of concerns such as these, this list of criteria was dropped from *DSM–IV*.

Recognizing these difficulties with the *DSM–III–R* description of psychotic prodrome, we performed our own pilot study by restrospectively reconstructing the prodromes preceding initial psychotic episodes in a series of 21 recent-onset psychosis patients (Yung and McGorry, in press). Phenomena were diverse and varied widely among patients. Again, many nonspecific prodromal features were found, including anxiety (86%), irritability (86%), depressed mood (76%), low energy (62%), and social withdrawal (71%). Other features seemed to be attenuated forms of psychotic symptoms, including perceptual disturbances (62%), delusional mood (62%), and suspiciousness (71%). Importantly, nonspecific features tended to occur early and were followed by more frank deviations from normal, such as the attenuated psychotic symptoms, which occurred much closer to the onset of actual psychosis. This finding supports the hypothesis that these features may represent early signs of actual disorder. In general, findings from this study agreed with previous literature on prodromal features in schizophrenia (Cameron 1938; Varsamis and Adamson 1971).

The literature review, pilot study, and critical appraisal of the validity and reliability of the *DSM–III–R* criteria for prodrome informed our thinking as we considered ways of identifying individuals at high risk of incipient psychosis. A major limitation of the work we reviewed is that no one knows how common these symptoms are in similarly aged persons with no disorder. This knowledge gap applies not just to nonspecific prodromal symptoms, but even to the attenuated psychotic symptoms. The base rates of these so-called prodromal symptoms in the general community need to be identified and their implications for prospective research examined.

Prospective Identification of At-Risk Mental States. Lack of specificity makes identifying psychotic prodromes difficult. Mental states that resemble prodromes may or may not progress to psychosis for two reasons. First, changes in mental state may not represent vulnerability but a different underlying pathology—for example, an incipient anxiety, depressive disorder, or situational crisis. Second, enhanced coping, increase in social support, or some other circumstance may prevent, delay, or modify changes that do indicate an at-risk mental state. The former group could be called the "true false positives"; the latter group, the "false false positives." The term false false positives is used because this group of patients would have the same vulnerability markers as the true positives, who do progress from an at-risk mental state to psychosis but, because of resilience or protective factors, do not make the transition. Conceptually, the false false positives may be thought to have early manifestations of the disorder but to make a "recovery" before the frank psychosis develops. The fact that these groups cannot be distinguished cross-sectionally has implications for the measurement of markers. In true positives, specific markers are

present; in false positives specific markers are absent. Specific markers are also present in false false positives, but the individuals' course over time is the same as that of the false positives, that is, nonprogression to frank psychosis.

The problem of false positives arose in Falloon's preliminary attempt at intervention in the schizophrenic prodrome. This study used the presence of the *DSM–III–R* criteria for prodrome as the basis for treatment (Falloon 1992). How many of the people presenting with these *DSM–III–R* features would not have made the transition to psychosis is not known, however. Falloon himself acknowledged that some individuals may have been treated unnecessarily.

Our recent community survey of Australian high school students, which assessed the presence of the nine *DSM–III–R* schizophrenia prodrome features has further highlighted the issue of false positives (McGorry et al. 1995). This study found a high level of endorsement of the prodromal features: at the time of the survey, nearly half the sample (49.2%) had two or more symptoms and hence met the criteria for *DSM–III–R* schizophrenic prodrome. We then raised the threshold for diagnosis of prodrome to include only the more positive of the nine features such as magical ideation and unusual perceptual experiences, and specified that symptoms needed to be present for more than 1 week but less than 5 years (thereby excluding features that might be considered personality traits). As a result 10 to 15 percent of the group met the criteria for schizophrenic prodrome. Several factors could account for this unrealistically high figure. For one thing, the prevalence of *DSM–III–R* prodromal features does not necessarily reflect the presence of a true psychotic prodrome. Also, the study relied on questionnaires to assess the level of symptomatology. (A replication study incorporating a semistructured interview component to validate findings is planned.) Another possibility is that some of the students were undergoing "outpost syndromes," that is, syndromes that resemble schizophrenic prodromes but that resolve spontaneously. These have been found in some individuals who ultimately progress to manifest schizophrenia (Huber et al. 1980). Thus, individuals with outpost syndromes who developed psychotic disorders some years later could in retrospect be thought of as having been false false positives at the time of the outpost syndrome. Alternatively, if the symptoms had been present from an early age, some students may have had schizotypal personality traits. Finally, an important factor is that many of these high school students likely represent true false positives.

The Challenge of False Positives for Early Intervention. The lack of specificity of prodromal features and the problem of false positives create a major challenge for attempts at early intervention. One study design, developed to overcome this problem in high-risk research, combines risk factors to enhance the true positive pickup rate. This is called a "close in" strategy (Bell 1992). Its application in early intervention in psychotic disorders involves combining *trait* risk factors, such as a family history of psychotic disorder (Gottesman and Shields 1982) or schizotypal personality traits (Claridge 1987; Meehl 1989), with the presence of low-grade psychopathology (an at-risk mental state), which is a *state* risk factor, to identify truly high-risk individuals and reduce the number of false positives. Because adolescence and early adulthood represent the peak age of onset for psychotic disorders, particularly schizophrenia (Kosky and Hardy 1992), age is the other risk factor that could be included. This close-in strategy thus involves focusing on a group of individuals at high risk of developing a psychosis in the *near future* because they are in the developmental period most at risk, have genetically increased risk, *and* have already begun to manifest mental state changes possibly indicating impending psychosis.

As alluded to previously, the other groups that need to be investigated regarding their relative risks for psychosis are those whose members have histories of transient psychotic symptoms with spontaneous resolution (the TIA model) and those whose members develop attenuated or subthreshold forms of psychotic symptoms (the angina model). The age risk factor can be added to these state risk factors to further increase the likelihood of transition to psychosis in these groups.

In 1994 we set up a specialized outpatient service to monitor and care for young people thought to be at high risk for psychosis. The specific inclusion criteria for the clinic, based on the above considerations, were intended to minimize false positives so the young people most at risk could be served. Targeted patients belonged to one of three groups, and ranged in age from 16 to 30 years.

Group 1 consisted of those with a combination of trait risk factors and state risk factors, that is, a first- or second-degree relative with a history of any psychotic disorder or a schizotypal personality disorder, both as defined by *DSM–III–R*, combined with a change in mental state or functioning indicating development of a probable prodromal state as defined by the presence of two or more of the nine criteria for *DSM–III–R* schizophrenic prodrome. Although problems in using this *DSM–III–R* definition of prodrome were recognized, no other operationalized criteria for this phase were available.

Group 2 consisted of those who had developed attenuated or subthreshold psychotic symptoms, that is, who had one or more of the positive prodromal features from the *DSM–III–R* criteria for schizophrenia prodrome: markedly peculiar behavior; digressive, vague, overelaborate, or metaphorical speech; odd or bizarre ideation or magical thinking; or unusual perceptual experiences.

Group 3 consisted of young people with a history of fleeting psychotic experiences that spontaneously resolved (called brief limited intermittent psychotic symptoms, or BLIPS) within 1 week. The exclusion criteria were the presence of a known organic brain disorder or a history of previous psychosis lasting longer than 1 week (treated or untreated).

Having defined the inclusion and exclusion criteria for the clinic, we then faced the issues of how to identify these high-risk individuals in the community and how to deliver appropriate clinical services to them.

Epidemiological and Service Delivery Issues

Identifying High-Risk Individuals in the Community. Case finding and promoting access to services are the crucial first stage in an intervention that targets high-risk individuals. The literature indicates that significant delays exist in recognizing and referring young people with frank psychotic symptoms and suggests that educating the public, particularly primary caregivers such as general practitioners, could enhance detection and reduce referral delays (Clausen et al. 1982; Helgason 1990). Falloon's uncontrolled study in Buckinghamshire, England, which attempted to identify prodromal adults, used a two-stage approach of (1) training all the general practitioners in the area to recognize and refer patients with possible prodromal symptoms and (2) providing a readily accessible system for assessment by specialized mental health workers (Falloon 1992). (See the description in Falloon et al. 1996, this issue.) Notwithstanding the methodological and conceptual issues described previously, Falloon's results in case finding and responding to referrals were promising.

Our approach to detecting young people at incipient risk of psychosis has been similar, though the health care climate in which we work is different. Under the British health care system, the vast majority of the population is registered with a general practitioner (GP). In Australia, however, many young people are not linked to a particular general practice and do not see a GP regularly. Hence, we targeted other primary care facilities and networks of individuals who come into contact with young people frequently, including school counselors, teachers, and youth workers.

We used our connections with the Early Psychosis Prevention and Intervention Centre (EPPIC) in establishing our clinic. This comprehensive integrated service, which specializes in assessing and managing young people in the early stages of psychotic illnesses (McGorry 1993), is described in detail in this issue (McGorry et al. 1996, this issue). One arm of this service is the mobile Early Psychosis Assessment Team, which, through extensive community networking, comes into contact with not only young people experiencing psychosis but also some "doubtful" cases who may be in the prodromal phase. EPPIC's outreach to primary care facilities and the general public has been expanded to include education about the new service for high-risk individuals and about prodromal states and other risk factors. Because the first author is the consultant psychiatrist with both EPPIC's mobile team and the new service, the links between EPPIC's mobile assessment team and our clinic are particularly strong. After establishing ties with EPPIC, we prepared literature explaining the principles of the new service and describing in plain language possible prepsychotic symptoms. The literature was mailed to GPs in the area, as well as to secondary and tertiary student counseling services and community mental health services.

Service Delivery to High-Risk Individuals. In developing an accessible, responsive clinical service for high-risk young people, we

were mindful of the potential for stigmatization associated with attending a psychiatric facility. This potential can affect referrals, as primary caregivers may be afraid of the perception that they are labeling young people detrimentally (Steinberg et al. 1980). Stigma can also lead to attendance problems. For this reason, we chose to name the service Personal Assistance and Crisis Evaluation (PACE). We avoided names suggesting impending psychosis or schizophrenia because it was unclear just how many of the patients would make the transition to frank psychotic disorder. The site was also important. We chose to locate the PACE Clinic at the Centre for Adolescent Health, a generalist outpatient service and health promotion center, so patients would not risk the potentially stigmatizing effect of attending a psychiatric facility. In its first year of operation, PACE was staffed by a consultant psychiatrist, two clinical psychologists, and a research assistant, all working one to two sessions per week. The clinic was open 2 half-days a week.

The Clinical Model. There is little research about the effectiveness of different interventions in the at-risk phase. Falloon's study used the stress-vulnerability paradigm (Zubin and Spring 1977) and a combination of low-dose, symptom-targeted neuroleptic medication and psychological interventions such as stress management and individual and family psychoeducation. The patients who were treated presented with possible prodromal syndromes identified using *DSM–III–R* criteria (Falloon 1992). A possible reduction in the incidence of schizophrenia resulted.

Others have intervened in the prodromal period preceding relapse in patients with established psychotic disorders such as schizophrenia (Herz et al. 1989; Birchwood 1992; Marder et al. 1994). Typically, low-dose neuroleptic medication is reintroduced or increased in these patients to avert relapse. Other relapse prevention efforts in schizophrenia have involved psychosocial strategies, including family education and support, family conflict reduction (Leff et al. 1982; Falloon et al. 1984), and cognitive therapy for patients aimed at increasing self-esteem, enhancing coping, and producing a sense of control and mastery over the illness and other stressful life circumstances (Vaccaro and Roberts 1992).

Informed by this work, we focused on a psychosocial treatment strategy aimed at reducing stress and enhancing coping, with an emphasis on individualized case management and support, problem solving, and stress management. Monitoring patients' symptomatology and functioning and establishing the "natural history" of at-risk mental states were important roles of the clinic. Family support was also provided, with the young person's consent. Most of the individuals referred to us were keen to participate in this exploratory program and attended regularly. Our nonspecific interventions were important because the young people attending the clinic had various concerns and needs and were often quite disabled by their symptoms. The study of Jones and colleagues (1993) reflects this phenomenon, reporting evidence of significant psychosocial decline before onset of first psychotic episode in schizophrenia.

Additionally, monitoring the young people enabled intervention to occur as early as possible if psychosis emerged, thereby potentially minimizing the severity of, and disruption caused by, psychosis.

Aware that many of the young people we were seeing could be false positives, we carefully weighed the potential benefits of receiving treatment during the at-risk mental state versus the risks involved, if such treatment was unnecessary. The timing of the decision to treat may be influenced by the mode of treatment. For instance, psychosocial interventions may be justified when nonspecific symptoms only are present. But prescribing neuroleptic medication may not be justified, because of the risk of side effects including tardive dyskinesia, until more specific signs occur. Using neuroleptic medication at this early stage may be highly effective, however; hence, the duration of neuroleptic treatment may only need to be brief, thereby reducing the likelihood of short- and long-term side effects. Because the actual transition rate to frank psychosis in our patients was unknown, we opted for a more conservative approach and generally withheld neuroleptics. Additionally, we acknowledged that the decision to treat should not be based on the presence or absence of positive symptoms alone. Level of disability and handicap and other factors such as suicidality were also taken into account. Thus, neuroleptics were used in one case where there was a high suicide risk accompanied by attenuated psychotic symptoms (see case 4 below).

How long clinical management should continue was unclear. We estimated that a followup period

of at least 1 year would be required, recognizing that this was roughly the median duration of schizophrenic prodrome in our own retrospective pilot study (Yung and McGorry, in press) and in others (e.g., Beiser et al. 1993). Many of the patients improved in both functioning and symptomatology over time, however; hence, a mutually acceptable termination date from the clinic was negotiated with them.

Other ethical issues we confronted were whether to inform patients about the risk of developing a psychotic disorder and what information to give them as a rationale for treatment. PACE clinicians did not emphasize the risk of transition to psychosis or schizophrenia, deciding that the degree of risk and likely transition rate were not known with any certainty in the sample we were managing. Thus, there was a desire to avoid prematurely stigmatizing or worrying the patients and their families. The need for intervention was explained in relation to patients' presenting problems. For example, the focus might be on helping a young person with social skills and coping at school. Some of the young people, particularly those with family histories of psychotic disorder, wanted to learn about psychosis and their likely risk. In such cases, psychoeducation was also given and the rationale for monitoring their mental states and providing stress management underlined.

Preliminary Finding From the PACE Clinic

Several agendas had to be addressed in the clinic's pilot phase.

Case Detection. We needed to evaluate our ability to find appropriate cases in the community by our various networking strategies. We therefore needed to determine the total number of referrals and the proportion of them who met the intake criteria. In the first 20 months of operation, the PACE clinic received a total of 110 referrals, the majority from EPPIC (n = 56, 50.9%). Other referral agencies included other community psychiatric facilities (n = 25, 22.7%), secondary and tertiary education centers (n = 12, 10.9%), generalist health settings such as GPs and community health centers (n = 11, 10%), family or self (n = 3, 2.7%), and forensic services (n = 2, 1.8%). Thus, the PACE clinic's close association with EPPIC, an already established clinical service specializing in managing psychotic adolescents and young adults, was an important factor in our ability to generate referrals.

All referrals were screened by an initial phone call to the intake worker (C.A.M.). Fifteen (14%) clearly did not meet intake criteria. If there was any doubt about appropriateness for the clinic, the individual would be accepted for a clinical assessment interview by the intake worker and the PACE consultant psychiatrist (A.R.Y.). Twenty-four referrals (22%) provisionally accepted over the telephone never kept the appointment, often because the initial referrer lost contact with the patient. Seventy-one (65%) of the 110 referrals were assessed with a clinical interview, and from this group a total of 52 patients were found to meet the intake criteria. This number represents nearly three-quarters (73%) of all clinical assessments conducted and approximately half (47%) of all referrals ever received.

Demographic Characteristics of the PACE Sample. Table 1 outlines the basic demographic characteristics of the patients who met intake criteria and who attended for clinical management. This clinical sample was composed of subjects who met one or more of the three criteria: 15 patients (28.8%) met the selection criteria for having a family history plus any change in mental state and 39 (75%) were assessed as having either attenuated psychotic symptoms or previous transient psychotic symptoms; 2 (3.8%) had both a family history and attenuated symptoms.

Symptoms and Disability in the PACE Sample. The level of symptomatology, disability, and handicap found in the high-risk sample also had to be established in the pilot phase. Doing so would allow us to more accurately determine the resources the clinic required. To investigate this issue further, a subsample of 33 of the 52 PACE patients (63.5%) was recruited into the research sample. Reasons for not being recruited included refusing to participate (n = 12), moving out of the metropolitan region (n = 2), or being lost to contact (n = 5). The proportion of the research sample meeting each of the intake criteria was similar to the clinical sample. Equal numbers of males and females did not participate in the research, which constitutes a higher fallout rate for women than for men overall. The women who dropped out tended to be unemployed (50%), while male dropouts tended to be secondary school students (66%). There was no difference in age between the research sample and the refusers, however. Two subjects were not

Table 1. Demographic characteristics of the Personal Assistance and Crisis Evaluation (PACE) clinical and research samples

	PACE clinical sample			PACE research sample		
Characteristic	**Total**	**Males**	**Females**	**Total**	**Males**	**Females**
Mean age	18.7	18.7	18.7	19.0	18.9	18.9
Age range	14–26	14–26	14–26	15–26	15–26	16–25
n	52 (100%)	34 (65%)	18 (35%)	31 (100%)	23 (74%)	8 (26%)
Present occupation						
Full-time student	21 (40.4%)	12 (35.4%)	9 (50%)	11 (35.5%)	6 (26.1%)	5 (62.5%)
Part-time student	1 (1.9%)	1 (2.9%)	0 (0%)	1 (3.2%)	1 (4.3%)	0 (0%)
Full-time employment	6 (11.5%)	4 (11.7%)	2 (11.1%)	5 (16.1%)	4 (17.4%)	1 (12.5%)
Part-time employment	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Unemployed	24 (46.2%)	17 (50.0%)	7 (38.9%)	14 (45.2%)	12 (52.2%)	2 (25.0%)

included in the analysis: one who had been recruited after treatment with low-dose neuroleptics and one who is still completing the research battery.

Patients in the research sample were assessed using a number of measures of psychopathology, functioning, and disability. The Royal Park Multidiagnostic Instrument for Psychosis (RPMIP; McGorry et al. 1990*a*, 1990*b*), a semistructured interview schedule designed to assess symptoms and signs of the first psychotic episode, includes specific probes for estimating illness onset, including prodrome, and for the nine *DSM–III–R* schizophrenia prodrome items. This measure was used to determine frequency and duration of these items. The RPMIP items for alcohol and other drug use were also included. The Brief Psychiatric Rating Scale (BPRS; Overall and Gorham 1962), the Schedule for Assessment of Negative Symptoms (SANS; Andreasen 1982), and the Quality of Life Scale (QLS; Heinrichs et al. 1984) were used to assess psychopathology and disability. Demographic data for the 31 subjects are outlined in table 1.

The reasons for referral in the PACE research sample ($n = 31$) were recorded and give an idea of the chief complaints of the group. Subjects usually had more than one reason for referral. Most common were suspiciousness or other magical ideas ($n = 17$) and perceptual abnormalities ($n = 10$), probably because these phenomena formed part of the inclusion criteria. Nonspecific symptoms such as depressed mood ($n = 14$), anxiety ($n = 11$), and social withdrawal ($n = 11$) were also frequently reported. Somatic symptoms were noted by referrers in six subjects, obsessive-compulsive phenomena in five, deterioration in role functioning in four, and suicidal ideas or attempts in four.

The presence and duration of *DSM–III–R* schizophrenia prodrome items are shown in table 2. The most frequently occurring *DSM–III–R* prodromal symptoms were magical thinking, perceptual disturbance, and impaired role function, present in 67.7, 54.8, and 54.8 percent of the subjects, respectively. Again, this finding reflects the number of patients in the sample who had attenuated or brief transient psychotic symptoms. Note that these symptoms were more commonly found on assessment by the clinician than identified by the referring agent. Least frequent symptoms were the items reflecting digressive or vague speech and markedly impaired hygiene. Overall, the duration of symptoms ranged from 1 day to 9 years. The three most prevalent symptoms were highly skewed because of an outlier at the upper end of each symptom's range.

Substance use was measured in 30 subjects of the PACE research sample (1 subject was missed). Analysis of these data revealed that 20 (66.7%) of the 30 subjects did not use or only occasionally used alcohol and that 22 (73.3%) did not use or only occasionally used other drugs. Conversely, one-third (10) of the 30 subjects used alcohol moderately to heavily, and 8 (26.7%) used other drugs at least moderately.

The PACE group was compared to a sample of recovering first-episode psychosis patients, assessed 6 months after their initial presentation on BPRS, SANS, and QLS, to compare levels of symp-

Table 2. Presence and duration of *DSM–III–R* prodrome items in the Personal Assistance and Crisis Evaluation research sample

Item	Presence of symptom, *n* (%)			Duration of symptom when present (days)			
	Present	Questionable	Absent	Mean	Standard deviation	Median	Range
Social isolation	16 (51.6)	4 (12.9)	11 (35.5)	388	340.2	273	30–1095
Impaired role function	17 (54.8)	3 (9.7)	11 (35.5)	691	687.0	548	30–2920
Markedly peculiar behavior	4 (12.9)	2 (6.5)	25 (80.6)	273	323.0	166	30–730
Markedly impaired hygiene	0 (0)	1 (3.2)	30 (96.8)	0	0	0	0
Blunted affect	5 (16.1)	4 (12.9)	22 (71.0)	213	215.7	213	60–365
Digressive/vague speech	3 (9.7)	4 (12.9)	24 (77.4)	548	—	548	(1)
Magical thinking	21 (67.7)	3 (9.7)	7 (22.6)	461	406.8	365	21–1825
Perceptual disturbance	17 (54.8)	1 (3.2)	13 (41.9)	523	804.3	180	1–3285
Marked lack of energy	12 (38.7)	4 (12.9)	15 (48.4)	485	251.1	502	92–730

Note.—DSM–III–R = Diagnostic and Statistical Manual of Mental Disorders. 3rd ed., revised (American Psychiatric Association 1987).

[1] No range given, as only 1 subject could give a valid estimate of the duration of this symptom. The other 2 subjects were rated positive for this symptom on observation alone and did not report the symptom themselves.

tomatology and disability across groups. These first-episode subjects were recruited from EPPIC during 1993, and 6-month followup data were collected during 1993 and 1994. The characteristics of this sample, including intake data, are described in more detail elsewhere in this issue (McGorry et al. 1996, this issue). Forty-one first-episode subjects were assessed. The SANS score was calculated by adding the individual item scores and the global scores and averaging them for the groups. The mean age of the EPPIC first-episode sample was 22.0 years, compared to 18.7 years in the PACE sample. The lower mean age in the PACE sample would be expected if we really were identifying a group of individuals in the prepsychotic phase. Results of the comparison of symptomatology and functioning measures are shown in table 3.

Total scores on the BPRS indicated that high-risk subjects had a higher mean level of general psychopathology than the recovering first-episode patients. Levels of negative symptoms and impairment in functioning, measured by the SANS and QLS, were also found to be higher in the high-risk sample than in the first-episode sample. These findings suggest that the putatively high-risk group (PACE sample) was indeed symptomatic and displayed difficulty in functioning, thus justifying identification and intervention in this group. One could also hypothesize that these findings indicate that, in terms of symptomatology and disability, the prodromal phase lies between the acute psychotic episode and the recovery phase.

We also estimated the rate of transition of the high-risk patients

Table 3. Comparison of symptomatology and disability measures across samples

	PACE research sample (n = 31)		First-episode sample (n = 41)		
Measure	**Mean**	**SD**	**Mean**	**SD**	**Significance**
BPRS	19.9	6.0	8.1	6.0	$p < 0.001$
SANS	30.1	17.3	17.7	18.5	$p < 0.01$
QLS	67.8	27.2	82.7	24.2	$p = 0.019$

Note.—PACE = Personal Assistance and Crisis Evaluation, BPRS = Brief Psychiatric Rating Scale (Overall and Gorham 1962), SANS = Schedule for Assessment of Negative Symptoms (Andreasen 1982), QLS = Quality of Life Scale (Heinrichs et al. 1984).

to frank psychosis to gain an idea of how long this might take. We arbitrarily defined the point at which psychosis began by the presence of at least one of the following symptoms: hallucinations as defined by *DSM–IV*, or a score of 3 or more on the hallucinations scale of the BPRS; delusions as defined by *DSM–IV*, a score of 4 or more on the unusual thought content scale of the BPRS, or delusions being held with strong conviction as defined by a score of 3 or more on the Comprehensive Assessment of Symptoms and History (CASH) rating scale for delusions (item 266) (Andreasen 1987); or formal thought disorder as defined by a score of 4 or more on the BPRS. In addition, the symptoms had to occur at least once a day, and change in mental state had to have lasted longer than 1 week. In the first 20 months of operation, 7 of the 33 patients (21%) in the research sample progressed to psychosis. Data comparing those who became psychotic in the 20 months to those who did not have not yet been analyzed.

Case Examples. Some typical cases of high-risk young people managed in the clinic follow. Each illustrates different issues associated with the PACE work.

Case 1: Resolution of an apparently incipient psychosis. M.S., a 17-year-old single, unemployed male, was initially referred to the local State psychiatric hospital by his father. The father had noted that M.S. was becoming suspicious—for example, becoming worried about cars following him and about his friends turning against him. These symptoms, which had been present for about 4 or 5 days, had been distressing for him and had resulted in some social withdrawal. He had begun to feel wary about going out with friends and leaving the house for extended periods of time. M.S.'s father was concerned about these features because when he was in his twenties he himself had had a brief psychotic episode, which responded to neuroleptic medication.

On mental state examination, M.S. exhibited persecutory ideas as described above, but they were not held with delusional intensity. He was able to see that he might be misinterpreting events in the environment. He was anxious when talking about these symptoms, but affect was reactive and warm. There was no thought disorder nor were there any other psychotic features. He was keen for help.

M.S. was considered to be at high risk for developing a psychosis because of the positive family history of psychotic disorder in his father and because he was experiencing attenuated psychotic symptoms. He was managed with supportive counseling and stress management in the PACE clinic. The psychological techniques used included challenging his persecutory ideas and getting him to suggest alternative explanations for others' apparent negative behavior toward him. Because M.S. himself recognized that his persecutory ideas worsened with high anxiety levels, he was also instructed in relaxation techniques.

M.S. was monitored for any worsening of symptoms. His mental state improved, and after 2 months of therapy he felt well, his persecutory ideas had resolved completely, and he had started a technical course. He was followed up for 2 more months, then discharged from the PACE clinic. According to our protocol, attempts will be made to follow up with M.S. at 2 and 5 years to determine his long-term outcome, particularly with regard to the development of any psychotic disorder.

Case 2: Fluctuating symptoms, possibly related to stress. C.C. was a 17-year-old single female living with her parents and older sister. She was referred to the PACE clinic by a psychiatrist at an adolescent community mental health clinic who noted several months of perceptual abnormalities, unusual ideas, and in-

creasing anxiety against a background of lifelong generalized anxiety. There was no family history of psychotic disorder.

C.C. described a sense that someone else was in the room with her every time she was left alone. At night when she went to bed she could hear noises such as chairs moving and footsteps and again sensed a presence in the room with her. These symptoms, which caused her marked anxiety and initial insomnia, had been occurring several times a week for the preceding few months. She suspected that the devil had something to do with her experiences but was unsure and said that she feared she would be thought crazy if she expressed these ideas.

In the weeks before referral, she had also developed a feeling that God and the devil knew about things that she did. She was unsure about this, however, and also acknowledged that it was a strange belief to hold and that others would think she was crazy if she told them about it. She believed that she had to smile as she walked past a church so that God would see that she was happy and would protect her. She also described how in recent weeks she had felt distressed at school if a graph in the shape of a cross were drawn on the blackboard, as this would remind her of God and the devil. These unusual thoughts were not present all the time, and she had some days when she did not experience them at all. On other days she could have them several times.

C.C. was still able to attend school, but she had moved into the kitchen to do her homework to avoid being alone. She felt anxious about her symptoms and was concerned that there might be something wrong with her. She was pleasant and cooperative during the interview, at which time there was no thought disorder present nor any other perceptual abnormalities. She was thought to be presenting with attenuated psychotic symptoms. There was a hypnagogic component to her auditory phenomena, and her bizarre ideas were not held with delusional intensity and fluctuated during the course of the day.

C.C. was managed with supportive counseling and stress management techniques similar to those described in Case 1, and she was monitored for any worsening of symptoms. Her family was also involved. Her symptoms remained fairly constant for the first 2 months of treatment, with some fluctuations according to other stressful events in her life. After about 5 months she gradually improved. The perceptual abnormalities and bizarre thoughts resolved, but she was still preoccupied with religious themes, which was out of keeping with her background. This mental state remained until 12 months after initial presentation, when there was another increase in the severity of her symptoms after her mother was diagnosed with cancer. Again, these symptoms decreased following stress management and other psychosocial interventions. Currently she still attends the clinic, is doing well at school, and intends pursuing a university course next year. It is not clear how long followup should continue.

Case 3: A possible false positive. J.S. was a 22-year-old single, unemployed man with a family history of schizophrenia in his father. He telephoned the local State psychiatric hospital for help and was referred to PACE via the Early Psychosis Assessment Team. His presenting complaint was one of a vague despair and a feeling that he was different from others in some way. He stated that his personality had changed over the 4 years since he left school. He had been popular and sociable at school and was seen as the class clown by his schoolmates. He was academically poor, barely literate, and had failed year 9 at school twice. Since leaving school, he had drifted away from his circle of friends and begun to feel increasingly alienated from others. Uncomfortable in social situations, he had resigned from his factory job some 10 months earlier, becoming increasingly withdrawn over the next few months. At the time of presentation he was seeing only his roommate and one other friend from school. J.S. had been using cannabis almost daily over the past few years. There was no diurnal mood variation or sleep or appetite disturbance. On examination, J.S. exhibited no psychotic features, but there was marked dysphoria and some circumstantiality of speech. He expressed a desire to attend the clinic to explore his ideas about the world further with a therapist.

J.S. therefore presented with nonspecific features and deterioration in functioning that could be attributed to depression, "existential despair," or substance use. The symptoms were understandable in the context of his change in role and loss of status and friends since leaving school. They could also indicate a prodrome to a psychotic disorder, particularly given his family history of schizophrenia. At this stage, 15 months after ini-

tial presentation, he is still attending the clinic for supportive therapy and continues to be monitored for changes in mental state. A 1-month trial of paroxetine failed to improve his symptoms, and he was reluctant to try any other medication. He is being encouraged to increase his activities and to cease cannabis use. Essentially, his mental state is unchanged.

Case 4: Early neuroleptics in "attenuated psychosis" with resolution of symptoms and improvement in functioning. T.P. was a 19-year-old apprentice mechanic with a family history of schizophrenia in his mother. He described about 5 months of increasing social anxiety, compounded in the few weeks before PACE contact by a sense that others were talking about him. He realized that he was being "paranoid" but still felt uncomfortable around others, even strangers. He was also scared that he was becoming like his mother and reported anxiety, sleeplessness, irritability, and increasing depression. In the weeks leading up to his referral, he had begun contemplating suicide. On examination there was no evidence of frank psychosis. He was in fact quite insightful and requested treatment. Because of the nature of his symptoms, which resembled an attenuated form of psychosis, and his risk of suicide, T.P. was started on a low dose of haloperidol (1.5 mg at night) and was seen weekly for support and monitoring, including a cognitive behavioral approach to his anxiety in social situations (this included homework assignments) and practical help and support in dealing with his mother's illness. He showed marked improvement within 1 week of starting treatment and continued to improve over the following few months. He was no longer suicidal. The optimal duration of neuroleptic therapy in such a case is not known. In T.P.'s case it was continued for 6 months, then ceased. Five more months have now elapsed with no return of symptoms, and T.P. no longer attends for followup. He has been advised to recontact the clinic if symptoms return.

Case 5: The transition from at-risk mental state to frank psychosis. J.J. was a 19-year-old single, unemployed male living with his parents. His case manager at the Commonwealth Employment Service had referred him to a community mental health clinic because of his poor motivation, sleep disturbance, and unusual countenance. The community mental health clinic referred him to the Early Psychosis Assessment Team, who referred him to PACE. There was no family history of psychotic disorder.

At initial presentation J.J. described longstanding lack of interest in things, poor motivation, anhedonia, and poor peer relationships. He had no friends, and on leaving school at 17 had made no attempt to look for work and was not interested in doing so. He described having ruminations about the nature of the world and was unsure of his place in it. Since the age of 15, he had had intermittent hypnagogic auditory phenomena of unrecognized voices calling his name. He also had intermittent, vague persecutory ideas. For example, he sometimes became very frightened at night if his dog started barking because he believed that someone might be breaking into the house to harm him. Sometimes he would not answer the telephone because he believed it might be someone with malicious intent toward him. At times he thought that cars might be following him. He thought sometimes that he was "just being paranoid." These persecutory ideas, which occurred once every 2 to 4 weeks, were fleeting, never lasting more than a few hours. The interviewer also noted a blunted affect and a decreased sense of rapport and observed occasional facial grimaces.

J.J. had been treated 3 years before by a psychiatrist with clomipramine to reduce the anxious ruminations and any depressive component to his presentation. This treatment had failed to change his symptoms or functioning, and after 6 months he discontinued the medication and the psychiatric followup. He had been diagnosed as having Tourette's syndrome 2 years before by another psychiatrist who had performed an organic workup including head computed tomography scan and electroencephalogram, all of which were normal. The diagnosis of Tourette's was based on repetitive tics in his hands and on facial grimaces. Haloperidol treatment had been recommended; however, J.J. had not taken this and did not attend further appointments with this psychiatrist.

Premorbidly, J.J. had been a below-average student but had completed his final year at school. He was socially isolated, and his only interests were playing the guitar and swimming in the sea near his home, even in extremely cold weather. His parents had always considered him an unusual boy.

J.J. was followed up in the PACE clinic for 18 months and was treated with psychosocial interventions including case management, relaxation and stress management, and practical help such as advice on self-improvement courses, social skills groups, and so on. He was reluctant to attend any groups but regularly arrived for his individual sessions. During that time his symptoms fluctuated. Sometimes his persecutory ideas would occur more often, but they were never present every day and were never of delusional intensity. He developed fleeting auditory hallucinations that sometimes occurred during the day as well as when he went to sleep. These consisted of tapping noises and soft voices calling his name and mumbling something he could not quite hear. He always had insight into the abnormal nature of these phenomena. At other times the symptoms would decrease in frequency and intensity and would sometimes go away for a few weeks at a time. Rapport with him increased over time, and he was able to smile and even joke with his PACE clinician. His affect remained blunted, and grimaces still occurred intermittently. His functioning remained poor. He made some attempts to start courses organized through the Employment Service but was unable to persist with them.

After 18 months of followup he presented for several appointments in a row with increasing frequency and intensity of his persecutory beliefs. When his paranoid ideas had been present for most of the day for 1 week and he was becoming increasingly convinced of them and distressed by them, he was considered to be psychotic. Haloperidol 3 mg daily was commenced. After 1 week of treatment he reported feeling much improved, more relaxed, and less concerned by his symptoms. After 2 weeks he continued to improve, and he has now been engaged in the EPPIC program and attends the group program there.

Discussion of Cases. These cases raise certain issues. First is the question of the stage at which to intervene in high-risk cases and the treatment to provide. The case of M.S. illustrates how attenuated psychotic symptoms can resolve with nonspecific psychosocial management. This young man was able to return to a normal mental state and functioning without being given a psychotic disorder label or having to take neuroleptic medication. C.C. similarly improved with psychosocial interventions, though her symptoms still seem to be apparent at times of stress. It is possible that nonspecific interventions have prevented both M.S. and C.C. from experiencing full-blown psychotic episodes thus far. T.P. was treated with low-dose neuroleptic medication for his attenuated psychotic symptoms and responded rapidly. Medication was chosen as the treatment of choice because of his high suicide risk. All three of these young people are likely to remain at high risk of psychotic disorder and may well experience a psychosis in the future, hence the importance of long-term followup. The fact that psychosis may have been delayed is important in itself, however. This delay has enabled patients to achieve important developmental tasks, such as completing school, and to continue personality development. As Sullivan (1927/1994) noted, "The longer psychotic collapse is escaped, the less the chance of a grave disorder, and the less typical any illness which ensues. In other words, a psychosis occurring in a psychopathic youth under, say, the age of 22, is in all likelihood frankly schizophrenic; but an initial psychosis occurring at, say, 30 will probably be a brief excitement—even if decidedly schizophrenic in type" (p. 137). A recent article highlighing this issue suggests that the educational attainment of people with early-onset psychiatric disorders is truncated (Kessler et al. 1995).

J.J.'s case highlights the issue of definition of onset of psychosis. He presented with subthreshold auditory phenomena, overvalued persecutory ideas, and ideas of reference. He also had a number of nonspecific symptoms such as anxious ruminations, sleep disturbance, and deterioration in role functioning. This picture was occurring against a background of poor premorbid functioning including schizoid personality traits and a previous diagnosis of Tourette's syndrome. His course fluctuated as the frequency and intensity of his attenuated symptoms varied over time. Psychosis was deemed to be present in his case when the persecutory ideas developed a degree of conviction considered delusional and were present for most of the day for 1 week. Should J.J. have been considered psychotic earlier and a diagnosis of brief psychotic disorder been made as soon as the delusions had been present for most of the day for 1 day? Given his previous fluctuating course, it might have been reasonable to consider that his symptoms would decline again rapidly without pro-

gression. One could argue that he should have been medicated earlier, thus enabling quicker and more complete remission, as research examining time to remission and degree of remission in first-episode schizophrenia has suggested (Loebel et al. 1992). J.J. did, however, receive appropriate medication as soon as psychotic symptoms persisted. Thus, the duration of untreated psychosis in his case was minimal. Additionally, his PACE contact resulted in engagement in a clinical service and a strong therapeutic alliance with his PACE clinician, who, because of dual roles at both PACE and EPPIC, will be able to continue to manage him at EPPIC.

Future Directions

Redefining the Criteria to Increase the Proportion of True Positives. The first year of the PACE clinic's operation has demonstrated that it is possible to identify and follow possibly prodromal individuals in the community. This finding indicates that there is an opportunity for developing a number of strands of research using our unique access to high-risk individuals, some of whom will experience onset of frank psychosis during followup. Many of the patients monitored during the pilot phase did not make the transition to psychosis and to date must be considered false positives, however. On these grounds we revised our inclusion criteria to include more true positives by narrowing the family history criteria to include only those with a first-degree relative with psychotic disorder. The criteria for attenuated psychotic symptoms were changed to include operationalized definitions of these features, as our impression from the pilot phase was that these symptoms tended to precede onset of frank psychosis in patients making the transition. We also operationalized the degree of disability and deterioration in functioning necessary for inclusion. The age range remained 16 to 30 years.

The revised criteria for group 1 were a combination of a first-degree relative with a history of any psychotic disorder as defined by *DSM–IV* or a schizotypal personality disorder as defined by *DSM–IV and* any change in mental state or functioning resulting in a loss of 30 points or more on the Global Assessment of Functioning (GAF; American Psychiatric Association 1987) scale, including nonspecific "neurotic"-type presentations such as anxiety and depressive syndromes.

For group 2 the revised criteria were attenuated psychotic symptoms as defined by the presence of at least one of the following symptoms as defined in *DSM–IV* schizotypal personality disorder: ideas of reference, odd beliefs or magical thinking, perceptual disturbance, odd thinking and speech, paranoid ideation, or odd behavior or appearance. The symptom should deviate significantly from normal as defined by a score of 2 or more on the unusual thought content scale of the BPRS or be held with a reasonable degree of conviction as defined by a score of 2 on the CASH rating scale for delusions. It should occur at least several times per week. Finally, the change in mental state should have been present for at least 1 week.

Inclusion in group 3, according to the revised criteria, was determined by a history of transient psychotic symptoms (BLIPS) as defined by the presence of at least one of the following symptoms: hallucinations as defined by *DSM–IV*; delusions as defined by *DSM–IV*, or a score of 4 or more on the unusual thought content scale of the BPRS, or held with strong conviction as defined by a score of 3 or more on the CASH rating scale for delusions; or formal thought disorder as defined by a score of 4 or more on the BPRS. The duration of each BLIPS had to be less than 1 week, before spontaneous resolution.

Prospective Study of At-Risk Individuals. Using these revised criteria, the major area of current research in the clinic is the predictive power of a number of putative trait markers of schizophrenia. Included in the study are neurobiological markers such as increased ventricular brain ratio and ventricular enlargement (Lieberman et al. 1993), neurochemical markers such as reduced dopamine uptake by platelets (Dean et al. 1992), and neuropsychological markers such as information processing deficits (Cornblatt and Keilp 1994). The predictive power of a number of psychopathological features, including various attenuated psychotic symptoms, is also being examined.

Another research component is the assessment of current disability afforded by these prodromal states. The process of transition from at-risk mental state to psychosis is also being studied, as well as factors that favor it (risk/vulnerability factors) and inhibit it (resilience factors) and fluctuations in its course.

Intervention in High-Risk Individuals. Research currently in progress is focusing on specific interventions in the high-risk group. The first stage will compare the transition rate to psychosis in a group receiving a combination of psychosocial treatment and low-dose neuroleptics with that of a control group receiving no intervention. The second phase will compare the efficacy of the two types of treatment applied independently in the high-risk group, that is, psychosocial interventions versus medication.

Followup of PACE clinic patients who go on to develop a psychotic disorder is possible through our links with EPPIC, the service to which they will be referred for ongoing management. This allows further strands of research, such as examination of outcome in patients in whom duration of untreated psychosis has been minimized and intervention for prodromal symptoms provided. Reexamination of putative trait markers after the onset of psychosis and comparison of results in the same patients before onset of psychosis is also possible. For example, measures of information processing reassessed after recovery from the first psychotic episode could indicate whether any abnormalities originally found are true trait markers or reflect mental state at the time of testing.

Conclusion

The prospect of intervening in the prodromal phase of schizophrenia and other psychotic disorders has long been seen as a worthy goal. The PACE clinic was established to access and intervene in vulnerable individuals possibly at imminent risk of psychosis.

The PACE clinic has provided clinicians and researchers access to significant numbers of young people at high risk for becoming psychotic in the near future. From a clinical perspective, followup of these at-risk young people affords the opportunity for prevention of, or early intervention in, psychotic disorders. Followup is aided by our links with the clinical service specializing in management of recent-onset psychosis, the EPPIC. From a research perspective, the clinic's design enables a number of prospective investigations to occur. Unlike other long-term followup studies of high-risk groups such as children of psychotic parents (Watt et al. 1984), the "close in" strategy of the clinic focuses on individuals who have already developed some low-grade psychopathology. Thus, the followup time to psychotic episode is considerably shortened. Studies examining biological, neuropsychological, and psychopathological measures before and after the onset of frank psychosis with the aim of identifying specific markers of psychosis are therefore possible. The process of transition from prodromal state to psychosis can also be studied, and factors influencing this transition can be examined. The clinic thus may contribute to the investigation of the pathogenesis of psychotic disorders and to the development of measures to prevent them.

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