Review Article

A Risk Reduction Approach for Schizophrenia: The Early Psychosis Intervention Programme

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Abstract

Schizophrenia is a serious mental disorder with a profound impact on patients, their caregivers and society. Most patients who develop schizophrenia experience a prodromal phase where there is a change in premorbid functioning prior to the onset of frank psychotic symptoms. Once psychosis sets in, the subsequent course can be variable but schizophrenia tends to run a chronic course, resulting in considerable disabilities. The prognosis of schizophrenia could potentially be improved by reducing the duration of untreated psychosis (DUP). The Early Psychosis Intervention Programme (EPIP) in Singapore adopts a risk-reduction approach. It seeks to reduce the DUP through public education, networking with the primary healthcare providers (general practitioners, counsellors, traditional healers), and the screening of conscripts into the Singapore Armed Forces. Integral to this programme is a service for those in the prodromal phase of psychosis, that addresses the concerns of stigmatisation and pharmacotherapeutic interventions. Our tertiary prevention strategies aim to reduce mortality and morbidity, and to improve the quality of the lives of the individuals diagnosed with this disorder through a comprehensive and holistic management programme that comprises case-management, the judicious use of antipsychotics, and various psychosocial interventions. Since EPIP's initiation in April 2001, there has been a steady increase in the number of individuals screened and accepted into the programme. Our networking strategy is gaining momentum and there has been a significant increase in the number of primary healthcare providers whom we have trained to identify early signs of psychosis. However, there remain various challenges which we are yet to overcome.

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Introduction

Schizophrenia is a serious mental disorder with a profound impact on patients, their caregivers and society. The Global Burden of Disease lists schizophrenia among the top 10 contributors to health burden and disability around the world.[1] Costs of treatment can be direct (costs of resources required to provide services to those who are ill), indirect (loss of resources that could have been invested in other areas and the loss of productivity by the patients and caregivers), or intangible (pain, suffering and grief of patients and caregivers). It is estimated that, in 1990, the cost of schizophrenia in America was $32.5 billion, of which $16 billion (49%) was spent on treatment and other healthcare services.[2] Costs are expected to escalate over time.

The age-corrected annual incidence rate of schizophrenia is between 10 and 40 new cases per 100,000 population. The age-corrected point prevalence rate ranges from 100 to 1700 with a mean of 580 per 100,000 population.[3] With a population of about 4 million, there would be about 23,200 people with schizophrenia in Singapore. The lifetime morbid risk (defined as the proportion of a population meeting the criteria for schizophrenia at any time during life, provided they live through the entire age range of risk) for schizophrenia is about 1%. The peak incidence of onset for males is between 15 and 25 years, and 25 and 35 years in

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females.[4] However, a significant proportion of patients experience their first psychotic symptoms before reaching 20 years of age.

High-risk studies and epidemiological research[5-7] indicate that risk factors for schizophrenia comprise family history (genetic risk), season of birth, urban birth, migrant/minority status, perinatal (including obstetric) complications, neurodevelopmental deficits, family dysfunction, behavioural maladjustment, and substance abuse.

Schizophrenia is a complex disorder where genetic and environmental factors interact in the expression of the illness. Schizophrenia is best conceptualised as a "multiple-hit" illness where individuals have a genetic predisposition and other environments need to act on to "release" the expression.[8]

Most patients who develop schizophrenia have a prodromal phase which involves a change from premorbid functioning and extends up to the time of the onset of frank psychotic symptoms.[9-11] The average length of the prodromal phase is between 2 and 5 years, during which there may be substantial psychosocial impairment.[12] Common early prodromal symptoms are generally non-specific, such as sleep disturbance, anxiety, irritability, depressed mood, poor concentration and fatigue, and behavioural changes such as deterioration in role functioning and social withdrawal.[13,14] Symptoms such as perceptual abnormalities, ideas of reference and suspiciousness develop late and herald the imminent onset of psychosis.[15] It is the non-specificity of these symptoms that confounds our ability to predict who will convert to psychosis.

When psychosis sets in, the subsequent course can be variable, but schizophrenia tends to run a chronic course which results in considerable disabilities. Ten per cent of people with schizophrenia kill themselves. However, what was formerly pessimism has been replaced by some measure of optimism. This has been partly due to the growing body of evidence that early treatment could result in a significant reduction in morbidity, and better quality of life for the patients and their families.[9,16,17] By reducing the duration of untreated psychosis (DUP) – defined as the time between the onset of the first psychotic symptoms and the first adequate treatment – the outcome of schizophrenia could be changed. A recent review[18] has reported that approximately two thirds of the 25 studies on DUP have shown a significant association between shorter DUP and better outcome of 1 or more measures.

The Problems

However, many studies have also shown that there is a considerable delay for those with psychosis in receiving appropriate treatment. The average DUP has been found to be between 1 and 2 years in most Western countries.[17,19] In Singapore, we found that the average duration of DUP of patients with schizophrenia is 33 months.[20]

It is likely that there are many determinants of DUP, but a few of them would be ignorance, stigma, denial, lack of motivation, absence of information about early psychosis, and lack of access to appropriate interventions.[21,22] Furthermore, in Singapore, the manifestations of psychosis are often attributed to supernatural causes. Indeed, we have found that about 24% of patients with first-episode psychosis had sought the help of traditional healers at the first onset of illness.[20]

Long DUP is associated with more frequent and longer hospitalisations,[23] slower and less complete recovery, and more frequent relapses.[24] There is also some suggestion that untreated psychosis may be neurotoxic and induces irreversible brain damage leading to lifelong deficits, and vocational and social disabilities.[25] This hypothesis of the neurotoxic consequence of psychosis, however, is still controversial. Untreated psychosis not only causes distress to the individual but also to family members who are often baffled and frightened, and have to shoulder a heavy burden of care.

The Early Psychosis Intervention Programme

These considerations led to the development of the Early Psychosis Intervention Programme (EPIP), which was initiated in April 2001 and is supported by the Ministry of Health, Singapore. This programme takes a risk-reduction approach:

- Universal preventive interventions that are targeted at the general public, who are not identified to have any specific risk factors,
- Selective preventive interventions targeted at individuals or subgroups of the population whose risk for developing psychosis is significantly higher than average,
- Indicated preventive interventions for high-risk individuals who are identified as having minimal but detectable signs or symptoms foreshadowing psychosis but who do not meet diagnostic criteria for the mental disorder at the current time.

The goals of the programme are:

- Raise awareness of the early signs and symptoms of psychosis,
- Reduce stigma associated with psychosis,
- Establish strong links with primary healthcare providers to work as "partners" in the detection and referral of potential EPIP clients,
- Improve the outcome and quality of life of those with psychosis and therefore reduce the burden of care for their families.

Our outcome indicators:

- Increased number of patients with previously undiagnosed psychosis referred to EPIP,
- Decreased DUP in Singapore,
- Increase in public knowledge about psychosis, its symptoms and where to seek help,
- Decreased level of disability,
- Decrease in suicide rate,
- Better quality of life for patients and families,
- Reduced admissions and reduced hospitalisation days,
- Reduced need for long-stay hospitalisation beds in the Institute of Mental Health,
- Lower health costs.

Strategies

We have implemented a number of our strategies:

- Education of the general public in various ways: public forums, television programmes, newspaper and magazine articles, web site, publication of a book on psychosis for lay persons, and art exhibitions. A study done in Norway demonstrated that a public education campaign (carried out on television, in cinemas, and in newspapers) that focused on psychosis could reduce the DUP over time.[26]
- Networking with primary healthcare providers (who are at the frontline of healthcare in Singapore) is indispensable as more than two thirds of patients with first-episode psychosis would choose to see primary healthcare providers (general practitioners, polyclinic doctors, counsellors and traditional healers) first.[20]
- Providing decentralised and accessible service. This includes the establishment of clinics within the community, onsite consultations at the counselling centres of the polytechnics and universities, and a hotline service.
- Secondary prevention through intervention in the prodromal phase of schizophrenia, which would reduce the proportion of patients making the full transition to schizophrenia, hence decreasing the cost and burden of the illness. In a study conducted from 1984 to 1988, Falloon[27] trained 16 general practitioners (GPs) within the Buckingham county (population of 35,000) in England to detect early cases of psychosis in the prodromal phase using the symptoms checklist in DSM-III-R.[28] The suspected cases were then referred for specialised mental health assessment and treatment. Altogether 16 patients were detected in the 4-year period and 1 was subsequently diagnosed to have schizophrenia. There was a 10-fold reduction in the annual incidence rate: from 7.4 per 100,000 per year to 0.75 per 100,000 per year. The Melbourne group used a "close-in" strategy[29] and developed a set of criteria for identifying ultra high-risk individuals based on recent onset functional decline plus genetic risk (a first-degree relative diagnosed with a psychosis or with a schizotypal personality disorder) and onset of attenuated (subthreshold) positive psychotic symptoms or brief limited intermittent psychotic symptoms i.e. symptoms which spontaneously resolved within 1 week. They found that those with these *a priori* risk factors have a conversion rate of 40% within a year.
- Tertiary prevention, aimed at reducing mortality and morbidity, and ultimately, the future progression of the illness, is effected through phase-specific and patient-centred interventions provided by a multidisciplinary team (psychiatrists, case managers, psychologists, social workers, occupational therapists and nurses). These measures include the optimal and judicious use of medications, psychotherapy, psychoeducation, family therapy, patient and family support groups, rehabilitation, case management, and clinical pathway. Case management is a core competency of our programme and it ensures both the continuity and integration of care. The case manager functions mainly as a broker in ensuring that the patient and family receive co-ordinated, comprehensive and continuous services tailored to their needs. For example, a case manager would ensure that a patient comes regularly for his treatment and receives financial or vocational assistance if necessary. Even childcare arrangements for patients who are parents, but find it difficult to look after their children, can be arranged. Other than psychoeducation and counselling, the programme uses an individualised form of psychotherapy called Personal and Strategic Coping Therapy which takes into account the patient's beliefs regarding his symptoms, coming to an understanding between the therapist and patient, and working out strategies to cope with the various symptoms and problems.
- Research is vital as we are responsible to the stakeholders of the programme i.e. the patients and their families, and our funding partners to ensure that our programme is cost-effective and efficacious. Research is also needed to determine which treatment strategies are effective in reducing the risk of progression to a psychotic disorder.

Results

General Public

A series of 8 public forums (English and Chinese) have been held. To date at least 17 articles on psychosis and the services of EPIP have been published in national newspapers and magazines. In conjunction with Singapore's Health Promotion Board, the Institute of Mental Health, Mental Health Education and EPIP, a docudrama on psychosis called *Mind Matters* was produced. In 2003, the EPIP team published its first book, *Delusions, Possession or Imagination? Experiencing and Recovering from Psychosis.* This is the first easy-to-read, specific book on

psychosis in Singapore for patients, families and care providers.

General Practitioners

A bimonthly newsletter *(EPIP Connect)* containing educational articles regarding different aspects of psychosis, is sent directly to EPIP's mailing list of more than 2,500 GPs in Singapore. The newsletter also contains information on upcoming EPIP events for GPs. We hold lunchtime talks at the various polyclinics around Singapore to which doctors from the polyclinics and private GPs from the surrounding area are invited. We have conducted 27 forums and workshops. In addition, a flip chart for GPs and counsellors has been developed. This chart is an easy-to-access information tool, with information regarding symptoms and the appropriate measures to be taken if a GP or counsellor suspects that a client/patient is experiencing a psychotic episode.

Singapore Armed Forces (SAF) and Singapore Civil Defence Force (SCDF)

EPIP has been integrated into the Medical Service of SAF, where training is provided for medical officers, counsellors and paracounsellors, and psychiatric care is provided for personnel with psychosis.

Counsellors (Universities, Polytechnics, Family Service Centres)

EPIP has established strong relationships with student counsellors from the various universities and polytechnics in Singapore. Counsellors at services run by non-government organisations, such as Family Service Centres, and associations such as the Singaporean Anglican Welfare Council, the Singapore Association for Mental Health and the Singapore Children's Society, have also been the focus of our networking through training and consultation. There is an ongoing training programme (21 talks and workshops have been conducted to date) for these counsellors.

EPIP has also started an assessment clinic within the Personal Guidance and Counselling Service of the National University of Singapore.

Traditional Chinese Medicine Practitioners

Several dialogue sessions with the Singapore Chinese Physicians' Association have been held, resulting in an invitation to give lectures on psychosis in the course for trainees in Traditional Chinese Medicine.

Preliminary Analysis

These efforts have resulted in an increase in individuals referred to the programme. The number of new referrals to EPIP in the first year of its inception (April 2001 to March 2002) was 162, with 135 accepted into the programme. In the following year, the number of referrals grew to 341 (110% increase from previous year), with 214 (59% increase from previous year) accepted into the programme. As of October 2003, we have screened 781 individuals and accepted 516 patients into the programme.

In a preliminary analysis of our first year of operation, we found the average length of stay of our patients within the programme to be 12.8 days (compared to the mean of 19 days for patients with schizophrenia outside the programme). The percentage of unplanned readmission was 7.4% (the Key Performance Indicator for the Institute of Mental Health is ≤10%). There was no suicide among our patients in the first year, and no patient had required a long-stay bed in the Institute of Mental Health. We would like to stress that these 2 indicators will require longitudinal monitoring before a more definitive conclusion regarding the effectiveness of the programme can be made.

A preliminary analysis has shown that in the year following the start of the programme, the DUP of patients coming into our programme was shorter than in the year before the programme suggesting that public education campaigns have been effective in getting individuals to seek help earlier (unpublished data).

Challenges

Weighing the Consequences

There is concern that participation in the early intervention programme would classify the person as a 'psychiatric case', leading them to face the stigmatisation of others or to experience self-stigmatisation, resulting in demoralisation and depression. The counter-argument[30-32] posits that without early intervention and treatment, those who would convert to psychosis will experience greater stigmatisation once the psychosis evolves. Also, these people belong to a treatment-seeking group and are experiencing severe distress with their symptoms.[15] These symptoms are highly distressing to both the patients and their families,[15,33] and the patients have a lower quality of life as compared to treated first-episode psychosis patients.[33,34] They come already accepting the label and role of a patient.

Identification of those who are in imminent risk of developing psychosis is a challenge but in recent years, there has been significant improvement in identifying the prodromal phase. There are 2 instruments: the Comprehensive Assessment of At Risk Mental States (CAARMS) and the Structure Interview for Prodromal Syndromes (SIPS) which have demonstrated good predictive validity.[29,35] Despite the improved sensitivity and specificity of these instruments, there is the risk that some individuals who are falsely labelled as prodromal will never develop schizophrenia at all (false positive

cases).[36-38] Although there have been attempts to improve on the identification of these individuals with genetic analysis and neuropsychological testing,[39] close monitoring and frequent visits will help to reduce that risk, and rapidly detect the initial onset of psychosis, where treatment could be started rapidly.

How to Treat the Prodromal Patients

One of the strongest debates arises from what could be considered as appropriate and effective interventions in the treatment programmes for prodromal patients.

Two recent trials involving new generation anti-psychotic medications have been conducted in prodromal patients. The Australian group conducted the first study,[40] comparing low-dose risperidone (mean dosage, 1.3 mg/d) along with cognitive therapy and supportive case management (n = 31) to case management alone (n = 28). The rates of conversion to psychosis at 6 months were 9.7% (3 out of 31) for the risperidone treatment group and 35.7% (10 out of 28) for the case management group ($P = 0.03$). Minimal side effects were observed. Risperidone was discontinued after the 6 months and all patients were offered ongoing case management. After a further 6-month follow-up, another 3 patients in the risperidone treatment group developed psychosis. It appears that specific pharmacological and psychotherapy treatment in the prodromal group reduced the risk of early transition to psychosis, although the relative contribution of each form of treatment could not be determined.

The second trial is a double-blinded randomised study[41,42] comparing the efficacy and safety of olanzapine treatment (n = 30) of prodromal symptoms to placebo (n = 29). The short-term (8 weeks) results revealed significant symptomatic improvements in the olanzapine treatment group. Weight gain was the principal adverse effect observed in this group. Cognisant of the potential adverse effects of anti-psychotic medications and the unresolved length of treatment for this group of individuals, we will be embarking on a research project to clarify some of these issues.

Responsible Public Education and Funding Issues

Public education campaigns are generally expensive, and as the bulk of our budget is allocated to manpower which has to be increased to respond to the growing patient volume, we have worked hard to obtain corporate sponsorship. Almost all of our public education is funded by such sponsorship. However, other than charitable foundations, great care has to be exercised to ensure that such projects are not influenced by the corporate sponsor's agenda.

Addressing the misconception surrounding psychosis continues to be a challenge, especially in certain groups of the population e.g. other traditional healers like temple mediums, and *bomohs* (Malay medicine men), who are not organised as a body.

The limitations of funding have also restricted our ability to establish a more extensive service outside a hospital or an outpatient setting, which would avoid premature "labelling" and stigmatisation. Although we have established such a service within the National University of Singapore, this service is only available to the university population.

Newer Medications

Another concern is the limited availability of second-generation antipsychotics (SGAs), none of which are on the standard list, and which are more expensive. These SGAs cause substantially less extrapyramidal side-effects than the first-generation antipsychotics (FGAs), which results in better acceptance. Furthermore, some SGAs are more efficacious than FGAs as they alleviate a greater variety of symptoms, resulting in more complete rehabilitation.[43]

Conclusion

Schizophrenia remains a major economic burden to the society and has a profound impact on the sufferers and their caregivers. Focusing on secondary prevention in the prodromal phase of schizophrenia is aimed at preventing the transition to overt psychosis. Recent evidence supports further development in this field. Studies have supported the effectiveness of early intervention programmes in shortening the DUP and reducing the morbidities associated with the disorder. Such specialised programmes should feature in any basic mental healthcare plan and deserve to be a public health priority.

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