British Medical Journal

Early detection and intervention evaluation for people at risk of psychosis: multisite randomised controlled trial

Re: Early detection and intervention evaluation for people at risk of psychosis: multisite randomised controlled trial

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Dear Sir/Madam

We read with interest Morrison et al. 'Early detection and intervention evaluation for people at risk of psychosis: a multisite randomised controlled trial' as well as the subsequent coverage in the Guardian http://www.guardian.co.uk/society/2012/apr/06/drugs-psychosis-schizophre...

The authors' concluded that cognitive therapy did not significantly reduce transition to psychosis or symptom related distress. However, the most surprising finding of the study was the low transition rate (8%), which meant that the study was not sufficiently powered to detect a true difference between the interventions. The authors suggest several reasons for this: the exclusion of participants at risk of imminent transition; the sampling and recruitment strategy may have led to including participants who, due to their pathways into care and degree of help-seeking, may not have been 'risk enriched' [1-3]; those most at risk may not be willing to enter trials; the relatively short follow-up period; and that the 'control' condition (monitoring of mental state, with warm, empathic supportive listening) may itself have reduced transition rates. Whatever the reasons, the transition rate was much lower than that reported in the existing literature. A recent meta-analysis of 27 studies found that in a combined sample of about 2500 subjects, the transition rate was 18% at 6 months after onset of symptoms, 22% at 1 year, 29% at 2 years, and 32% at 3 years [4]. In agreement with the meta-analytic cohort findings, substantially higher 12 months transition rates (12.5% to 37.5%) were observed in the control conditions of earlier randomised controlled intervention trials in this population [5-10].

It would be interesting to know how many of the cohort remitted from the at-risk mental state during their time in the study, and whether this was influenced by the two interventions [11]. The clinical significance of the results is difficult to interpret because the ordinal CAARMS intensity scales appear to have been weighted by the corresponding frequency ratings to create a 'severity scale' which was statistically analysed as though it were a continuous variable. The authors then commented that a 4 point reduction in this severity scale represented clinically significant change. However, spread across the four subscales examined this might actually reflect a modest clinical change.

The authors reported that of n=634 participants assessed for eligibility, n=346 were excluded and n=288 were randomised. Of those excluded, 156 either were taking antipsychotic

medication or were found to be psychotic (24.6%) and n=110 were sub threshold for psychosis (17.35%). It is worth bearing in mind that many of those on anti-psychotics will not have had a psychotic disorder, but have been at-risk subjects with a relatively high risk of transition [12]. Hence, excluding this group may have contributed to the low transition rate. In the study by Morrison et al, 45.4% of those assessed met inclusion criteria. However, in an earlier publication from the same group that described the study design [13], the authors indicated that n=867 participants had been referred to the study, suggesting that n=233 were not assessed. This was reported as being due to a loss of contact or subjects lacking interest. However, this loss of potential participants is another potential source of bias, as these individuals may be those who are the most distressed or disadvantaged, and hence at greatest risk of psychosis. Without knowing more about the sampling procedures employed by the study, such as how the team tried to engage with those with whom they had lost contact, and demographic data comparing this subgroup to those included in the study, it is hard to know whether this may have also contributed to the low transition rate.

The authors suggest that the low transition rate that they identified raises questions about the validity of the At Risk Mental State. However, given how atypical the rate is relative to that in the literature, this may be premature. The concept of the At Risk Mental State has stimulated a body of new research that has significantly advanced our knowledge of the mechanisms underlying psychosis [14-22], and has led to the development of clinical services that permit the earlier detection and management of mental health problems [23, 24]. Research at this stage is a particularly powerful way of investigating the mechanisms underlying psychosis, as the same individual can be studied before and after the onset of illness, without the confounding effects of previous treatment or long-lasting disease-related effects [25]. Nevertheless, the data from this and other studies [26-29] suggest that the existing inclusion criteria, which are relatively recent and mainly based on positive psychotic symptoms [11, 30-35], could certainly be improved. In particular, it would be useful to include items relating to affective and negative psychotic symptoms, and self-perceived [36] and cognitive changes [37] or through the introduction of second step risk stratification [38, 39].

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