Early intervention in psychosis: concepts, evidence and future directions

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The rise of the early intervention paradigm in psychotic disorders represents a maturing of the therapeutic approach in psychiatry, as it embraces practical preventive strategies which are firmly established in mainstream health care. Early intervention means better access and systematic early delivery of existing and incremental improvements in knowledge rather than necessarily requiring dramatic and elusive breakthroughs. A clinical staging model has proven useful and may have wider utility in psychiatry. The earliest clinical stages of psychotic disorder are non-specific and multidimensional and overlap phenotypically with the initial stages of other disorders. This implies that treatment should proceed in a stepwise fashion depending upon safety, response and progression. Withholding treatment until severe and less reversible symptomatic and functional impairment have become entrenched represents a failure of care. While early intervention in psychosis has developed strongly in recent years, many countries have made no progress at all, and others have achieved only sparse coverage. The reform process has been substantially evidence-based, arguably more so than other system reforms in mental health. However, while evidence is necessary, it is insufficient. It is also a by-product as well as a catalyst of reform. In early psychosis, we have also seen the evidence-based paradigm misused to frustrate overdue reform. Mental disorders are the chronic diseases of the young, with their onset and maximum impact in late adolescence and early adult life. A broader focus for early intervention would solve many of the second order issues raised by the early psychosis reform process, such as diagnostic uncertainty despite a clear-cut need for care, stigma and engagement, and should be more effective in mobilizing community support. Early intervention represents a vital and challenging project for early adopters in global psychiatry to consider.

Key words: Early intervention, psychosis, staging, health care reform, youth mental health

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Psychotic disorders and particularly schizophrenia are serious and sometimes fatal illnesses which typically emerge during the sensitive developmental period of adolescence and emerging adulthood (1). For over a century, a corrosive blend of pessimism, stigma and neglect have confined therapeutic efforts to delayed and inconsistent palliative care. Much of this can be attributed to the conceptual error underpinning the concept of schizophrenia, namely that a true disorder could be validly defined by its (poor) outcome. This error was, in turn, a legacy of the 19th century degeneration theory, which has been allowed to influence the field well beyond its use-by date (2). Although Kraepelin himself and some of his contemporaries ultimately recognized the fallacy, his dichotomy (between dementia praecox and manic depressive insanity) has withstood several challenges and has been strongly reinforced with the advent of operational diagnostic systems. This has not only hampered neurobiological research, but has caused widespread iatrogenic harm and inhibited early diagnosis because of an exaggerated fear of the expected outcome.

Until recently, apart from transient and illusory optimism generated by the mental hygiene movement in the 1920s, early intervention for psychotic disorders has been the furthest thing from the minds of clinicians and researchers. Ironically, however, since the early 1990s, this hitherto barren landscape has seen the growth of an increasingly rich harvest of evidence, and widespread national and international efforts for reform in services and treatment approaches, setting the scene for more serious efforts in early intervention in other mental disorders (3-5).

DEVELOPMENT OF EARLY INTERVENTION SERVICES

Building on seminal research on first episode psychosis from the 1980s (6-8), frontline early psychosis clinical services were established, first in Melbourne (9) and soon after in many key locations in the UK, Europe, North America and Asia (10). There are now hundreds of early intervention programs worldwide, of varying intensity and duration, which focus on the special needs of young people and their families. International clinical practice guidelines and a consensus statement have been published (11) and clinical practice guidelines for the treatment of schizophrenia now typically have a major section on early psychosis (12,13). The International Early Psychosis Association (www.iepa.org.au), an international organization which seeks to improve knowledge, clinical care and service reform in early psychosis, has been in existence for over ten years, led by a highly collegial leadership group of clinicians and researchers. This association has over 3000 members from over 60 different countries, and by 2008 will have held six international conferences, stimulating and capturing a large volume of research and experience.

In recent months, responding to the widespread international momentum, the US National Institute of Mental Health has announced a large new funding initiative to study and promote the development of better services for patients with first episode psychosis (www.nimh.nih.gov).

Shift in thinking: pessimism to optimism

The advent of preventive thinking has required a shift in the way schizophrenia and other psychotic disorders are viewed. Rather than seeing them as having inevitably poor prognoses with deterioration in social and functional outcome as the norm, more recent thinking backed up by evidence from large international studies (14-25) views the course of these disorders as much more fluid and malleable.

Examination of risk factors which can influence outcome has revealed that many of these may be reversible. For example, disruption of peer and family networks and vocational drop-out commonly occur around and even before the onset of a first psychotic episode. Attention to these areas as part of treatment has the potential to limit or repair the damage.

Comorbid depression, substance use, personality dysfunction and post-traumatic stress disorder (PTSD) are all factors which may influence outcome in a person with first episode psychosis. Again, early and vigorous management of these problems can result in better outcomes (26).

What is early intervention?

Early intervention is a potentially confusing term. Because there is no aetiopathological basis for diagnosing psychotic disorders, they can only be diagnosed by symptoms or combinations of symptoms. In addition, we have no known malleable causal risk factors which predict onset of psychotic disorder with any specificity. Thus, it seems that primary prevention is currently out of our reach. Early intervention, therefore, means early *secondary* prevention.

In keeping with the clinical staging model (27) articulated below, early intervention in psychosis can be defined as comprising three foci or stages: ultra-high risk, first episode, and the recovery or critical period. The principal reason for making such distinctions relates to the underlying risk of chronicity, and specifically the timing and duration of prescription of antipsychotic medication, since psychosocial interventions are needed at all stages, though these interventions too vary by stage.

What is the target for early intervention: schizophrenia or psychosis?

Clinicians and researchers have debated whether to focus on the preventive target of schizophrenia or of psychotic disorders more broadly. There are several reasons for stepping out of the current diagnostic silos and preferring a relatively broad target.

As described above, schizophrenia is conceived and defined in part as an outcome as much as a diagnosis. While it is very stable once applied (28-31), it is intrinsically difficult to apply until the patient has been ill for a prolonged period of time. Within a sample of ultra-high risk cases (already defined in order to preferentially predict transition to non-affective psychosis), only 75% of those who go on to develop a first episode psychosis will progress to a schizophrenia diagnosis (32). So, the false positive rate is higher for schizophrenia than for first episode psychosis. Even within a first episode psychosis sample, only 30-40% will meet criteria for schizophrenia, and this percentage will increase over time with additional diagnostic flux. Thus, some cases of first episode psychosis which do not meet criteria for schizophrenia can be seen as being at risk for this in the future (33). Schizophrenia, therefore, is to some extent a more distal target than psychosis, which is a better and broader initial waystation for critical treatment decisions. An even earlier and broader point for intervention is the ultra-high risk clinical stage, where there is a need for care prior to the positive psychotic symptoms having become severe and sustained.

In addition, due to fear and stigma derived from the notion of intrinsic poor prognosis, clinicians are reluctant to use the label "schizophrenia" early on anyway, justifiably concerned about iatrogenic effects on hope and the potential for recovery (34). This has led some countries, such as Japan, to change their diagnostic terminology and eschew the word "schizophrenia" (35). Our preferred alternative is to retain it for the time being, as one subtype of psychotic disorder outcome, admittedly a major one, among a small range of distal targets.

Psychosis itself is a variable syndrome, defined by the presence of positive psychotic symptoms, especially delusions and hallucinations, and typically features one or many comorbidities, including negative symptoms, mood syndromes, personality disorders, substance use disorders, medical diseases and PTSD. The relative prominence of the positive symptoms and comorbidities varies, and this leads to a more heterogeneous group of patients. As a consequence of this, a broader range of clinical skills will be required in early psychosis programs than in narrower schizophrenia programs.

Some have argued that the schizophrenia focus allows the other psychotic disorders, especially psychotic mood disorders and psychoses associated with certain personality disorders and PTSD, to be treated in more appropriate settings. However, provided there is a flexible attitude and a broad range of clinical expertise available, both groups of patients benefit more from this broad, early, and inclusive focus on the spectrum of psychosis. It provides a good balance between specialization and addressing common needs, and also facilitates both clinical and aetiological research, which increasingly needs to transcend traditional diagnostic barriers.

ENHANCING THE VALUE OF DIAGNOSIS: THE CLINICAL STAGING MODEL

Many of the problems of categorical diagnosis flow from a telescoping of syndromes and stages of illness which conceals and distorts the natural ebb and flow of illness, remission and progression. In addition to augmenting categorical approaches with symptom dimensions, consideration needs to be given to the dimensions of time, severity, persistence and recurrence.

The notion of staging can be borrowed

and adapted from mainstream medicine to assist us here. A clinical staging model provides a heuristic framework allowing the development and evaluation of broad and specific interventions as well as the study of the variables and processes underlying the evolution of psychiatric disorder (27,36).

What is clinical staging?

Clinical staging is simply a more refined form of diagnosis (37,38). Its value is recognized in the treatment of malignancies, where quality of life and survival rely on the earliest possible delivery of effective interventions. However, it also has applicability in a diverse range of diseases. Clinical staging differs from conventional diagnostic practice in that it defines the extent of progression of disease at a particular point in time, and where a person lies currently along the continuum of the course of illness (36).

The differentiation of early and milder clinical phenomena from those that accompany illness extension, progression and chronicity lies at the heart of the concept. It enables the clinician to select treatments relevant to earlier stages, and assumes that such interventions will be both more effective and less harmful than treatments delivered later in the course.

While staging links treatment selection and prediction, its role in the former is more crucial than in the latter, particularly since early successful treatment may change the prognosis and thus prevent progression to subsequent stages. In addition to guiding treatment selection, a staging framework, which moves beyond the current diagnostic silos to encompass a broader range of clinical phenotypes, and which at the same time introduces subtypes along a longitudinal dimension, has the potential to organize endophenotypic data in a more coherent and mutually validating fashion (36).

How do we define the stages of a disorder?

In other medical conditions, clinical stages are defined by the degree of extent, progression and biological impact of illness in the patient, which in turn must correlate with prognosis. This approach usually depends upon a capacity to define pathologically as well as clinically the limits or extent of the disease process.

In clinical psychiatry, this could involve not only a cross-sectional clinical definition, but a wider biopsychosocial definition of extent or progression. Therefore, in addition to the severity, persistence and recurrence of symptoms, biological changes (e.g., hippocampal volume loss), and the social impact of the disorder (e.g., the collateral damage affecting social relationships and employment), could also be drawn into the definition. Ultimately, something approaching a clinicopathological model could emerge.

What are the potential benefits of staging?

On the clinical side, defining discrete stages according to progression of disease creates a prevention-oriented framework for the evaluation of interventions. The key positive health outcomes are prevention of progression to more advanced stages, or regression to an earlier stage. This requires an accurate understanding of those broad social, biological and personal risk and protective factors which influence progression from one stage to the next.

Furthermore, we need to know the relative potency of these risk factors and which of them may be responsive to current interventions. While some factors may operate across several or all stage transitions, others may be stage-specific, for example substance abuse or stress may be especially harmful in triggering onset of the first episode of illness, yet be less toxic subsequently (or vice versa). Gene-environment interactions almost certainly underpin and mediate these transitions, where environmental variables – such as substance abuse, psychosocial stressors, cognitive style, medication adherence and social isolation – may interact with genetic and other biological risk factors (39-41).

From an aetiological perspective, over a century of research with traditional diagnostic categories of psychosis and severe mood disorders has failed to relate these flawed concepts to any discrete pathophysiology (42,43). A clinical staging model, which allows the relationship of biological markers to stage of illness to be mapped, may help to validate the boundaries of current or newly defined clinical entities, distinguish core biological processes from epiphenomena and sequelae, and enable existing knowledge to be better represented and understood.

THE STAGES OF EARLY PSYCHOSIS

Stage 1: Ultra-high risk

In psychotic disorders, an early prepsychotic stage is known to exist, one in which much of the collateral psychosocial damage is known to occur (44). This earliest stage could, in retrospect, be termed the "prodrome", i.e., the precursor of the psychotic stage. However, since we can only apply the term "prodrome" with certainty if the definitive psychotic stage does indeed develop, terms such as the "ultra-high risk" (34) or "clinical high risk" (45) stage have been developed to indicate that psychosis is not inevitable and that false positive cases also occur. This symptomatic yet prepsychotic stage is the earliest point at which preventive interventions for psychosis can concurrently be conceived (46).

The challenge in detecting such a stage prospectively is firstly to define the clinical frontier for earliest intervention and "need for care" which represents the boundary between normal human experience and pathology. Secondly, a set of clinical and other predictors need to be defined which identify a subgroup at imminent risk for psychotic disorder. This is a complex task and the key issues involved have been covered in many recent publications (47-55). Earlier writers (56) aspired to the diagnosis of schizophrenia in the prodromal phase. German psychopathologists in the mid 20th century emphasized subtle changes in experience and behaviour, though

their complexity meant that they had little impact on Anglophone psychiatry initially. A practical operational definition of a prepsychotic "at risk" or "ultra-high risk" mental state, which could be shown to confer a substantially high risk of fully fledged psychosis within a 12 month period, was then developed and tested in the early 1990s (57). This has captured the attention of the field and has been the focus of much subsequent research, focusing on prediction, treatment and neurobiological aspects.

These criteria do indeed predict an "ultra-high risk" group for early transition to psychosis (32), leading to a relative risk of 40% compared to the incident rate of psychotic disorders in the general population (58). However, there is still a significant false positive rate of 60-80%, though they typically are or turn out to be true positives for other disorders, notably depression and anxiety disorders. While the predictive power for psychosis can be substantially sharpened *post-hoc* by the use of key variables such as genetic risk, depression, functional impairment and substance use (58,59), this is of limited utility due to the "prevention paradox". This means that increasing the positive predictive value reduces the number and percentage of cases that can benefit. So, if the sample is narrowed, one is on firmer ground, but most cases who do go on to develop the disorder are missed due to the narrower focus (51). We know already that most cases of first episode psychosis are already missed by prodrome clinics.

There have been a series of clinical trials of relatively small sample size examining both antipsychotics and/or cognitive therapy as preventive treatment strategies for ultra-high risk patients (60-62). These trials suggest that cognitive therapy and antipsychotics may prevent or at least delay the onset of psychotic disorder and reduce symptomatology. A second generation of single site clinical trials has recently been completed, with interesting results for a range of psychosocial and biological therapies, including cognitive therapy (62), lithium (63), omega-3 fatty acids (64), and atypical antipsychotics (60).

However, treating young people in the putative prodromal phase does cause some understandable concern that patients might be exposed to unnecessary and potentially harmful treatments. This has created controversy in the US in particular around this type of research. This in turn has led to so-called "naturalistic designs" (58,65) being preferred above the traditional randomized designs. Paradoxically, the ethical considerations that drove this thinking have allowed the same treatments that could not be researched under rigorous conditions of informed consent within a randomized controlled trial to be used off label in a widespread and uncontrolled fashion in these naturalistic studies. Hence the term "naturalistic" becomes a misnomer, since the natural course may be profoundly influenced by uncontrolled treatment. These "naturalistic" studies reveal that extensive non-evidence-based use of antipsychotic medications seems to be common in clinical settings in the US, ironically side by side with long delayed and inadequate treatment of first episode and established psychotic disorders (66).

Next steps

Clinical trial data is crucial to determining the risks and benefits of various forms of treatment in a new clinical focus and creating solid foundations for an evidence-based approach. This is the best antidote to fears on widespread and potentially harmful and unnecessary use of antipsychotic medications in particular. The "prodromal" or ultra-high risk field remains in clinical equipoise, since we do not yet know which treatments will be most helpful and acceptable to patients, and crucially in which sequence or combination.

Prospective or naturalistic data can best be collected in the most sound and interpretable fashion in the context of a large well-funded multicentre clinical trial, with an "effectiveness" rather than efficacy design and a minimal intervention arm, to which non-consenters to randomisation can be assigned.

We can readily accept that antipsychotics and indeed antidepressants (67) and neuroprotective agents such as omega-3 fatty acids and lithium are legitimate therapies to be further researched, but their use in research should be protocolized within rigorous study designs. In the meantime, the international clinical practice guidelines on early psychosis (11), which advocate a conservative approach to the use of antipsychotic medications and more liberal use of psychosocial interventions, should be followed. This rather conservative approach to treatment of ultra-high risk individuals is even more imperative, as recently it has been discovered that the rates of early transition to first episode psychosis have been falling in the more established prodromal centres (52), with a much higher rate of so-called "false positives" being accepted into these services. This may be due to sampling variation, earlier detection of ultra-high risk cases, or improved efficacy of interventions provided (52).

This reduction in transition rate and uncertainty over treatment in the ultra-high risk group has led to valid concerns about identification of and intervention with these individuals. Yet help-seeking patients defined by the ultra-high risk criteria for first episode psychosis are at risk not only for schizophrenia or psychosis but for other adverse mental health outcomes (68). We may need to define an even broader pluripotential initial clinical stage with a range of possible exit or target syndromes. Consequently, we have broadened our own clinical and research strategy (69), cross-sectionally with the development of a broader and more accessible system of clinical care for those in the peak age of risk for all types of mental disorders (70-72), and longitudinally with the creation of a clinical staging model for psychotic, mood and anxiety disorders (27).

This enables a serial enriching strategy to unfold to ensure that the declining transition rates in ultra-high risk samples (52) and the consequently high false positive rate can be handled in future clinical trials, and that other exit syndromes and indeed remission and resolution can be included. These strategies help us to move beyond some of the obstacles to early diagnosis and

intervention: namely the "false positive" issue, potential problems with stigma, the challenge of comorbidity, and lack of predictive specificity. As we move further down this road, the problems with our historically determined classification systems loom larger and the need to loosen the shackles becomes more apparent.

Stage 2: Early detection and treatment of first episode psychosis

The second stage involves a therapeutic focus on the period after the onset of fully-fledged psychosis (often known as "first episode psychosis"). This is divided into the period before psychosis is detected and the period after detection. Unfortunately, the undetected or untreated phase can be prolonged, even in developed countries (73). Of course, even when psychosis is detected, the initiation of effective treatment may still be delayed. The goal is to minimize this duration of untreated psychosis (DUP). Post-detection, the intervention goals are engagement and initiation of pharmacological and psychosocial treatments. Intensive interventions aimed at maximal symptomatic and functional recovery and the prevention of relapse are ideally delivered during the early weeks and months of treatment.

The controversy surrounding the importance of DUP and treatment delay in first episode psychosis seems to have been largely resolved following the publication of some key systematic reviews (74,75) and recent influential longitudinal research. These studies have now established that longer DUP is both a marker *and* independent risk factor for poor outcome. The Early Treatment and Identification of Psychosis (TIPS) study in Scandinavia has shown, through the best possible design, that reducing DUP leads to early benefits in reducing suicidal risk and severity of illness at initial treatment and sustained benefits in terms of negative symptoms and social functioning (18-21). The relationship between DUP and outcome is robust, being sustained over many years of follow-up (76,77). However, these studies do show that, though being a malleable risk factor, DUP accounts for a relatively modest amount of outcome variance, underlining the importance of treatment access and quality during the early years of illness.

There is an extensive literature attesting to the benefits of comprehensive care of the first psychotic episode. This is summarised in the International Clinical Practice Guidelines for Early Psychosis (11), published in 2005. Since 2005, the growth in research in this area has continued. This has led to the emergence of the following findings.

The large multicentre European First Episode Schizophrenia Trial (EUFEST) has shown that in the treatment of first episode schizophreniform and schizophrenic disorders, atypical or second-generation antipsychotics have some clear-cut advantages (78). While most patients responded surprisingly well to both typical and atypical medications, with no significant efficacy differences, discontinuation rates and tolerability were clearly superior for atypical agents. This was true even when contrasted with very low-dose haloperidol. While the authors' conclusions and recommendations were conservative, highlighting the equivalent efficacy of the two classes of drug, the EUFEST findings contrast markedly with those of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study (79) in chronic schizophrenia, where no dramatic advantages were found for atypicals using similar outcome measures. The EUFEST data support the recommendations of the International Clinical Practice Guidelines in Early Psychosis (11), which favor the use of atypicals as first line therapy, because of better tolerability (a crucial issue in drug-naïve first episode patients) and reduced risk for tardive dyskinesia. However, some atypicals have a particularly high risk of weight gain and metabolic problems, and these risks need to be carefully managed and prevented wherever possible. A recent paper (80), however, suggests that weight gain is a problem in the first year of therapy for first episode patients on both typicals and atypicals, with the key difference being the rate at which it develops.

Psychosocial treatments in early psychosis have been extensively studied, and there are positive findings pointing to the value of cognitive therapies in accelerating and maximizing symptomatic and functional recovery (81,82). Increasingly there has been attention to the fact that medications, while assisting in symptomatic recovery, do not, by themselves, contribute to a return to functioning. This has led to an increased focus on the need to enhance social recovery (68) especially educational and vocational aspects (83-85), through the combination of effective psychosocial interventions with well-managed medication. There is also an increasing focus on targeted cognitive remediation (86) to limit the degree of cognitive decline that is often found as illness progresses.

Next steps

Initial scepticism regarding DUP has slowly melted in the face of evidence but also the logic of early diagnosis. If we believe we have effective interventions in psychosis, it is perverse to argue that delayed treatment is acceptable. Sceptics find themselves being asked how long a delay is acceptable: 2 months? 6 months? 2 years? In reducing the DUP the two key components of intervention are community awareness and mobile detection services. Both are important, as the data from TIPS (87) and other studies (88) have shown. When both are in place, it is possible to achieve very low levels of DUP (a median of a few weeks only). These strategies also result in a less risky and traumatic mode of entry into care and enable patients to be engaged without a surge of positive symptoms or disturbed behaviour being required to force entry into poorly accessible or highly defended service systems. They should be available in all developed communities and a standard feature of all mental health systems.

In terms of the specific elements of first episode psychosis intervention, a number of trials have shown that atypical antipsychotics in low dose are superior for first episode patients where tolerability and safety are at a premium, though

some may be ruled out on exactly these grounds in many patients. The recent EUFEST study is especially compelling (78). The place of new injectables and clozapine needs to be clarified, as well as that of adjunctive neuroprotective agents such as omega-3 fatty acids, lithium and N-acetyl cysteine. Cognitive behavioural therapy and vocational rehabilitation (89) are the key psychosocial interventions in early psychosis and need to be much more intensively and widely deployed. Assertive community treatment for the subset of poorly engaged patients is vital (11). Family interventions are also an essential element of care, even though the formal evidence is not yet fully available (90).

Stage 3: The critical period of the first 5 years after diagnosis

This third stage involves the critical early years beyond the first episode, which can be viewed as the critical period (91). Treatment goals in this phase are the management of effective medication and the use of effective psychosocial interventions to minimize the development of disability and maximize functioning. Proof of concept is now established for these strategies (14,15). However, there remains a large gap in most communities between what works and what is available, even in high income countries and certainly in the low and middle income countries (92).

Beyond the first episode, we know that the first 2-5 years post-diagnosis are crucial in setting the parameters for longer term recovery and outcome. This is the period of maximum risk for disengagement, relapse and suicide, as well as coinciding with the major developmental challenges of forming a stable identity, peer network, vocational training and intimate relationships. It makes sense that a stream of care specially focused on young people and on this stage of illness is required to maximize the chances of engagement, continuity of care, appropriate lifestyle changes, adherence to treatment, family support and vocational recovery and progress. Indeed, the available evidence from naturalistic and randomized studies strongly supports the value of specialized early psychosis programs in improving outcome in the short term (89,93). If these programs are only provided for 1-2 years, there is also evidence that some of the gains are eroded, suggesting that, for a substantial subset at least, specialized early psychosis care needs to be provided for a longer period, probably up to 5 years in many cases (77,94,95).

Next steps

The best available evidence indicates that streamed care provides superior outcomes in the short to medium term compared to generic care (16,17). While this may be insufficient to meet the most stringent Cochrane criteria, such evidence, combined with face validity and obvious poorly met need, has been sufficient to convince mental health policy makers and service providers in hundreds of locations worldwide to adopt, adapt and implement this model. The randomized controlled trials so far have only tested partial versions of this streaming, with a specialized assertive community treatment model being the main feature evaluated. Even so the results are positive for the first 2 years of care. It seems likely that, for a significant subset at least, if these gains are to be maintained, the streamed early psychosis model must be continued for longer, perhaps up to 5 years (89). At this point, persisting illness and disability may be present in a much smaller percentage of people, whose needs may subsequently be well met by more traditional mental health services for older adults. This may be a much better point to transfer care.

THE PROCESS OF REFORM

The pace of reform is typically slow in health care. While early intervention in psychosis has made great progress in recent years, dissemination remains in many ways frustratingly slow. Many developed and most developing countries have made no progress at all, and even those countries which have made significant investments have only achieved partial coverage. We have previously commented on this inertia and some of the reasons for it (92,96).

Evidence-based health policy (97) can be seen as a blend of evidence-based health care and public policy analysis, in which evidence is only one of a range of influential variables. Pure evidence-based health policy derives from a technical perspective and regards the task as identifying and overcoming barriers to smooth flow of best available evidence into practice. This has been characterised as "naïve rationalism" (98), since cultural and political values and the dynamics of change and reform are other key influences on policy making. Evidence is a product as well as a driver of reform and the evidence-based paradigm, by setting impossible prerequisite standards, and by shifting the goalposts once evidence is forthcoming, can be used as a weapon to frustrate and delay overdue reform in a manner that would be unacceptable in other branches of medicine (99).

In better understanding this phenomenon, it is worthwhile to reflect on how innovation and reform in health care works. Diffusion of innovations is a major challenge in all industries, from agriculture to manufacturing. The study of diffusion of innovation has a long history in the social sciences. Many nations have established centres and strategies to understand and promote this in health care (100,101).

There are many contextual factors involved, but there are also predictable characteristics of individuals and health care systems which influence the process (102). Firstly, we must consider perceptions of the innovation. There must be perceived benefit; the innovation should be compatible with the values and needs of those considering it. It should be simple or capable of simplification and, in the process of spread, it is vital that innovations be adapted and reinvented in relation to local needs. Secondly, there are several groups of adopters involved in the process of innovation. The innovators are the smallest group and create the novel ideas and skills. They are novelty seekers who form wider national and international networks or cliques

and they invest energy in these connections. They may be thought of as mavericks heavily invested in a specialized issue. The early adopters are a larger group of opinion leaders who draw on the innovators and cross-pollinate with one another. They are open to a range of new ideas and have the resources and risk tolerance to try new things. Most importantly, they are closely watched by the next group, the early majority, who are more local in their focus and more risk averse. The early majority look to the early adopters for guidance about what is safe to try. The fourth group, the late majority, are even more conservative and look to the early majority, adopting an innovation only when it appears to be the new status quo. Finally, we have the laggards, apparent members of a modern day flat earth society, whose point of reference is the past. To be fair, this description underestimates their value, since they usefully point to the need to retain some valuable elements of current and prior practice. However, they are also exposed defending the indefensible and demanding impossible and unrealistic levels of evidence before accepting change. Furthermore, the evidence standards demanded for innovations are rarely if ever applied to the status quo, which in mental health at least is typically less evidence-based than the new approach. This active rearguard action is aided and abetted by the tendency of systems to rapidly build inertia and reinstitutionalize after periods of progress.

Despite the welcome progress in early intervention, the laggards have been prominent in the early intervention field. While evidence-based medicine is by far the best antidote for taking wrong and potentially dangerous and wasteful turns in health care, opponents of change have been observed to misuse the paradigm to frustrate change which is overdue and in the best interests of the community. There is regrettably insufficient debate about where the onus of proof lies in such matters, and what considerations other than evidence should influence decisions, especially where changes have high face validity, such as emergency care and indeed early intervention. Finally, it is unlikely that oncologists would debate the relative value of early diagnosis and palliative care, which is where psychiatry has got stuck repeatedly.

Berwick points out that the dissemination of innovation has a tipping point (103), usually around 15-20% adoption. Certainly, once the early majority have swung in behind an innovation, the late majority are likely to feel comfortable to move as well. This is a process that can be facilitated by several strategies. These include identifying sound innovations, leading by example, supporting innovators and early adopters with resources and time, making the activities of early adopters highly visible, and valuing reinvention as a form of learning rather than requiring exact replication of innovations.

CONCLUSIONS

Many of the obstacles to early intervention are the same ones which impede progress in mental health more widely, as illustrated in the Lancet Series on Global Mental Health (104). They include stigma, pessimism, the silence that surrounds the mentally ill, and a consequent failure to invest. Developed and rapidly developing countries need to recognize the public health importance of untreated and poorly treated mental disorders. A key aspect which is beginning to be recognized is that mental disorders are the chronic diseases of the young (105). Most adult type mental disorders – notably psychotic, mood, anxiety, substance use and personality disorders – have their onset and maximum impact in late adolescence and early adult life. A broader focus for early intervention would solve many of the second order issues raised by the early psychosis reform process, such as diagnostic uncertainty despite a clear-cut need for care, stigma and engagement, and should be more effective in mobilizing community support for investment and reform in mental health. This is occurring in Australia (106,107) and Ireland (108), and is attracting increasing attention in a number of other countries, along the lines of the innovation process described above. It currently represents a vital and challenging project for early adopters in global psychiatry to consider.

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