

## Duration of untreated symptoms in common mental disorders: association with outcomes

International study

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**Summary** Studies have assessed the association between a longer duration of untreated symptoms and outcome for psychoses in specialist care. We investigated the effect of longer duration on the outcome of common psychiatric disorders in primary care, where most patients are treated. Patients presenting to primary care for new episodes in 10 countries were recruited into a prospective cohort study. Information on duration of untreated symptoms and psychosocial status was collected for 351 individuals using standardised instruments and this was repeated 1 year later. At 1-year follow-up, longer duration was associated with worse psychiatric outcome even after controlling for potential confounders.

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Studies on the duration of untreated symptoms focus on time to admission for severe mental illness such as schizophrenia and affective psychosis in Europe, Australasia and North America, rather than on common mental disorders in primary care (Craig *et al*, 2000; Drake *et al*, 2000; McGorry, 2000). The longer depression, anxiety and somatic disorders last, the worse the response to appropriate intervention: inadequacy of treatment leading to symptom persistence may be one reason. The kindling hypothesis suggests that longer waits for treatment may also contribute (Kendler *et al*, 2000).

### METHOD

We investigated the effect of duration of untreated symptoms on 1-year outcome in primary care, using data from the

1990–1993 World Health Organization Collaboration Study of Psychological Problems in General Health Care (Ustun & Sartorius, 1995). Data were available for Ankara, Athens, Bangalore, Groningen, Ibadan, Manchester, Rio de Janeiro, Santiago, Seattle and Verona. Overall study methods are described elsewhere (Sartorius *et al*, 1993; Ustun & Sartorius, 1995). Studies of duration of untreated psychosis indicated that up to 250 participants were required to have an 80% chance of detecting a statistically significant result at the 95% level (Craig *et al*, 2000; Drake *et al*, 2000).

We focused on overall psychiatric morbidity as our outcome, because patients in primary care are more likely to have a mixture of depression, anxiety and somatoform symptoms than discrete syndromes. We analysed psychiatric outcome as a continuous variable, instead of dichotomously (e.g. caseness), to obtain more information on severity, including subclinical symptoms.

We screened patients aged between 16 and 65 years who had not visited the clinic in the previous 3 months, using the 12-item General Health Questionnaire (GHQ; Goldberg & Williams, 1988). A stratified random sample of the study population (weighted towards higher GHQ scorers) were then interviewed, using the primary healthcare version of the Composite International Diagnostic Interview (CIDI-PHC; Robins *et al*, 1988; Sartorius *et al*, 1993). This included the Pathways to Care Interview to record the onset and duration of presenting symptoms (depressive, anxious or somatic); whether this was the initial visit for this problem; the profession of each person consulted for those symptoms; and the main treatment offered at each step. We calculated the duration of untreated symptoms by subtracting the time from first seeking treatment in any setting and arriving at the participating clinic (duration of pathway in treatment) from the total duration of presenting symptoms. We only included people whose current presentation was their

initial visit to the participating clinic for this problem. Duration of untreated symptoms was assessed in weeks; zero meant symptoms had lasted less than a week.

We used the CIDI-PHC sections on somatisation, anxiety, depression, hypochondriasis and neurasthenia to measure psychiatric morbidity. Medically explained and unexplained somatic symptoms were counted using a flow chart to establish aetiology (Robins *et al*, 1988). We assessed disability using the Groningen Social Disability Schedule (GSDS), a semi-structured interview that considers local norms (Wiersma *et al*, 1990).

At baseline, the family physician completed a questionnaire on the presence of psychiatric disorder and any treatment offered. All patients with significant psychological problems, and a 20% random sample of 'non-cases', were contacted for 12-month follow-up. Bangalore and Seattle followed up every patient. We repeated the CIDI-PHC and collected information on visits to the participating clinic or other clinics and any hospital admissions, irrespective of diagnosis, during the intervening year.

The interviewer–observer reliability coefficient for the CIDI-PHC (including the Pathways to Care Interview) was 0.92, and 0.85 for the GSDS (Sartorius *et al*, 1993).

We restricted our analysis to patients who had not visited the practice previously for their presenting problem and who had an ICD-10 (World Health Organization, 1992) psychiatric diagnosis, as determined by the CIDI-PHC. We excluded patients with non-psychiatric presentations such as visits for family planning or antenatal care.

### RESULTS

In all, 3321 patients completed the baseline interview, of whom 2767 were eligible for follow-up. Details of duration of untreated symptoms were available for 2579 people (93%). Of these, 1791 (70%) were successfully followed-up.

Those who had not previously visited the participating practice for their presenting problem numbered 900, of whom 351 met our remaining criteria of reason for presentation and psychiatric caseness. The majority had depression ( $n=210$ ); 73% were women or girls ( $n=256$ ); 81.9% had an educational level of less than grade 12 (usually age 18 years) ( $n=290$ ); 40.7% were single ( $n=143$ ); and 21.4% were unemployed ( $n=75$ ). Age ranged from 15 to

50 years with a mean of 37.7 years (s.d.=12.9).

Duration of untreated symptoms was skewed, with a mean of 19.1 weeks (s.d.=74.1) and a median of 1. We normalised the duration by taking the logarithm of the base, rather than dichotomising or dividing into quintiles, to maximise power. We added one to each value before transformation because of zeros (Kirkwood, 1992). The mean was 0.57 (s.d.=0.67).

We obtained information on health service use for 317 participants. Patients averaged five visits to the participating clinic and three to other clinics; 12% ( $n=41$ ) had been admitted to hospital at least once.

On multiple regression, the duration of untreated symptoms showed a significant association with overall psychiatric symptoms 1 year later ( $B=3.61$ , s.e.=1.60,  $P=0.02$ ), as did initial psychiatric symptom count, older age, lower educational levels, medically unexplained somatic symptoms, and visits to the participating clinic (see data supplement to the online version of this paper for results on all variables).

The duration of untreated symptoms also showed an association with anxiety symptoms ( $B=0.46$ , s.e.=0.18,  $P=0.02$ ) and depression ( $B=0.97$ , s.e.=0.49,  $P=0.05$ ), using the same model. There was no statistically significant association when using untransformed duration of symptoms ( $B=0.01$ , s.e.=0.02,  $P=0.37$ ).

## DISCUSSION

The outcome and response to treatment for common psychological disorders such as depression and anxiety are inversely proportional to their chronicity (Seivewright *et al*, 1998). One explanation is that inadequate intervention leads to persistence of symptoms, and collaboration between specialists and family practitioners can help address this (Andrews, 2001; Roy-Byrne & Wagner, 2004). We suggest another explanation, i.e. longer waits for treatment. This association is modest, but still significant, after controlling for other variables including demographics, centre attended and initial severity of symptoms (see online data supplement).

These results support the kindling hypothesis of depression (Kendler *et al*, 2000), which has parallels with the critical period hypothesis in early psychosis

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(Birchwood *et al*, 1998). The association between depressive episodes and adverse life events weakens with successive illnesses, suggesting biological or psychological adaptation so that psychosocial precipitants are no longer necessary for relapse.

Limitations include our demonstration of only an association between duration of untreated symptoms and subsequent psychiatric morbidity, not direct causation. Furthermore, our analysis may have been confounded by variables for which we were unable to control. We considered new episodes of care and not necessarily first presentations of an illness. There may have been selection bias, as patients with a short duration may have improved and never sought care (McGorry, 2000). Depression or anxiety may be harder to recognise than psychosis, and we did not get corroboration from family members. Data were collected a decade ago, and so may be less applicable now. However, it is unethical to collect further data, with the consequent cost and inconvenience to patients, without first analysing available datasets.

Our results provide a wider perspective on the duration of untreated symptoms. Research on the effects of such duration in psychosis is conflicting. Explanations have included differences in demographic characteristics, diagnostic criteria, measures of onset (first symptom or full syndrome), treatment definition (medication or hospital admission), outcome measures and follow-up periods. Studies that use transformation to normalise the positive skew of duration tend to show an association with outcome in contrast to those that do not (Norman *et al*, 2005). This supports our negative finding, and that of others, when using untransformed duration of symptoms (Drake *et al*, 2000).

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