Chapter 7
Early Intervention in the Indian Context

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1 Introduction

Psychotic disorders such as schizophrenia afflict the young, are highly disabling, rob patients of their most productive years, cause huge suffering and place enormous burden on families and carers. India, with a population of 1.2 billion, a national median age of less than 25 years, and only 3,500 psychiatrists, has a large pool of undetected and untreated patients with psychotic disorders (between 7 and 8 million) living mainly in remote rural areas (Saxena and Sharan 2004). Evidence-based packages of care for these disorders have been developed and piloted for such settings. However, the actual delivery of treatments remains a significant challenge and is a global mental health priority (Lamers et al. 2006; Sullivan and Ghushchyan 2006; Chisholm et al. 2007; Patel et al. 2008; Saxena et al. 2011). The greatest hope for reducing the burden of schizophrenia in India comes from identifying and treating psychotic patients early and offering evidence-based interventions. Such cohorts also offer unique opportunities to explore the sociocultural and neurobiological influences on outcome of schizophrenia.

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2 Rationale for Early Intervention

The concept of intervening early in psychosis is neither new nor revolutionary; in 1938, Cameron observed that "the therapeutic results to be obtained [in schizophrenia] are considerably better in patients in whom there is little progression towards chronicity" and advocated a public health approach to early detection of cases in the community (Cameron 1938). The mid-twentieth century witnessed the major service reform of deinstitutionalisation, driven by clinical, sociopolitical and financial imperatives. Antipsychotics had engendered therapeutic optimism in schizophrenia, the anti-psychiatry movement had revealed a disturbing violation of the rights of the incarcerated mentally ill, and funding restraints necessitated the development of community-based alternatives, thought to be both cheaper and more humane. The focus of these changes was where and how care was delivered, rather than the quality and effectiveness of that care (Geller 2000).

Studies in the 1980s (Johnstone et al. 1986; Rabiner et al. 1986) and Wyatt's seminal papers (Wyatt 1991) confirmed the prognostic influence of length of untreated psychosis on outcome. In the 1990s, three emerging and interwoven strands of evidence supported the case for specialised early intervention (EI) services. First, the existence of an early window of opportunity, "the critical period", was postulated on the basis of strong evidence that early trajectory and disability were strongly predictive of long-term course and outcome (Wiersma et al. 1998; Harrison et al. 2001), and the greatest impact on the illness might be made during this period of neuronal and psychosocial plasticity (Birchwood et al. 1998). Second, the association between longer periods of untreated psychosis and poorer outcomes became firmly established (Marshall et al. 2005; Perkins et al. 2005). Third, it became clear that even well-resourced community services were not meeting the needs of young people in their first psychotic episode and had not improved their outcomes (Singh et al. 2000, 2003). Politically, an important lever for change was pressure from service users and their carers determined to tackle the "scandal of delays in care" for young people with emerging psychosis (Rethink 2002).

This chapter reviews the rationale for early intervention, describes the range of early interventions, summarises their evidence base and considers clinical and policy implications of implementing early intervention strategies in an Indian context.

3 Duration of Untreated Psychosis (DUP) and Outcome

DUP refers to the time period between the emergence of psychotic symptoms and the commencement of adequate treatment. Since frank psychotic symptoms are usually preceded by non-psychotic symptoms and behavioural changes, DUP is distinguished from duration of untreated illness (DUI), which is the period between the start of the "prodrome" and the commencement of treatment. The conceptual, clinical and methodological problems in ascertaining DUP and DUI have been well documented (McGorry 2000; Norman et al. 2001; Singh et al.

2005; Malla et al. 2011). Several structured instruments and methods have been proposed for measuring DUP and are routinely used in clinical and research settings (Hafner et al. 1992; Singh et al. 2005; Singh 2007; Large et al. 2008).

Two systematic reviews have explored the relationship between DUP and outcomes in psychosis. Marshall et al. (2005) reviewed 26 first-episode studies to find that while baseline presentation in first-episode studies was not poorer in those with longer DUP, there was a significant correlation between DUP and outcome at 6 months (for all symptoms and overall functioning), 12 months (for symptoms, functioning and quality of life) and 24 months (for positive symptoms, functioning and quality of life). The association between DUP and positive symptoms at follow-up was significant even after controlling for pre-morbid functioning. In a review of 43 studies, Perkins et al. (2005) found an association between shorter DUP and better antipsychotic treatment response as measured on psychopathology, positive and negative symptom severity, and global functioning. Both reviews concluded that there was convincing evidence of an association between DUP and outcome following treatment. However, several questions remain. The relationship between DUP and outcome is not linear (longer the DUP, poorer the outcome), but is there a critical cut-off beyond which longer DUP predicts poorer outcome? Is DUP confounded by pre-morbid and illness-related variables? Is DUP neurotoxic? Is reducing DUP at a population level a worthwhile public mental health strategy? (Verdoux et al. 2001; Friis et al. 2004; Killackey et al. 2007; Singh 2007; Malla et al. 2011).

4 DUP in the Resource-Poor Settings

Early intervention services (EISs) exist mainly in the developed world and are the source of the bulk of DUP data (Chiliza et al. 2012). A review of 11 studies from eight low- and middle-income (LAMI) countries including India, Mexico, Poland, China, Turkey, Brazil, South Africa and Indonesia found that longer DUP was associated with lower treatment response in these settings (Farooq et al. 2009a, b). Given the paucity of mental health services in LAMI, it is reasonable to anticipate that those coming into psychiatric care will have long DUP. Average mean DUP is indeed longer in countries with lower gross domestic product in the LAMI. DUP is reduced by 6 weeks for each US$1,000 GDP purchasing power increase (Large et al. 2008). However, this relationship between DUP reduction and rising GDP does not hold true for high-income countries. A study of untreated patients from Chennai, South India (Tirupati et al. 2004), found that treatment response is evident even in cases with DUP longer than 15 years. In this study, a DUP of less than 5 years predicted good clinical but not occupational outcome.

Recent studies from LAMI suggest that the relationship between DUP, service availability, economic development and outcomes is complex. In Pakistan, Naqvi et al. (2009) reported a mean DUP of 64 weeks in a cohort of patients with schizophrenia. Most patients had a psychiatric contact as their first help-seeking encounter, highlighting the scarcity of primary care or community-based services in the study area. Since this was not an epidemiologically ascertained cohort, it is difficult to draw conclusions

about undetected and untreated patients in the base population. In Sao Paulo Brazil, Oliveira et al. recruited an epidemiological cohort of first-episode psychosis (FEP) ($n = 200$) and found a very short DUP (median 4.1 weeks), with longer DUP length associated with patients living alone. A South African study of first hospitalisation patients found an association between longer DUP and spiritual/traditional attributions for psychosis causation and help-seeking through traditional healers (Burns et al. 2011).

5 The Range of Early Interventions

Some of the controversy surrounding early intervention is generated by the different ways in which the term "early intervention" is used. It can mean improving outcomes in established cases of psychosis by facilitating and consolidating recovery, detecting hidden morbidity in the community by identifying untreated cases or preventing the emergence of psychosis through pre-psychotic interventions. These are different aims, requiring different service models and strategies, and have differing levels of supporting evidence.

6 Prodromal Interventions

Preventing psychosis by intervening in the prodrome remains ethically contentious and clinically challenging, given the non-specificity of prodromal symptoms and their low predictive power in identifying cases that will make a transition to psychosis. Table 1 summarises the potential benefits and pitfalls of pre-psychotic and prodromal interventions, as articulated by proponents from both sides of the debate (McGorry 1998; Yung et al. 1998; Warner 2002, 2005; McGorry et al. 2003). In the absence of markers of true prodrome, it is unclear whether the risks of mislabelling and inappropriately treating the "false positives" outweigh the potential benefits of preventing the illness in the "true positives". McGlashan et al. (2001) considers our knowledge in the area to be in "equipoise", i.e. genuine uncertainty, justifying clinical intervention but demanding greater research in the efficacy of such interventions.

Table 1 Pros and cons of prodromal interventions

Against intervention	For intervention
No good screening tests	Help-seeking, symptomatic population with dysfunction and disability
No effective preventive strategy	Targeted rather than universal screening/treatment
Unnecessary treatment of acute and transient psychoses and "false positives"	Safe and efficacious treatments available
Unnecessary stigmatisation	Challenging stigma is part of the solution, not the problem
Research samples are highly selected	Help-seeking groups with prodromal presentation come to clinical services

Correll et al. (2010) reviewed seven randomised trials (a total of 603 "at-risk" individuals), three of which were placebo controlled. Many interventions were used including antipsychotics alone, antipsychotics with CBT, CBT alone and omega 3 fatty acids. Of these, five showed reduced transition rates with CBT (Bechdolf et al. 2004; Morrison et al. 2004); amisulpride (Ruhrmann et al. 2008); ethyl EPA (Berger et al. 2008); and risperidone plus CBT (McGorry et al. 2002). One negative study had a very high dropout, but trend favouring olanzapine (McGlashan et al. 2006). A second negative study had very low transition rates in both groups (Yung et al. 2008). Lower rates of transition ion the active treatment group last only as long as patient receive active treatment; on stopping active treatment, intervention arm patients catch up with control arm in transition rates, with the exception of one study of omega 3 fatty acids (Ethyl EPA). However, this last finding has as yet not been replicated. Another review and meta-analysis of "at-risk" studies concluded that while the benefits for any specific intervention have not been robustly proven, there is tentative evidence that it might be possible to delay or prevent transition to psychosis (Stafford et al. 2013).

Correll et al. (2010) also reviewed specific risk markers such as neuroanatomical abnormalities and cognitive dysfunction predating the emergence of frank psychotic symptoms and concluded that currently valid markers of true psychosis remain unknown. It is unclear whether the risks of mislabelling and inappropriately treating the "false positives" outweigh the potential benefits of preventing the illness in the "true positives". McGlashan et al. (2001) consider our knowledge of the value of treating the prodrome to be in a state of equipoise or genuine uncertainty, justifying needs-based clinical intervention but demanding greater research in the efficacy of such interventions.

7 Early Detection in the Community

In mental health, the routes of access to care are diverse and varied. Patients with FEP access care through a number of agencies, including social services and the criminal justice systems (Singh and Grange 2006). There have been some attempts at developing and evaluating early detection strategies for FEP with mixed results. The first comprehensive trial was the Scandinavian TIPS study which ran over 4 years in four health sectors in Norway and Denmark (Friis et al. 2005; Johannessen et al. 2005; Melle et al. 2005). Both the intervention and control area had similar specialised EISs. In addition, in the intervention arm, GPs and other health professionals were trained face-to-face, schools visited for providing information on psychosis to students, teachers and counsellors, and general public educated about psychosis and help-seeking through information leaflets and a media campaign. TIPS also conducted a historical comparison with DUP data prior to the development of early detection services. Despite a short median DUP in the control area, the TIPS trial found significant further reduction in DUP in the intervention arm. Patients from early detection sectors presented with less severe psychotic symptoms and milder functional deficits prior to treatment initiation. Early detected

cases had significantly less suicidal ideation and suicidal attempts at baseline. TIPS is the first large and comprehensive study to show that a community's median DUP can be significantly reduced with clinical advantages both at intake and at follow-up.

Lloyd-Evans et al. (2011) conducted a systematic review of 11 studies which used eight early detection initiatives. They found that general practitioner education campaigns and dedicated EISs do not reduce DUP or increase the number of patients seeking help for psychotic disorders. Multi-focus initiatives such as a mixture of public education campaigns combined with ease of access to care had better, but still mixed results. The authors concluded that the most promising evidence was for identifying hidden cases in the community via intensive public awareness campaigns.

Facilitating recovery in first-episode psychosis: There is now considerable evidence from EISs around the world that effective and assertive intervention in first-episode psychosis improves short- and medium-term outcomes. Besides several naturalistic studies, there have been 12 trials comparing specialised EISs with standard care from Denmark, Spain, Australia, UK, Holland, USA and China. Of these, the OPUS study from Denmark (Nordentoft et al. 2006; Bertelsen et al. 2007, 2008) is the largest (sample size 547), and also the one of two with a 5-year follow-up, the other being the LEO trial (Craig et al. 2004). In the OPUS study, participants received integrated care consisting of high-fidelity assertive community treatment supplemented by behavioural family therapy and social skills training. Standard care consisted of care at a community mental health centre. At 2 years, participants receiving specialist EIS care had better clinical outcomes, including better symptom control and functioning and reduced hospitalisation. After 2 years of specialist input, all patients in the trial received standard care and were followed up for further 3 years. At the five-year follow-up, there were no differences between the two groups on clinical outcomes although the EIS-treated group were more likely to be living independently. Similarly, the LEO trial in the UK showed that specialised EIS was better than a generic community team in improving short-term outcomes in FEP (Craig et al. 2004).

Specialised teams also appear to be cost-effective. McCrone and Knapp (2007) conducted Markov modelling to compare costs between specialist and generic team care for FEP and found that specialist teams incurred lower costs, primarily due to lower hospitalisation and readmission rates. Similar cost savings have been demonstrated from Danish, Swedish and Italian studies (Valmaggia et al. 2009).

Overall, trials confirm that FEP patients treated under specialist EIS teams have better outcomes than standard care. However, the effect of specialist care lasts only as long as the early intervention approach is maintained. Like the OPUS 5-year results, findings from longer follow-up of LEO sample also showed loss of early intervention gains when patients were discharged back to standard care (Gafoor et al. 2010). It appears therefore that once the EI "grip is relaxed", clinical gains are lost; interventions are therefore effective only as long as actively implemented. This suggests that the heterogeneous trajectories of early psychosis require differentiation, with EI provision being tailor-made for longer periods for those with poorer early outcomes. EIS is a complex intervention with several interacting components, and we are yet to determine the active "therapeutic ingredients" within EIS and how these are exerting their effect (Singh 2010).

8 Early Intervention in the Indian Context

Many patients with emerging psychosis in India receive little or no treatment, with major barriers to access and availability of care and the economic impediments especially for the remote and rural population groups. It is hard to justify setting up prodromal services in such a context, given the limited evidence for such interventions and the clinical, resource and policy imperative of prioritising care for those already ill over those who may become ill in the future. Detection of all, not just first-episode, untreated cases in the community is, however, a public mental health priority. Treating these cases effectively in the first episode and preventing relapse must be another key priority demanding urgent action. In countries such as India, schizophrenia is the sixth leading cause of years lost due to disability (DALYs), higher than iron deficiency anaemia, and only slightly less than cataract. The goal of an integrated approach to meeting the challenge of untreated psychosis should combine a public awareness programme particularly dealing with stigma and lack of awareness of treatment options, training primary care workers and general practitioners identifying cases and using the emerging power of the Internet and the voluntary sector in India.

Farooq et al. (2009a, b), Farooq (2013) have argued for a public health approach to psychosis similar to those being applied for infectious and non-communicable diseases. This would require public education campaigns with particular focus on traditional healers and care provision through a network of primary care workers and social welfare organisations. Such an approach is being used by non-profit organisation such as Schizophrenia Research Foundation (SCARF) in Chennai, which is providing early intervention programmes with emerging evidence of success (Rangaswamy et al. 2012). Telepsychiatry is another promising innovation which can allow clinician access to remote areas overcoming the obstacles of time and travel and using mobile connectedness of rural India to considerable advantage (Thara et al. 2008; Thara 2012; Malhotra et al. 2013; Thara and Sujit 2013). Widespread adoption of these innovative models will depend upon policy makers prioritising mental health care and integrating mental health provision into general health care delivery especially in rural and remote areas. In the West, user voice was eventually heard after a sustained campaign by carers, voluntary organisations and concerned clinicians. The emerging economic power of India should not leave behind among the most vulnerable of its citizens, the untreated psychotic patients languishing in the community.

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