Early intervention in psychotic disorders: detection and treatment of the first episode and the critical early stages

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ABSTRACT

- The two main goals of early intervention in psychotic disorders are to reduce the period of time between the onset of psychosis and the commencement of effective treatment, and to provide consistent and comprehensive care during the critical early years of illness.
- Effective care during the critical early years involves proactive engagement and initiation of drug and psychosocial treatments, aiming for maximal symptomatic and functional recovery and the prevention of relapse.
- Over the past 15 years, an increasing number of specialised or streamed treatment delivery systems for early psychosis have been established around the world. There is now evidence that these services can reduce the duration of untreated psychosis and produce better symptomatic and functional recovery. In addition, they are more cost-effective than standard models of mental health care for these patients.
- Fully fledged, specialised early intervention services should be established, with full integration with local communities, as well as enhanced primary care systems focused on young people.

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Schizophrenia and other psychoses represent the most severe of the mental disorders, with a peak of onset in adolescents and young adults. Until recently, this area of mental health has been marked by pessimism and neglect. Over the past 15 years, however, this apparently unpromising environment for early intervention has seen the emergence of an increasingly sound bank of evidence, and widespread national and international efforts to reform services and develop treatment approaches for early psychosis.[1-3] There are now close to 200 early intervention centres worldwide that focus on the special needs of young people and their families.[4-6] Clinical practice guidelines for the treatment of schizophrenia now typically have a major section on early psychosis.[7]

In keeping with the clinical staging model articulated in this Supplement (McGorry et al, *page S40*), the evidence for the effectiveness of interventions in early psychosis can be considered in two stages. The principal reason for making this distinction relates to the timing and duration of prescription of antipsychotic medication, as psychosocial interventions are needed at all stages.

- The first stage involves intervention before the onset of full threshold psychosis. This is characterised by efforts to accurately identify and intervene in young people with evident clinical disorders but who are in the "prodromal" or "ultra high risk" phase of a psychotic disorder.[8,9] This is covered later in the Supplement (Yung et al, *page S43*).
- 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.

Of course, even when psychosis is detected, the initiation of effective treatment may still be delayed. The goal is to minimise the duration of untreated psychosis (DUP). After detection, the intervention goals are therapeutic engagement and initiation of drug and psychosocial treatments. Intensive interventions aimed at maximal symptomatic and functional recovery as well as the prevention of relapse are ideally delivered during the critical early years after diagnosis.[10] Proof of concept is now established for these strategies; however, there remains a large gap between what works and what is available in most communities around Australia.

Duration of untreated psychosis and outcome

When early intervention studies began, a disturbing finding was the length of time that people had been frankly psychotic before they received treatment.[2] This delay in treatment was almost certainly linked to poor outcomes both in the short- and longer-term. This issue was initially controversial because some researchers failed to find the link, and others asserted on theoretical grounds that the relationship between DUP and outcome was confounded by underlying illness severity, which produced both delayed treatment and also worse outcomes. So the key questions were: Was DUP robustly related to outcome?; Could it be reduced?; and, If this were done, would better outcomes ensue? The answer to all these questions is almost certainly yes.

Two meta-analyses to answer these questions found that there was a consistent, small-to-moderate effect of DUP on a range of outcome variables, including symptomatic and functional recovery.[11,12] Both meta-analyses found that the effect of DUP on outcome was independent of potential confounders,[13] and that prolonged DUP had a negative impact on recovery. The weight of evidence therefore seems to agree with the proponents of the early intervention model — that DUP is related to poor outcome. This then leads to a consideration of the effectiveness of early intervention programs in reducing DUP, and whether such reductions produce better outcomes.

The influential Norwegian TIPS study[14] evaluated whether a specialised community education and mobile detection program can actually reduce DUP. Comparing two health service regions in which an early psychosis detection program was introduced with two areas without such a program, it was found that DUP could be substantially reduced to a matter of weeks, with a much greater reduction in the experimental regions where community education and mobile detection teams were provided.[15] Patients entering care in the early detection regions were in better clinical condition and had been at less risk of suicide.[15,16] Positive clinical differences were maintained at the 3-month follow-up, and at 1 year the level of negative symptoms was significantly less and social recovery was better in the sample detected early.[17] This finding was still present and had strengthened at the 2-year follow-up (Tor K Larsen, Associate Professor of Psychiatry, Stavanger University

Hospital, Norway, personal communication, 3 June 2007). While other dimensions of recovery were not affected, negative symptoms have been the most troublesome to treat, so this is seen as a positive result. While it remains possible that sampling issues could provide an alternative explanation for the results, the general consensus is that evidence increasingly supports the need to establish early detection and engagement strategies across the board to reduce treatment delays.

First-episode psychosis and the critical period

In recent years, the specific elements of the treatment of first-episode psychosis have been carefully studied, specified and distinguished from the treatment of established schizophrenia and severe mood disorders.[7] Another aspect is the need for specialised or streamed treatment delivery systems to engage and retain such patients during the crucial early stages of treatment, and to ensure the key components of treatment are effectively provided.

Two trials have used a randomised design to access the effectiveness of outcomes of specialised first-episode services. The OPUS trial in Denmark randomly assigned 547 patients to an integrated treatment program (in which they were provided with 2 years of enhanced service) or to standard treatment.[18] The integrated treatment was more intense and assertive and covered a wider range of domains, including family therapy and social skills training. The caseload for clinicians was 1 : 10 compared with standard treatment in Copenhagen or Aarhus (the two largest cities in Denmark) in which caseloads were higher (1 : 25). The results indicated that the integrated treatment had beneficial effects on symptomatic and functional outcomes at 1 and 2 years,[18,19] as well as a perceived reduction in family burden.[20] The more assertive nature of the early intervention model is seen in the fact that patients having integrated treatment had an average of 77 contacts over the 2 years, compared with 27 in the standard treatment group.[18]

The second trial was the Lambeth Early Onset (LEO) trial.[21] In the LEO trial, people in Lambeth, England, presenting with a first-episode psychosis (or a second episode where there had been failure to engage previously) were randomly allocated to receive treatment from standard services or from a new early intervention service. Results indicated a beneficial effect of early intervention on readmissions, relapses and drop-outs, although the relapse rate became non-significant[21] when potential confounders were taken into account. More importantly, the intervention group adhered more closely to their medication regimen, spent more time engaged in educational or vocational pursuits, and were better able to establish or re-establish relationships than the control group.[22] The LEO trial showed that early intervention systems can produce gains in clinical, functional and social aspects of early psychosis.[23]

One question that may be asked is whether or not the more intense nature of the early intervention service is cost-effective. A partial answer to this question is found in the 3-year results of the Parachute Project,[24] which compared an early intervention model of service with both a historical control and a high-quality prospective control. Although there were no differences in patient cost between the programs in the second and third years of the project, in the first year the total costs of early intervention care were significantly lower than the costs for the prospective control group ($11 614 v $23 192).[24] This was mainly due to lower inpatient costs, as the early intervention model was more focused on treatment in the community. This was also found previously by the Early Psychosis Prevention and Intervention Centre (EPPIC) program in Melbourne,[25] a finding now confirmed at long-term follow-up, by which time the costs associated with patients treated in the EPPIC model were half of those treated initially in standard care.[26] Economic modelling based on the LEO data is also strongly in favour of the specialised model of care for early psychosis (Dr Paul McCrone, Senior Lecturer in Health Economics, Institute of Psychiatry, London, personal communication, 5 June 2007).

A final question is, for what period should "early" intervention continue? Birchwood and Fiorillo identified the first 5 years as a critical period,[27] and yet many early intervention programs provide only 18 months or, at best, 3 years of streamed care. While many outcome studies look at 1-year outcomes,[28,29] the high cumulative rate of relapse and suicide risk in the first 5 years of illness in young people with psychosis[30] has led some to suggest that a longer tenure of care is warranted, and that there may even be ethical issues associated with referral to mainstream or generic services during this critical period.[31] Suicide rates and functional outcomes, initially better in early psychosis programs, erode if the service is withdrawn after 2 years (Professor Merete Nordentoft, Bispebjerg Hospital, Denmark, and Meredith Harris, Research Fellow, University of Queensland, personal communication, 24 May 2007). Clearly, the tenure of care required in early psychosis services warrants further investigation, but the best estimate currently is that 5 years would be optimal, supporting Birchwood and Fiorillo's notion.[27]

As the field of early intervention in psychosis enters its 15th year, a number of important findings are emerging. Logic, face validity, and the best available evidence converge to demand that proactive and specialised early intervention services be established as new streams of care within the mental health system, connected with local communities and linked to enhanced primary care systems focusing on young people.

Two domains that still need to be addressed are relapse and functional recovery. Much effort has gone into being able to identify people early and initiate treatment. One of the neglected areas that is beginning to receive attention is relapse prevention.[30,32] Likewise, a key focus in recovery has been the remission of positive symptoms. While this has been beneficial, and most first-episode patients now make good symptomatic recoveries,[12] research on vocational and social recovery has lagged behind.[33] Addressing these areas will be crucial to ensuring that people with first-episode psychosis make more complete and sustainable recoveries that give them every opportunity to participate fully in life.

Competing interests

None identified.

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