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Author's reply to: Difficulties of diagnosing and managing dementia in people with Down syndrome

We thank Drs Smith and Chicoine for their interest in our work and highlighting some of the practical issues in diagnosing and managing dementia in this group. The association between trisomy 21 and early-onset Alzheimer's disease is well established[1] and dementia is now the most common cause of death in adults with Down syndrome. Despite this, there exists relatively little evidence on which to base treatment decisions.

Using a naturalistic study design, we report the effects of antidementia medication on the survival and function of 310 people with Down syndrome and dementia. Notwithstanding the limitations typical of observational studies (discussed in the paper), this work addresses a significant gap in the literature. Kaplan–Meier survival curves demonstrate significantly increased survival in the group prescribed antidementia medication. Baseline differences between those prescribed and not prescribed antidementia medication were accounted for, where possible, in a Cox regression model. This adjusted analysis showed that protection in the treated group remained, although it did not reach statistical significance because of less power and broader confidence intervals.

Functional impairment was measured using the Dementia in Learning Disabilities scale,[2] a standardised informant questionnaire that covers several skill domains. These data show an early protective effect of medication in mitigating cognitive decline, as is observed in individuals with Alzheimer's disease without Down syndrome.[3] We appreciate the concern of Drs Smith and Chicoine for quality of life. Unfortunately, there are no well-validated measures of quality of life for this group and proxy measures have been subject to limitations in people with intellectual disability. Development of such measures and their use in research studies and routine clinical care would be welcome and could focus efforts on providing optimal holistic support.

The Cochrane reviews that Drs Smith and Chicoine cite highlight the lack of evidence in this field, rather than negative results of drug intervention studies. Two of these Cochrane reviews did not include any studies at all, and the third included only one, small randomised controlled trial. The authors of these reviews, now some years old, highlight the paucity of evidence and conclude that the reviews cannot be used to guide practice.

Our cohort was recruited from specialist memory clinics for people with intellectual disability. Clinician diagnosis of dementia in such clinics is valid and reliable[4] and we are confident that clinicians will have adequately assessed potentially reversible causes of decline. It is important not to overlook dementia as an early diagnosis can facilitate prompt pharmacological and psychosocial treatments and effective care planning.[5] When dementia is diagnosed, a decision to use medication is, of course, an individual one, and should take account of the views of families and carers. Our paper provides additional evidence that could inform the decision-making process. People with Down syndrome and dementia should not be denied access to antidementia drugs.

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An alternative perspective on Cooper *et al*'s finding of a high incidence of mania in individuals with intellectual disabilities

Cooper *et al* (2018) note that despite high use of mood stabilisers (22.4%), the 2-year incidence of mania in individuals with intellectual disabilities is 1.1%.[1] This is higher than in the general population. They infer that clinicians need to consider mania in their differential diagnosis, highlighting the risk of misdiagnosis. The authors specifically note the similarity of symptoms across diagnostic categories, including those for mania, attention-deficit hyperactivity disorder (ADHD) and problem behaviours.

This raises an interesting point of symptom overlap between ADHD and bipolar disorder, which, as the authors suggest, can lead to diagnostic overshadowing. However, it is possible that this overlap could result in clinicians primarily diagnosing bipolar disorder, with ADHD remaining undiagnosed. This alternative perspective could offer an explanation for the high incidence of mania in the context of high mood stabiliser use.

In Cooper *et al*'s (2007) original study, it is of interest that there were no individuals with ADHD identified within the cohort of mild intellectual disability.[2] Although the authors acknowledged they might not have fully identified this group, the finding is noteworthy given the average prevalence in the general population is 3.4% (range 1.2–7.3%).[3] This baseline comparative data used in Cooper *et al*'s (2018) report underlines their comments pertaining to the diagnostic challenge of mental illness in the population with intellectual disabilities.[1]

Overall, Cooper *et al*'s recent paper highlights a need for clinicians to be more aware of symptom overlap in the area of

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intellectual disabilities, particularly between ADHD and mania.[1] By raising awareness, the apparent undercurrent of diagnostic overshadowing may be better managed.

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Author's reply

We thank our colleagues for their interest in our paper, and agree with them of the importance of careful diagnosis. We disagree though that primarily diagnosing bipolar disorder and underdiagnosing ADHD accounts for the high incidence of mania in the context of high mood stabiliser use. Our study was an incidence study with adults; therefore, by definition, all those who experienced onset of mania within the 2-year period did not have mania at the first time point, and all those who experienced onset of a bipolar depressive episode in the 2-year period had previously had a manic episode that had resolved. Despite some similarities in symptoms between mania and ADHD, there are also key differences: bipolar disorder is a cyclical disorder (hence, with onset of episodes and remission from them) whereas ADHD is not; and ADHD has onset in early childhood so could not account for the onset of new manic psychopathology in these adult participants. The 15 of 651 participants with ADHD had this consistently across the 2-year period. The psychiatric assessments we conducted for the purpose of our study were detailed and included an instrument to detect hyperkinetic disorders, developmental histories, were undertaken by two consultant learning disabilities psychiatrists and all were case-conferenced to apply the four sets of diagnostic criteria. We restate our evidenced-view that the incidence of mania is higher in adults with intellectual disabilities than in the general population, despite the high use of mood stabilisers.

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