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Early and delayed treatment of bipolar disorder

Using Danish registry data, Kessing *et al* examined the relationship between lithium response and the timing of treatment (early *v.* delayed).¹ Early treatment was associated with an increased probability of lithium response. This is a clinically important finding, given the increasing emphasis on early intervention in bipolar disorder. The results of the Kessing *et al* study are sobering. Only few patients, particularly among those for whom treatment was delayed, responded to lithium. Several factors may have contributed to the reported results.

The study did not – and possibly could not – control for the cycle shortening that is observed after successive episodes of bipolar disorder. Although the interpretation of such cycle shortening has been debated,² it is well established that early cycles are significantly longer than those occurring later; consequently, early in the course of illness one would expect longer spontaneous remissions regardless of treatment. This effect may be partially responsible for the greater treatment response in patients receiving early intervention in the Kessing *et al* study.

Naturalistic studies typically demonstrate full response in about 30% of participants³ (that is, no recurrences, or the Kessing *et al* criterion, in treatment-adherent patients), which is markedly greater than the response rate observed by Kessing *et al*. This discrepancy could be related to age at first contact. The average age of participants whom Kessing *et al* reported as having received early and late treatment was 46.7 years and 49.1 years, respectively. The natural history of bipolar disorder includes an average age at onset in the second or third decade of life. The trajectory of the illness, where mania typically develops as the last stage, delays the diagnosis of bipolar disorder. Also, there is often a substantial delay in starting treatment even following the diagnosis of bipolar disorder.^{4,5} These reports, in conjunction with the advanced age at index presentation, and high rates of antidepressant, antipsychotic and anticonvulsant use in the Kessing *et al* study suggest that participants may have been afflicted with bipolar disorder for some time before ‘first contact’. In a sample of 450 participants, Baldessarini *et al* reported a negative relationship between treatment latency and effect of treatment on time spent ill.⁵ If the aforementioned findings are generalisable to the Danish sample, the reduced overall treatment responses may be interpreted as a consequence of relatively advanced participant age.

Finally, Kessing *et al* analysed data collected since 1995. Is it possible that participants had received lithium during the years prior? This would further complicate the interpretations of sample responsiveness to lithium, regardless of early or late initiation. In conclusion, we suggest that the findings presented by Kessing *et al* are limited by the lack of control for inter-participant differences in the manifestation of the natural history of bipolar disorder. Such control may be difficult, or in some cases impossible, to achieve using registry-based observational data, but is nevertheless imperative to understanding the effects of early *v.* late treatment prophylaxis in relapsing–remitting illnesses such as bipolar disorder.

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Authors’ reply: We are confident that the relatively low response rates to lithium in our study relate to the narrow definition of lithium response, rather than to characteristics of the included patients.¹ Thus, we intended to characterise patients who had an excellent response to lithium monotherapy; that is, patients who were ‘cured’ from further affective episodes following a start-up period of lithium as in a prior study.² We used two robust clinical indicators to define excellent lithium response: (a) lithium prescribed in monotherapy; and (b) no need for psychiatric hospital admission. By doing this, we defined lithium response in a rather rigorous way, resulting in relatively low rates of response. We do not find that our definition of lithium response hampered the finding of the study that early treatment with lithium was associated with increased probability of excellent lithium response compared with delayed treatment, or hampered the generalisability of this finding. Although cycle acceleration occurs on average in bipolar disorder^{3,4} the results of our study may suggest that early treatment with lithium might prevent progression of bipolar disorder.

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‘Reasonable adjustments’ for vulnerable patients

We support the views of Tuffrey-Wijne & Hollins¹ and their argument for the NHS to take an organisational approach to embed documentation and provision of reasonable adjustments for those with protected characteristics under the Equalities Act 2010. Lord Darzi defined quality for the NHS as comprising three dimensions: safety, effectiveness and patient experience.² The provision of reasonable adjustments is central to each of these.

Safety – Tuffrey Wijne & Hollins rightly identify the lack of provision of reasonable adjustments as being a patient safety issue. The Confidential Inquiry into Premature Deaths of People with

Learning Disabilities (CIPOLD)³ demonstrated an underlying culture in which people with intellectual disabilities were disadvantaged in accessing equitable healthcare and at risk of premature death because equality for disabled people was assumed to mean treating them the same as others. It does not. Alternative methods of making services available have to be found in order to achieve equality of outcomes. Mizen *et al*, for example, demonstrated that clinical guidelines can actually increase health inequalities for people with intellectual disabilities if reasonable adjustments are not made.⁴ If the lack of reasonable adjustments threatens to compromise safety as, in very many cases, it does for people with intellectual disabilities, this needs to be reported and reviewed as a patient safety issue.

Effectiveness – evidence put forward by Tuffrey-Wijne *et al* suggests that ward culture, staff attitudes and staff knowledge are crucial in ensuring that hospital services are accessible to vulnerable patients.⁵ Effective care is that which is tailored to the needs of the patient, and this must involve an understanding of the adjustments they need in order to be able to receive appropriate medical and nursing care. In our view, we should go further than Tuffrey-Wijne & Hollins' requirement for Care Quality Commission inspections in England and Wales to oversee patient-specific recording of reasonable adjustments. We also need to be confident that such adjustments are being delivered, and for evidence to be provided of adequate arrangements being in place.

Patient experience – Turner & Robinson note that it is difficult for people with intellectual disabilities and their families to influence policy and practice in healthcare systems if they are not visible within them and if involvement mechanisms such as surveys and focus groups are not accessible to them.⁶ Both the Death by Indifference⁷ and CIPOLD reports highlighted the lack of attention paid to the views of patients and their families, preventing them from becoming active partners in their care; the CIPOLD report additionally noted the devastating impact on future care that a poor experience of healthcare can have for some people with intellectual disabilities. The provision of reasonable adjustments needs to extend to the ways in which we garner the views of people with intellectual disabilities, communicate with them, and place them at the centre of their care.

The CIPOLD report made 18 recommendations, which included (a) clear identification of people with intellectual disabilities on the NHS central registration system and in all health care records, and (b) reasonable adjustments required by, and provided to, individuals, to be audited annually and examples of best practice shared across agencies and organisations.³

It is now 4 years since the Equalities Act 2010 came into force. Our adherence to the Act must be sharpened in the light of the health inequalities faced by people with protected characteristics, including those with intellectual disabilities, so clearly demonstrated in successive reports. We all have a responsibility, and we all have a role to play, in ensuring equal outcomes for

vulnerable people through the provision of reasonable adjustments, but strong leadership is central to making it happen.

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- 5 Tuffrey-Wijne I, Goulding L, Giatras N, Abraham E, Gillard S, White S, et al. The barriers to and enablers of providing reasonably adjusted health services to people with intellectual disabilities in acute hospitals: evidence from a mixed-methods study. *BMJ Open* 2014; **4**: e004606.
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Authors' reply: We welcome the detailed response from Heslop *et al* giving more evidence in support of our recommendation for the effective use of reasonable adjustments during in-patient care. They also draw attention to the need for these to be properly audited by staff who understand the Equality Act 2010, which in our view would require an extensive educational programme, as there is no evidence that current audits are much more than a box-ticking exercise.

They repeat an earlier and often made recommendation that people with intellectual disabilities should be identified on a national NHS database. NHS England has already decided to set up a national learning-disability mortality review function, which will require a national database. Regrettably, this cannot commence until data linkages have been enabled by the NHS and the Health and Social Care Information Centre and it seems unlikely that this will be achieved until next summer.¹ Strong advocacy is needed to ensure there are no further delays in giving priority to this work.

- 1 Hansard. HL Deb 30 July 2014 vol 755 col 1583.

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Corrections

Aripiprazole once-monthly for treatment of schizophrenia: double-blind, randomised, non-inferiority study. *BJPsych*, 205, 135–144. Figure 3(a), p. 141: x-axis label should be 'Days from randomisation'. The online version of this paper has been corrected post-publication, in deviation from print and in accordance with this correction.

Cost-effectiveness of injectable opioid treatment *v.* oral methadone for chronic heroin addiction. *BJPsych*, 203, 341–349. In the abstract,

the second sentence of the Results should read: 'Costs overall were highest for oral methadone (mean £15 805 *v.* £13 410 injectable heroin and £10 945 injectable methadone; *P*=n.s.) due to higher costs of criminal activity'. These data were reported correctly in the body of the paper (Table 2, p. 344). The online version of this paper has been corrected post-publication, in deviation from print and in accordance with this correction.

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