# Effectiveness of early intervention in psychosis

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**Purpose of review**

Over 15 years, early intervention in psychosis has grown to become a mainstream funded approach to clinical care. This review examines recent developments in evaluating the effectiveness of early intervention. It considers identification and treatment of those at risk of psychosis, as well as interventions in the postonset phase of illness.

**Recent findings**

Development of methods identifying those at risk of psychosis continues to evolve. Promising results in the prevention and delay of transition to psychotic disorder from a high-risk state have been found. Psychological and psychosocial interventions are important components of these preventive programmes. Two recent meta-analyses indicate that there is a consistent relationship between duration of untreated psychosis and outcome independent of other factors. Further evidence shows that early intervention reduces the duration of untreated psychosis, produces better outcomes in terms of symptomatic and functional domains, and is cheaper than standard models of care.

**Summary**

There is evidence that early intervention is effective for early psychosis. Some challenges remain. These include developing a greater focus on functional recovery and prevention of relapse.

**Keywords**

early intervention, early psychosis, effectiveness, first episode psychosis, postonset, preonset

Curr Opin Psychiatry 20:121–125. © 2007 Lippincott Williams & Wilkins.

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**Current Opinion in Psychiatry** 2007, 20:121–125

**Abbreviation**

**DUP** duration of untreated psychosis


0951-7367

## Introduction

After 14 years of development of the early intervention model [1,2], this field of psychosis has moved through the initial years of rapid expansion [3] to become a part of the mainstream approach to psychotic illnesses, particularly with regard to research and clinical practice. After the first 10 years of development, conclusions as to the effectiveness of early intervention were unable to be drawn conclusively [4]. This review revisits the issue.

The early intervention paradigm can be divided into two sections for the examination of effectiveness. The first is intervention prior to the onset of psychosis. This part is characterized by efforts to accurately identify those at risk of onset of psychotic disorder and then interventions to prevent this [5]. The second section is postonset of psychosis, and is characterized by early initiation of treatment [i.e. minimized duration of untreated psychosis (DUP)], symptomatic and functional recovery, and the prevention of relapse [6].

### Identification and intervention in the prepsychotic phase

The primary aim of intervention before the onset of psychosis is to prevent, delay or ameliorate the onset of illness [7,8]. There are two elements that are necessary in order to achieve this. The first is to be able to accurately identify those at risk of developing the illness. Second, there is the need for treatments that are effective in slowing or preventing progression to illness.

#### *Identification*

Identification of people at risk for developing psychosis is the key element of preonset intervention. It is also difficult [9]. Psychotic illnesses have low base rates, and therefore large-scale screening of the general population is not viable [10]. To solve this problem, several strategies have been developed in order to identify high-risk groups. One is 'multiple-gate screening' and 'close in' follow-up. This requires an individual to meet a number of conditions to be included in the high-risk sample, rather than just one condition, as in traditional genetic high-risk studies. These conditions, for example, could be age in the period of highest risk plus subthreshold psychotic symptoms, or family history of psychotic disorder plus social deterioration. The aim is to minimize the inclusion of false positive, that is, those not truly at high risk of psychosis [11]. Based on this concept and the idea of indicated prevention [12], 'Ultra High Risk' criteria were developed at the PACE clinic in

Melbourne, Australia, and then adapted or implemented in several different centres around the world [7,13–17]. In some European countries, criteria based on basic symptoms have been used in a similar way [17]. Studies using these varying criteria have produced transition rates between 9.4 and 70%, with a mean of 31% [7].

While going from a general population rate of 1% to being able to identify a population with a rate of 30% is a positive development towards eventually more accurate identification [18], the methods developed to identify people at risk of psychosis have been criticized [19–21]. One of the criticisms is that the screening process would not be effective in the general population because of the lower base rate of psychotic illness in that population [20]. While this is true, preonset identification is predicated on indicated, high-risk samples rather than on general population samples [2], and in a previous review it was commented that the application of these strategies at a population level would not be supported [18]. The second criticism is that there is a high false-positive rate in all of these studies, with the majority of participants not developing a psychotic disorder. Proponents of early intervention argue that the answer to this is the application in psychiatry of the clinical staging model, which is well known in other areas of medicine [22••,23]. In this model, earlier identification would be associated with less invasive treatments (e.g. psychoeducation rather than medication). If the symptoms progressed, increasing levels of treatments would be able to be used. It also allows for other disorders apart from psychotic disorders to be treated in a timely manner if they arise. The understanding and development of clinical stages in psychiatry is the next phase of development of early intervention and preonset identification [22••].

*Interventions in the preonset phase*

The main aims of intervention in the preonset phase are, first, to prevent or delay transition to psychosis and, second, to treat current problems, such as comorbid depressive or anxiety symptoms or syndromes. A secondary aim is to ensure that should transition occur, the individual is already well engaged with treatment, thereby minimizing the DUP and facilitating nontraumatic entry into an early intervention programme [7]. Psychotherapy and pharmacotherapy have been the main forms of intervention in preonset clinics. Psychotherapy (usually cognitive-behavioural in orientation) [7,24], can be targeted specifically at positive symptoms, or at comorbid syndromes or symptoms such as depression or anxiety. Similarly, pharmacotherapy can be targeted at mood or anxiety disorders, which are frequently present in people presenting to preonset clinics [7,25–27]), or specifically at subthreshold psychotic symptoms, and could include the use of low-dose antipsychotic medication.

To date there have been four studies that have examined the effectiveness of various strategies in reducing transition to psychosis [24,28•,29,30•]. Three strategies found a significant difference in the transition to psychosis between intervention and control groups [24,29,30•], whereas the fourth [28•] found a nonsignificant difference but with a trend in the direction of medication being effective. Two of the three studies that found a difference used a combination of psychosocial and pharmacological intervention [29,30•] whereas Morrison *et al.* [24] used cognitive therapy alone. In contrast, the McGlashan *et al.* study [28•] was the only one to use a pharmacological intervention alone. This would seem to indicate that psychological and psychosocial interventions either alone or in combination with pharmacotherapy may be more effective than pharmacological interventions alone. It has been observed that an increase in stressful life events precedes a psychotic episode [16] and it may be that the psychological and psychosocial elements of treatment affect this domain more directly than medication. The nonsignificant difference in the McGlashan *et al.* trial, however, may be a result of the under-powering of the study. Further research is required to resolve which elements of an intervention are essential at this time point and for how long they need to be applied. Development of this knowledge would be a useful contribution towards the elucidation of a working clinical staging model [22••].

One of the criticisms of intervention in the preonset phase is that people will be mislabelled, potentially stigmatized, and exposed to treatments that they did not need [20,24] because they were not going to develop psychosis ('false positives'). This is particularly a criticism targeted at interventions utilizing antipsychotic medication. Morrison *et al.* [24] specifically address this criticism in their choice of using only a psychological intervention, which they argue is less likely to lead to deleterious side effects than a pharmacotherapy. While criteria for identification of those at risk of psychosis continue to evolve and there are large numbers of false positives, even the leading proponents of preonset intervention advocate cautious use of medication [29], as do guidelines for treatment in this phase [31•].

In the last 10 years since the establishment of the first preonset clinic, great advances have been made in developing criteria to identify those at risk of developing psychosis. Treatment for this identified group has been developed which, in a majority of studies, shows an ability to significantly reduce the rate of transition to psychosis and reduce symptomatology. While this is promising, critics raise some valid concerns. In order to address these concerns, two key developments are required. The first development is the continued improvement of the accuracy of predictive tools, thus reducing the

false-positive rate as much as possible. The second one is developing a knowledge of which interventions are required at what stage so as to reduce the exposure of people to unnecessary iatrogenic damage.

## Postonset

In considering the effectiveness of early intervention after the onset of psychosis, there are three key areas to examine. The first is to clarify the ongoing debate about whether or not duration of untreated psychosis is related to poorer outcome in first-episode psychosis, as has been suggested [32–34]. Duration of untreated psychosis has been claimed to be a key target of the early intervention movement because it represents one of the few obviously malleable variables [10]. The second area is whether early intervention programmes can reduce DUP, as has long been claimed by the proponents of early intervention [32,35]. This claim has been a controversial one [19,36] and was not yet at a point of resolution when Drake and Lewis last wrote in this journal about this topic [18]. The third area to examine is whether or not early psychosis programmes produce good outcomes in terms of both symptomatic and functional recovery. Critics of early intervention services in psychosis have argued that early intervention involves discontinuity of care and diversion of resources from other areas of mental healthcare [37], and that the costs outweigh the benefits of innovation in the treatment of psychotic illnesses [38].

### *Duration of untreated psychosis and outcome*

For some time there has been debate about whether or not DUP is related to outcome, as has been suggested by the early interventionists, or whether it is itself brought about by a third variable that independently leads to prolonged avoidance of help seeking, such as insidious onset or social withdrawal [20,35,36,39]. Many studies have examined whether or not DUP was related to outcome in first episode groups [32–35,40]. There have been criticisms of studies with findings that supported and of studies with findings that did not support DUP being associated with poorer outcome [10,20]. Reviews that have appeared in this journal were not able to resolve conclusively this important question [2,18].

Two meta-analyses of this question have now been conducted [41••,42••]. Both studies found that there was a consistent small to moderate effect of DUP on a range of outcome variables, including symptomatic and functional recovery. More importantly, both studies reviewed whether or not this effect was independent of potential confounding effects such as premorbid functioning [18]. Both meta-analyses found that the effect of DUP on outcome was independent of potential confounders, and that prolonged DUP had a negative impact on recovery. It would therefore seem that the weight of evidence agrees 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 programmes at acting to reduce DUP.

### *Programmes for reducing duration of untreated psychosis*

The Norwegian TIPS study [43••] is the best study thus far of whether a specialized programme can act to reduce DUP [18]. Comparing two regions with an early psychosis detection programme and community awareness campaign to two areas without, it was found that DUP can be reduced, with medians being 5 weeks and 16 weeks, respectively [44]. There were differences in favour of the early detection group at baseline on a number of symptomatic variables [44], and also reduced suicidality [45•]. There was no difference, however, between quality of life or social functioning [46]. The authors suggest that this functional deterioration may precede symptom onset. While it would be valuable if the TIPS study were replicated, the evidence from this one study suggests that a combination of service provision and public education can act to reduce the duration of untreated psychosis.

### *Treatment of the first episode*

There have been two trials that have used a randomized design to access the effectiveness of outcomes of first episode services. The OPUS trial in Denmark [47] randomly assigned 547 patients to either an integrated treatment in which they were provided with 2 years of service or to standard treatment. The integrated treatment provided was intense and assertive and covered a wide range of domains including family therapy, and social skills training. The caseload was 1 : 10. The control condition was treatment at a standard service in Copenhagen or Aarhus in which caseloads were higher (1 : 25). The results from the study indicated that the integrated treatment had beneficial effects on symptomatic and functional outcome at 1 and 2 years [47,48••], as well as a perceived reduction in family burden [49]. The more assertive nature of the early intervention model is seen in the fact that patients in the integrated treatment had an average of 77 contacts over the 2 years compared with 27 in the standard treatment group [47].

The second trial was the Lambeth Early Onset (LEO) trial [50]. The LEO trial randomized people in Lambeth, UK presenting for a first episode psychosis (or a second episode where there had been failure to engage previously) to either receive treatment from standard services or from a new early intervention service. It was found that there was a beneficial effect of the early intervention on readmissions, relapses and dropouts. When adjustments were made, however, the relapse rate became nonsignificant [50]. Further analysis of this study showed that the intervention group were more compliant with medication, spent more time engaged in educational

or vocational pursuits, and established or re-established relationships better than the control group [51]. The LEO trial shows that early intervention can achieve gains in both clinical and functional aspects of early psychosis.

One question that may be asked is whether or not the more intense nature of the early intervention service is so expensive as to be not viable. An answer to this question is found in the 3-year results of the Parachute project [52•], which compared an early intervention model of service with both an historical control and a high-quality prospective control. Although there were no differences in patient cost between the programmes in the second and third years of the project, in the first year the total costs of the early intervention condition were significantly lower than the prospective control condition ($11 614 compared with $23 192, $P < 0.05$) [52•]. This was mainly due to lower inpatient costs, as the early intervention model is more focussed on treatment in the community.

A final question that may be asked is for what period should 'early' intervention continue? Birchwood [53] identified the first 5 years as being a critical period, and yet many early intervention programmes provide only 18 months or, at best, 3 years. While many outcome studies examine 1-year outcomes [54,55], the high rate of relapse in young people with psychosis [56] has led to suggestions that a longer continuity of care within first episode programmes is warranted, and that there may even be ethical issues about referral to mainstream agencies during this critical period [57]. Clearly, the length of treatment required in optimal early psychosis services warrants further investigation.

## Conclusion

As the field of early intervention in psychosis enters its 15th year, a number of important findings are emerging. Intervention in the prepsychotic period is an area of rapid growth in which indicated prevention is being aggressively pursued. There is good evidence that this area has the ability to limit transition to psychosis at best, and at worst, to ensure that there are minimal periods of untreated psychosis for those who develop psychosis. This area faces challenges, however, in refining the techniques it uses to identify those at risk of developing psychosis to ensure that they are ever more accurate and specific.

Intervention in the postonset period has also made gains in the period since Drake and Lewis reviewed it [18]. As they foreshadowed, meta-analyses of the influence of DUP on outcome have shown that there is a relationship between prolonged DUP and poor outcome. Further, studies have shown that early psychosis programmes can act to reduce DUP. Both the LEO and the TIPS projects show that early intervention can produce superior outcomes to regular psychiatric services for people with first episode psychosis, and the Parachute project demonstrates that this can be cost effective.

There are areas that still need to be addressed with regard to early intervention. The two main domains are those of relapse and functional recovery. Much effort has gone into being able to identify people early and initiate treatment. It is apparent that one of the neglected areas in this development is relapse, an area that is now beginning to get attention [56,58]. Similarly, a key focus in recovery has been the remission of positive symptoms. While this has been beneficial and many patients now make good symptomatic recoveries, research on functional recovery has lagged behind [59•]. Addressing these areas will be important to ensure that people with first episode psychosis make sustained recoveries that give them every opportunity to participate fully in life.

## Acknowledgements

The authors wish to acknowledge the extremely helpful assistance of Magenta Simmons in gathering literature for this article.

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