# Letters

COMMENT & RESPONSE

## Child vs Adult Onset of Attention-Deficit/Hyperactivity Disorder

**To the Editor** Two longitudinal studies of epidemiological cohorts published in *JAMA Psychiatry*—one conducted in Brazil[1] and the other in the United Kingdom[2]—have found evidence for adult-onset attention-deficit/hyperactivity disorder (ADHD) in substantial proportions of adults with ADHD. These studies, plus an earlier one from New Zealand,[3] challenge the longstanding conceptualization of ADHD as a disorder necessarily beginning in childhood. The strengths of these studies include large sample sizes and longitudinal prospective birth cohort designs. Thus, the childhood diagnostic data were collected in childhood and not dependent on retrospective (and possibly biased) reports.

Nevertheless, I submit that these unexpected results may reflect the method used to diagnose the disorder in children. Specifically, the *DSM-III* ADHD diagnostic criteria in use at the time of initiation of the New Zealand study did not allow for diagnosis of the inattentive subtype or presentation of ADHD, which comprises 45%[4] of all children with ADHD. Children with the inattentive subtype would similarly not have been recognized in the Brazil study,[1] which used the 5-item hyperactivity subscale of the Strengths and Difficulties Questionnaire to screen the participants. Exclusion of predominantly inattentive cases would result in a significantly reduced occurrence of childhood ADHD among the adults with ADHD. Children in the UK study[2] were diagnosed as having the disorder on the basis of the full *DSM-IV* criteria for ADHD, which recognized the subtypes, which may explain why it reports a much higher percentage of adults with ADHD having onset in childhood (32.5%) than did the New Zealand study (10%) or the Brazil study (12.6%).

I see 100 adults per year for evaluation and/or treatment of ADHD, most of whom have clear onset of symptoms in childhood, with an additional number reporting onset in adolescence. Thus, I believe it would be premature to implement a diagnosis of an "adult-onset ADHD" without understanding more fully why clinical samples differ from the epidemiological samples reported in these studies.

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1. Caye A, Rocha TB, Anselmi L, et al. Attention-deficit/hyperactivity disorder trajectories from childhood to young adulthood: evidence from a birth cohort supporting a late-onset syndrome. *JAMA Psychiatry*. 2016;73(7):705-712.

2. Agnew-Blais JC, Polanczyk GV, Danese A, Wertz J, Moffitt TE, Arseneault L. Evaluation of the persistence, remission, and emergence of attention-deficit/hyperactivity disorder in young adulthood. *JAMA Psychiatry*. 2016;73(7):713-720.

3. Moffitt TE, Houts R, Asherson P, et al. Is adult ADHD a childhood-onset neurodevelopmental disorder? evidence from a four-decade longitudinal cohort study. *Am J Psychiatry*. 2015;172(10):967-977.

4. Willcutt EG. The prevalence of *DSM-IV* attention-deficit/hyperactivity disorder: a meta-analytic review. *Neurotherapeutics*. 2012;9(3):490-499.

**In Reply** We thank Solanto for her interest in our article[1] and for providing some thoughtful ideas on how to understand these intriguing similar findings from 3 population samples that challenge the notion of attention-deficit/hyperactivity disorder (ADHD) as only a child-onset neurodevelopmental disorder.[2,3] Solanto suggests that our study[1] might have missed a substantial proportion of cases of ADHD predominantly inattentive type (ADHD-PI) in childhood, consequently decreasing the rate of adult ADHD with roots in childhood. She based this hypothesis on the idea that we had collected data on ADHD symptoms in childhood before *DSM-IV* criteria.

In fact, the 1993 Pelotas Birth Cohort collected data on childhood ADHD in 2004, a decade after *DSM-IV* was launched. However, as mentioned in the article,[2] we assessed childhood ADHD with a screening instrument that emphasizes hyperactive-impulsive symptoms. Considering the potential lower performance of the instrument for ADHD-PI subtype, Solanto's hypothesis makes sense and warrants proper testing.

In 2004, a subsample of 288 participants at age 11 years was also assessed with the Development and Well-Being Assessment, a semistructured interview that generates *DSM-IV* diagnoses, including ADHD-PI. In this subsample, 24% of the ADHD cases were of ADHD-PI, 40% of which were not detected by the screening instrument. Therefore, we can conclude that 10% (40% of 24%) of the childhood ADHD cases were not included in the childhood ADHD group. Extrapolating for the entire sample at 11 years of age, the scenario suggests that the 393 cases in childhood represent 90% of the real ADHD cases and the ADHD-PI cases that were not diagnosed by the instrument would add 44 new cases. It is important to note that this mathematical reasoning addresses only the issue related to ADHD-PI. It does not take into account the performance of the screening for other subtypes of ADHD.

Although the ADHD combined type seems to be the most persistent subtype,[4] let us assume conservatively that all these ADHD-PI cases in childhood would continue to present ADHD in young adulthood. This assumption would increase the proportion of young adults with ADHD with childhood history of ADHD symptoms from 13% (reported in the article) to 21%. Thus, we cannot throw the baby out with the bath water. We were also surprised with our findings and explored our data from diverse angles to assess potential flaws. Others did the same.[5] The main message continues to be that most young



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adults with the ADHD phenotype do not have a childhood history of significant ADHD symptoms.

Finally, we are in complete agreement with Solanto's proposal that the translation of data from population-based to clinical studies is challenging and that more studies are needed to understand the reasons for this surprising rate of adult-onset ADHD cases in population samples. Indeed, a group of researchers interested in this controversial issue has begun to work on numerous data-driven hypotheses.[6]

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**In Reply** Solanto asks whether the exclusion of inattentive symptoms in childhood—based on *DSM* criteria at the time of study inception—resulted in a reduced occurrence of childhood attention-deficit/hyperactivity disorder (ADHD) among adults with ADHD in 2 recent longitudinal epidemiological cohort studies from Brazil[1] and New Zealand,[2] possibly artificially inflating rates of the newly observed group of late-onset ADHD.

Our study,[3] using data from a contemporary longitudinal cohort in the United Kingdom, also reports a high rate of late-onset ADHD among the population of adults with ADHD (68%). However, we did not identify an excess of inattentive vs hyperactive/impulsive symptoms in childhood among individuals with late-onset ADHD: Table 1 of our article[3] indicates that late-onset individuals had an average of 1.7 inattentive symptoms in childhood compared with 2.4 hyperactive/impulsive symptoms. Additionally, eFigure 1 in the Supplement to our article[3] illustrates that the distribution of inattentive symptoms was very similar to that of hyperactive/impulsive symptoms at age 12 years among the late-onset ADHD group. This distribution is similar to that of participants who never met diagnostic criteria for ADHD (than to those with persistent or remitted ADHD). This suggests that in childhood, inattentive symptoms do not appear to be overrepresented among those with late-onset ADHD at age 18 years.

The question remains whether Dunedin Study cohort members who were diagnosed as having ADHD in their 30s, but never diagnosed as having it as children, might have had inattentive subtype when young. Could their condition have gone undiagnosed in childhood because the then-current *DSM* lacked an inattentive subtype? This possibility is intriguing but unlikely to explain adult-onset cases in the Dunedin Study. There are 3 lines of evidence. First, Dunedin Study adult-onset ADHD cases performed normally on all childhood neuropsychological tests and therefore had no evidence of attentional deficits that typify childhood ADHD.[2] Incidentally, the adult-onset cases also performed normally on adult attention tests, including a continuous-performance test of attentional vigilance and the Wechsler Working Memory index. Second, the adult-onset cases did not meet diagnostic criteria in childhood according to *DSM-III*, which, in addition to impulsivity/hyperactivity criteria, required the child meet at least 3 of 5 inattention criteria. Figure 3 of the article[2] showed adult-onset ADHD cases lacked symptoms in childhood. In addition to the diagnosis of "ADD with Hyperactivity" (314.01), *DSM-III* included a diagnosis of "ADD without Hyperactivity" (314.00), which the study made if criteria were met. Third, in the 1980s, the Dunedin Study was among the first to report a syndrome of inattention separable from hyperactivity in a series of articles that helped push *DSM-IV* to include the inattentive subtype.[4,5] Thus, the cohort included children who had a primary inattentive presentation, but these were not the same individuals who emerged with adult-onset ADHD.

Solanto calls for caution with implementing a new "adult-onset ADHD" diagnosis. We agree and also believe that more research is needed to better understand the heterogeneity in the population of young adults with ADHD identified in these recent population-based longitudinal studies. We need further research not only to clarify the differences between



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clinical and epidemiological samples, but also to elucidate the causes, course, and optimal treatment of late-onset ADHD.

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**3**. Agnew-Blais JC, Polanczyk GV, Danese A, Wertz J, Moffitt TE, Arseneault L. Evaluation of the persistence, remission, and emergence of attention-deficit/hyperactivity disorder in young adulthood. *JAMA Psychiatry*. 2016;73(7):713-720.

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## Increasing the Use of Lithium and Clozapine in US Suicide Prevention

**To the Editor** The rising US suicide rate since 1999 is a significant public health issue, being the tenth leading cause of death overall. In *JAMA Psychiatry*, Hogan[1] highlighted that much can be done to reduce the US suicide rate but did not mention the potential role of lithium and clozapine for directly treating suicidality. The importance of these biologic interventions is often underestimated in suicide prevention strategies.[2]

Lithium is recognized as a highly effective acute and maintenance treatment for bipolar disorder. The rate of suicide in this population is 10 times higher than in the nonpsychiatric population.[2] A recent systematic review confirmed lithium's role in the prevention of suicide for mood disorders.[2] Lithium was associated with a reduced risk of suicide (odds ratio, 0.13; 95% CI, 0.03-0.66) when compared with placebo for mood disorders (unipolar and bipolar disorders).

However, lithium use is in marked decline in the United States owing to the aggressive marketing of patentable medications for bipolar disorder that have no antisuicidal properties.[3] The lithium prescription rates in the United States are markedly lower than that of England.[3]

The lifetime rates of suicide for patients with schizophrenia is up to 10%.[4] Clozapine is the gold-standard medication for treatment-resistant schizophrenia and is also approved by the US Food and Drug Administration as an antisuicide treatment. This is based on the outcomes of a 2-year randomized prospective study comparing the risk for suicidal behavior in 980 patients with schizophrenia or schizoaffective disorder, all with high risk of suicide, when treated with either clozapine or olanzapine.[4] Clozapine-treated patients in this trial had significantly reduced suicide attempts, fewer hospitalizations, and required less coadministration of antidepressants compared with the olanzapine-treated group.

The US clozapine prescription rates for schizophrenia is less than 5%.[5] This prescription rate is well below other developed countries, with the recommended rate being at least 20% based on overall treatment-resistant schizophrenia rates of 30%.[5]

The US National Institutes of Health, Centers for Disease Control and Prevention, and psychiatrists should specifically recommend, monitor, and aim to increase the currently low US prescription rates of lithium (particularly for bipolar disorder) and clozapine. Improved educational efforts, financial incentives, and policies to increase lithium and clozapine use[5] may also be required. Increased use of lithium and clozapine has the potential to reduce the high and rising US suicide rate, especially when combined with other evidence-based public health and psychosocial interventions.

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**In Reply** In response to a Viewpoint urging action to improve suicide prevention in health care settings,[1] Bastiampillai et al emphasize the effectiveness of lithium (for patients with bipolar disorder) and clozapine (for patients with schizophrenia) in reducing suicide. They note the low prescription rates of both medications in the United States and urge efforts to increase use of these effective treatments as a key suicide prevention strategy.



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