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## Annual Research Review: Attention-deficit/ hyperactivity disorder in girls and women: underrepresentation, longitudinal processes, and key directions

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Attention-deficit/hyperactivity disorder (ADHD) - and its underlying behavioral dimensions of inattention and hyperactivity-impulsivity - have been understudied in females. We first cover the conceptual issues of prevalence, diagnostic practices, diversity, comorbidity, and causal factors, plus forces limiting awareness of ADHD in females. After a narrative review of cross-sectional and longitudinal findings, we conclude the following. (a) Girls meet diagnostic criteria for ADHD at just under half the rates of boys, a ratio that becomes much closer to equal by adulthood. (b) Girls and women with ADHD show a predominance of inattention and associated internalizing problems; boys and men display greater levels of hyperactive-impulsive symptoms and associated externalizing problems. (c) Sex differences in ADHD symptoms and related outcomes depend heavily on the clinical versus nonreferred nature of the samples under investigation. (d) Females with ADHD experience, on average, serious impairments, with a particularly heightened risk for problems in close relationships and engagement in self-harm. (e) Clinicians may overlook symptoms and impairments in females because of less overt (but still impairing) symptom manifestations in girls and women and their frequent adoption of compensatory strategies. Our review of predictors and mediators of adult outcomes highlights (a) the potential for heterotypically continuous pathways in females with childhood ADHD and (b) developmental progressions to self-harm, intimate partner violence, unplanned pregnancy, and comorbid psychopathology. Focusing on ADHD in females is necessary to characterize causal and maintaining mechanisms with accuracy and to foster responsive interventions, as highlighted in our closing list of clinical implications and research priorities. Keywords: ADHD; developmental psychopathology; self-harm; girls and women.

### Introduction

Attention-deficit/hyperactivity disorder (ADHD) involves developmentally extreme and crosssituational manifestations of (a) inattention and/or (b) hyperactivity-impulsivity. Considerable research reveals substantial impairments in key domains of functioning throughout the life span for individuals either surpassing or falling just below diagnostic thresholds (Hinshaw, 2018). Given space limitations, we direct readers to the masterful review of developmental origins of ADHD in Nigg, Sibley, Thapar, and Karalunas (2020) and the provocative overview of biological correlates of ADHD during adolescent development in Shaw and Sudre (2021). Until recently, however, almost all research in this area has focused on boys and men. Female presentations have been largely overlooked in both clinical and research settings (Young et al., 2020). To redress this historical neglect, we provide current evidence on both (a) sex differences with respect to ADHD across the life span, and (b) female-specific impairments, mechanisms, and developmental pathways

(see Williamson & Johnston, 2015, for an incisive review of gender differences in adult ADHD).

Male-dominated samples have long characterized a great many behavioral science and biomedical endeavors (including animal research; see Beery & Zucker, 2011). Three decades ago, calls emerged for equitable representation of females in science and medicine (see U.S. guidelines [National Institutes of Health, 1994], which have received periodic updates; see also updated U.K. guidelines [Great Britain Home Office, 2018]). Eating disorders and depression, which both display female overrepresentation, are exceptions to this widespread trend. Yet even when mixed-sex samples are available, many scientists fail to examine sex-related differences or moderator effects (for enhancing research on sex differences, see Rich-Edwards, Kaiser, Chen, Manson, & Goldstein, 2018; Tannenbaum, Greaves, & Graham, 2016). Merit also exists in considering conditions like ADHD in an all-female context (Hinshaw, 2018; Owens, Zalecki, & Hinshaw, 2017).

Despite growing commitment to diversify research samples, a lack of substantial progress toward full female representation remains (Hartung & Lefler, 2019; Mazure & Jones, 2015; see also Eagly, Eaton, Rose, Riger, & McHugh, 2012). A similar critique can

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be made regarding the lack of research on, for example, males with eating disorders or depression. A core objective of gender-representative samples is generalizability, a point that also pertains to socioe-conomic and racial diversity. Empirically questioning the assumption of universal etiologies, developmental pathways, and/or therapeutic processes across males and females should result in better understanding of the underlying mechanisms. Similarly, comprehending sex differences in and female presentations of ADHD should enhance both scientific accuracy and clinical prowess.

As discussed below, the prevalence of ADHD in boys is 2-2.5 times higher than its prevalence in girls. A male predominance is the case for most if not all neurodevelopmental disorders (Rutter, Caspi, & Moffitt, 2003). We therefore open with three conceptual issues about sex differences. First, theories exist regarding the nature of psychopathology with lower prevalence in either sex (Eme, 1979, 1992; Gualtieri & Hicks, 1985). According to the 'gender paradox' (Loeber & Keenan, 1994), the sex with lower prevalence is expected to display more severe features as well as higher rates of comorbid disorders. Two explanatory models are relevant. (a) The polygenetic multiple threshold model holds that the lowerprevalence sex (e.g., females with ADHD) would need to have greater levels of family history and a higher genetic 'load' and/or environmental disadvantage to meet diagnostic criteria (see Taylor et al., 2016). (b) In the constitutional variability model, boys are slower to mature than girls, leading to a greater propensity for exhibiting a wide spectrum of neurodevelopmental symptoms. Given the extreme gender atypicality of her symptoms in relation to other females, a girl with significant ADHD would thus be likely to have demonstrable neural dysfunction.

Second, even in representative samples, the sex ratio of diagnosed ADHD approaches 1.5:1 or lower during the adult years (Kessler et al., 2006; Nussbaum, 2012). For one thing, girls are more likely than boys to display inattention as the predominant symptom domain (Biederman et al., 2002), and inattentive symptoms are more likely to persist through adulthood (e.g., Döpfner, Hautmann, Görtz-Dorten, Klasen, & Ravens-Sieberer, 2015; Larsson, Dilshad, Lichtenstein, & Barker, 2011). Thus, females appear prone to display a more 'lifepersistent' form of ADHD. As well, symptom lists for ADHD are biased toward male behaviors (e.g., physical overactivity or extreme risk-taking) as opposed to female-related manifestations (e.g., excessive verbalizations or more subtle indicators of impulsivity; see Quinn & Madhoo, 2014; Young et al., 2020). Furthermore, females are less likely than males to display disruptive behaviors (or at least have a later onset of such), curtailing early detection. Finally, children are rated for ADHD via parent and teacher reports, but adult assessment is typically based on self-report - with women more likely to disclose

relevant problems (e.g., Millenet et al., 2018; Vildalen, Brevik, Haavik, & Lundervold, 2019).

Third, as reviewed by Asherson and Agnew-Blais (2019), over the last decade several birth-cohort studies challenged the assumption that ADHD is a neurodevelopmental disorder inevitably beginning in childhood. Strikingly, adult-onset individuals in these investigations comprised half or more women. Yet (a) many such cases have heightened but subthreshold ADHD symptoms in childhood, (b) comorbidities explain a substantial proportion of so-called adult-emergent cases, and (c) far more evidence exists for adolescent or very-early adult onset of ADHD than in later adulthood. Regardless, ADHD is increasingly salient for females by the adult years.

We provide a final note on terminology, as to whether discussion should focus on *gender* versus *sex* differences (Gentile, 1993). Following convention, we use *sex* to denote biological male or female status (acknowledging that this designation is not a binary) and *gender* to depict the social and/or cultural roles applied to biological sex or the personal identification with such roles.

# ADHD and psychopathology: background issues

The topic of ADHD is the subject of a voluminous and still-growing literature. Issues regarding this diagnosis are often controversial in both science and the public eye (Hinshaw, 2018). We contend that a developmental psychopathology perspective is essential (Hinshaw, 2017). Rather than viewing ADHD as a static diagnostic entity, a focus on its dimensional components is often fruitful (see the Research Domain Criteria [RDoC]; Cuthbert & Insel, 2013). Furthermore, incorporating concepts such as transactional models of development, multiple levels of analysis, heterotypic continuity, and the confluence of heritable and psychosocial underpinnings of symptom domains will continue to be illuminating.

### Prevalence, including race/ethnicity

Given the lack of validated biomarkers for any mental health or neurodevelopmental syndrome, it is impossible to gauge the actual prevalence of conditions like ADHD. Diagnosed prevalence rates of ADHD in the United States have been rising steadily over the past several decades in both boys and girls (Hinshaw & Scheffler, 2014). According to population surveys, 9.4% of all children and adolescents aged 2-17 years have received an ADHD diagnosis, as reported by parents, with a male: female sex ratio of 2.3:1 (Danielson et al., 2018). Such estimates are above those of nearly every other country on earth with relevant data, especially when rarely diagnosed 2- to 3-year-olds are excluded (Polanczyk, De Lima, Horta, Biederman, & Rohde, 2007; Polanczyk, Willcutt, Salum, Kieling, & Rohde,

2014). We note, however, that regional differences are evident in the United States and other countries. One potential explanation has to do with schooltesting policies known as consequential accountability statutes (Fulton, Scheffler, & Hinshaw, 2015). An unintended consequence is that rates of ADHD diagnosis rise precipitously for a state's most impoverished children when such 'test scores at all costs' policies are enacted (Hinshaw & Scheffler, 2014). In addition, Caye et al. (2020) review the effect of 'relative age' – that is, being young for one's grade level – on the propensity for ADHD diagnosis. In both instances, sex differences are unclear.

Regarding adult ADHD, prevalence estimates are confounded by the developmental reality that physical activity and behavioral impulsivity decline from childhood through adulthood (e.g., Larsson et al., 2011). After the teen years, it becomes difficult to ascertain when symptom levels are indicative of remission. Accordingly, estimates of the percentage of children who maintain the diagnosis into adulthood range widely, from under one-third to a substantial majority (Guelzow, Loya, & Hinshaw, 2017; Sibley et al., 2021). Still, a growing consensus is that well over half of diagnosed children display impairing adult symptoms even when strict diagnostic criteria are no longer met (Biederman et al., 2010; Uchida, Spencer, Faraone, & Biederman, 2018).

The racial composition of who gets diagnosed with ADHD has shifted substantially of late, at least in the United States. Although diagnosis was reserved largely for White, middle-class boys during the 20th century, Cénat et al. (2021) documented that Black youth have now surpassed White youth in terms of diagnosed prevalence, in both sexes (see also Danielson et al., 2018). Furthermore, although Latinx youth have traditionally had lower diagnostic rates than other ethnic groups, the gap is closing (Hinshaw & Scheffler, 2014). Greater awareness among professionals is relevant, but it is possible that ADHD may become - or has recently become - a convenient diagnostic label for youth experiencing impoverishment and/or trauma (Hinshaw & Scheffler, 2014).

### Diagnostic practices

Related to this last point, we comment briefly on the kinds of assessment practices typically used to diagnose ADHD in clinical as opposed to research settings. Despite evidence-based guidelines prepared by the American Academy of Child and Adolescent Psychiatry (Pliszka & AACAP Work Group on Quality Issues, 2007) and the American Academy of Pediatrics (Wolraich et al., 2019) in the United States, and the National Institute for Health and Care Excellence (2019) in the U.K., general pediatricians and adult practitioners are often not sufficiently trained in (or reimbursed for, in the United States) such evidence-based assessments. A 15-

minute office visit without normed informant rating scales, developmental histories, medical examinations, or testing to consider comorbid psychiatric and learning conditions may lead to both overdiagnosis and underdiagnosis, with the former more likely for boys but the latter for girls (Hinshaw & Scheffler, 2014). Major dividends should accrue from adequate resources for accurate assessments, including the recognition that ADHD clearly exists in girls and women. In addition, inattentive symptoms should be accounted for across the life span, especially during transitions from elementary to secondary school, which present new challenges with less adult scaffolding, and to pregnancy and parenthood, including hormonal changes that may exacerbate symptoms (Young et al., 2020). Finally, mood and anxiety symptoms frequently accompany female ADHD, mandating careful differential and/or additional diagnosis, particularly given the high risk for self-harm in females with ADHD.

### Clinical vs. representative samples

Biases accrue from making generalizations about causal mechanisms, symptom profiles, or treatment responses in clinically referred versus nonreferred/population-based samples (Goodman et al., 1997; LeWinn, Sheridan, Keyes, Hamilton, & McLaughlin, 2017). As highlighted below, conclusions about sex differences in levels of ADHD-related symptoms and/or impairments can differ dramatically depending on referral source.

### Comorbidity and associated psychopathology

Individuals with any given mental condition are highly likely to experience additional syndromes (Angold, Costello, & Erkanli, 1999; Caron & Rutter, 1991). By definition, such comorbidity comprises the joint presence of two or more independent manifestations of psychopathology. Yet the extraordinarily high rates of comorbidity - far above levels predictable if the underlying conditions were truly independent – lend strong suspicion to the idea that other mechanisms are at play. Supposedly independent disorders may be linked in terms of risk factors and even symptoms. Moreover, a general liability to all forms of mental disorder is increasingly investigated, with respect to the so-called general psychopathology (or 'p') factor (e.g., Caspi et al., 2014). Finally, what appears to be the sequential presence of different categorical diagnoses – for example, from early ADHD to later conduct disorder, followed by substance use disorders and adult antisocial personality disorder for males and self-harmful behaviors and adult borderline personality disorder for females (e.g., Beauchaine, Hinshaw, & Bridge, 2019) - may actually reflect heterotypic continuity (Hinshaw, 2017). This concept denotes the stability of an underlying predisposition that yields changing

symptoms across development as the result of a range of biological and contextual forces.

### Heritable and psychosocial influences

Genetically informative investigations reveal that ADHD, appraised dimensionally or categorically, is strongly heritable (e.g., Faraone & Larsson, 2019; Thapar, 2018; for an informative review of potential genetic and endocrine mechanisms potentially underlying sex differences, see Davies, 2014). Yet high heritability does not imply that symptom presentation and/or impairment are devoid of environmental input (e.g., Lahey, 2021). Indeed, extreme environmental deprivation may engender inattention and overactivity (usually linked with highly aberrant attachment; see Kreppner, O'Connor, & Rutter, 2001). In more typical cases, negative parent-child interactions often maintain and exacerbate heritable tendencies toward impulsivity and dysregulation (Beauchaine & McNulty, 2013), even in adoptive families (Sellers et al., 2021). For girls with ADHD, parenting stress related to caring for such a daughter can magnify the underlying tendencies and predict subsequent impairment in adolescence and beyond (Gordon & Hinshaw, 2017).

Nonheritable biological risk factors - such as prenatal maternal alcohol or nicotine use, low birthweight, or exposure to toxic substances early in life - are implicated in some cases of ADHD. Genetic vulnerability may well statistically interact with environmental triggers in the genesis of significant symptoms; inflammatory processes may also play a role (Nigg et al., 2020). All too little research exists on sex differences in the unfolding of such transactional processes (see Martin et al., 2018, for findings related to common-versus rare-variant genotypes in males versus females). Important intraindividual mechanisms linked to ADHD - dysregulated attention, poor executive functions (e.g., working memory, response inhibition), low intrinsic motivation, and emotion dysregulation (for at least a subgroup) - are well established (Sonuga-Barke & Halperin, 2010). Still, most of the relevant research emanates from predominantly or exclusively male samples.

Loyer Carbonneau, Demers, Bigras, and Guay (2020) provided a comprehensive meta-analysis of symptoms and underlying mechanisms related to sex differences in youth with ADHD. In short, objective indicators revealed that boys show greater hyperactivity than girls but statistically equivalent levels of inattention. Yet teachers rate boys as higher on both, with the clear implication that adult ratings may lead to underreporting and underdiagnosis of ADHD in girls (see Abikoff, Courtney, Pelham, & Koplewicz, 1993, regarding halo effects in adult informant ratings). Regarding executive functions, girls with ADHD have, on average, greater cognitive

flexibility, and better motor response inhibition than boys, although the sexes are similar with respect to interference control and working memory (Loyer Carbonneau et al., 2020). Overall, it is essential to examine sex differences in, and female-specific manifestations of, both symptoms/impairments and mechanistic processes.

### Girls with ADHD: what do we know?

Pioneering work in the systematic investigation of females with ADHD began four decades ago (e.g., Ackerman, Sykman, & Oglesby, 1983; Kashani, Chapel, Ellis, & Shekim, 1979; for other early empirical studies, see Berry, Shaywitz, & Shaywitz, 1985; Biederman et al., 1994; James & Taylor, 1990; Mannuzza & Gittelman, 1984; McGee & Feehan, 1991). Because many mixed-sex samples had extremely small female subsamples (e.g., Barkley, Fischer, Smallish, & Fletcher, 2002), calls for focus on girls and women with ADHD have continued (Barkley, 2002; Nussbaum, 2012; Quinn & Madhoo, 2014; Staller & Faraone, 2006).

Key reasons for the longstanding underrepresentation of females with ADHD include the following: (a) long-term scientific/professional insistence that the condition was vanishingly rare in girls (and even more so in women, as ADHD was assumed to be childhood-limited); (b) predominance of the inattentive (and less visibly impairing) presentation in females (e.g., Biederman et al., 2002; Lahey et al., 1994); (c) lower rates of co-occurring disruptive behavior disorders in girls or later onset of such (Uchida et al., 2018), suppressing the visibility and salience of female symptoms (Mowlem, Rosenqvist, et al., 2019); (d) clinician bias that ADHD symptoms are indicative of the diagnosis in boys but not girls (Bruchmüller, Margraf, & Schneider, 2012); (e) the finding that parent and teacher ratings systematically underreport female, as opposed to male, ADHD behavior patterns, even when objectively observed behaviors are matched between the sexes (Meyer, Stevenson, & Sonuga-Barke, 2020); and (f) higher rates of compensatory behaviors in females (Mowlem, Agnew-Blais, Agnew-Blais, Taylor, & Asherson, 2019). We selectively review findings in childhood through mid-adolescence.

In an intriguing early study, James and Taylor (1990) extracted a small sample of 61 boys and 18 girls with diagnosed hyperkinetic disorder – a diagnosis far more stringent than the current ADHD criteria – from a large clinical sample. The female subsample was overrepresented with language disorders and low IQ scores compared with the male subsample (see Berry et al., 1985, who also found greater peer rejection in their female sample; see also Rokeach & Wiener, 2018, regarding relationship quality in female vs. male adolescents with ADHD). Such a pattern is just what would be predicted from the constitutional variability model.

Yet clinical samples are, by definition, not representative of the population (Goodman et al., 1997). The importance of sampling issues cannot be overstated: The important, early meta-analytic reviews of sex differences in ADHD (Gaub & Carlson, 1997; Gershon, 2002) gave ample evidence that the type of sample investigated (clinical versus nonreferred/community) had considerable effect on conclusions. Gaub and Carlson (1997) found that, overall, boys display greater symptom severity and externalizing comorbidity levels than girls, whereas the latter reveal greater cognitive impairments. Yet both referral source and informant (e.g., parent vs. teacher) were crucial moderators, as opposite patterns of findings for the two types of samples and raters sometimes emerged. Additional clinical samples yield contradictory outcomes regarding whether girls with ADHD have equivalent social impairment as boys (Greene et al., 2001) or greater social/ academic deficits (Rucklidge & Tannock, 2001; see also Elkins, Malone, Keyes, Iacono, & McGue, 2011). If girls with ADHD actually have fewer/less severe symptoms than boys, a core tenet of the gender paradox would be violated, obviating the need for polygenetic multiple threshold versus constitutional variability explanations.

A major step forward occurred via the Massachusetts General Hospital (MGH) studies of boys and girls with ADHD (see Uchida et al., 2018, for review of relevant publications). Both boys and girls with ADHD and those without (all aged 6–17 years) were recruited from psychiatric and pediatric referral sources and followed over time. Note that the sample was predominantly White and initially diagnosed using DSM-III-R criteria, but important methodological advantages (e.g., blinded assessments, ascertainment of familiality, measures of educational and cognitive functioning beyond symptoms/diagnoses per se) yielded crucial findings. Indeed, in this unprecedentedly large sample of carefully diagnosed girls with ADHD (n = 140), comorbidities and impairments were clearly evident, belying the view that ADHD was nonexistent or of trivial importance for females. In fact, functional impairment levels matched those of their male ADHD sample, as did rates of comorbid disorders (although girls showed later onset of disruptive behavior problems; Biederman et al., 1994). Most female impairments were evident when covarying comorbid conditions, signaling that ADHD itself predicted impairment.

An equal-sized sample of ethnically and socioeconomically diverse girls with ADHD aged 6–12 years at baseline – plus 88 age- and ethnicity-matched comparison girls – was described in Hinshaw (2002) and Hinshaw, Carte, Sami, Treuting, and Zupan (2002). Participants were carefully diagnosed with ADHD using DSM-IV criteria and took part in a 5-week naturalistic research summer program, affording behavioral observations and peer sociometric

nominations in addition to adult informant reports and individualized testing data (the investigation is termed the Berkeley Girls with ADHD Longitudinal Study, or BGALS). In relation to the comparison group, the ADHD participants were impaired in all domains of measured functioning (e.g., symptoms, associated psychopathology, family stress, peer relationships, academics, neuropsychological measures, use of special services, self-perceptions), with effect sizes ranging from medium to extremely large. Findings held with stringent covariation of demographic and cognitive factors and, in most cases, comorbidities. In the first systematic contrast of Inattentive versus Combined presentations in girls, both subgroups were highly impaired in relation to the comparison participants but differed significantly from each other only for externalizing behaviors and peer rejection, with the Combined subgroup scoring higher for each. Five-year prospective follow-up into middle adolescence (Hinshaw, Carte, Fan, Jassy, & Owens, 2007; Hinshaw, Owens, Sami, & Fargeon, 2006) revealed enduring impairment in all domains examined. Additionally, the proportion of the ADHD sample meeting criteria for overall positive adjustment was distressingly low (Owens, Hinshaw, Lee, & Lahey, 2009). Selected additional findings from BGALS data are reviewed in Owens et al. (2017).

In a large community survey of girls meeting criteria for hyperactivity, conduct problems, or both, followed from childhood to mid-adolescence, Young, Heptinstall, Sonuga-Barke, Chadwick, and Taylor (2005) found that hyperactivity was particularly predictive of pervasive adolescent academic and interpersonal problems. Lahey et al. (2007) found that ADHD in preschool predicted subsequent early-adolescent comorbidities in both sexes, with predictions to internalizing comorbidities especially strong for girls.

Overall: First, sex ratios reveal a male predominance of over 2:1 for ADHD in childhood and adolescence (Danielson et al., 2018). Second, subtle yet important differences in symptoms exist, with respect, for example, to greater verbal overactivity in females versus physical overactivity in males (Young et al., 2020). Also, many girls with ADHD, particularly those with predominant inattention, may compensate with intensive effort and coping strategies (including family coping), masking key impairments and lowering the chance for recognition (Mowlem, Agnew-Blais, et al., 2019). Third, comorbidity (regarding categorical diagnoses) and associated features (regarding dimensional variables) differ, as males reveal stronger linkages with externalizing problems (at least in childhood) and females with internalizing problems and possibly language disorders and neurological problems (e.g., Tung et al., 2016). Fourth, ADHD is highly impairing in girls during childhood and adolescence regarding major domains of life functioning (Hinshaw, 2018).

# Developmental progressions, mediators, and heterotypic continuity by adulthood

The core questions here pertain to outcomes encountered by girls with ADHD by adulthood, along with childhood predictor variables and adolescent mediator processes that may presage long-term impairments. We also summarize selected cross-sectional investigations of women with ADHD. Some studies of quite-small female subsamples have yielded provocative exploratory findings (e.g., Barkley et al., 2002; Sarver, McCart, Sheidow, & Letourneau, 2014). Additionally, Babinski et al. (2010) followed 34 young women with childhood-diagnosed ADHD and 24 without, to the end of adolescence. ADHDrelated impairments emerged for some domains (e.g., conflict with parents, depression, fewer romantic relationships) but not for others (e.g., job performance, substance use).

In the MGH sample, follow-up revealed continuing symptoms and impairments in girls with carefully diagnosed baseline ADHD (Biederman et al., 2010; see also Biederman et al., 2006). Although half or fewer of such participants met full diagnostic criteria by early adulthood, over two-thirds revealed above-normative symptom levels plus clear functional impairments (Uchida et al., 2018; see also Owens et al., 2017; Sibley et al., 2021). As for comorbid disorders, Biederman et al. (2010) demonstrated that rates of antisocial, mood, anxiety, developmental, addictive, and eating disorders were substantially elevated beyond those of the comparison participants. Furthermore, compared with the MGH males who also were followed longitudinally, the female sample showed lower rates of adult antisocial behaviors but higher rates of mood and anxiety disorders. Executive functioning performance was also compromised (Seidman et al., 2006). These findings withstood stringent statistical adjustment for potentially confounding variables (see Mick et al., 2011, for data on predictors of follow-up status).

In the BGALS follow-ups through an average age of 20 (Hinshaw et al., 2012) and then 26 years (Owens et al., 2017) – for which participant retention rates ranged from 93% to 95% - the focus was on functional impairments. Findings revealed large and statistically significant impairment relative to the comparison sample, even with stringent statistical adjustment for demographic and cognitive factors. Noteworthy were academic underperformance (especially in mathematics), internalizing disorders, poor executive functions (Gordon & Hinshaw, 2020), employment-related problems, unplanned pregnancy rates (43% in the ADHD sample versus 11% of comparisons), high risk for intimate partner violence (Guendelman, Ahmad, Ahmad, Meza, Owens, & Hinshaw, 2016), and early engagement in oral sex (Halkett & Hinshaw, 2021). Yet evidence

for beyond-normative substance use problems (except nicotine), driving problems, and eating problems was not found.

Other investigations corroborate serious impairment. In a relatively early longitudinal study, Dalsgaard, Mortensen, Frydenberg, and Thomsen (2002) discovered that girls with ADHD (especially those with comorbid conduct problems) had significantly higher risk than parallel boys for subsequent adult inpatient psychiatric admissions. In a large Norwegian investigation of women and men with ADHD in adulthood, Fredriksen et al. (2014) found larger incidence of lifetime work-related disability in the female subsample; inattentive symptoms were especially predictive of such difficulties. Furthermore, marked risk for teen motherhood - 15% for females with ADHD versus 3% for comparisons - was revealed in the Swedish cohort study of Skoglund et al. (2019), who also found elevated prenatal and perinatal complications related to those births.

Given its rising rates (especially in females) and clear public-health importance, we focus on self-harm, including nonsuicidal self-injury (NSSI) and suicidal behavior. Population studies have revealed a sizable risk for such behaviors among individuals with ADHD (Chen et al., 2014; Hurtig, Taanila, Moilanen, Nordström, & Ebeling, 2012; see review in Garas & Balázs, 2020). As for longitudinal findings, Chronis-Tuscano et al. (2010) found that, among preschoolers with ADHD reassessed in early to late adolescence, rates of depression and suicide attempts were elevated in relation to comparison youth, despite stringent use of covariates. Crucially, these rates were significantly higher in the female compared with male subsample. In more recent research, women with ADHD had particularly high rates of NSSI (Balázs, Győri, Horváth, Mészáros, & Szentiványi, 2018), suicidal ideation (Babinski, Neely, Ba, & Liu, 2020), and suicidal behavior (Fitzgerald, Dalsgaard, Nordentoft, & Erlangsen, 2019), even as compared with their male counterparts.

For the initial BGALS indication of increased risk for self-harm, Hinshaw et al. (2012). reported that, by early adulthood, girls with childhood ADHD-Combined (but not Inattentive) presentation had markedly higher rates of attempted suicide (22% for ADHD-C, 8% for ADHD-I, and 6% for comparisons) and moderate-to-severe NSSI (51%, 29%, and 19%, respectively), even with stringent use of key covariates (see also Owens et al., 2017). A series of theoretically driven mediator analyses followed. (a) Swanson, Owens, and Hinshaw (2014) found that early-to-mid-adolescent internalizing behaviors (as reported by parents, teachers, and participants) significantly and partially mediated the link between childhood ADHD and subsequent suicide attempts, but adolescent externalizing behaviors (parent- and teacher-reported) and an objective indicator of poor executive functioning were parallel mediators of NSSI. (b) Regarding peer relationships, Meza, Owens, and Hinshaw (2016) reported that teacherreported peer rejection in adolescence significantly and partially mediated the link to subsequent suicide attempts, whereas self-reported peer victimization mediated the link to NSSI. (c) As for maltreatment, Guendelman, Owens, Owens, Galan, Gard, and Hinshaw (2016) utilized multi-informant, blinded ratings of each BGALS participant for evidence of physical abuse, sexual abuse, and/or neglect in childhood through early adolescence. For one thing, ADHD participants showed greater incidence of maltreatment than the comparisons. Next, and crucially, among ADHD participants the experience of one or more forms of such maltreatment predicted both depression and elevated risk for suicide attempts by early adulthood. In fact, the rate of such attempts was over 33% for participants with childhood ADHD who had also experienced one or more forms of maltreatment. In short, the combination of maltreatment and highly heritable ADHD symptoms was linked to an extraordinarily high risk for suicidal behavior - paralleling work on bipolar disorder, also highly heritable, for which maltreatment predicts heightened risk of suicidality (Brown, McBride, Bauer, & Williford, 2005). In short, reductionistic accounts of relevant risk as either exclusively heritable or exclusively contextual are not accurate.

Meza, Owens, and Hinshaw (2020) examined childhood predictors of NSSI, suicidal ideation, and suicide attempts in BGALS participants followed through their mid-20s. Key predictors of NSSI were childhood ADHD symptoms, externalizing behaviors, poor executive functioning, and participant perceptions of paternal (but not maternal) negative parenting. The significant childhood predictors of suicidal ideation were low perceived self-competence and a history of adverse child experiences; for attempted suicide, the significant predictors were elevatedchildhood ADHD symptoms (both inattention and hyperactivity-impulsivity), adverse childhood experiences, and low perceived self-competence. Interacpredictor tions between variables emerged, indicating moderation effects. For example, regarding lifetime NSSI, 80% of participants with this form of self-injury had childhood externalizing and internalizing scores in the clinical range plus poor childhood executive functioning.

In short, for substantial numbers of girls with ADHD, a heterotypically continuous trajectory from early impulsivity (and in some cases, high levels of concurrent early inattention) is salient. Associated psychopathology (internalizing and/or externalizing), executive dysfunction, maltreatment or other early adverse experiences, negative father-daughter interactions, low self-worth, and peer victimization/rejection are implicated. Such process-oriented findings may aid with intervention (see O'Grady & Hinshaw, 2021, for commentary).

Regarding unplanned pregnancy, Owens and Hinshaw (2020) found that mid-adolescent academic underachievement was part of a serial mediation pathway, whereby childhood ADHD predicted low academic performance in mid-adolescence, which in turn mediated late-adolescent engagement in risky sexual behavior, with resultant high rates of unplanned pregnancy. In addition, low academic performance in adolescence mediated the linkage between childhood ADHD and the later experience of intimate partner violence (Guendelman, Ahmad, et al., 2016).

Finally, Owens and Hinshaw (2016) presented a complex set of serial, indirect effect, mediator models, from childhood neurocognitive vulnerability through early- and late-adolescent psychological processes and then to internalizing/externalizing comorbidity in adulthood. Such comorbidity was marked by adolescent paths incorporating (a) poor self-control/delay of gratification and (b) academic underachievement/school failure. In all, relevant developmental processes for females are variegated, embedded in intraindividual, family-related, and school contexts.

# Unresolved issues and core recommendations for future directions

Unresolved issues

First, given significant female impairments linked with ADHD, a core issue is whether girls and women should be diagnosed in relation to overall norms (emanating from both males and females) versus female-specific norms. With the latter, girls would more easily meet symptom thresholds, as they would be compared with the 'lower bar' of average female levels of ADHD symptoms (Reid et al., 2000). A parallel argument might be made for depression in males: More men would be diagnosed if their symptoms were compared with male norms, partly redressing the doubled female:male sex ratio for depression that begins in adolescence. Yet we urge caution. It would need to be definitively established that girls qualifying for an ADHD diagnosis (or men, for depression) on the basis of sex-specific norms reveal clear impairments. Otherwise, rates of diagnosis in females with ADHD could become overinflated. In the absence of such evidence, it may be preferable to ensure that (a) diagnostic items reflect both male- and female-specific manifestations, (b) subtle indicators of inattention/disorganization are probed, and (c) clinicians inquire about such factors as compensatory behaviors and life transitions in girls and women (Young et al., 2020).

Second, we note that important issues of culture, diversity, and stigma with regard to ADHD need amplification. Despite critics' contentions that ADHD is an exclusive product of major pressures for educational and vocational success, Western

culture, unresponsive schools (including compulsory education), or lax parenting, the relatively consistent prevalence rates around the world (Polanczyk et al., 2007) and the strong contributions of psychobiological risk factors argue otherwise (for a classic debate, see Timimi & Taylor, 2004). Still, rates and types of various treatments vary substantially around the world (Hinshaw et al., 2011). As well, cultural and social forces markedly affect personal and family acceptance as well as adaptation (Asherson et al., 2012) - as well as high rates of diagnosed prevalence in the United States (Hinshaw & Scheffler, 2014). Far too little is known about the experience of ADHD in non-Western/post-industrial cultures and in racial groups beyond Whites. Especially given increased recognition and diagnosis of ADHD in Black youth (Cénat et al., 2021) and lower-SES individuals (Hinshaw & Scheffler, 2014), it is essential to include diverse participants in research investigations, including girls and women with ADHD beyond middle-class, majority individuals.

As for stigma, a review by Nguyen and Hinshaw (2020) highlights considerable evidence for public stigma, internalized stigma, and associated stigma for youth and adults with ADHD (for a general review, see Martinez & Hinshaw, 2016; for negative adult attitudes regarding youth ADHD, see Pescosolido et al., 2008). Despite the belief that stigmatization is reserved for psychotic conditions such as schizophrenia, it is highly likely that disorders marked by inconsistency of performance, like ADHD, can fuel harsh castigation – perhaps because of the belief that insufficient effort is the underlying cause. Furthermore, for girls and women, traditionally valued for social skills and cohesion, interpersonal difficulties related to ADHD may be particularly stigmatized (e.g., Blachman & Hinshaw, 2002).

Third, space limitations preclude any kind of systematic review of sex differences in ADHD-related treatment response. Evidence does not reveal major differences in female versus male responses to psychosocial or pharmacologic interventions. In a recent review of medications, Kok, Groen, Fuermaier, and Tucha (2020) found that girls with ADHD were less likely to be treated with medications than boys (see also Mowlem, Rosenqvist, et al., 2019), yet overall results revealed sex-equivalent outcomes in response to medication. Still, females appear to encounter more adverse reactions to stimulants and may respond preferentially to nonstimulants like selective norepinephrine reuptake inhibitors. And, in the largest clinical trial ever conducted for children with ADHD, including 20% girls among its 579 participants, both behavioral and stimulant medication-related treatment effects were not moderated by sex (MTA Cooperative Group, 1999). Yet female samples or subsamples are sufficiently small in most investigations to preclude detection of sex-specific findings.

Authoritative sources such as Quinn and Madhoo (2014) and Young et al. (2020) caution that

psychosocial interventions should be tailored to female-specific manifestations and sensibilities (e.g., prioritizing group interventions, focusing on inattention and on relationship issues). A model intervention in this regard is the Child Life and Attention Skills curriculum, designed for both boys and girls with the Inattentive presentation. It revealed positive benefits in a randomized controlled trial (Pfiffner et al., 2014). Finally, unless girls and women are accurately detected for ADHD during the evaluation and diagnostic process, they may never receive evidence-based treatments.

### Recommendations and brief research agenda

Based on the preceding review, we present a brief, bullet-point listing of recommended practices regarding assessment and treatment, as well as research priorities.

Regarding evaluation and assessment:

- The assumption that girls and women simply do not exhibit ADHD or do so only rarely is no longer tenable.
- A thorough, evidence-based evaluation is essential, including assessment of comorbid behavioral, emotional, and learning issues.
- Many assessment scales laden are with items emphasizing male forms of ADHD but do not focus sufficiently on potential female-relevant behaviors (e.g., hyper-verbal behavior versus overly active physical behavior). Moreover, teachers may underreport ADHD symptoms in girls.
- Many girls with actual ADHD may be hard to identify given their tendency to present with exclusive inattention, relative lack of externalizing behaviors, comorbid presence of anxiety and/ or depression, and use of compensatory strategies and family supports that may mask core symptoms (see Young et al., 2020, who also emphasize that highly structured environments can mask ADHD).
- Times of life transition to formal schooling, secondary education, challenging university/ vocational venues; economic independence; and pregnancy/childbearing may well be triggering of symptom exacerbation. Thus, developmental histories are essential.
- Evaluation of strengths in the assessment process is crucial, as their elucidation may be important targets for treatment planning.

### Regarding treatment:

 Families of girls with ADHD are marked by stress, discordant parenting, and potential invalidation of their daughter (Beauchaine et al., 2019; Gordon & Hinshaw, 2017). Parent management interventions (including emotion regulation skills for parents), combined with school-

- based programs and active promotion of social skills, are evidence-based ideals.
- There are no definitive data that ADHD medications reveal greatly different effects in females than males, although nonstimulants may be indicted more in girls and women.
- Beyond symptom reduction, treatments should emphasize academic engagement/skills, monitoring of peer interactions, reduction in risk for maltreatment, and building of self-concept (not falsely but through development of competencies). Education around sexuality, protected sex, and prevention of partner violence are also clearly in order.

### In terms of research priorities:

- A key direction should be not only more precise estimates of sex differences in symptoms and impairments but also female-specific elucidation of heterotypically continuous developmental pathways to self-harm, relationship difficulties, unplanned pregnancy, and subsequent parenting of the next generation. Although expensive, prospective longitudinal research is necessary for such elucidation.
- Greater female representation (of both parents and offspring) is needed in genetic and epigenetic investigations; in follow-up of prenatal and perinatal risk factors; and in studies of the roles of parenting practices, parenting stress, and parental psychopathology. Also, studies of biological and psychosocial changes related to transitions to puberty and subsequently to childbirth and childrearing as well as perimenopause and menopause in women are sorely needed.

- In the transition to adolescence and adulthood, self-report is more widely utilized for assessment than exclusively informant report. Additional research is needed on the validity of self-report, particularly for adolescent girls and women. It may be that female self-report is more accurate than that of men, with implications for the decreasing sex ratio of ADHD diagnosis by adulthood.
- Determination of later life health risks, including neurodegenerative disorders – along with relevant underlying mechanisms – is a priority. Far too little is known about such topics, particularly in women.

In closing, we hope that our review has highlighted the importance of ADHD in girls and women, the ways in which the historical neglect of this population has at last inspired renewed research and clinical efforts, and the importance of examining female-specific mechanisms and trajectories beyond the search for sex differences per se. There is much to gain, scientifically and clinically, by full representation of the sexes (as well as other crucial individual and cultural differences) in future efforts within this and other domains of psychopathology.

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### **Key points**

- Until recently, almost all research on ADHD has focused on boys and men, with female presentations having been largely overlooked in both clinical and research settings.
- In childhood, the prevalence of ADHD in boys is 2–2.5 times higher than its prevalence in girls. By adulthood, this ratio becomes closer to equal.
- Females are more likely to present inattention symptoms and associated internalizing problems, whereas males are more likely to display hyperactive-impulsive symptoms and associated externalizing problems.
- ADHD is highly impairing in girls during childhood and adolescence regarding major domains of life
  functioning, with longitudinal studies showing these impairments to persist through adulthood. Notably,
  self-harm continues to be a major impairment in girls and women with ADHD throughout adolescence and
  adulthood.
- Ongoing efforts exploring developmental pathways and casual mechanisms linking female presentation of ADHD to long-term outcomes will further scientific understanding and foster responsive interventions.

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