

assigned 1202 extremely low birthweight infants, soon after birth, to receive indomethacin (0.1 mg/kg) or placebo intravenously once daily for three days.¹⁰ The primary outcome, a composite of death, cerebral palsy, cognitive delay, deafness, and blindness at a corrected age of 18 months, was not significantly different in the intervention and placebo cohorts. However, in the indomethacin group, there was a significantly reduced incidence of patent ductus arteriosus (24% *v* 50% in the placebo group), and requirement for subsequent indomethacin therapy (17% *v* 46%), or surgical duct ligation (7% *v* 12%). The incidence of severe periventricular haemorrhage, but not of other evidence of intracranial abnormalities seen on cerebral ultrasound, was reduced in the indomethacin group (9% *v* 13%). The study did not find any evidence that prophylactic indomethacin affected other outcomes such as chronic lung disease, necrotising enterocolitis, and retinopathy.

This major collaborative effort, involving infants from 32 centres in five countries, further shows that it is possible to do large, pragmatic trials to address clinically relevant questions in neonatology. Previous randomised controlled trials did not find any evidence for a longer term neurodevelopmental effect of prophylactic indomethacin in very low birthweight infants. These were done in the era before the frequent use of antenatal steroids and exogenous surfactant therapy,¹¹ or were limited by small sample size and incomplete follow up.¹² Now, Schmidt and colleagues have provided, with near complete follow up, an unbiased assessment of longer term neurological outcomes in a population of extremely low birthweight infants who had the opportunity to get antenatal steroids and surfactant therapy.¹⁰ This, and the fact that the cohort size was sufficient to detect a modest effect (roughly 20% difference in risk) on the primary outcome, improves confidence in using the findings in everyday practice.

Is indomethacin prophylaxis beneficial for extremely low birthweight infants? The answer depends on which outcomes are considered most important. Prophylaxis with indomethacin reduces the incidence of severe intraventricular haemorrhage, but survival without neurological disability, the outcome of major importance to parents and carers, is not improved. However, parents and carers may value the finding that prophylactic indomethacin reduces the frequency of patent ductus arteriosus and the need for

subsequent surgery to close the patent ductus arteriosus. Applying the effect size estimated by the study, for every 100 extremely low birthweight infants who get prophylactic indomethacin, patent ductus arteriosus will be prevented in about 20 and about five will not need surgical closure. The reduced need for surgery may be of particular importance in neonatal centres where infants need to be moved to specialist cardiology and thoracic surgery centre. As with many perinatal and neonatal interventions, the decision to use prophylactic indomethacin will depend on the values attached by parents and carers to these benefits.

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Bipolar affective disorder—left out in the cold

Too late for the national service framework but local initiatives may be possible

The national strategic framework for mental health states that “one person in 250 will have a psychotic illness such as schizophrenia or bipolar affective disorder.” It goes on to cite bipolar affective disorder as one of the 10 leading causes of disability worldwide in adults aged 15-44.¹ How surprising then that the service needs of people with bipolar affective disorder receive no specific consideration in this major policy document.

There are four reasons why the national service framework should have given special consideration to

the needs of people with bipolar affective disorder. Firstly, most patients with bipolar affective disorder have the potential, with optimal treatment, to return to normal function and contribute to the economy. With suboptimal treatment, however, many will have a poor long term outcome and needlessly become a burden to families and society.² Yet there is evidence that treatment is generally suboptimal. For example, a survey (n=1004) of members of the Manic Depression Fellowship, a British organisation for people with bipolar affective disorder, found that only 19% were in full

time work, although 40% were graduates and 69% wanted to work.³ Longitudinal observational studies suggest that the very high lifetime prevalence of suicide attempts in people with bipolar affective disorder (50%³) could be reduced by maintenance drug treatment and adequate treatment of depression and comorbid alcohol and drug abuse.⁴

Secondly, achieving optimal treatment of bipolar affective disorder is challenging and requires long term commitment from health services.^{4 5} For example, an expert review shows that the need to balance the benefits of mood stabilisers, neuroleptics, and antidepressants against the risk of iatrogenically inducing depression, mania, or rapid cycling mood.⁵ Moreover, despite the benefits of drugs such as lithium shown in a Cochrane review, pharmacological treatment for bipolar disorder is potentially toxic.⁶ Failure to adequately monitor lithium leads to well known, serious, largely preventable complications such as renal failure, hypothyroidism, or irreversible neurological damage through intoxication.⁵ Observational research, however, shows that deficiencies in monitoring lithium in primary and secondary care are commonplace.⁷

Thirdly, bipolar affective disorder is characterised by high rates of relapse and high rates of disabling mood symptoms between relapses. For example, a prospective observational study has shown that after a manic episode, 50% of people with bipolar affective disorder will relapse in the next 12 months.⁸ In a survey of people with bipolar affective disorder 23% had been admitted to psychiatric inpatient care in the previous 12 months.⁹

Fourthly, relatives of people with bipolar disorder are not only subject to the usual stresses of caring but are also at high risk of developing unipolar depression or bipolar disorder themselves.⁹

The national service framework is primarily concerned with finding the right service structures rather than advocating particular individual treatments. Perhaps the problem with bipolar affective disorder was that there was no off the shelf model of care such as existed for schizophrenia, in the form of assertive outreach.¹ Yet people with bipolar affective disorder do not necessarily fit well into structures of care developed primarily for those with schizophrenia. It is not clear, for example, that people with bipolar affective disorders who maintain high levels of functioning and compliance when well are likely to benefit from assertive outreach, even if they have frequent episodes of mania or depression.

Does the omission of bipolar affective disorder from specific service provision matter in practice? It does if resources are diverted away from services that are principally used by people with bipolar affective disorder. National surveys reveal a 14% shortage of consultant psychiatrists in the United Kingdom,¹⁰ with similar shortages of trained nursing, social work, and other mental health staff.

Some of the service innovation outlined in the national service framework for mental health and the NHS plan must result in the shift of staff from mainstream services that bipolar affective disorder patients frequently use,^{2 11} such as community mental health teams, outpatient sessions with consultant psychiatrists and inpatient services, to new services such as assertive outreach teams, early intervention teams, and crisis teams that will occasionally be used by

bipolar affective disorder patients. The long term care needs of most people with bipolar affective disorder may not be well served by these services.

However, there are some opportunities in the local implementation of the national service framework for mental health for improving services for people with bipolar affective disorder. A randomised controlled trial showed that crisis teams might prevent mania and improve function if they are set up to access and implement contingency care plans that have been previously agreed between psychiatrist and patient should there be a relapse.¹¹ Another randomised controlled trial found that psychoeducation for people with bipolar affective disorder and their carers can reduce relapse, improve depressive symptoms, and reduce caregiver burden.¹² Observational research suggests the benefit of adopting protocols for prescribing and monitoring mood stabilising drugs (lithium and anticonvulsant) across both primary and secondary care. It is too late to include these initiatives formally in the national service framework,¹ but they could be among the targets for local, regional, and national service framework implementation teams.

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