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Adults with Persistent ADHD: Gender and Psychiatric Comorbidities – A Population-Based Longitudinal Study–

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Abstract

Objective—Evaluate associations between ADHD and comorbid psychiatric disorders, among adults from a population-based birth cohort.

Method—Subjects were recruited from all children born 1976–1982 remaining in Rochester, MN after age five. Subjects with childhood ADHD (N=232; mean age 27.0 years; 72% men) and non-ADHD controls (N=335; mean age 28.6 years; 63% men) completed a structured interview (M.I.N.I.) assessing current ADHD status and comorbid psychiatric disorders.

Results—Among 232 with childhood ADHD, 68 (49 men, 19 women) had persistent adult ADHD. Compared to non-ADHD controls and non-persistent ADHD subjects, adults with persistent ADHD were significantly more likely to have any or each of 12 psychiatric comorbidities. The associations retained significant or marginally significant when stratified by gender. Externalizing psychiatric disorders were more common in men (74%) and internalizing disorders in women (58%).

Conclusion—Persistent ADHD is associated with an increased risk of comorbid psychiatric disorders in adult men and women.

Keywords

ADHD; gender; adults; psychiatric comorbidity; epidemiology

Attention-deficit/hyperactivity disorder (ADHD), characterized by developmentally inappropriate and disabling levels of inattentiveness, impulsivity, and/or hyperactivity, has been reported in adult populations, frequently accompanied by a variety of internalizing and externalizing psychiatric comorbidities (Hesson & Fowler, 2015; Kessler et al., 2006; Kooij

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Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

et al., 2012; Mao & Findling, 2014; Moore, Sunjic, Kaye, Archer, & Indig, 2013; Newcorn, Weiss, & Stein, 2007; Roncero et al., 2015; Rucklidge, Downs-Woolley, Taylor, Brown, & Harrow, 2014; Williamson & Johnston, 2015), complicating the recognition and accurate diagnosis of ADHD in adults(Mao & Findling, 2014). We have previously reported that boys and girls with ADHD from a population-based birth cohort were at significantly increased risk for a broad range of comorbid psychiatric disorders through age 19 years, compared to their non-ADHD peers(Yoshimasu et al., 2012). We found no significant gender $\times$ ADHD interaction for overall risk for psychiatric comorbidity prior to 19 years of age. However, among children with ADHD, girls were significantly more likely to have internalizing comorbid disorders, while boys were more likely to have externalizing disorders. To date, there are no similar, population-based studies of the effect of gender on the risk for specific psychiatric comorbidities among adults with ADHD that has persisted from childhood.

The National Comorbidity Survey Replication (NCS-R), a large epidemiological study of the US population, revealed that the likelihood of psychiatric comorbidity with adult ADHD increased for several psychiatric disorders, such as mood disorders, anxiety disorders, substance use disorders, and intermittent explosive disorders(Kessler, et al., 2006), some of which are not evident in childhood (e.g., substance use disorders). Characteristics of psychiatric comorbidities among adults with ADHD were reviewed in detail by Kooij et al. (Kooij, et al., 2012). They classified psychiatric comorbid disorders frequently observed in adult ADHD into six categories: (1) mood disorders, (2) substance use disorders, (3) learning disabilities, (4) sleep disorders, (5) anxiety disorders, and (6) impulse control/personality disorders(Kooij, et al., 2012). These internalizing and externalizing mental disorders are likely to become more apparent in adulthood due to difficulties in coping with various life circumstances.

The majority of the previous epidemiological studies conducted on this issue have been cross-sectional(Hesson & Fowler, 2015; Kessler, et al., 2006; Moore, et al., 2013; Vingilis et al., 2014) or clinic-based studies(Roncero, et al., 2015; Rucklidge, et al., 2014) and they may have been affected by referral bias. Previous prospective studies that have followed childhood ADHD cases into adulthood have primarily included boys and/or employed clinic-referred subjects, and therefore could not contribute to understanding gender differences in risk for adult psychiatric comorbidities among the general population of adults with ADHD(Barkley, Fischer, Smallish, & Fletcher, 2002; Biederman, Petty, Evans, Small, & Faraone, 2010; Gittelman, Mannuzza, Shenker, & Bonagura, 1985). Men with ADHD often are referred for any level of impairment, regardless of the level of severity, whereas female adults who are referred to clinics are usually those with significant impairment, which leads to clinical samples that may not be truly representative of the general population of adults with ADHD(Kooij, et al., 2012). Therefore, it has been suggested that any observed gender differences are more likely to be the result of referral bias than a true gender effect(Biederman et al., 2005). Furthermore, gender differences on the prevalence of psychiatric comorbidity are still inconclusive, since very few studies have included comparison groups of adults without ADHD(Hesson & Fowler, 2015; Williamson & Johnston, 2015). Given the previous epidemiological research showing gender differences of childhood ADHD(Gaub & Carlson, 1997; Hasson & Fine, 2012; Yoshimasu, et al., 2012), it is reasonable to explore whether gender may moderate comorbid features of ADHD in

adults, as understanding the relation between gender and ADHD in adulthood is critical in improving both the quality of ADHD research and clinical practice(Williamson & Johnston, 2015).

We have previously conducted an epidemiological study of comorbid psychiatric disorders among childhood ADHD cases and their non-ADHD peers from a population-based birth cohort(Yoshimasu, et al., 2012). The purpose of the current prospective study of this same birth cohort is to evaluate the psychiatric comorbidities among adults whose childhood ADHD has persisted into adulthood, with explicit assessment for gender differences in the rates and pattern of psychiatric comorbidities.

Method

Study Setting and Data Source

Rochester, Minnesota, is 90 miles southeast of Minneapolis-St Paul, the closest major urban center. In 1990, when subjects in this birth cohort were school-aged children, there were 70,745 residents: 96% white, 72% 45 years of age, and primarily middle class. The demographic characteristics of Olmsted County (Rochester Standard Metropolitan Statistical Area) residents resembled those of the US white population during the timeframe relevant to this study(Melton, 1996).

The capacity for population-based epidemiological research on psychiatric comorbidities of ADHD in Rochester, MN is the result of a unique set of circumstances. First, Rochester is relatively isolated in southeastern Minnesota, and as a result, virtually all medical care is provided locally by Mayo Clinic and Olmsted Medical Center and their three affiliated hospitals. Through the Rochester Epidemiology Project, which is characterized by a unique medical record-linkage system of Rochester and Olmsted County residents, all diagnoses and surgical procedures recorded at affiliated medical facilities are continuously indexed for automated retrieval(Kurland & Molgaard, 1981; Melton, 1996). The medical record includes the detailed history of all medical encounters in the community, including psychiatry and psychology reports, psychological test results, all correspondence regarding treatment provided by private psychiatric treatment facilities, as well as ambulatory medical and social services, hospitals, emergency departments, and home visits, from birth until the patient no longer resides in the community. Second, through a contractual research agreement, all 41 public and private schools in Minnesota Independent School District (ISD) No. 535, the school system for the city of Rochester, MN, gave us permission to access their richly documented cumulative educational records for every child in the birth cohort. These cumulative school records are permanently maintained for all children who have attended public, private or home school in the district. Third, under a separate research agreement we also obtained permission to access the resources of the only private community psychiatric practice in the area. The study was approved by the Institutional Review Boards of Mayo Clinic and Olmsted Medical Center.

Birth Cohort

Our birth cohort consisted of all children born between January 1, 1976 and December 31, 1982 to mothers residing in the townships comprising Minnesota ISD No. 535 ($n = 8548$). The target population consisted of 5,718 children (2,956 boys and 2,762 girls) who still lived in Rochester at or after the age of five years (Katusic et al., 2005a, 2005b), who were followed retrospectively from birth. Among the 5,718 children, 19 subjects with severe intellectual disability were excluded. The steps and resources used for identification and follow-up of this birth cohort, and analysis of potential influence of migration bias, have been previously reported (Katusic, Colligan, Barbaresi, Schaid, & Jacobsen, 1998).

Persistent ADHD Incidence Cases—Identification and Case Definition

Our strategy in identifying childhood ADHD incident cases consisted of several steps, used multiple sources of information, and relied on recorded history of symptoms, individual test results, and treatment. This case-identification approach was previously described in detail (Barbaresi et al., 2002; Katusic, et al., 2005a). Subjects were defined as childhood research-identified ADHD incidence cases if their school and/or medical records included various combinations of the following three different categories of information: 1) meets DSM-IV criteria for ADHD, 2) positive ADHD questionnaire results, 3) clinical diagnosis of ADHD documented (Barbaresi, et al., 2002; Katusic, et al., 2005a). Thus, a total of 379 childhood ADHD cases were identified. As previously reported, five additional subjects who participated in the prospective study were reclassified as childhood ADHD cases, therefore all subsequent analyses included these five subjects as childhood ADHD cases (Barbaresi et al., 2013). Among all 384 subjects with childhood ADHD, 367 provided continued permission to access their medical records for research, and all of them were invited to participate in the current prospective study. However, seven were deceased and 10 were incarcerated at the time of recruitment, thus, 350 were ultimately invited to participate in the study (Figure 1).

Because there are no agreed-upon, norm-referenced diagnostic criteria for adult ADHD, we utilized the distribution of the number of symptoms of inattention and hyperactivity/impulsivity endorsed by non-ADHD controls to establish cutoffs to diagnose persistent, adult ADHD. Persistent ADHD into adulthood was defined using the M.I.N.I.-International Neuropsychiatric Interview (M.I.N.I.), including the module for adult ADHD (Sheehan et al., 1997; Sheehan et al., 1998), in accordance with the following two criteria: 1) childhood ADHD cases who exceeded two standard deviations above mean number of M.I.N.I. ADHD items describing current inattentive and/or hyperactive impulsive symptoms endorsed by non-ADHD controls, and 2) who endorsed M.I.N.I. item on adverse impact of adult ADHD symptoms in two or more settings (Barbaresi, et al., 2013).

Non-ADHD Controls

To ensure enrollment of non-ADHD controls, a random sample of 801 adults from the same population-based birth cohort was invited to participate. Among them, five subjects were reclassified as childhood ADHD cases as described above. The detailed procedures of recruiting controls have been previously described (Barbaresi, et al., 2013).

Adult Psychiatric Disorders

All participants in this prospective study were administered the M.I.N.I. by one of two interviewers who were trained by a clinical psychologist and/or a developmental-behavioral pediatrician. One of the investigators was available at all times, to address any questions or concerns during study visits; so that all issues could be immediately resolved before the study visit was completed. The M.I.N.I. is a structured diagnostic interview for DSM-IV and ICD-10 mental disorders. The M.I.N.I. was selected for several reasons. It was specifically “designed to meet the need for a short but accurate structured psychiatric interview for multicenter clinical trials and epidemiology studies (Sheehan, et al., 1997; Sheehan, et al., 1998).” The M.I.N.I. deals with 17 Axis I of DSM-IV mental disorders based on the standard of a 12-month prevalence of 0.5% or more (Sheehan, et al., 1997), among which we chose major depressive disorder (MDD), dysthymia, post-traumatic stress disorder (PTSD), social phobia, obsessive-compulsive disorder (OCD), hypomanic episode, generalized anxiety disorder, antisocial personality disorder, alcohol dependence/abuse, panic disorder, suicidality, and substance dependence/abuse, as potential candidate disorders associated with persistent ADHD. Among 20 instruments to diagnose depression, the M.I.N.I. was shown to have excellent sensitivity and specificity (Pettersson, Bostrom, Gustavsson, & Ekselius, 2015) and to be useful for epidemiological studies in adult populations (Algorta et al., 2013; Gunter et al., 2008; Kumar, Faden, & Steer, 2011).

Data Analysis

Demographic and perinatal factors were compared among subjects with childhood ADHD that persisted into adulthood (i.e. “persistent ADHD”), those whose childhood ADHD did not persist (i.e., “non-persistent ADHD”), and non-ADHD controls using the chi-square test or Fisher’s exact test for categorical values and the F test from an analysis of variance model for age and maternal age. The presence of each comorbid psychiatric disorder was compared between males and females with persistent ADHD using the chi-square test.

Logistic regression models were fit to evaluate the association of persistent ADHD (vs. non-ADHD) with each of the comorbid psychiatric conditions, for both genders combined and separately by gender. Multivariable models were fit adjusting for gender, maternal age, and maternal education. Additional models were fit to evaluate the association of a) persistent ADHD (vs. non-persistent ADHD) and b) non-persistent ADHD (vs. non-ADHD) with each of the comorbid psychiatric conditions. All associations were summarized using the odds ratio (OR) and corresponding 95% confidence intervals (CI). *P*-values (two-sided) less than 0.05 were considered statistically significant. All analyses were performed using the SAS version 9.3 software package (SAS Institute, Inc., Cary, NC).

Results

Among 367 childhood ADHD cases and 796 non-ADHD controls, 232 adults with research-identified childhood ADHD (61% of original cohort of childhood ADHD cases) and 335 non-ADHD controls (42.1%) participated in the current, prospective outcome study. As we reported previously, among these 232 childhood ADHD cases, 68 cases (29.3%, 95% CI

23.5–35.2, 29.3% for males and 29.2% for females) fulfilled the criteria for persistent adult ADHD (Figure 1)(Barbarese, et al., 2013).

Demographic differences among subjects with persistent-ADHD, non-persistent ADHD, and controls are shown in Table 1. Subjects with persistent or non-persistent ADHD were more likely to be male ($P=0.07$), and have younger mothers at birth ($P=0.054$), compared to non-ADHD controls. There were no significant differences regarding perinatal factors among the three groups. As reported previously, a comparison of socio-demographic factors between participating and non-participating childhood ADHD cases showed no significant differences, with the exception of higher high school graduation rates among the participating childhood ADHD cases(Barbarese, et al., 2013).

Table 2 includes the rates of each comorbid psychiatric disorder separately among men and women with persistent ADHD. Internalizing disorders such as depression (major depressive disorder, $P=0.10$; and dysthymia, $P=0.008$) or anxiety disorders ($P=0.10$) were more common in women with persistent ADHD, while externalizing disorders such as substance dependence/abuse ($P=0.06$) or alcohol-related disorders ($P=0.001$) and antisocial personality disorders ($P=0.05$) were more common in men.

Table 3 demonstrates the associations between persistent ADHD (vs. non-ADHD controls) and each psychiatric disorder assessed by the M.I.N.I. in both genders combined. Persistent ADHD was significantly associated with an increased risk for all psychiatric disorders assessed by the M.I.N.I. When assessed in men and women separately, (Table 4) persistent ADHD (vs. non-ADHD controls) was significantly associated with an increased risk for seven psychiatric disorders within both genders. Of the remaining psychiatric disorders, alcohol-related disorders (externalizing disorders) were significantly associated with persistent ADHD in men but not in women. Conversely, dysthymia and PTSD (internalizing disorders) were significantly associated with persistent ADHD in women but not in men. However, only the gender $\times$ ADHD interaction for dysthymia reached statistical significance (adjusted OR=3.8 for men vs. 44.2 for women; $P=0.049$).

Adults with persistent ADHD were also at an increased risk for all of these psychiatric disorders compared to adults with non-persistent ADHD (Table 5). When assessed in men and women separately (Table 6), persistent ADHD (vs. non-persistent ADHD) was significantly associated with an increased risk for four psychiatric disorders within both genders: social phobia, hypomanic episode, generalized anxiety and major depressive disorder. Of the remaining psychiatric disorders, persistent ADHD was significantly associated with OCD, antisocial personality disorder, alcohol dependence/abuse, panic disorder, suicidality, and substance dependence/abuse among men, but not in women. Conversely, persistent ADHD was significantly associated with dysthymia and PTSD in women, but not in men. However, the statistical power was limited for the evaluation among women given the sample size, and the only gender interaction effect that approached statistical significance was for alcohol dependence/abuse (unadjusted OR=3.8 for men vs. 0.8 for women; $P=0.09$).

When risk for comorbid psychiatric disorders among adults with non-persistent ADHD was compared to non-ADHD controls, non-persistent ADHD was significantly associated with an increased risk of only three disorders: major depressive disorder (OR 2.8, 95%CI 1.1–7.0), antisocial-personality disorder (OR 2.3, 95%CI 1.1–5.1), and suicidality (OR 1.9, 95%CI 1.1–3.3) (all data not shown).

Discussion

The core of this epidemiological study is the population-based birth cohort with carefully defined, research-identified childhood as well as adult ADHD cases and their comorbid psychiatric conditions. These adult population-based data add significantly to our understanding of the comorbidity between persistent ADHD and various psychiatric disorders, as well as their gender differences. Our study clearly indicates strong associations between persistent ADHD (i.e., adults with childhood ADHD that persists into adulthood) and a broad range of psychiatric disorders, including mood disorders, anxiety disorders, antisocial personality disorders, alcohol-related disorders, and suicidality, which is consistent with previous studies (Hesson & Fowler, 2015; Kessler, et al., 2006; Kooij, et al., 2012; Williamson & Johnston, 2015). Especially strong associations were observed between persistent ADHD and mood disorders, anxiety disorders, and substance use disorder, also generally consistent with previous community-based findings (Hesson & Fowler, 2015; Kessler, et al., 2006; Williamson & Johnston, 2015). We found that adults with persistent ADHD have an approximately eight-fold increased risk of having any psychiatric disorder compared to adults without a history of childhood ADHD. Similarly, adults with persistent ADHD also had increased risk for any psychiatric disorders compared with the adults whose childhood ADHD did not persist into adulthood (about 5-fold increased risk). These findings suggest that persistent adult ADHD confers much higher risks of psychiatric comorbidities in adulthood not only compared to non-ADHD controls but also compared to cases with childhood ADHD only. Interestingly, the association between some anxiety disorders (PTSD, general anxiety disorder) and persistent ADHD was more evident in comparison with non-persistent ADHD subjects than with non-ADHD controls (OR=13.5 vs. 10.0 for PTSD, 7.9 vs. 4.7 for generalized anxiety disorder). This occurred because the prevalence of these disorders in adulthood was relatively low among cases with non-persistent ADHD. Remission of ADHD symptoms in adulthood may bring emotional stability to reduce the risk of such disorders.

Among subjects with persistent ADHD, the overall rate of comorbid psychiatric disorders was similar for males (84%) and females (74%). However, internalizing disorders, such as depression and anxiety, were more common in women with persistent ADHD, while externalizing disorders, such as personality disorders and substance use disorder, were more common in men with persistent ADHD. These findings are consistent with previous findings including both community and referral samples (Hesson & Fowler, 2015; Rasmussen & Levander, 2009; Rucklidge, 2008, 2010; Williamson & Johnston, 2015). However, previous studies have had several shortcomings. There have been very few studies on this issue that have included non-ADHD controls (Williamson & Johnston, 2015). Even if controls were included, the range of comorbid psychiatric disorders examined typically has been limited,

and the diagnosis of ADHD has been based on unconfirmed self-report(Hesson & Fowler, 2015).

Overall, our current findings in a population-based birth cohort did not detect significant gender $\times$ ADHD interactions on the risk for psychiatric comorbidities in a comparison of persistent ADHD cases with non-ADHD controls, suggesting that the strength of the association between ADHD and psychiatric comorbidities among adults does not generally differ between men and women. A significant interaction was observed only for dysthymia, in which the association between persistent ADHD and dysthymia was significantly stronger in women compared to men. There has been little evidence regarding gender $\times$ ADHD interaction on risk for psychiatric disorders in the adult population. Only five adult studies regarding gender differences on psychiatric comorbidities have been conducted using non-ADHD controls(Babinski et al., 2011; Biederman, Faraone, Monuteaux, Bober, & Cadogen, 2004; Hesson & Fowler, 2015; Minde et al., 2003; Rucklidge, et al., 2014), of which only one study assessed gender $\times$ ADHD interaction on risk for psychiatric disorders that were evaluated by the Structured Clinical Interview for DSM-III-R(Biederman, et al., 2004). In this study, Biederman et al.(Biederman, et al., 2004) found no significant gender $\times$ ADHD interactions, consistent with our findings except for our finding on risk for dysthymia. However, since the Biederman et al. study used a referred sample of adult ADHD cases, some effects of referral bias must be considered. Our study is the first that evaluates gender $\times$ ADHD interactions on psychiatric disorders in a non-referred, adult population.

Findings from this study of psychiatric comorbidities among adults are strikingly similar to those from our earlier study of this issue among children with and without ADHD in this birth cohort(Yoshimasu, et al., 2012). Recent meta-analyses have revealed that the prevalence of childhood and adult ADHD are estimated to be 7.2% and 2.5%, respectively(Simon, Czobor, Balint, Meszaros, & Bitter, 2009; Thomas, Sanders, Doust, Beller, & Glasziou, 2015), indicating that persistence of ADHD into adulthood can be estimated to be 34.7% (2.5/7.2). This is consistent with our findings that the incidence of childhood ADHD among our sample was 7.4%(Barbaresi, et al., 2002) and almost 30% of these childhood cases met criteria for adult ADHD, which suggests that our sample can be regarded as representative of the general population and comparable between childhood and adulthood. Our earlier study in childhood was also strikingly similar, with boys having greater risk for externalizing psychiatric comorbidities, girls having greater risk for internalizing psychiatric comorbidities, and the gender $\times$ ADHD interaction was not significant for any psychiatric comorbidity(Yoshimasu, et al., 2012). Thus, our findings suggest that the pattern and risk for psychiatric comorbidities among males versus females with ADHD is similar in both childhood and adulthood. In addition, it should be noted that persistent ADHD might be more likely among severe childhood ADHD cases, but further study is needed to address this issue. Lastly, the findings from this study suggest a potential framework in which to better understand the association between ADHD and other psychiatric disorders. Our findings may be attributed to the impact of childhood ADHD symptoms on the emotional development of affected children and adolescents, as well as the continuing impact of ADHD symptoms in adulthood. While it is already clear from decades of research that persons with ADHD have genetically determined differences from their non-ADHD peers, it is also possible that there are distinct, genetically determined differences in

the neurobiology of individuals with childhood ADHD that does versus does not persist into adulthood. This study represents an important step in understanding the association between ADHD and other adult psychiatric disorders; however, further research is needed to disentangle the genetic, developmental and other potential explanations for this association.

Although our study employed a unique, population-based approach, with prospective follow-up and direct assessment of childhood ADHD cases and controls, our study does have several limitations. Though ADHD subtype has been shown to be an important variable in connection with risk of comorbid psychiatric disorders(Rucklidge, et al., 2014; Soendergaard et al., 2014; van Emmerik-van Oortmerssen et al., 2014), we were unable to obtain precise information about ADHD subtypes for our cases due to the nature of data available to determine childhood ADHD case status and the changes in terminology for ADHD subtypes over time. Thus, we were unable to address the issue of ADHD subtype on adult comorbidity and gender differences. Further, we did not have sufficient data to evaluate the severity of the psychiatric comorbidities. In addition, at the time of the study, Rochester, Minnesota was primarily a white, middle class community, so inferences to other populations or settings may be limited. However, the residents of Rochester have excellent access to medical care and comprise a homogeneous population (95% white) thereby minimizing the confounding effects of ethnicity and race on the study questions. Since we could not ascertain age of onset of the psychiatric disorders, it is unclear whether persistent ADHD preceded the development of psychiatric comorbidities. It may be that the persistent ADHD criteria can appear to be met because of the presence of adult mental disorders or that persistence of ADHD is a strong contributor to the development of other adult psychiatric disorders(Rutter et al., 2008). As suggested by Olazagasti et al.(Ramos Olazagasti et al., 2013), since children with ADHD can develop conduct disorder or antisocial personality disorder during adulthood, symptoms suggestive of persistent ADHD may be noted among adults with these disorders, even when they do not truly have adult ADHD. Finally, the limited number of females in our study limits comparison with males, as the 95% confidence intervals are extremely wide for some disorders in women.

Our findings in this population-based cohort demonstrate that persistent adult ADHD is associated with a significantly increased risk for a broad range of psychiatric comorbidities in both men and women. In contrast, risks for psychiatric disorders among adults with non-persistent ADHD are comparatively small. The strength of associations between psychiatric disorders and persistent ADHD did not differ between men and women, except that persistent ADHD was more strongly associated with dysthymia in adult women. Further, significant associations were observed between persistent ADHD and dysthymia as well as panic disorders in women, while persistent ADHD was significantly associated with alcohol and substance-related disorders in men. These findings highlight the need for careful consideration of psychiatric comorbidities among adults with ADHD, with heightened attention to possible internalizing disorders among women and externalizing disorders among men. Our findings also emphasize that the recognition and diagnosis of adult ADHD can be seriously complicated by the presence of comorbid psychiatric disorders(Mao & Findling, 2014). Future large scale studies are warranted to evaluate the comprehensive management for adults with ADHD with comorbid psychiatric disorders.

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Robert C. Colligan, PhD, is a former elementary and junior high school teacher, and consulting school psychologist. Later, he served as Head of Section–Psychology, Department of Psychology & Psychiatry at Mayo Clinic and was recipient of their Distinguished Career Award, and received a Lifetime Achievement award from the Minnesota Psychological Association. He is now Emeritus Consultant to the Mayo Clinic Department of Psychology & Psychiatry. He is Diplomate of the American Board of Professional Psychology (ABPP), Fellow of the Societies for Personality Assessment, Clinical Child and Adolescent Psychology, Clinical Psychology and Child and Family Policy. He has served as Co-Investigator on grants from several organizations, including the National Institutes of Mental Health and the National Institute of Health.

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Slavica K. Katusic, MD, is Associate Professor of Epidemiology and Pediatrics. As MD and Epidemiologist, she has more than 25 years of experience in assembling huge population based birth cohorts, maintaining a long standing research relationship with 41 public and private schools, and in getting the access to detailed birth certificate data. All of this, together with comprehensive medical records data available to every member of the birth cohort, allowed her and her team to study childhood development disorders (ex. ADHD) and their adult outcomes.

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FIGURE 1.

Flow diagram showing steps in the identification of persistent and non-persistent adult ADHD cases.

Table 1

Demographic and Perinatal Risk Factors^a among Adults with and without Persistent ADHD and Non-ADHD Controls

Factor	Persistent ADHD (N = 68)	Without Persistent ADHD (N = 164)	Non-ADHD Controls (N = 335)	P-value
Children				
Age on 12/31/2009, mean (SD)	30.2 (1.9)	30.0 (1.9)	30.2 (2.0)	0.50
Males, <i>n</i> (%)	49 (72.1)	118 (72.0)	210 (62.7)	0.07
White, <i>n</i> (%)	68 (100.0)	163 (99.4)	328 (98.2)	0.54
Birth weight <2500 gm, <i>n</i> (%)	3 (4.4)	7 (4.3)	16 (4.8)	0.96
Parents				
Mother's age, mean (SD)	25.5 (4.6)	26.1 (4.6)	26.8 (4.4)	0.05
Mother White, <i>n</i> (%)	68 (100.0)	163 (99.4)	329 (98.5)	0.59
Married, <i>n</i> (%)	61 (89.7)	151 (92.1)	313 (93.4)	0.54
Mother's education level, <i>n</i> (%)				0.23
<12	4/64 (6.2)	9/148 (6.1)	17/302 (5.6)	
12	28/64 (43.8)	60/148 (40.5)	96/302 (31.8)	
13–15	20/64 (31.2)	54/148 (36.5)	110/302 (36.4)	
16+	12/64 (18.8)	25/148 (16.9)	79/302 (26.2)	
Pregnancy/Labor/Delivery				
Pregnancy complications, <i>n</i> (%)	5 (7.4)	19 (11.6)	37 (11.0)	0.62
Labor/delivery complications, <i>n</i> (%)	19 (27.9)	65 (39.6)	115 (34.3)	0.21
Congenital anomalies, <i>n</i> (%)	0	2 (1.2)	0	0.17

^a Computerized birth certificate information for all birth cohort children were obtained from the Minnesota Department of Health.

Table 2

Burden of Comorbid Psychiatric Disorders among Adult Subjects with Persistent ADHD by Gender

M.I.N.I. Psychiatric Disorders	Persistent ADHD		P-value
	Men (N=49) N (%)	Women (N=19) N (%)	
Any psychiatric comorbidity	41 (83.7)	14 (73.7)	0.49
PTSD – current	2 (4.1)	4 (21.1)	0.047
Social phobia – current	5 (10.2)	5 (26.3)	0.13
OCD – current	11 (22.5)	3 (15.8)	0.74
Hypomanic episode – current or past	16 (32.7)	8 (42.1)	0.46
Generalized anxiety disorder – current	13 (26.5)	9 (47.4)	0.10
Dysthymia – current	4 (8.2)	7 (36.8)	0.008
MDD – current	11 (22.5)	8 (42.1)	0.10
Antisocial personality disorder	20 (40.8)	3 (15.8)	0.05
Alcohol dependence/abuse (12 mo.)	26 (53.1)	2 (10.5)	0.001
Panic disorder – lifetime	6 (12.2)	3 (15.8)	0.70
Suicidality – current	17 (34.7)	7 (36.8)	0.87
Substance dependence/abuse (12 mo.)	16 (32.7)	2 (10.5)	0.06

M.I.N.I.: The M.I.N.I.-International Neuropsychiatric Interview, PTSD: post-traumatic stress disorder, OCD: obsessive-compulsive disorder, MDD: major depressive disorder

Table 3

Risk of Comorbid Psychiatric Disorders among Adults with Persistent ADHD and Non-ADHD Controls

M.I.N.I. Psychiatric Disorders	Adult ADHD status		OR (95% CI)	
	Persistent ADHD (N=68) N (%)	Non-ADHD Controls (N=335) N (%)	Unadjusted	Adjusted ^a
Any psychiatric comorbidity	55 (80.9)	117 (34.9)	7.9 (4.1–15.0)	7.8 (4.0–15.3)
PTSD – current	6 (8.8)	3 (0.9)	10.7 (2.6–44.0)	10.0 (2.9–35.0)
Social phobia – current	10 (14.7)	4 (1.2)	14.3 (4.3–47.0)	12.8 (4.2–39.4)
OCD – current	14 (20.6)	8 (2.4)	10.6 (4.2–26.5)	8.0 (3.3–19.2)
Hypomanic episode – current or past	24 (35.3)	12 (3.6)	14.7 (6.9–31.4)	16.5 (7.2–37.4)
Generalized anxiety disorder – current	22 (32.4)	30 (9.0)	4.9 (2.6–9.1)	4.7 (2.4–9.0)
Dysthymia – current	11 (16.2)	4 (1.2)	16.0 (4.9–51.9)	19.0 (5.4–66.1)
MDD – current	19 (27.9)	9 (2.7)	14.0 (6.0–32.8)	15.2 (6.2–37.4)
Antisocial personality disorder	23 (33.8)	13 (3.9)	12.7 (6.0–26.8)	12.2 (5.3–27.9)
Alcohol dependence/abuse (12 mo.)	28 (41.2)	51 (15.2)	3.9 (2.2–6.9)	3.6 (2.0–6.7)
Panic disorder – lifetime	9 (13.2)	17 (5.1)	2.9 (1.2–6.7)	2.6 (1.1–6.2)
Suicidality – current	24 (35.3)	35 (10.5)	4.7 (2.5–8.6)	4.9 (2.6–9.4)
Substance dependence/abuse (12 mo.)	18 (26.5)	22 (6.6)	5.1 (2.6–10.2)	4.4 (2.1–9.1)

^a Adjusted for gender, maternal age, and maternal education. Statistically significant adjusted odds ratios (p<0.05) are indicated in bold font.

Table 4

Risk of Comorbid Psychiatric Disorders among Adults with Persistent ADHD and Non-ADHD Controls by Gender

	Men		Women	
	Persistent ADHD (N=49) vs. Non-ADHD controls (N=210)		Persistent ADHD (N=19) vs. Non-ADHD controls (N=125)	
M.I.N.I. Psychiatric Disorders	OR (95% CI)		OR (95% CI)	
	Unadjusted	Adjusted ^a	Unadjusted	Adjusted ^a
Any psychiatric comorbidity	8.5 (3.8–19.0)	7.6 (3.3–17.5)	6.4 (2.2–19.1)	7.5 (2.4–23.6)
PTSD – current	4.4 (0.6–32.2)	3.6 (0.7–17.7)	33.1 (3.5–315.6)	30.2 (4.2–217.6)
Social phobia – current	7.8 (1.8–34.0)	5.7 (1.5–21.5)	31.5 (4.7–211.4)	45.6 (6.3–329.8)
OCD – current	8.4 (3.1–23.0)	6.0 (2.3–16.0)	23.3 (2.3–237.1)	13.5 (2.5–72.5)
Hypomanic episode – current or past	16.5 (6.0–45.2)	17.6 (5.8–53.4)	14.4 (4.2–49.1)	17.6 (4.4–70.6)
Generalized anxiety disorder – current	3.6 (1.6–8.0)	3.0 (1.3–6.8)	9.3 (3.1–27.8)	9.5 (3.0–29.8)
Dysthymia – current	6.1 (1.3–28.4)	3.8 (1.0–14.7)	72.3 (8.2–638.0)	44.2 (7.5–261.2)
MDD – current	11.9 (3.9–36.1)	8.3 (2.9–23.8)	22.0 (5.7–84.8)	21.1 (5.2–85.5)
Antisocial personality disorder	13.8 (5.9–32.4)	14.1 (5.2–38.4)	7.6 (1.4–41.0)	7.3 (1.6–32.5)
Alcohol dependence/abuse (12 mo.)	4.5 (2.3–8.7)	4.3 (2.2–8.4)	1.5 (0.3–7.6)	1.7 (0.4–7.2)
Panic disorder – lifetime	2.8 (0.96–8.1)	2.0 (0.7–6.2)	3.2 (0.7–13.5)	3.8 (0.9–15.7)
Suicidality – current	7.4 (3.3–16.6)	5.8 (2.6–13.0)	2.9 (1.02–8.2)	3.5 (1.1–10.9)
Substance dependence/abuse (12 mo.)	4.9 (2.3–10.4)	4.3 (1.9–9.6)	4.8 (0.7–30.7)	4.4 (0.9–21.1)

^a Adjusted for maternal age and maternal education. Statistically significant adjusted odds ratios (p<0.05) are indicated in bold font.

Table 5

Risk of Comorbid Psychiatric Disorders among Subjects with Childhood Research-Identified ADHD With Versus Without Adult Persistent ADHD

M.I.N.I. Psychiatric Disorders	Adult ADHD status		OR (95% CI)	
	Persistent ADHD (N=68) N (%)	Without Persistent ADHD (N=164) N (%)	Unadjusted	Adjusted ^a
Any psychiatric comorbidity	55 (80.9)	77 (47.0)	4.8 (2.4–9.4)	5.1 (2.5–10.1)
PTSD – current	6 (8.8)	1 (0.6)	15.8 (1.9–133.6)	13.5 (2.4–74.5)
Social phobia – current	10 (14.7)	3 (1.8)	9.3 (2.5–34.8)	8.7 (2.6–28.6)
OCD – current	14 (20.6)	5 (3.1)	8.2 (2.8–24.0)	8.1 (2.8–23.8)
Hypomanic episode – current or past	24 (35.3)	11 (6.7)	7.6 (3.4–16.7)	8.5 (3.7–19.4)
Generalized anxiety disorder – current	22 (32.4)	11 (6.7)	6.7 (3.0–14.7)	7.9 (3.3–18.6)
Dysthymia – current	11 (16.2)	5 (3.1)	6.1 (2.0–18.4)	7.1 (2.2–23.1)
MDD – current	19 (27.9)	11 (6.7)	5.4 (2.4–12.1)	5.8 (2.5–13.5)
Antisocial personality disorder	23 (33.8)	16 (9.8)	4.7 (2.3–9.7)	5.7 (2.6–12.5)
Alcohol dependence/abuse (12 mo.)	28 (41.2)	33 (20.1)	2.8 (1.5–5.1)	3.2 (1.6–6.2)
Panic disorder – lifetime	9 (13.2)	8 (4.9)	3.0 (1.1–8.1)	2.9 (1.1–7.6)
Suicidality – current	24 (35.3)	27 (16.5)	2.8 (1.5–5.3)	2.7 (1.4–5.3)
Substance dependence/abuse (12 mo.)	18 (26.5)	20 (12.2)	2.6 (1.3–5.3)	2.6 (1.2–5.7)

^a Adjusted for gender, maternal age, and maternal education. Statistically significant adjusted odds ratios (p<0.05) are indicated in bold font.

Table 6

Risk of Comorbid Psychiatric Disorders among Subjects with Childhood Research-Identified ADHD With Versus Without Adult Persistent ADHD, By Gender

M.I.N.I. Psychiatric Disorders	Men Persistent ADHD (N=49) vs. Non-persistent ADHD (N=118)	Women Persistent ADHD (N=19) vs. Non-persistent ADHD (N=46)
	Unadjusted OR (95% CI) ^a	Unadjusted OR (95% CI) ^a
Any psychiatric comorbidity	6.3 (2.7–14.6)	2.6 (0.8–8.3)
PTSD – current	12.5 (0.6–269.0)	12.0 (1.2–115.9)
Social phobia – current	6.6 (1.2–35.2)	16.1 (1.7–149.3)
OCD – current	16.8 (3.6–79.1)	2.7 (0.5–14.7)
Hypomanic episode – current or past	7.7 (2.9–20.3)	7.6 (1.9–30.1)
Generalized anxiety disorder – current	8.2 (2.7–24.5)	6.0 (1.7–20.8)
Dysthymia – current	5.2 (0.9–29.1)	8.4 (1.9–37.3)
MDD – current	5.4 (1.9–15.6)	6.0 (1.6–21.9)
Antisocial personality disorder	5.6 (2.5–12.5)	2.7 (0.5–14.7)
Alcohol dependence/abuse (12 mo.)	3.8 (1.9–7.7)	0.8 (0.1–4.3)
Panic disorder – lifetime	4.0 (1.1–14.8)	2.0 (0.4–9.8)
Suicidality – current	3.6 (1.6–8.1)	1.7 (0.5–5.2)
Substance dependence/abuse (12 mo.)	2.7 (1.2–5.9)	2.6 (0.3–19.9)

^aStatistically significant unadjusted odds ratios (p<0.05) are indicated in bold font. Odds ratios adjusted for maternal age and maternal education are not reported by gender due to the limited number of women in the two comparison groups.