Published in final edited form as:

JAMA Psychiatry. 2016 July 01; 73(7): 713–720. doi:10.1001/jamapsychiatry.2016.0465.

Persistence, Remission and Emergence of ADHD in Young Adulthood: Results from a Longitudinal, Prospective Population-Based Cohort

Jessica C Agnew-Blais, ScD[1], **Guilherme Polanczyk, MD, PhD**[2], **Andrea Danese, MD, PhD**[1,3,4], **Jasmin Wertz, MSc**[1], **Terrie E. Moffitt, PhD**[1,5,6], and **Louise Arseneault, PhD**[1]

[1]MRC Social Genetic and Developmental Psychiatry, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK

[2]Department of Psychiatry, University of São Paulo Medical School, São Paulo, Brazil; and the Department of Psychiatry, Federal University of Rio Grande do Sul, Porto Allegre, Brazil

[3]Department of Child and Adolescent Psychiatry, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK

[4]National and Specialist Child Traumatic Stress and Anxiety Clinic, South London and Maudsley NHS Foundation Trust, London, UK

[5]Department of Psychology and Neuroscience, Duke University, Durham, NC, USA

[6]Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, NC, USA

Abstract

Importance—ADHD is now recognized to occur in adulthood and is associated with a range of negative outcomes. However, less is known about the prospective course of ADHD into adulthood, the risk factors for its persistence past childhood, and the possibility of its emergence in young adulthood in non-clinical populations.

Objective—To investigate childhood risk factors and young adult functioning of individuals with persistent, remitted and late-onset ADHD.

Design, Setting and Participants—The study sample is the Environmental Risk (E-Risk) Longitudinal Twin Study, a UK nationally-representative birth cohort of 2,232 twins born in England and Wales in 1994–1995.

Main Outcome Measures—ADHD diagnoses were assessed in childhood at ages 5, 7, 10, and 12 and in young adulthood at age 18. Childhood predictors included pre/perinatal factors, child clinical characteristics and aspects of the family environment. Age-18 outcomes included ADHD symptoms and associated impairment, overall functioning and other mental health disorders.

Correspondence concerning this article should be addressed to Louise Arseneault, Institute of Psychiatry, Psychology & Neuroscience, SGDP Centre, London, SE5 8AF, UK. louise.arseneault@kcl.ac.uk.

Results—Among individuals with childhood ADHD (n=247), 21.1% met diagnostic criteria for the disorder at age 18. Persistence was associated with higher levels of symptoms and lower IQ in childhood. Persistent individuals had more functional impairment and higher rates of other mental health disorders at age 18 compared to those who remitted. Among individuals with adult ADHD (n=162), 67.9% did not meet criteria for ADHD at any assessment at or prior to age 12. In childhood, individuals with late-onset ADHD showed fewer behavior problems and higher IQ compared to the persistent group; at age 18, they showed comparable ADHD symptoms and impairment and similarly elevated rates of mental health disorders compared to the persistent group.

Conclusion and Relevance—In this general population cohort, the persistence of ADHD was largely driven by childhood ADHD severity and poorer neuropsychological functioning. Additionally, we identified heterogeneity in the adult ADHD population such that this group consisted of a large late-onset ADHD group with no childhood diagnosis and minimal neuropsychological impairment, and a smaller group with persistent ADHD and associated neuropsychological impairment. Our findings call into question the conceptualization of adult ADHD as a childhood-onset neurodevelopmental disorder.

Introduction

Attention deficit hyperactivity disorder (ADHD) is increasingly recognized to occur in adulthood,[1–3] and has been associated with several negative outcomes, including depression and substance abuse,[1] lower educational attainment,[4] unemployment,[1,5] and excess mortality.[6] To date, adult ADHD has been conceptualized as a continuation of childhood ADHD. However, recent findings have suggested that for some, ADHD may not arise until adolescence or adulthood and may be associated with different risk factors and outcomes than childhood ADHD.[7] In the current study, we take a prospective, developmental approach to clarifying the origins and correlates of adult ADHD in a UK general population cohort.

While ADHD was originally described as childhood-limited,[8,9] prospective follow-up studies of clinic-referred children with ADHD indicate that approximately 15% will continue to meet diagnostic criteria, and 65% will continue to have impairing ADHD symptoms as young adults.[10] These studies have identified childhood risk factors associated with a more persistent course, including higher levels of symptoms, comorbid oppositional-defiant disorder (ODD), lower IQ, and family socioeconomic disadvantage.[11–15] However, the vast majority of follow-up studies of children with ADHD have been conducted with clinical samples, which may not represent the overall ADHD population.[16] Additionally, individuals who do not meet diagnostic criteria in childhood are generally not included in studies following children with ADHD, resulting in a limited understanding of the potential emergence of the disorder in later life.

Our investigation aims to characterize adult ADHD by examining the persistence of the disorder from childhood to age 18, and its possible emergence in young adulthood. First, we examined childhood predictors of persistent ADHD, including pre/perinatal, clinical, and family environmental factors. Second, we assessed whether some individuals who did not have an ADHD diagnosis in childhood developed the disorder by age 18, and described

childhood risk factors among these individuals. Third, we investigated the functioning of persistent and late-onset ADHD groups at age 18 to understand how these groups differ or resemble one another in young adulthood.

Methods

Study cohort

Participants were members of the Environmental Risk (E-Risk) Longitudinal Twin Study, which tracks the development of a birth cohort of 2,232 British children. The sample was drawn from a larger birth register of twins born in England and Wales in 1994–95.[17] Full details about the sample are reported elsewhere.[18] The E-Risk sample was constructed in 1999–2000, when 1,116 families (93% of those eligible) with same-sex 5-year-old twins participated in home-visit assessments. This sample comprised 55% monozygotic and 45% dizygotic twin pairs; sex was evenly distributed within zygosity (49% male). Families were recruited to represent the UK population with newborns in the 1990s, on the basis of residential location throughout England and Wales and mother's age. Teenaged mothers with twins were over-selected to replace high-risk families who were selectively lost to the register through non-response. Older mothers having twins via assisted reproduction were under-selected to avoid an excess of well-educated older mothers. At follow up, the study sample represented the full range of socioeconomic conditions in the UK.[19]

Follow-up home visits were conducted when the children were aged 7 (98% participation), 10 (96%), 12 (96%), and 18 years (93%). With parents' permission, questionnaires were mailed to the children's teachers, who returned questionnaires for 94% of children at age 5, 93% of those followed up at age 7, 90.1% at age 10, and 83% at age 12. A total of 2,066 participants took part in assessments at age 18. There were no differences between those who did and did not take part at age 18 in socioeconomic status when the cohort was initially defined, or age 5 IQ, internalizing or externalizing problems.[20] Home visits at ages 5, 7, 10, and 12 years included assessments with participants and their mother; home visit at age 18 included interviews only with participants. Each twin was assessed by a different interviewer, and was asked to identify individuals to act as co-informants; 99.3% of participants at age 18 had complete co-informant data. The Joint South London and Maudsley and the Institute of Psychiatry Research Ethics Committee approved each phase of the study. Parents gave informed consent and twins gave assent between 5–12 years and then informed consent at age 18.

Childhood ADHD diagnosis

We ascertained ADHD diagnosis on the basis of mother and teacher reports of 18 symptoms of inattention and hyperactivity-impulsivity according to DSM-IV criteria.[21–23] Participants had to have six or more symptoms reported by mothers or teachers in the past 6 months, and the other informant must have endorsed at least two symptoms. For the current study, we considered participants to have a diagnosis of childhood ADHD if they met criteria at age 5, 7, 10 or 12. Participants who had ADHD information on at least two of the four childhood assessments and did not to meet diagnostic criteria at any available assessments were classified as not having the disorder in childhood. Two children whose symptoms fell below

threshold for diagnosis but were taking ADHD medication were included in the ADHD group. In total, 247 participants (12.1%) met criteria for ADHD in childhood. A previous study in this cohort identified a heritability of ADHD symptoms at age 5 of 74%.[23]

Adult ADHD diagnosis

We ascertained ADHD diagnosis at age 18 based on private structured interviews with participants regarding 18 symptoms of inattention and hyperactivity-impulsivity according to DSM-5 criteria.[7] Symptoms were reported for the preceding 12 months. Consistent with DSM-5 criteria for ADHD in adulthood, participants had to endorse five or more inattentive and/or five or more hyperactivity–impulsivity symptoms to be diagnosed. We also required that symptoms interfered with individual's "life at home, or with family and friends" and "life at school or work" as rated 3 or higher on a scale from "1=mild interference" to "5=severe", thereby meeting criteria for impairment and pervasiveness. The DSM-5 requirement of symptom onset prior to age 12 was met if parents or teachers reported 2 or more ADHD symptoms at ages 5, 7, 10 or 12. Of the 2,066 participants interviewed at age 18, 2,061 had information on adult ADHD. Analyses were restricted to 2,040 individuals with information on ADHD in childhood and adulthood. Of these, 153 participants met criteria for adult ADHD based on symptoms and impairment. At age 18, 13 individuals were taking ADHD medication, of whom 9 did not otherwise meet criteria, but were included in the adult ADHD group for a total of 162 (7.9%) participants with ADHD at age 18. We fitted an ACE model and identified a heritability estimate of ADHD symptoms of 35% (95% CI: 25–41%).

Persistent, remitted, and late-onset ADHD groups

Among individuals who met diagnostic criteria for ADHD in childhood or adulthood, we identified three mutually exclusive groups (Figure 1): individuals with persistent ADHD who met diagnostic criteria both in childhood and at age 18 (n=52, 2.5% of the total sample); individuals with remitted ADHD who met diagnostic criteria in childhood but not at age 18 (n=195, 9.6%); and individuals with late-onset ADHD who did not meet diagnostic criteria in childhood but did at age 18 (n=110, 5.4%). A total of 1,683 (82.5%) participants did not meet criteria for ADHD in childhood or adulthood.

Statistical analyses

First, we compared ADHD groups on pre/perinatal, childhood clinical and family factors; we compared individuals with childhood and adult ADHD, in turn, to the reference group who never met criteria, using logistic regressions. To understand childhood predictors of ADHD persistence to age 18, we compared individuals who persisted to those who remitted by age 18. Second, to characterize childhood features of the late-onset group, we compared persistent individuals to those with late-onset ADHD. Third, we examined functional outcomes at age 18 among these groups. To understand the impact of remission, we compared the persistent and remitted groups on age-18 correlates. We also compared persistent and late-onset groups on these factors to understand whether the presence of ADHD in childhood influenced age-18 functioning. Table 1 lists the measures used to describe childhood risk factors and age-18 correlates of ADHD. Analyses were corrected for

the non-independence of twin observations with tests using the sandwich variance estimator in Stata version 11.[24]

Results

Predictors of childhood and adult ADHD

Participants who met diagnostic criteria for ADHD in childhood and those who met diagnostic criteria for ADHD in adulthood both differed from controls on pre/perinatal factors, clinical features and family environment (Table 2). As these two ADHD groups were not mutually exclusive, similar correlates are unsurprising. However, the gender distribution differed between ADHD groups: males were overrepresented in the childhood ADHD group, while the gender ratio was nearly equal in the adult ADHD group.

Childhood characteristics of persistent versus remitted ADHD

Among individuals who met diagnostic criteria for ADHD in childhood, 21.1% still had the disorder by age 18. Few childhood characteristics distinguished individuals with persistent and remitted ADHD (Table 2): persistent individuals had more symptoms across childhood and lower performance IQ compared to those who remitted. Overall, characteristics of the family environment did not distinguish individuals who persisted from those who remitted, except that families of persistent individuals had comparatively higher maternal warmth and less maternal depression.

Childhood characteristics of late-onset versus persistent ADHD

Among individuals with adult ADHD, 67.9% had late-onset ADHD. Comparing mutually exclusive groups of individuals with persistent and late-onset ADHD, late-onset individuals were less likely to be male and, controlling for gender, had fewer childhood behavioral problems and less cognitive impairment than persistent individuals (Table 2). Pre/perinatal factors and characteristics of the family environment did not differ between these groups.

Young adult functioning of persistent versus remitted ADHD

At age 18, co-informants rated individuals with persistent ADHD as having more symptoms compared to remitted individuals, and interviewers rated them as less conscientious, diligent and persevering than remitted peers (Table 3). While persistent individuals had lower IQ and life satisfaction than remitted individuals, these differences were marginally significant. Persistent individuals had elevated rates of generalized anxiety disorder, conduct disorder and marijuana dependence compared those who remitted. However, compared to controls, individuals with remitted ADHD had more self-rated ADHD symptoms and impairment at home and with friends, more ADHD symptoms as rated by co-informant, lower life satisfaction and job preparedness, and higher rates of major depression and conduct disorder.

Young adult functioning of late-onset versus persistent ADHD

Individuals with late-onset ADHD differed from the persistent group on few variables at age 18 (Table 3). Co-informants rated symptoms as lower for the late-onset than the persistent group, and interviewers rated them as more conscientious, diligent and persevering. Age-18

IQ was higher in the late-onset than the persistent group. However, persistent and late-onset ADHD groups were similar on levels of ADHD symptoms and functional impairment, life satisfaction, job preparedness, and rates of being in formal education. Late-onset and persistent ADHD individuals were also similar on age-18 psychiatric comorbidity: both had elevated rates of generalized anxiety disorder, conduct disorder, and marijuana dependence. Late-onset individuals had significantly elevated alcohol dependence compared to those who persisted.

Discussion

Our study was uniquely suited to investigate the persistence and emergence of adult ADHD, given its prospective follow-up of a general population sample of children with and without ADHD from early childhood to young adulthood. We found that ADHD persistence was largely driven by severity of the childhood disorder and associated neuropsychological impairment. Additionally, our results suggest that adult ADHD is more complex than a straightforward continuation of the childhood disorder, with 70% of individuals with adult ADHD never having a diagnosis in childhood.

Persistence driven by childhood ADHD severity

While we examined a wide range of risk factors, we found persistence to be predominantly accounted for by severity of childhood ADHD symptoms. That childhood ADHD severity was related to persistence is consistent with several,[11,25] but not all,[12,26] prospective studies in clinical samples. We also found that lower IQ, especially performance IQ, was associated with persistence. However, after adjusting for number of childhood ADHD symptoms, IQ was no longer significant, suggesting that its effect on persistence may be due to the co-occurrence of lower IQ with more ADHD symptoms. While most pre-/perinatal and family environment factors were associated with the incidence of ADHD in childhood, overall they were not associated with its persistence into adulthood.

Most children with ADHD will remit by age 18 but impairment remains

The majority of individuals with ADHD in childhood no longer met criteria at age 18; however, while remitted individuals showed better functioning than those with persistent ADHD, they remained impaired. Relatively few childhood factors predicted remission. Recent findings point to a large genetic influence on the course of ADHD symptoms across development,[27] such that remission may be related to a genetic predisposition for more transient symptoms.

Additionally, it could be that concurrent lifestyle factors are more important for determining adult ADHD. Individuals with ADHD often do not exhibit symptoms when engaged in tasks they find rewarding.[28] As children with ADHD get older, they are given more opportunities to shape their lives and pursue interests they find engaging. In this way, young adults in milieus adapted to their ADHD at age 18 may be more likely to consider themselves in remission, independent of earlier life differences.

ADHD was more likely to remit among individuals whose mothers had depression and showed less warmth. Possibly some children exhibit symptoms in response to poor family

environments, but once these individuals move away from home, symptoms abate. Other aspects of the environment were not more compromised in the remitted group, suggesting that if this association is causative, it may be specific to pathways related to maternal-child bonding.

What is late-onset ADHD?

The high proportion of individuals with late-onset ADHD calls into question the conceptualization of the disorder as a neurodevelopmental condition originating in childhood. Recent studies suggest the possibility of ADHD emergence after childhood: findings from the Dunedin Study found that 90% of the individuals with adult ADHD at age 38 did not met diagnostic criteria for the disorder in childhood.[7] We found that already by age 18 late-onset individuals constitute a large proportion of adult ADHD. This is consistent with recent studies that identified individuals for whom ADHD symptoms increased in adolescence and adulthood.[27,29]

However, many questions remain as to the nature of late-onset ADHD and its relationship to ADHD as currently conceptualized. One explanation could be that these individuals have an underlying liability for ADHD, but that the disorder was not yet apparent in childhood. For some individuals, childhood symptoms may be compensated for by supportive family environments or highly developed cognitive skills. In such cases, symptoms may not become impairing until youths face the increased challenges of later, more intellectually demanding schooling.[28]

A second possibility is that late-onset individuals do not have ADHD at age 18, but rather a different disorder presenting with similar symptoms. We found that late-onset individuals exhibit elevated rates of anxiety, depression, marijuana dependence and alcohol dependence. To investigate whether the late-onset group is entirely accounted for by ADHD-like symptoms from other disorders, we excluded individuals with diagnoses of anxiety, depression, marijuana, and alcohol dependence. We found that the remaining 33.6% (n=37) of the late-onset group still presented with full ADHD criteria, indicating that these disorders do not entirely explain the presence of late-onset ADHD.

A third explanation is that late-onset ADHD is a distinct disorder. In childhood, the late-onset group shows important differences from the persistent group, including less neuropsychological impairment. We also found that the heritability of adult ADHD was lower than for childhood ADHD. Furthermore, late-onset ADHD was equally common among males and females, while childhood ADHD is more frequent in boys. As women and girls are understudied in ADHD research,[30] this gender-specific finding warrants further research. Given that the current conceptualization of ADHD is of a highly genetic neurodevelopmental disorder originating in childhood, the absence of these distinctive features in the late-onset group is suggestive of differing etiologies.

Limitations

First, our use of self-reports at age 18 is a limitation. However, adult self-reports have been found to be valid;[31] also our co-informants rated the persistent group as having more symptoms than the remitted group, corroborating self-reports. We also found childhood risk

factors for persistence were similar when age-18 symptoms were reported by co-informants (Appendix 1).

Second, it is both a limitation and a strength that our criteria for adult ADHD were restricted to those with at least two childhood symptoms. This could be viewed as a limitation, as the late-onset group, by definition, has young adult onset of the ADHD *syndrome* rather than *symptoms*. It is also a strength, as our adult ADHD group meets DSM-5 criteria, which stipulate symptom onset before age 12. Our requirement of at least 2 symptoms in childhood does not identify a group with subthreshold ADHD in childhood; exhibiting at least 2 symptoms in childhood was quite normative, as 80% of our study population falls into this category.

Third, the sample comprised twins, so results may not generalize to singletons. However, our rate of persistence of 21.1% is slightly higher than found in a meta-analysis;[10] given the young age of our cohort, this is not unexpected. Our prevalence of childhood ADHD of 12% was higher than the 3.4–11% estimated previously,[32,33] possibly because we are capturing more cases by assessing ADHD at four ages across childhood.

Conclusions and implications

Due to the prospective, longitudinal design of the E-Risk study, we were able to identify heterogeneity in the adult ADHD population. Our findings highlight the importance of taking a developmental approach to understanding ADHD. A significant proportion of those presenting clinically with ADHD symptoms in adulthood may not have met criteria for the disorder in childhood. While many questions remain as to the nature of late-onset ADHD, we found this group showed significant levels of ADHD symptoms and impairment, as well as poor functioning and high rates of psychiatric comorbidity. Therefore, the absence of a clear childhood diagnosis of ADHD should not preclude adults with ADHD from receiving clinical attention. Whether individuals with late-onset versus childhood-onset ADHD respond differently to treatment is an open question, and further research is required to better understand the etiology, course and optimal treatment of late-onset ADHD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The E-Risk Study is funded by the Medical Research Council (UKMRC grant G1002190). Additional support was provided by Economic and Social Research Council grant RES-177-25-0013, by the National Institute of Child Health and Human Development grant HD061298, and by the Jacobs Foundation. Jasmin Wertz is supported by the National Institute for Health Research Mental Health Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London, UK.

We are grateful to the study mothers and fathers, the twins, and the twins' teachers for their participation. Our thanks to Avshalom Caspi, Michael Rutter and Robert Plomin, to Thomas Achenbach for kind permission to adapt the Child Behavior Checklist, CACI, Inc., and to members of the E-Risk team for their dedication, hard work, and insights.

References

1. Kessler RC, Adler L, Barkley R, et al. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey. Am J Psychiatry. 2006; 163(4):716–723. [PubMed: 16585449]
2. Faraone SV, Biederman J, Spencer T, et al. Attention-deficit/hyperactivity disorder in adults: an overview. Biol Psychiatry. 2000; 48:9–20. [PubMed: 10913503]
3. Simon V, Czobor P, Balint S, Meszaros A, Bitter I. Prevalence and correlates of adult attention-deficit hyperactivity disorder: meta-analysis. Br J Psychiatry. 2009; 194(3):204–211. [PubMed: 19252145]
4. Faraone SV, Biederman J. What is the prevalence of adult ADHD? Results from a population screen of 966 adults. J Atten Disord. 2005; 9(2):384–391. [PubMed: 16371661]
5. De Zwann M, Grub B, Muller A, et al. The estimated prevalence and correlates of adult ADHD in a German community sample. Eur Arch Psychiatry Clin Neurosci. 2012; 262:79–86. [PubMed: 21499942]
6. Dalsgaard S, Dinesen Ostergaard S, Leckman J, Mortensen P, Glorts Pederson M. Mortality in children, adolescents, and adults with attention deficit hyperactivity disorder: a nationwide cohort study. Lancet. 2015; 385(9983):2190–2196. [PubMed: 25726514]
7. 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 Epub head of print.
8. Laufer MW, Dehoff E. Hyperkenetic behavior syndrome in children. J Pediatrics. 1957; 50(4):463–474.
9. Biederman J, Faraone SV. Attention-deficit hyperactivity disorder. Lancet. 2005; 366:237–248. [PubMed: 16023516]
10. Faraone S, Biederman J, Mick E. The age-dependent decline of attention deficit hyperactivity disorder: a meta-analysis of follow-up studies. Psychol Med. 2006; 36(2):159–165. [PubMed: 16420712]
11. Molina B, Hinshaw S, Swanson J, et al. The MTA Study at 8 years: prospective follow-up of children treated for combined type ADHD in a multisite study. J Am Acad Child Adolesc Psychiatry. 2009; 48(5):484–500. [PubMed: 19318991]
12. Biederman J, Petty C, Clarke A, Lomedico A, Faraone S. Predictors of persistent ADHD: an 11-year follow-up study. J Psychiatric Res. 2011; 45:150–155.
13. Barkley R, Fischer M, Smallish L, Fletcher K. The persistence of attention-deficit/hyperactivity disorder into young adulthood as a function of reporting source and definition of disorder. J Abnorm Psychol. 2002; 111(2):279–289. [PubMed: 12003449]
14. Kessler RC, Alder LA, Barkley R, et al. Patterns and predictors of attention-deficit/hyperactivity disorder persistence to adulthood: results from the National Comorbidity Survey Replication. Biol Psychiatry. 2005; 57:1442–1451. [PubMed: 15950019]
15. Cheung CHM, Rijsdijk F, McLoughlin G, et al. Cognitive and neurophysiological markers of ADHD persistence and remission. Br J Psychiatry. 2015; 62:92–100.
16. Holbrook J, Cuffe S, Cai B, et al. Persistence of parent-reported ADHD symptoms from childhood through adolescence in a community sample. J Atten Disord. 2014:1–10. Epub ahead of print.
17. Trouton A, Spinath F, Plomin R. Twins Early Development Study (TEDS): a multivariate, longitudinal genetic investigation of language, cognition and behavior problems in childhood. Twin Res. 2002; 5(5):444–448. [PubMed: 12537874]
18. Moffit T. E-Risk Study Team. Teen-aged mothers in contemporary Britain. J Child Adolesc Psychiatry. 2002; 43(6):727–742.
19. Odgers C, Caspi A, Russell M, Sampson R, Arseneault L, Moffit T. Supportive parenting mediates neighborhood socioeconomic disparities in children's antisocial behavior from ages 5 to 12. Devel Psychopathol. 2012; 24(3):705–721. [PubMed: 22781850]
20. Goldman-Mellor S, Caspi A, Arseneault L, et al. Committed to work but vulnerable: self-perceptions and mental health in NEET 18-year olds from a contemporary British cohort. J Child Psychol Psychiatry. 2015 EPub ahead of print.

21. Polanczyk G, Caspi A, Houts R, Kollins SH, Rohde LA, Moffitt TE. Implications of extending the ADHD age-of-onset criterion to age 12: results from a prospectively studied birth cohort. J Am Acad Child Adol Psychiatry. 2010; 49(3):210–216.
22. Caspi A, Langley K, Milne B, et al. A replicated molecular genetic basis for subtyping antisocial behavior in children with attention-deficit/hyperactivity disorder. JAMA Psychiatry. 2008; 65(2): 203–210.
23. Kuntsi J, Eley TC, Taylor A, et al. Co-occurrence of ADHD and low IQ has genetic origins. Am J Med Genet Part B (Neuropsychiatric Genetics). 2004; 124B:41–47.
24. *STATA* [computer program]. Version 11. College Station, TX: StataCorp LP; 2009.
25. Cheung C, Rijdijk F, McLoughlin G, Faraone S, Asherson P, Kunsi J. Childhood predictors of adolescent and young adult outcome in ADHD. J Psychiatric Res. 2015; 62:92–100.
26. Biederman J, Petty C, O'Connor K, Hyder L, Faraone S. Predictors of persistence of in girls with attention deficit hyperactivity disorder: results from an 11-year controlled follow-up study. Acta Psychiatr Scand. 2012; 125:147–156. [PubMed: 22097933]
27. Pingault J, Viding E, Galera C, et al. Genetic and environmental influences on the developmental course of attention-deficit/hyperactivity disorder symptoms from childhood to adolescence. JAMA Psychiatry. 2015 EPub.
28. Brown, T. A new understanding of ADHD in childhood and adults: Executive function impairments. New York and London: Routledge Taylor & Francis Group; 2013.
29. Klein RG, Mannuzza S, Ramos Olazagasti MA, et al. Clinical and functional outcome of childhood attention-deficit/hyperactivity disorder 33 years later. Arch Gen Psychiatry. 2012; 69(12):1295–1303. [PubMed: 23070149]
30. Hinshaw SP. Preadolescent girls with attention-deficit/hyperactivity disorder: I. Background characteristics, comorbidity, cognitive and social functioning, and parenting practices. J Consult Clin Psychol. 2002; 70(5):1086–1098. [PubMed: 12362959]
31. Kooij JJS, Boonstra AM, Swinkels SHN, Bekker EM, de Noord I, Buitelarr JK. Reliability, validity, and utility of instruments for self-report and informant report concerning symptoms of ADHD in adult patients. J Atten Disord. 2008; 11(4):445–458. [PubMed: 18083961]
32. Polanczyk GV, Salum GA, Sugaya LS, Caye A, Rohde LA. Annual research review: a meta-analysis of the worldwide prevalence of mental disorders in children and adolescents. J Child Psychol Psychiatry. 2015; 56(3):345–365. [PubMed: 25649325]
33. Centers for Disease Control and Prevention. Increasing prevalence of parent-reported attention-deficit/hyperactivity disorder among children -- United States, 2003 and 2007. MMWR Morbidity and Mortality Weekly Report. 2010; 59(44):1439–1443. [PubMed: 21063274]
34. Bucker JM, Green M. Birth weight and head circumference standards for English twins. Arch Dis Child. 1994; 71(6):516–521. [PubMed: 7726611]
35. Maughan B, Taylor A, Caspi A, Moffitt TE. Prenatal smoking and child antisocial behaviour: testing genetic and environmental confounds. Arch Gen Psychiatry. 2004; 61:836–843. [PubMed: 15289282]
36. Achenbach, TM. Manual for the Child Behavior Checklist/4–18 and 1991 Profile. Burlington: University of Vermont, Department of Psychiatry; 1991.
37. Achenbach, TM. Manual for teacher's report form and 1991 profile. Burlington: University of Vermont, Department of Psychiatry; 1991.
38. Wechsler, D. Wechsler preschool and primary scale of intelligence--revised. London, England: The Psychological Corporation; 1990.
39. Sattler, J. Assessment of Children: WISC-III and WPPSI-R Supplement. San Diego, CA: Jerome M Sattler, Publisher, Inc; 1992.
40. Gerstadt CL, Hong YJ, Diamond A. The relationship between cognition and action: performance of children 3.5–7 years old on a Stroop-like day-night test. Cognition. 1994; 53(2):129–153. [PubMed: 7805351]
41. Baddeley AD. Exploring the central executive. Q J Exp Psychol. 1996; 49A:5–28.
42. Baddeley, AD. Working Memory. Oxford, England: Oxford University Press; 1986.

43. Robins, L., Cottler, L., Bucholz, K., Compton, W. Diagnostic Interview Schedule for DSM-IV. St. Louis, MP: Washington University School of Medicine; 1995.
44. Achenbach, TM. Manual for the young adult self-report and young adult behavior checklist. Burlington, VT: University of Vermont, Department of Psychiatry; 1997.
45. Selzer ML, Vinokur A, van Rooijen L. A self-administered Short Michigan Alcoholism Screening Test (SMAST). J Stud Alcohol. 1975; 36(1):117–126. [PubMed: 238068]
46. Skinner HA. The drug abuse screening test. Addict Behav. 1982; 7(4):363–371. [PubMed: 7183189]
47. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4. Washington, D.C: American Psychiatric Association; 1994.
48. Trzesniewski KH, Moffitt TE, Caspi A, Taylor A, Maughan B. Revisiting the association between reading achievement and antisocial behavior: new evidence of an environmental explanation from a twin study. Child Devel. 2006; 77(1):72–88. [PubMed: 16460526]
49. Caspi A, Moffitt TE, Morgan J, et al. Maternal expressed emotion predicts children's antisocial behavior problems: using monozygotic-twin differences to identify environmental effects on behavioral development. Dev Psychol. 2004; 40(2):149–161. [PubMed: 14979757]
50. Straus, MA. The Conflict Tactics Scale and its critics: An evaluation and new data on validity and reliability. In: Straus, MA., Gelles, RJ., editors. Physical Violence in American Families: Risk factors and adaptations to violence in 8,145 families. New Brunswick, NJ: Transaction Publishing; 1990. p. 49-73.
51. Dodge K, Pettit G, Bates J, Valente E. Social information-processing patterns partially mediate the effect of early physical abuse on later conduct problems. J Abnorm Psychol. 1995; 104(4):632–643. [PubMed: 8530766]
52. Kim-Cohen J, Caspi A, Rutter M, Tomas MP, Moffitt TE. The caregiving environments provided to children by depressed mothers with or without an antisocial history. Am J Psychiatry. 2006; 163(6):1009–1018. [PubMed: 16741201]
53. Benet-Martinez V, John OP. Los cinco grandes across cultures and ethnic groups: multitrait multimethod analyses of the Big Five in Spanish and English. J Pers Soc Psychol. 1998; 75:729–750. [PubMed: 9781409]
54. Wechsler, D. Wechsler Adult Intelligence Scale--Fourth Edition. San Antonio, TX: Pearson; 20078
55. Diener E, Emmons RA, Larsen RJ, Griffin S. The satisfaction with life scale. J Pers Assess. 1985; 49:71–75. [PubMed: 16367493]
56. Secretary's Commission on Achieving Necessary Skills. What Work Requires of Schools. U.S. Department of Labor; 1991.
57. American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-5. Washington, D.C: American Psychiatric Association; 2013.

Appendix 1

Childhood pre- and perinatal, clinical and social environment characteristics and age-18 informant report of ADHD symptoms

	Total ADHD symptoms at age 18 among individuals with childhood ADHD (N=239)
Pre- and perinatal factors	**Standardized β**
Male gender, n (%)	0.15 *
Birth weight (gr), mean (SD)	0.13
Stress during pregnancy, n (%)	0.19 *

	Total ADHD symptoms at age 18 among individuals with childhood ADHD (N=239)
Pre- and perinatal factors	**Standardized β**
Smoking during pregnancy, n (%)	0.12
Child ADHD characteristics	
Age 5–12 childhood ADHD symptoms	
Total inattention symptoms, mean (SD)	0.36***
Total hyp/impul symptoms, mean (SD)	0.34***
Total symptoms, mean (SD)	0.41***
Age 5–12 comorbidity	
ODD, n (%)	0.13~
CD, n (%)	0.17*
Internalizing score, mean (SD)	0.12~
Externalizing, mean (SD)	0.27**
Age-5 cognitive measures	
IQ, mean (SD)	−0.13~
Performance IQ, mean (SD)	−0.14~
Verbal IQ, mean (SD)	−0.07
Executive functioning, mean (SD)	−0.07
Family environment	
Parental antisocial behavior, n (%)	−0.07
Parental substance use problems, n (%)	−0.05
Maternal depression, n (%)	−0.01
Low social class, n (%)	−0.01
Maternal warmth, mean (SD)	0.04
Maternal negativity, mean (SD)	0.07
Domestic violence exposure, n (%)	−0.10
Child maltreatment, n (%)	0.03

* p<0.05,
** p<0.01,
*** p<0.001,
~ p<0.10

At a Glance

- The purpose of this study was to investigate childhood risk factors and young adult functioning of individuals with persistent, remitted and late-onset ADHD.
- In a general population cohort with prospective follow-up, the rate of persistence of ADHD from childhood to age 18 was 21.1%.
- Persistence of ADHD was largely driven by severity of ADHD and associated poorer neuropsychological functioning in childhood.
- Of the population of individuals with ADHD at age 18, 67.9% did not meet criteria for ADHD in childhood; these late-onset ADHD individuals were as impaired as individuals with persistent ADHD at age 18.
- The large proportion of the adult ADHD population with no childhood ADHD diagnosis calls into question the conceptualization of adult ADHD as a childhood-onset neurodevelopmental disorder.

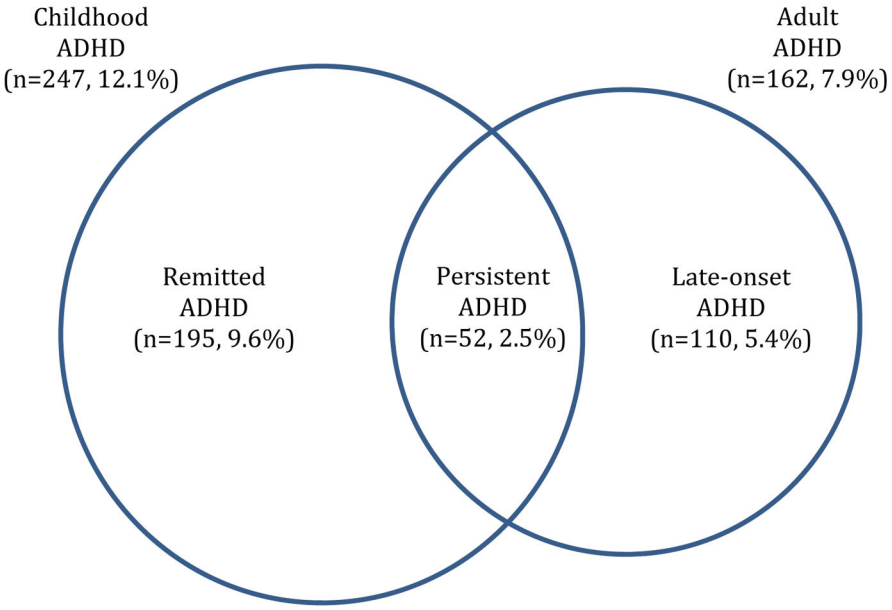

Figure 1.

Groups of individuals with childhood ADHD, adult ADHD, and subgroups of remitted, persistent and late-onset ADHD

Table 1

Description of the investigated risk factors and correlates of ADHD

Measure	Informant	Description of measure	Age, y	Reference
Pre- and perinatal factors				
Birth weight	Parents	Absolute values for weight were standardized with reference to birth weight in relation to gestational age of 1900 twins born in England from 1988 to 1992	Birth	34
Stress during pregnancy	Mother	Mothers' report of severe stress during pregnancy	Birth	
Smoking during pregnancy	Mother	Mothers' report of smoking at any time during pregnancy	Birth	35
Child clinical characteristics				
ODD diagnosis	Mother, teacher	DSM-IV symptoms of ODD were assessed using the Achenbach family of instruments including items: hot temper, argues, disobedient, annoying others on purpose, blames others, irritable, angry/hostile, spiteful	5, 12	36,37
CD diagnosis	Mother, teacher	Fourteen of 15 DSM-IV symptoms of CD were assessed using the Achenbach family of instruments and additional DSM-IV items covering aggressive and nonaggressive conduct problems, deceitfulness or theft, and rule violations	5, 7, 10, 12	36,37
Internalizing symptoms	Mother, teacher	CBCL/TRF Anxiety and Withdrawn subscales	5, 12	36,37
Externalizing symptoms	Mother, teacher	CBCL/TRF Delinquent Behavior and Aggressive Behavior subscales	5, 12	36,37
IQ	Participant	WPPSI Revised; children were administered 2 subtests: Vocabulary and Block design and IQ scores were prorated following procedures described by Sattler	5	38,39
Performance IQ	Participant	Age-adjusted Block Design score	5	38
Verbal IQ	Participant	Age-adjusted Vocabulary score	5	38
Executive functioning	Participant	Children were administered 3 executive functions tests: Mazes, a WPPSI subtest; Day-Night, a nonverbal analog of the Stroop task; and Sentence Working Memory, based on the Baddeley model of working memory	5	38,40–42
Social environment characteristics				
Parental antisocial behavior	Mother	Mothers' report of parents' history of antisocial behavior using the Young Adult Behavior Checklist	5	43,44
Parental substance problems	Mother	Mothers' report of parents' history of drug and alcohol problems taken from the short Michigan Alcoholism Screening Test and from the Drug Abuse Screening Test	5	45,46
Maternal depression	Mother	Maternal depression was assessed using a modified version of the Diagnostic Interview Schedule according to DSM-IV criteria; mothers asked to specify if and when they experienced any episodes of depression since the child's birth	5	43,47
Low social class	Parents	Lowest tertile of socioeconomic index, a composite of parental income, education, and occupation	5	48
Maternal expressed emotion	Mother, coded by independent raters	Assessed using a 5-minute speech sample eliciting expressed emotion from the mother; speech samples were audiotaped and coded by 2 independent raters. Maternal negativity indexes negativism expressed in the interview about the child; maternal warmth indexes warmth expressed in the interview about the child	5	49

JAMA Psychiatry. Author manuscript; available in PMC 2017 July 01.

Measure	Informant	Description of measure	Age, y	Reference
Domestic violence exposure	Mother	Mothers asked about own violence toward partner and partners' violence toward them during 5 years since the child's birth. Assessed by all 9 items from the Conflict Tactics Scale, Form R plus 3 items describing other physically abusive behaviors	5	[50]
Child maltreatment	Mother	Mothers answered questions about the extent and severity to which restrictive and harsh physical punishment were used by the parent(s), and the probability that each child experienced physical abuse	5	[51,52]
Young adult functioning				
Interviewer personality impressions	Interviewer	Following the interview, the interviewers completed a series of questions concerning their own impressions of the participant's mental health, physical health and personality	18	[53]
IQ	Participant	WAIS-IV; youth were administered 3 subtests: Information, Digit Symbol Coding and Matrix Reasoning	18	[54]
Life satisfaction	Participant	Assessed by the Satisfaction with Life Scale	18	[55]
Job preparedness	Participant	Participants asked to endorse phrases that describe themselves (e.g. "a leader", "tech or computer savvy") in the context of potential employment	18	[56]
Generalized anxiety disorder	Participant	Based on DSM-5 criteria for generalized anxiety disorder	18	[57]
Major depressive episode	Participant	Based on DSM-5 criteria for major depressive episode	18	[57]
Conduct disorder	Participant	Based on DSM-5 criteria for conduct disorder	18	[57]
Marijuana dependence	Participant	Based on DSM-5 criteria for marijuana dependence	18	[57]
Alcohol dependence	Participant	Based on DSM-5 criteria for alcohol episode	18	[57]

Table 2

Pre- and perinatal, clinical, and family environment factors in childhood among individuals with and without ADHD

	No ADHD dx *N (%) 1683 (82.5)*	Childhood ADHD dx *N (%) 247 (12.1)*	Adult ADHD dx *N (%) 162 (7.9)*	Persistent ADHD dx *N (%) 52 (2.5)*	Remitted ADHD dx *N (%) 195 (9.6)*	Late-onset ADHD dx *N (%) 110 (5.4)*	Persistent vs remitted	Persistent vs late-onset[a]
Pre- and perinatal factors								
Male gender, n (%)	744 (44.2)	176 (71.3)***	83 (51.2)	34 (65.4)	142 (72.8)	49 (44.6)		*
Birth weight (gr), mean (SD)	2448.5 (541.1)	2370.3 (510.9)~	2437.2 (520.3)	2357.0 (540.7)	2374.4 (503.1)	2476.5 (508.0)		
Stress during pregnancy, n (%)	329 (20.5)	62 (27.4)*	46 (28.9)*	17 (33.3)	45 (25.7)	29 (26.9)		
Smoking during pregnancy, n (%)	373 (23.3)	88 (40.4)***	56 (35.7)**	23 (45.1)	65 (38.9)	33 (31.3)		~
Child clinical characteristics								
Age 5–12 childhood ADHD symptoms								
Total inattention symptoms, mean (SD)	0.83 (1.2)	5.26 (2.8)***	3.22 (3.0)***	6.34 (3.1)	4.97 (2.7)	1.75 (1.3)	**	***
Total hyp/impul symptoms, mean (SD)	1.33 (1.5)	5.77 (2.7)***	3.79 (2.9)***	6.70 (3.1)	5.52 (2.5)	2.42 (1.6)	*	***
Total symptoms, mean (SD)	2.15 (2.4)	11.03 (4.6)***	7.01 (5.5)***	13.02 (5.4)	10.50 (4.3)	4.18 (2.5)	**	***
Age 5–12 comorbid problems								
ODD, n (%)	167 (9.9)	108 (43.7)***	50 (30.9)***	24 (46.2)	84 (43.1)	26 (23.6)		*
CD, n (%)	169 (10.0)	118 (47.8)***	58 (35.8)***	26 (50.0)	92 (47.2)	32 (29.1)		*
Internalizing score, mean (SD)	10.72 (6.2)	16.17 (8.6)***	14.25 (8.0)***	17.51 (9.4)	15.81 (8.4)	12.71 (6.7)		**
Externalizing score, mean (SD)	14.21 (9.8)	32.96 (15.7)***	26.89 (15.2)***	36.66 (18.0)	31.97 (14.9)	22.27 (11.1)	~	***
Age 5 cognitive measures								
IQ, mean (SD)	101.38 (14.6)	91.91 (14.8)***	94.10 (16.0)***	88.17 (14.9)	92.93 (14.6)	96.90 (15.8)	~	**
Performance IQ, mean (SD)	9.98 (2. 8)	8.29 (2.8)***	8.66 (3.0)***	7.44 (3.0)	8.52 (2.7)	9.24 (2.9)	*	**
Verbal IQ, mean (SD)	9.12 (3.0)	7.71 (3.0)***	8.10 (3.1)***	7.40 (2.8)	7.79 (3.1)	8.43 (3.2)		*

	No ADHD dx *N (%) 1683 (82.5)*	Childhood ADHD dx *N (%) 247 (12.1)*	Adult ADHD dx *N (%) 162 (7.9)*	Persistent ADHD dx *N (%) 52 (2.5)*	Remitted ADHD dx *N (%) 195 (9.6)*	Late-onset ADHD dx *N (%) 110 (5.4)*	Persistent vs remitted	Persistent vs late-onset[a]
Executive functioning, mean (SD)	11.84 (3.0)	10.56 (3.3)***	10.86 (3.0)***	10.64 (3.5)	10.55 (3.3)	10.96 (2.8)		
Family environment								
Parental antisocial behavior, n (%)	422 (25.2)	105 (42.7)***	60 (37.0)**	23 (44.2)	82 (42.3)	37 (33.6)		
Parental substance use problems, n (%)	383 (22.9)	91 (37.0)***	63 (38.9)***	23 (44.2)	68 (35.1)	40 (36.4)		
Maternal depression, n (%)	438 (26.2)	105 (42.9)***	49 (30.4)	15 (29.4)	90 (46.4)	34 (30.9)	*	
Low social class, n (%)	514 (30.5)	118 (47.8)***	69 (42.6)**	23 (44.2)	95 (48.7)	46 (41.8)		
Maternal warmth, mean (SD)	3.33 (1.0)	2.90 (1.1)***	3.18 (0.9)~	3.20 (1.0)	2.82 (1.1)	3.17 (0.9)	*	
Maternal negativity, mean (SD)	1.45 (0.9)	2.00 (1.1)***	1.81 (1.0)***	1.98 (1.1)	2.00 (1.1)	1.73 (1.0)		
Domestic violence exposure, n (%)	670 (40.1)	128 (52.0)**	84 (51.9)**	25 (48.1)	103 (53.1)	59 (53.6)		
Child maltreatment, n (%)	199 (11.8)	53 (21.5)***	31 (19.1)*	8 (15.4)	45 (23.1)	23 (20.9)		

*p<0.05,

**p<0.01,

***p<0.001,

~p<0.10

[a]Statistical comparisons controlled for gender

JAMA Psychiatry. Author manuscript; available in PMC 2017 July 01.

Table 3

Age-18 functioning among individuals with no ADHD, and persistent, remitted, and late-onset ADHD

	No ADHD dx[a] *N (%) 1683 (82.5)*	Persistent ADHD dx *N (%) 52 (2.3)*	Remitted ADHD dx *N (%) 195 (9.8)*	Late-onset ADHD dx *N (%) 110 (5.25)*	Persistent vs remitted	Remitted vs no ADHD[b]	Persistent vs late-onset[b]
Age-18 ADHD symptoms and impairment							
Self-report							
# inattentive sx, self-report, mean (SD)	2.64 (2.2)	5.69 (2.2)	3.54 (2.5)	6.14 (1.8)	***	***	
# hyp/impulsive sx, self-report, mean (SD)	2.45 (2.2)	5.67 (2.2)	3.34 (2.4)	5.28 (2.4)	***	***	
# total sx, self-report, mean (SD)	5.08 (3.9)	11.37 (3.5)	6.89 (4.3)	11.42 (3.2)	***	***	
ADHD interference at school or work, mean (SD)	1.93 (1.0)	3.73 (1.1)	2.03 (1.1)	3.91 (0.8)	***		
ADHD interference at home or with friends, mean (SD)	1.55 (0.8)	3.62 (1.0)	1.66 (0.9)	3.45 (0.7)	***	*	
Co-informant report							
# any informant ADHD sx, mean (SD)	0.35 (1.0)	2.02 (2.3)	1.01 (1.7)	1.16 (2.0)	**	***	*
Interviewer personality impressions							
Not conscientious, n (%)	151 (9.0)	20 (38.5)	39 (20.2)	21 (19.3)	*	***	*
Not diligent, n (%)	240 (14.4)	26 (53.1)	58 (29.9)	30 (27.8)	**	***	**
Not planful, n (%)	290 (17.3)	15 (29.4)	67 (34.7)	37 (33.6)		***	
Disorderly, n (%)	49 (2.9)	6 (11.8)	16 (8.3)	13 (11.8)		**	
Not focused, n (%)	219 (13.1)	18 (34.6)	51 (26.4)	25 (22.7)		***	
Not persevering, n (%)	134 (8.1)	19 (36.5)	36 (18.9)	18 (16.4)	**	***	**
Functioning							
IQ, mean (SD)	102.5 (14.5)	90.4 (14.7)	93.1 (16.0)	96.0 (14.3)		***	*
Life satisfaction, mean (SD)	3.92 (0.7)	3.49 (0.9)	3.74 (0.7)	3.45 (0.8)	~	**	
Job preparedness, mean (SD)	17.2 (2.4)	14.8 (4.0)	16.4 (3.0)	15.5 (2.9)	**	***	~
Currently studying, n (%)	1,231 (73.1)	33 (63.5)	113 (58.0)	71 (64.6)		***	
Comorbid diagnoses							
Generalized anxiety disorder, n (%)	108 (6.4)	12 (23.1)	12 (6.2)	18 (16.4)	**		
Major depressive episode, n (%)	301 (17.9)	18 (34.6)	42 (21.7)	47 (42.7)	~	*	

	No ADHD dx[a] *N (%)* ***1683 (82.5)***	Persistent ADHD dx *N (%)* ***52 (2.3)***	Remitted ADHD dx *N (%)* ***195 (9.8)***	Late-onset ADHD dx *N (%)* ***110 (5.25)***	Persistent vs remitted	Remitted vs no ADHD[b]	Persistent vs late-onset[b]
Conduct disorder, n (%)	201 (12.0)	19 (38.0)	46 (23.8)	38 (34.9)	~	**	
Marijuana dependence, n (%)	54 (3.2)	8 (15.4)	11 (5.6)	13 (11.8)	*		
Alcohol dependence, n (%)	182 (10.8)	7 (13.5)	32 (16.4)	35 (32.1)		~	*

*p<0.05,

**p<0.01,

***p<0.001,

~p<0.10

[a]Information for individuals with no ADHD presented for reference; statistical comparisons were not conducted with this group

[b]Statistical comparisons controlled for gender