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Childhood Factors Affecting Persistence and Desistence of Attention-Deficit/Hyperactivity Disorder Symptoms in Adulthood: Results From the MTA

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The Multimodal Treatment Study of Children with ADHD (MTA) was a National Institute of Mental Health (NIMH) cooperative agreement randomized clinical trial, continued under an NIMH contract as a follow-up study and finally under a National Institute on Drug Abuse (NIDA) contract. Collaborators from NIMH: Benedetto Vitiello, MD (Child and Adolescent Treatment and Preventive Interventions Research Branch), Joanne B. Severe, MS (Clinical Trials Operations and Biostatistics Unit, Division of Services and Intervention Research), Peter S. Jensen, MD (currently at REACH Institute and Mayo Clinic), L. Eugene Arnold, MD, MEd (currently at Ohio State University), Kimberly Hoagwood, PhD (currently at Columbia); previous contributors from NIMH to the early phases: John Richters, PhD (currently at National Institute of Nursing Research); Donald Vereen, MD (currently at NIDA). Principal investigators and co-investigators from the sites are: University of California, Berkeley/San Francisco: Stephen P. Hinshaw, PhD (Berkeley), Glen R. Elliott, PhD, MD (San Francisco); Duke University: Karen C. Wells, PhD, Jeffery N. Epstein, PhD (currently at Cincinnati Children's Hospital Medical Center), Desiree W. Murray, PhD; previous Duke contributors to early phases: C. Keith Conners, PhD (former PI); John March, MD, MPH; University of California, Irvine: James Swanson, PhD, Timothy Wigal, PhD; previous contributor from UCLA to the early phases: Dennis P. Cantwell, MD (deceased); New York University School of Medicine: Howard B. Abikoff, PhD; Montreal Children's Hospital/McGill University: Lily Hechtman, MD; New York State Psychiatric Institute/Columbia University/Mount Sinai Medical Center: Laurence L. Greenhill, MD (Columbia), Jeffrey H. Newcorn, MD (Mount Sinai School of Medicine); University of Pittsburgh: Brooke Molina, PhD, Betsy Hoza, PhD (currently at University of Vermont), William E. Pelham, PhD (PI for early phases, currently at Florida International University). Follow-up phase statistical collaborators: Robert D. Gibbons, PhD (University of Illinois, Chicago); Sue Marcus, PhD (Mt. Sinai College of Medicine); Kwan Hur, PhD (University of Illinois, Chicago). Original study statistical and design consultant: Helena C. Kraemer, PhD (Stanford University). Collaborator from the Office of Special Education Programs/US Department of Education: Thomas Hanley, EdD. Collaborator from Office of Juvenile Justice and Delinquency Prevention/Department of Justice: Karen Stern, PhD.

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Abstract

Objective—To determine childhood factors that predict attention-deficit/hyperactivity disorder (ADHD) persistence and desistence in adulthood.

Method—Regression analyses were used to determine associations between childhood factors and adult ADHD symptom persistence in 453 participants (mean age = 25 years) from the Multimodal Treatment of ADHD study (MTA). Childhood IQ, total number of comorbidities, child-perceived parenting practices, child-perceived parent-child relationships, parental mental health problems, marital problems of parents, household income levels and parental education were assessed at a mean age of 8 years in all participants. Adult ADHD persistence was defined using *DSM-5* symptom counts either with or without impairment as well as mean ADHD symptom scores on the Conners' Adult ADHD Rating Scale (CAARS). Age, sex, MTA site and childhood ADHD symptoms were covaried.

Results—The most important childhood predictors of adult ADHD symptom persistence were initial ADHD symptom severity (OR = 1.89, SE = .28, $p = .025$), comorbidities (OR = 1.19, SE = .07, $p = .018$), and parental mental health problems (OR = 1.30, SE = .09, $p = .003$). Childhood IQ, socioeconomic status, parental education and parent-child relationships showed no associations with adult ADHD symptom persistence.

Conclusion—Initial ADHD symptom severity, parental mental health and childhood comorbidity affect persistence of ADHD symptoms into adulthood. Addressing these areas early on may assist in reducing adult ADHD persistence and functioning problems.

Keywords

Attention-deficit/hyperactivity disorder (ADHD); adulthood; family; comorbidity; IQ

INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is a childhood-onset neurodevelopmental condition characterised by symptoms of hyperactivity, impulsivity and inattention.¹ Once considered to be childhood-limited, ADHD is now widely recognised to persist long into adolescence and adulthood.² Studies suggest that of all children with ADHD, 45%–85% are symptomatic in adolescence while 50%–60% continue to show symptoms in adulthood.^{3–6} The large heterogeneity in persistence rates is partly determined by the age at which symptoms are assessed; symptoms of ADHD, particularly hyperactivity/impulsivity, decrease with age leading to lower persistence rates at adulthood than adolescence.^{3,5,7}

Further, heterogeneity in persistence rates also result from the varying definitions of persistence employed by studies. Nevertheless, it is agreed that only some individuals with a childhood diagnosis may improve sufficiently to not be diagnosed with ADHD in adulthood (desisters) while others continue to show symptoms and qualify for a diagnosis (persisters) in adult life.

Persisters and desisters differ in a number of characteristics. Persisters are more likely than desisters to have comorbid oppositional, addiction, anxiety and depression problems as well as functioning difficulties in social, educational, emotional and cognitive domains.⁸⁻¹² It is not understood whether such differences are cause, effect, or simply associated through some third factor. More importantly, it is not known if such differences in functioning are already present at an early age and predate the divergence in ADHD symptom profiles into persistent and desistent types.

A number of studies have assessed effects of childhood functioning and family characteristics on ADHD persistence showing that ADHD severity, comorbid oppositional and conduct problems, cognitive difficulties and functional impairments increase the risk for persistence in late childhood and early adolescence.^{10,12,13-14} Few studies, though, have followed up children with ADHD into late adolescence and adulthood.¹⁵⁻¹⁹ Of these, Biederman et al,¹⁵ Biederman et al,¹⁶ and Cheung et al¹⁷ have assessed the effects of several factors on ADHD persistence, but include participants with a wide age-range at follow-up. As participants with persistent ADHD in both mid-adolescence and adulthood were included, it is not clear which factors were associated specifically with adult persistence. A few other studies have included a narrower age range, restricting assessment of persistence to adulthood.¹⁸⁻²⁰ However, these studies too may be limited as they assess effects of only a few childhood factors (such as comorbid internalising/externalising problems, ADHD symptom severity) on adult ADHD symptoms.

Most previous studies have assessed effects of parental mental health and childhood comorbidity on ADHD symptoms.^{11-12,21-22} While these are important predictors of persistence, effects of other family and child characteristics cannot be ignored. For example, socioeconomic status (SES) and family relationships affect children's upbringing and their coping abilities.²³⁻²⁶ Similarly, poor parenting and low parental education may be associated with impaired prognosis.²⁷⁻²⁸ Such factors can have far-reaching downstream effects on functioning, and should arguably worsen ADHD persistence. Finally, concurrent IQ levels distinguish between young adults with and without persistent ADHD.²⁹ Thus, childhood IQ may too be an important predictor of adult ADHD persistence.

This study aims to assess effects of family characteristics and childhood functioning on risk for persistence of ADHD into early adulthood. It is important to determine, specifically, the predictors of adult persistence, which may differ from predictors of adolescent persistence. Though adolescence is associated with increased social requirements, adulthood is associated with demands for independent functioning. Such demands may lead to differences in coping abilities at adolescence and adulthood and consequently produce differences in effects of early factors on persistence at the two time-points. We include a

wider range of early factors than previous studies, and assess their effects on ADHD symptom persistence.

METHOD

Sample

This study was based on data from the National Institute of Mental Health – Multimodal Treatment Study of Children with ADHD (MTA) cohort. The MTA was a 14-month randomized treatment study of 579 children with ADHD, aged 7–10 years, with naturalistic follow-ups to 16 years after baseline. Follow-up assessments were made in childhood (3 years after baseline), adolescence (6, 8 and 10 years after baseline), and adulthood (12, 14 and 16 years after baseline). The current study uses data from participants assessed at the adult follow-up assessments and from their baseline measurements ($n = 453$, 21.8% females, mean age = 24.7 years, age range = 19–28 years). Further details on the MTA sample are available in previous publications.^{30–34} For a comparison of the sample and participants lost to follow-up, see Table S1, available online.

The study was approved by Institutional Review Boards and procedures were carried out in accordance with the Declaration of Helsinki. All participants were informed of the study procedures and provided written consent.

Measures

Outcome—The Conners' Adult ADHD Rating Scale (CAARS) was used to assess symptoms of ADHD at the adult assessments. Scores from the last available time point of 12, 14 or 16 years were used. Presence of an ADHD symptom was defined as a score of 2 or more on the four-point CAARS scale (0 = never, 1 = once in a while, 2 = often, 3 = very frequently) when endorsed by either parent or participant. Persistence of ADHD in adulthood was defined using *DSM-5* symptom cut-off criteria (at least 5 inattentive or 5 hyperactive-impulsive symptoms).

Baseline Predictors—(i) IQ was measured using the Wechsler Intelligence Scale for Children, 3rd ed. (WISC-III). The predictor variable used was full scale IQ, which is a composite measure of performance on all verbal and non-verbal subtests.³⁰ (ii) Childhood comorbidity was defined as the total number of comorbid diagnoses present according to *DSM-III-R* criteria as assessed by the Diagnostic Interview Schedule for Children – Parent version (DISC-P).^{30–31} (iii) Parental mental health was assessed using the Structured Clinical Interview for *DSM* Disorders – Non Patient (SCID-NP). Presence of either a maternal or paternal mental health condition was considered as a parental diagnosis. Parental morbidity was defined as the total number of parental diagnoses (either mother or father) on the SCID-NP. (iv) Socioeconomic status was defined as the total household income level, measured on categorical scale of 1–10 (1 < \$10,000 per annum and 10 = \$75,000 per annum). (v) Parental education was the highest education received between mother and father. (vi) Parental marital relationship was the total number of separations/divorces (of mother/father figure) experienced by the child. (vii) Parent-child relationships were assessed with the parent-child relationship questionnaire;³⁴ child reports were used to minimize

bias.³⁵ Children rated their relationship quality with 40 items on a five-point scale (1 = hardly, 2 = not too much, 3 = somewhat, 4 = very much, 5 = extremely). Composite scores reflected five domains of parent-child relationships: possessive/protective, affectionate/admiring, conflicting, nurturing/intimate, participating/involved. (viii) Parenting styles were assessed using the child-reported Alabama Parenting Questionnaire (APQ). A total of 51 items are rated on a five-point scale (1 = never, 2 = almost never, 3 = sometimes, 4 = often, 5 = always) and composite scores were used to define six domains of parenting practices: parental involvement, positive parenting, inconsistent discipline, low monitoring and supervision, appropriate discipline, harsh discipline.³⁴ A low score indicated poor performance in that domain.

Covariates—Age (at baseline), sex, original MTA site of randomization, and ADHD symptom scores (at baseline) were included as covariates. ADHD symptom severity at baseline was defined as mean parent- and teacher-reported scores on the Swanson, Nolan, and Pelham (SNAP) scale.³¹

Analyses

Of the 453 participants, 49.2% had missing data on one or more variables. Missingness on baseline predictors ranged from 1.1% to 39.3% (Table S2, available online). We performed multiple imputations by chained equations and assumed that data were missing completely at random (MCAR) or missing at random (MAR). Logistic regression was performed to determine if missingness could be predicted by all baseline variables. Results showed that baseline predictor variables individually explained 14% to 24% of the variance (Nagelkerke R^2) partly supporting the assumption of MAR. We created models for data imputation wherein all variables that were correlated (bivariate correlations ≥ 0.1) with missingness in the data were included. Multiple imputation was performed using fully conditional specification in which separate models specify the distribution for each variable with missing data.³⁶ Predictive mean matching was used to impute missing data for continuous variables, while ordered logit models and multinomial logit models were used to impute ordinal and categorical variables, respectively. As the recommended number of imputations should equal the percentage missingness,³⁷ 39 imputed datasets (for maximum missingness = 39.1%) were constructed with 10 iterations each. Results from each imputed dataset were pooled according to Rubin's method for multiple imputation inference.³⁸

Binary logistic regressions were used to determine associations between baseline predictors and adult ADHD persistence. First, all predictors were entered in the regression model, including the covariates age at baseline, sex, and MTA site. Next, baseline ADHD symptom scores were added to the model as an additional covariate to test for unique prediction from the hypothesized childhood variables after controlling for overlap with childhood ADHD symptomatology.

Sensitivity analyses were carried out to further explore the associations of childhood factors with adult ADHD symptom persistence. First, individuals were regrouped as persistent or desistent depending on the presence of functioning impairment in adulthood, in addition to the *DSM-5* symptom cutoffs. Impairment was defined as a score of 3 or more on either self-

or observer-rated Impairment Rating Scales (IRS).³⁹ Logistic regression analyses were rerun (first with only age, sex and site as covariates and second with baseline ADHD symptoms as an additional covariate) using the new persistence classification as outcome measure. Second, continuous adult ADHD symptom scores were used as the outcome measure. Adult ADHD symptoms were defined as mean scores on self- and observer-reported CAARS ratings. Linear regression analyses were used to determine associations between baseline factors and continuous adult ADHD symptom scores, controlling for age, sex, and site in the first step and baseline ADHD symptoms additionally in the next step.

Statistical analyses were conducted with R software, version 3.1.1. Multiple imputation was performed using the *mice* package. All results at a two-sided value of $p < .05$ were considered significant given the long 16-year window of prediction.

RESULTS

Based on *DSM-5* symptom count, 226 (49.9%) of participants were classified as symptom persisters and 227 (50.1%) as symptom desisters. Table 1 presents distributions of baseline variables in the complete-case dataset (Table S3, available online, presents distributions of variables in the imputed dataset).

Logistic regression analyses on the imputed dataset showed that childhood comorbidity was associated with a 15% likelihood of ADHD symptom persistence (OR = 1.15, SE = 0.07, $p = .035$). Parental mental health problems were associated with a 35% likelihood (OR = 1.35, SE = 0.09, $p = .004$) and parental marital relationships with a 36% likelihood (OR = 1.36, SE = 0.15, $p = .038$) of persistence. Appropriate parental discipline was associated with a 39% likelihood of desistance (OR = 1.39, SE = 0.13, $p = .013$). No associations were found between childhood IQ, child-perceived parent-child relationships, parental education, SES and ADHD symptoms at adulthood (Table S4, available online).

Table 2 presents results of logistic regression analyses after controlling for childhood ADHD symptoms. ADHD symptom severity in childhood was associated with a 39% likelihood of adult persistence. Parental mental health problems were associated with a 28% risk of ADHD persistence. Appropriate parental discipline was associated with a 38% likelihood of ADHD symptom desistance in adulthood. No significant associations of childhood comorbidity or parental mental health with persistence were found (Table 2).

Sensitivity analyses – using impairment ratings with symptom cut-offs to define persistence – showed that 34.7% ($n = 157$) of the participants met criteria for persistence. Logistic regression analyses using this new grouping of persisters showed associations of childhood comorbidity (OR = 1.21, SE = .07, $p = .007$) and parental mental health problems (OR = 1.31, SE = .09, $p = .002$) with ADHD persistence. After covarying childhood ADHD symptoms (OR = 1.89, SE = .28, $p = .025$), associations were still found between childhood comorbidity and persistence (OR = 1.19, SE = .07, $p = .018$) as well as parental mental health and persistence (OR = 1.30, SE = .09, $p = .003$). Further, linear regressions were used to determine effects of baseline factors on continuous adult ADHD scores (mean = 0.96, SD = .50). Results showed associations of childhood comorbidity ($B = .05$, SE = .02, $p = .001$)

and parental mental health problems ($B = .07$, $SE = .02$, $p < .001$) with adult ADHD symptoms. After covarying baseline ADHD symptoms ($B = .15$, $SE = .06$, $p = .011$), childhood comorbidity ($B = .04$, $SE = .02$, $p = .005$) and parental mental health ($B = .07$, $SE = .02$, $p = .001$) were associated with adult ADHD symptomatology. No associations of IQ, parent-child relationships, parenting styles, parental education, parental marital problems, SES with adult ADHD persistence (defined with impairment ratings) or adult ADHD symptom scores were found. Table 3 presents an overview of results from all analyses.

DISCUSSION

This study investigated childhood factors that predict a risk for persistence of ADHD into adulthood. Childhood psychiatric comorbidity, parental mental health, parental marital relationships and parenting styles were associated with persisting ADHD symptomatology. Of the four above-mentioned predictors, only childhood comorbidity and parental mental health were consistently associated with adult ADHD symptom persistence. We found no associations of IQ, household income, parental education, or parent-child relationships with adult ADHD persistence.

Throughout all analyses carried out in this study, we consistently found no associations of IQ, income and parental education with adult ADHD symptom persistence. Research suggests that IQ and ADHD symptoms are related both concurrently as well as prospectively. It is possible though, that ADHD symptom levels are a stronger predictor of IQ than the other way around. One study reported that IQ levels predicted ADHD persistence in late adolescence and young adulthood.²⁹ These results are different from ours and may be related to the inclusion of participants with a wider age range at baseline (including both children and adolescents).²⁹ With regards to the effects of parental education and household income on ADHD, results from prior studies are heterogeneous. According to Biederman, Petty, O'Connor et al.,¹⁶ household income and parental education levels did not affect ADHD persistence between the ages of 15 and 30 years. Similarly, Hurtig et al.²¹ found no effects of household income on ADHD persistence in late adolescence (16 to 18 years). In contrast to these two studies Law, Sideridis, Prock, and Sheridan,⁴⁰ found an association of low income and parental education levels with ADHD persistence at the age of ten. It is possible that income and parental education levels predict ADHD symptomatology through childhood but not later on in life when other factors more proximal to adult outcome become relevant. In a recent study, however, Cheung et al.¹⁷ reported that parental occupational classes (a measure reflecting both income and parental education) predicted ADHD persistence from 12 to 25 years of age. Further research may be needed to examine the effects of income and parent education on ADHD symptomatology and resolve discrepancies in findings. Key mediators, such as ultimate educational attainment by the child, which is known to be affected by parent education and occupation, may need to be tested.

Previously, studies have provided mixed evidence on effects of family environment on persistence.^{15–16,21} While one study found an effect of family cohesion and conflict on persistence,¹⁶ another reported no associations between the same family characteristics and ADHD symptoms in adulthood.¹⁵ A third study, in a general population sample, found no

relationship of parental marital status with adolescent ADHD persistence.²¹ In our study too, we did not find an effect of parent-child relationships with persistence of symptoms. We did find an association of parental marital problems with (the *DSM-5* symptom cut-off based definition of) persistence, though these effects too became non-significant after controlling for baseline ADHD symptoms. According to a recent study, high parenting stress but not parenting/discipline style distinguished persisters and remitters.¹² In contrast to this study, we found a good parental disciplining style to protect against adult ADHD symptom persistence. However, neither marital problems nor parenting styles were associated with adult ADHD symptoms when using continuous scores as outcomes or using impairment ratings in addition to symptom count to define 'persistence'. Thus, associations of family environments with persistence have been weak and more studies are needed to scrutinize these effects.

As seen in previous studies, childhood ADHD severity predicted a risk for adult symptom persistence.^{15,17,41} Similarly, the effects of parental psychopathology and childhood psychiatric comorbidity on persistence are in line with previous studies.^{12,18,21,41} Parental mental health problems, and in particular maternal psychopathology has been shown to predict ADHD persistence in adolescence and young adulthood.¹⁵ Studies have shown that the type of parental psychopathology affects ADHD symptoms: Biederman, Petty, O'Connor et al.¹⁶ reported that adolescents and adults with persistent ADHD were more likely to have a family history of ADHD or anxiety, while families of individuals under remission were more likely to show conduct problems. Our results extend this literature by showing that the total number of parental psychopathologies affects adulthood ADHD - an increase in the number of parental mental health problems adds to the risk for persistence. Further, Biederman et al.¹⁵ found that adolescents and adults with persistent ADHD were more likely than those with desistent ADHD to have ODD, CD and anxiety problems in childhood. Similarly, in a follow-up study of girls with ADHD, adolescent and adult persistence was associated with higher behavior, mood and anxiety problems in childhood.¹⁶ Here too we add to the existing knowledge and show that an increase in the number of comorbidities in childhood increases the risk for persistence of ADHD in adulthood. One caveat of these findings is that we did not find an association of childhood comorbidity with adult ADHD symptom persistence (as defined only with *DSM-5* symptom cut offs) after covarying baseline ADHD severity. This is a surprising finding as inclusion of impairment ratings and using continuous ADHD symptom scores as outcomes showed consistent associations with childhood comorbidity. Further studies may be needed to explore the discrepant associations of childhood comorbidity with adult ADHD symptom persistence.

Results from this study must be interpreted while bearing in mind certain limitations. First, persistence was assessed in young adulthood and persistent participants may remit at a later age. Research shows that not only young adults, but middle aged and older individuals show symptoms of ADHD and receive treatment for these symptoms.⁴²⁻⁴³ Further, prevalence rates of ADHD may decrease between young adulthood middle age and older ages,⁴⁴ suggesting that remission from ADHD symptoms could continue beyond young adulthood.¹⁸ The effects of childhood-based factors on persistence beyond early adulthood could not be assessed in this study. Second, the CAARS rating scale, used here to assess ADHD symptoms, does not inform about presence of symptoms in multiple settings. Thus,

we could not ascertain ADHD symptom persistence according to the full *DSM-5* criteria. Third, data were missing on a number of variables at baseline, which were subsequently imputed to avoid loss of subjects. Although, our analyses provided a measure of correction for missing data, 22% of participants from the original cohort were missing from the adult assessments and findings may have been influenced by their absence. Fourth, concurrent comorbidity may affect persistence of ADHD. However, the current study was aimed at assessing childhood correlates of adult persistence, and the effects of adult comorbidity were not accounted for in the analyses.

In summary, childhood factors such as a higher number of psychiatric comorbidities and greater ADHD severity, but not IQ, predict a risk for ADHD symptom persistence in adulthood. Amongst family factors, a risk for ADHD persistence is predicted by parental mental health problems, but not SES, parental education, or parent-child relationships. Our findings thus suggest that addressing ADHD severity and comorbidity in childhood may have long-term implications, although it is likely - given the findings of the MTA³³ - that one year of treatment in childhood would be insufficient to alter long-term trajectories. Further, interventions aimed at improving parental mental health may be beneficial. Future studies may explore if risk factors for adolescent, young adult and late adult persistence differ. These predictors should be integrated to identify the unfolding of risk and resilience that occurs across the adolescent bridge from childhood to adulthood. Further, sophisticated longitudinal modelling may be used to determine mechanisms through which early childhood factors affect persistence, critical periods during which such factors influence ADHD symptoms, and temporal relationships between childhood predictors and persistence. Ultimately, predictors of ADHD persistence may change with age, and an integrated view of risk dynamics for persistence is needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5®). Arlington, VA: American Psychiatric Pub; 2013.
2. Goodman DW. The consequences of attention-deficit/hyperactivity disorder in adults. *J Psychiatr Pract.* 2007; 13(5):318–327. [PubMed: 17890980]
3. Biederman J, Mick E, Faraone SV. Age-dependent decline of symptoms of attention deficit hyperactivity disorder: Impact of remission definition and symptom type. *Am J Psychiatry.* 2000; 157(5):816–818. [PubMed: 10784477]
4. Faraone SV, Biederman J, Spencer T, et al. Attention-deficit/hyperactivity disorder in adults: An overview. *Biol Psychiatry.* 2000; 48(1):9–20. [PubMed: 10913503]
5. Faraone SV, Biederman J, Mick E. The age-dependent decline of attention deficit hyperactivity disorder: A meta-analysis of follow-up studies. *Psychol Med.* 2006; 36:159–65. [PubMed: 16420712]
6. Mattingly G, Culpepper L, Babcock T, Arnold V. Aiming for remission in adults with attention-deficit/hyperactivity disorder: The primary care goal. *Postgrad Med.* 2015; 127:323–9. [PubMed: 25662296]
7. Srebnicki T, Kolakowski A, Wolanczyk T. Adolescent outcome of child ADHD in primary care setting: Stability of diagnosis. *J Atten Disord.* 2013; 17(8):655–659. [PubMed: 22408135]
8. Biederman J, Petty CR, Evans M, Small J, Faraone SV. How persistent is ADHD? A controlled 10-year follow-up study of boys with ADHD. *Psychiatry Res.* 2010; 177:299–304. [PubMed: 20452063]
9. Biederman J, Petty CR, Woodworth KY, Lomedico A, Hyder LL, Faraone SV. Adult outcome of attention-deficit/hyperactivity disorder: A controlled 16-year follow-up study. *J Clin Psychiatry.* 2012; 73(7):941–950. [PubMed: 22901345]
10. Gau SS, Lin YJ, Cheng AT, Chiu YN, Tsai WC, Soong WT. Psychopathology and symptom remission at adolescence among children with attention-deficit-hyperactivity disorder. *Aust N Z J Psychiatry.* 2010; 44(4):323–332. [PubMed: 20307165]
11. Mick E, Byrne D, Fried R, Monuteaux M, Faraone SV, Biederman J. Predictors of ADHD persistence in girls at 5-year follow-up. *J Atten Disord.* 2011; 15(3):183–192. [PubMed: 20332414]
12. Miranda A, Colomer C, Fernandez MI, Presentacion MJ, Rosello B. Analysis of personal and family factors in the persistence of attention deficit hyperactivity disorder: Results of a prospective follow-up study in childhood. *PLoS One.* 2015; 10(5):e0128325. [PubMed: 26024216]
13. Bussing R, Mason DM, Bell L, Porter P, Garvan C. Adolescent outcomes of childhood attention-deficit/hyperactivity disorder in a diverse community sample. *J Am Acad Child Adolesc Psychiatry.* 2010; 49(6):595–605. [PubMed: 20494269]
14. Holbrook JR, Cuffe SP, Cai B, et al. Persistence of parent-reported ADHD symptoms from childhood through adolescence in a community sample. *J Atten Disord.* 2016; 20:11–20. [PubMed: 24994874]
15. Biederman J, Petty CR, Clarke A, Lomedico A, Faraone SV. Predictors of persistent ADHD: An 11-year follow-up study. *J Psychiatr Res.* 2011; 45(2):150–155. [PubMed: 20656298]
16. Biederman J, Petty CR, O'Connor KB, Hyder LL, Faraone SV. Predictors of persistence in girls with attention deficit hyperactivity disorder: Results from an 11-year controlled follow-up study. *Acta Psychiatr Scand.* 2012; 125(2):147–156. [PubMed: 22097933]
17. Cheung CH, Rijdijs F, McLoughlin G, Faraone SV, Asherson P, Kuntsi J. Childhood predictors of adolescent and young adult outcome in ADHD. *J Psychiatr Res.* 2015; 62:92–100. [PubMed: 25680235]
18. Karam RG, Breda V, Picon FA, et al. Persistence and remission of ADHD during adulthood: A 7-year clinical follow-up study. *Psychol Med.* 2015; 45:2045–56. [PubMed: 25612927]
19. Klein RG, Mannuzza S, 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]

20. Barkley, RA.; Murphy, KR.; Fischer, M. ADHD in adults: What the science says. New York: Guilford Press; 2010.
21. Hurtig T, Ebeling H, Taanila A, et al. ADHD symptoms and subtypes: Relationship between childhood and adolescent symptoms. *J Am Acad Child Adolesc Psychiatry*. 2007; 46(12):1605–1613. [PubMed: 18030082]
22. Seco FL, Aguado-Gracia J, Mundo-Cid P, et al. Maternal psychiatric history is associated with the symptom severity of ADHD in offspring. *Psychiatry Res*. 2015; 226(2):507–512. [PubMed: 25747683]
23. Deault LC. A systematic review of parenting in relation to the development of comorbidities and functional impairments in children with attention-deficit/hyperactivity disorder (ADHD). *Child Psychiatry & Human Development*. 2010; 41(2):168–192. [PubMed: 19768532]
24. Johnston C, Mash EJ. Families of children with attention-deficit/hyperactivity disorder: Review and recommendations for future research. *Clin Child Fam Psychol Rev*. 2001; 4:183–207. [PubMed: 11783738]
25. Johnston C, Jassy JS. Attention-deficit/hyperactivity disorder and oppositional/conduct problems: Links to parent-child interactions. *J Can Acad Child Adolesc Psychiatry*. 2007; 16(2):74–79. [PubMed: 18392155]
26. Tarver J, Daley D, Sayal K. Beyond symptom control for attention-deficit hyperactivity disorder (ADHD): What can parents do to improve outcomes? *Child Care Health Dev*. 2015; 41(1):1–14. [PubMed: 24910021]
27. Chronis AM, Lahey BB, Pelham WE Jr, et al. Maternal depression and early positive parenting predict future conduct problems in young children with attention-deficit/hyperactivity disorder. *Dev Psychol*. 2007; 43(1):70–82. [PubMed: 17201509]
28. Russell G, Ford T, Rosenberg R, Kelly S. The association of attention deficit hyperactivity disorder with socioeconomic disadvantage: Alternative explanations and evidence. *J Child Psychol Psychiatry*. 2014; 55(5):436–445. [PubMed: 24274762]
29. Cheung CH, Rijdsdijk F, McLoughlin G, et al. Cognitive and neurophysiological markers of ADHD persistence and remission. *Br J Psychiatry*. 2016; 208:548–55. [PubMed: 26250744]
30. Jensen PS, Arnold LE, Swanson JM, et al. 3-year follow-up of the NIMH MTA study. *J Am Acad Child Adolesc Psychiatry*. 2007; 46:989–1002. [PubMed: 17667478]
31. Molina BS, Hinshaw SP, Swanson JM, et al. The MTA at 8 years: Prospective follow-up of children treated for combined-type ADHD in a multisite study. *J Am Acad Child Adolesc Psychiatry*. 2009; 48:484–500. [PubMed: 19318991]
32. MTA cooperative group. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. Multimodal treatment study of children with ADHD. *Arch Gen Psychiatry*. 1999; 56:1073–1086. [PubMed: 10591283]
33. MTA Cooperative Group. National institute of mental health multimodal treatment study of ADHD follow-up: Changes in effectiveness and growth after the end of treatment. *Pediatrics*. 2004; 113(4):762–769. [PubMed: 15060225]
34. Wells KC, Epstein JN, Hinshaw SP, et al. Parenting and family stress treatment outcomes in attention deficit hyperactivity disorder (ADHD): An empirical analysis in the MTA study. *J Abnorm Child Psychol*. 2000; 28(6):543–553. [PubMed: 11104316]
35. Taber SM. The veridicality of children's reports of parenting: A review of factors contributing to parent-child discrepancies. *Clin Psychol Rev*. 2010; 30(8):999–1010. [PubMed: 20655135]
36. van Buuren S, Groothuis-Oudshoorn K. Mice: Multivariate imputation by chained equations in R. *Journal of statistical software*. 2011; 45(3):1–68.
37. White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. *Stat Med*. 2011; 30(4):377–399. [PubMed: 21225900]
38. Rubin, DB. Multiple imputation for nonresponse in surveys. Vol. 81. Hoboken, NJ: John Wiley and Sons; 2004.
39. Sibley MH, Pelham WE Jr, Molina BS, et al. When diagnosing ADHD in young adults emphasize informant reports, DSM items, and impairment. *J Consult Clin Psych*. 2012; 80:1052–61.

40. Law EC, Sideridis GD, Prock LA, Sheridan MA. Attention-deficit/hyperactivity disorder in young children: Predictors of diagnostic stability. *Pediatrics*. 2014; 133(4):659–667. [PubMed: 24639272]
41. Lara C, Fayyad J, de Graaf R, et al. Childhood predictors of adult attention-deficit/hyperactivity disorder: Results from the world health organization world mental health survey initiative. *Biol Psychiatry*. 2009; 65(1):46–54. [PubMed: 19006789]
42. Das D, Cherbuin N, Butterworth P, Anstey KJ, Eastaun S. A population-based study of attention deficit/hyperactivity disorder symptoms and associated impairment in middle-aged adults. *PLoS One*. 2012; 7(2):e31500. [PubMed: 22347487]
43. McCarthy S, Wilton L, Murray ML, Hodgkins P, Asherson P, Wong IC. Persistence of pharmacological treatment into adulthood, in UK primary care, for ADHD patients who started treatment in childhood or adolescence. *BMC Psychiatry*. 2012; 12:219. [PubMed: 23216881]
44. Bernardi S, Faraone SV, Cortese S, et al. The lifetime impact of attention deficit hyperactivity disorder: Results from the national epidemiologic survey on alcohol and related conditions (NESARC). *Psychol Med*. 2012; 42(4):875–887. [PubMed: 21846424]

Clinical Guidelines

- Childhood ADHD symptoms, comorbidity, and parental mental health affect persistence of ADHD symptoms in adulthood
- Clinicians need to address ADHD symptoms to remission and not just improvement in their treatment of children with ADHD
- Clinicians need to assess and treat comorbidities in children with ADHD
- Evaluation of parental mental health and treatment, if needed, should be part of the clinical approach to improve prognosis of children with ADHD

Table 1
Distribution of Childhood Variables in Persistent and Desistent Groups in Complete Case Dataset

Baseline variables	Desisters Mean (SD)	Persisters Mean (SD)	t	p	Cohen's d
Age	7.78 (0.84)	7.80 (0.81)	-0.33	.74	0.02
Parenting styles					
Parental involvement	3.23 (0.69)	3.26 (0.68)	-0.40	.69	0.04
Positive parenting	3.90 (0.77)	3.95 (0.81)	-0.68	.50	0.06
Inconsistent discipline	2.39 (0.70)	2.52 (0.81)	-1.76	.08	0.17
Low monitoring and supervision	2.01 (0.71)	2.02 (0.72)	-0.22	.83	0.01
Harsh discipline	2.18 (0.94)	2.24 (0.91)	-0.63	.53	0.06
Appropriate discipline	2.61 (0.79)	2.54 (0.74)	0.96	.34	0.09
Parent-child relationships					
Possessive and protective	3.16 (0.81)	3.23 (0.78)	-0.73	.50	0.09
Affectionate and admiring	4.41 (0.72)	4.42 (0.67)	-0.12	.90	0.01
Conflicting	2.30 (0.73)	2.41 (0.69)	-1.27	.20	0.15
Nurturing and intimate	3.46 (0.79)	3.59 (0.76)	-1.40	.16	0.17
Participating and involved	3.30 (0.73)	3.45 (0.79)	-1.71	.09	0.20
IQ	102.14 (15.19)	102.24 (13.97)	-0.08	.09	0.01
Total child comorbidity					
	1.50 (1.58)	1.87 (2.00)	-2.12	.035	0.21
Parental marital relationships^a					
	0.43 (0.70)	0.71 (1.91)	-2.02	.045	0.20
Parental mental health problems					
	0.80 (1.01)	1.28 (1.58)	-3.17	<.001	0.36
ADHD severity					
	1.96 (0.45)	2.10 (0.44)	-3.22	.001	0.32
Baseline variables					
	Desisters N	Persisters N	χ²	p	Odds ratio
Sex (Females)	49	50	0.02	.89	0.97
Income levels (per annum)					
< \$10,000	19	20	0.03	.86	0.94

Baseline variables	Desisters Mean (SD)	Persisters Mean (SD)	t	p	Cohen's d
\$10,000 – \$20,000	25	26	0.03	.86	0.95
\$20,000 – \$30,000	29	29	0	>.99	0.89
\$30,000 – \$40,000	30	30	0	>.99	0.92
\$40,000 – \$50,000	24	33	1.67	.20	0.69
\$50,000 – \$60,000	30	18	3.3	.07	1.76
\$60,000 – \$70,000	19	25	0.94	.33	0.73
\$70,000 – \$75,000	14	9	1.12	.29	1.59
> \$75,000	24	31	1.05	.31	0.74
Parental education levels					
Eighth grade or less	1	0	0	>.99	-
Some high school	5	4	0	>.99	1.25
High school graduate	48	28	6.22	.01	1.90
Some college or post-high school	55	83	8.35	.004	0.55
College graduate	56	62	0.45	.50	0.86
Advanced graduate or professional degree	62	49	1.94	.16	1.36

Note: ADHD = attention-deficit/hyperactivity disorder.

^aTotal number of separations/divorces of parent figure.

Table 2

Results From Logistic Regression Analyses of Adulthood Attention-Deficit/Hyperactivity Disorder (ADHD) Persistence on Childhood Variables Controlling for Age, Sex, MTA Site and Baseline ADHD Symptom Scores

Baseline variables	OR	SE	<i>p</i>	CI
Parenting styles				
Parental involvement	-1.05	0.16	.77	-0.36 to 0.27
Positive parenting	1.14	0.16	.42	-0.18 to 0.44
Inconsistent discipline	1.17	0.13	.21	-0.09 to 0.42
Low monitoring and supervision	-1.07	0.13	.57	-0.32 to 0.18
Harsh discipline	1.07	0.15	.64	-0.22 to 0.36
Appropriate discipline	-1.38	0.13	.017	-0.58 to -0.06
Parent-child relationships				
Possessive and protective	1.01	0.18	.97	-0.35 to 0.36
Affectionate and admiring	-1.13	0.18	.50	-0.49 to 0.24
Conflicting	1.06	0.17	.75	-0.28 to 0.39
Nurturing and intimate	1.02	0.24	.93	-0.50 to 0.46
Participating and involved	1.25	0.24	.38	-0.27 to 0.70
IQ	1.004	0.01	.65	-0.01 to 0.02
Child comorbidity	1.13	0.07	.07	-0.01 to 0.26
Parental marital relationships^a	1.31	0.15	.06	-0.01 to 0.56
Parental mental health problems	1.28	0.09	.008	0.07 to 0.42
Income levels (per annum)^b				
\$10,000 – \$20,000	-1.41	0.53	.53	-1.39 to 0.71
\$20,000 – \$30,000	-1.16	0.53	.78	-1.20 to 0.90
\$30,000 – \$40,000	-1.20	0.52	.73	-1.19 to 0.84
\$40,000 – \$50,000	1.27	0.53	.65	-0.81 to 1.29
\$50,000 – \$60,000	-1.77	0.55	.30	-1.64 to 0.50
\$60,000 – \$70,000	1.20	0.57	.75	-0.94 to 1.30
\$70,000 – \$75,000	-1.86	0.69	.37	-1.97 to 0.72
> \$75,000	-1.03	0.55	.96	-1.10 to 1.05
Parental education levels^c				
Some high school	128.98	535.41	.98	-1040.92 to 1064.44
High school graduate	163.99	535.41	.98	-1040.60 to 1064.76
Some college or post-high school	163.99	535.41	.98	-1039.72 to 1065.64
College graduate	403.59	535.41	.98	-1039.71 to 1065.66
Advanced graduate or professional degree	270.46	535.41	.98	-1040.17 to 1065.19
Age	1.11	0.14	.45	-0.17 to 0.39

Baseline variables	OR	SE	<i>p</i>	CI
Sex	1.27	0.29	.40	−0.32 to 0.81
Original study site	−1.004	0.06	.95	−0.13 to 0.13
ADHD symptom severity	1.39	0.12	.006	0.09 to 0.56

Note:

^aTotal number of divorces/separations of parent figure.

^bCompared to income level group <\$10,000.

^cCompared to parental education level “eighth grade or less.”

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Table 3

Overview of Associations Between Adult Attention-Deficit/Hyperactivity Disorder (ADHD) Symptom Persistence and Baseline Factors

Analysis	Adult ^a ADHD symptom persistence definition	Covariates	Significant predictors of ADHD symptom persistence
1.	DSM-5 symptom count cut-offs ^b	Age, sex, and MTA site	<ul style="list-style-type: none"> • Childhood comorbidity • Parental mental health problems • Parental marital relationships • Appropriate discipline
2.	DSM-5 symptom count cut-offs	Age, sex, MTA site, AND baseline ADHD symptoms	<ul style="list-style-type: none"> • Parental mental health problems • Appropriate discipline
3.	DSM-5 symptom count cut-offs AND Impairment ratings ^c	Age, sex, and MTA site	<ul style="list-style-type: none"> • Childhood comorbidity • Parental mental health problems
4.	DSM-5 symptom count cut-offs AND Impairment ratings	Age, sex, MTA site, AND baseline ADHD symptoms	<ul style="list-style-type: none"> • Childhood comorbidity • Parental mental health problems
5.	Continuous ADHD symptom scores ^d	Age, sex, and MTA site	<ul style="list-style-type: none"> • Childhood comorbidity • Parental mental health problems
6.	Continuous ADHD symptom scores	Age, sex, MTA site, AND baseline ADHD symptoms	<ul style="list-style-type: none"> • Childhood comorbidity • Parental mental health problems

Note: MTA = Multimodal Treatment of ADHD study.

^aMean age 24.7 years.

^bAt least 5 inattentive or hyperactive/impulsive symptoms on self- or observer scores of the Conners' Adult ADHD Rating Scales (CAARS).

^cScores 3 on self- or observer-reported Impairment Rating Scales.

^dMean self- and observer scores on CAARS.