ADHD: Restricted Phenotypes Prevalence, Comorbidity, and Polygenic Risk Sensitivity in
ABCD Baseline Cohort

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Acknowledgements:

Effort on this project was supported by NSF GRP fellowship 2020239717 (Cordova) and NIH grant R37-MH59105 (PI: Joel Nigg). The authors have no reportable conflicts of interest to disclose. They are grateful for helpful comments on this work by Deanna Barch, Ph.D., Joan Kaufman, Ph.D., Stefanie Bodison, O.T.D., O.T.R./L., Anthony Dick, Ph.D., Ellen Leibenluft, M.D., Philip Shaw, B.M.B.Ch., Ph.D., and Argyris Stringaris, M.D., Ph.D., FRCPsych.

Key words: ADHD, comorbidity, prevalence, polygenic score, executive function

Abstract

Introduction. Estimates of prevalence and comorbidity of ADHD in the United States require additional national, multi-informant data. Further, it is unclear whether the polygenic, neurodevelopmental model of ADHD in DSM-5 is best modeled with a broad or restrictive phenotype definition.

Method: In the Adolescent Behavior Cognition Development (ABCD) study baseline data on 9-10 year old children, ADHD prevalence, comorbidity, and association with cognitive functioning and polygenic risk were calculated at four thresholds of definition of ADHD phenotype restrictiveness using multiple measures and informants. Multi-indicator latent variable and composite scores were created and cross validated for ADHD symptoms and for irritability. Missing data, sample nesting, and sampling bias were corrected statistically.

Results: Multi-informant estimate of ADHD prevalence by the most restrictive definition was 3.53% when restricted to children in which parent ratings and teacher ratings both converged with KSAD report of current ADHD. As stringency of the phenotype was increased, total comorbidity increased slightly, and associations with cognitive functioning and polygenic risk strengthened. Inclusion of children with past ADHD but now treated increased prevalence estimate without weakening detection of polygenic risk. Irritability and ADHD dimensional composite scores and latent variables achieved satisfactory model fit and expected external correlations.

Conclusion: The present report strengthens estimates of ADHD prevalence and comorbidity. Research on polygenic and other correlates of ADHD as a clinical category in the ABCD sample may benefit from using a restrictive, multi-informant operational definition

INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is a crucially important childhood condition due to its link to subsequent onset of other disorders, shortened life spans, and other serious life outcomes.^{1,2} This paper addresses two fundamental and closely related issues that impede progress on understanding ADHD: estimating prevalence and comorbidity, and evaluating the appropriate stringency of phenotype definition for detecting genetic and other mechanistic or predictive signals.

Prevalence and comorbidity. First, the prevalence of childhood mental disorders in the U.S. in general, and ADHD in particular, has been difficult to estimate due to the lack of an epidemiological study using adequate clinical evaluation. The multi-institute NIH-funded *Adolescent Behavior Cognition Development* (ABCD)³ study has unique advantages that can add to the quality of estimates of national prevalence and comorbidity rates for ADHD.

Previous information on ADHD prevalence and comorbidity in the U.S. has come primarily from two sources. First, national surveys of parents, such as those conducted by the Centers for Disease Control, estimate prevalence of ADHD at about 9%.⁴⁻⁶ but lack standardized multi-informant evaluation of ADHD. Local but non-representative studies using more stringent standardized direct evaluation of ADHD in children have yielded noticeably lower estimates of 2-4%.⁷ Standard meta-analyses have reached an interim value of 5-7% in children^{8,9} but are limited by combining studies using different methods of varying rigor. A Bayesian meta-analysis¹⁰ that attempted to correct that problem by estimating multi-informant cases, put worldwide prevalence at approximately 2%, and just over 3% in North America. (Further details on that literature are provided in the online supplement, p. S-11).

Phenotype refinement. Secondly, the DSM-5 defines ADHD in relation to a literature

that views it as a polygenic, multifactorial, neurodevelopmental condition. This makes it important to determine how ADHD should be operationalized—broadly (as in national parent surveys) or more stringently (using multi-method, multi-informant procedures) to best detect genetic liability and cognitive markers such as reduced executive functioning. Different studies have used widely varying ways of operationalizing ADHD as a diagnosis, and as a dimension. Here we evaluate several of these in relation to the important goal of understanding genetic liability as well as laboratory neurocognitive measures.

The ABCD study offers a unique opportunity for further insight these key issues by virtue of nationwide sampling, the availability of multiple informants, and prior work on propensity weighting to estimate actual prevalence.¹¹ Inclusion of both a structured interview and nationally normed ratings from informants who observe the child in two settings is a significant advantage compared to most prior studies using national data and may bring estimates closer to the intent of theory and of diagnostic criteria in DSM-IV and DSM-5. The same design enables evaluation of competing ways of defining ADHD that are used in various ways in the literature. As noted, the way to define ADHD for different purposes even in the ABCD sample has been unclear, with different methods used in different papers.

The present paper therefore aims to (a) provide an estimate of prevalence and comorbidity of ADHD using different operational definitions, (b) evaluate the value of different thresholds of restrictive phenotype definition for identifying external correlates of ADHD as a category, with particular emphasis on best methods for detecting polygenic risk, (c) evaluate methods of creating dimensional measures of ADHD in this sample, and (d) and to offer standardized options and recommendations for operationalizing ADHD in the ABCD sample. In the present study, we estimated *current* ADHD prevalence using 4 different thresholds of

stringency, while supplementing this with alternative methods that include past and current ADHD in these 9-10 year old children. We estimated rates of comorbidity and examined utility of these different definitions of ADHD by examining IQ, executive functioning, other cognitive functions, and polygenic risk scores for ADHD.

METHODS

Description of the ABCD sample and ADHD Evaluation

The ABCD study is the largest longitudinal study of child-adolescent neurodevelopment and mental health in the U.S.³ The ABCD cohort enrolled 11,878 participants between 9-10 years of age from among community volunteers, at 21 sites around the nation.

Participants were screened for basic inclusion eligibility information prior to enrollment. Wave 1 data collection included measures of mental health status with a recently developed and validated computerized parent-answered Kiddie Schedule of Affective Disorders and Schizophrenia for DSM-5 (KSADS-COMP).¹² It coded a positive diagnosis of ADHD when the parent report met DSM-5 criteria including duration. Note that the impairment criteria in this version of the KSADS-COMP required impairment in only one setting for the diagnosis of ADHD.^a We paired it with well-validated, nationally normed scales—the parent report Childhood Behavioral Checklist (CBCL)¹³ and the teacher-report Brief Problem Monitor (BPM)¹⁴. Child participants completed a computerized version of the WISC-V¹⁵ Matrix Reasoning subtest as an estimate of non-verbal IQ. They also completed the self-report KSADS-COMP for selected mood and anxiety modules. For testing of dimensional latent variable models, demographically matched split-half samples known as the ABCD Reproducible Matched Samples (ARMS)¹⁶ were used for replicability analyses (ARMS-1; N=5,786, ARMS-2;

^a The baseline KSADS-COMP assessment of major depression (MDD) failed to utilize impairment criteria. Both errors are being corrected, but data were not publicly available at this writing.

N= 5,786).

ADHD restrictive phenotypes

Four increasingly restrictive phenotypes were created using increasingly stringent filters to approximate the DSM-5 model of ADHD. For the specific measures and cutoffs used, and further rationale, see Online Supplement pages S2-S4.

ADHD-1: Met ADHD-current on the KSADS-COMP. (Criterion A). Exclude ADHD-past-only.

ADHD-2: ADHD-1 + rule out schizophrenia, bipolar disorder, or estimated IQ>70 (Criterion E).

ADHD-3: ADHD-2 + teacher BPM T-score ≥ 65 (Criterion C).

ADHD-4: ADHD-3 + parent CBCL attention scale or ADHD DSM5 scale T ≥ 65 (Criterion E).

Comorbid Disorders

Comorbid disorders were estimated by the report on the parent-report KSADS-COMP, supplemented by youth self-report on the KSADS-COMP for bipolar disorder, depressive disorders, and anxiety and fear disorders). When both parent and youth report were available, we used an “or” rule, in which the disorder was considered present if full criteria were endorsed by either reporter.

Three broad categories of comorbidity were used for ease of interpretation in the manuscript: *Mood Disorders*, *Disruptive Behavior Disorders*, and *Anxiety and Fear Disorders*. Their composition is noted in the results (results for all the individual disorders assessed are included in the Online Supplement as noted below). Substance use was exclusionary at baseline and autism spectrum disorder was not assessed in the ABCD baseline sample.

Full details on the rationale and evaluation for comorbid disorders are provided in the online supplement pp. S2-S4.

Creation of composite dimensional variables for secondary analysis and validity checks

ADHD dimension. Extensive evidence suggests that for some purposes ADHD can be treated as a trait dimension in the population rather than only as a categorical disorder. Therefore, dimensional measures of ADHD were created as a resource for the field and alternative to categorical ADHD analysis. These were validated by fitting structural equation models in a replication analysis using a split-half of the ABCD data set (see online supplement Table S6).¹⁶ The primary ADHD latent variable included indicators from both parent and teacher sources. Indicators comprised the CBCL attention scale t score, the teacher BPM attention scale t score as well as two item-level composites from the KSADS-COMP.

Irritability dimensions. A parent-rated child irritability score was created using the average of five CBCL and three KSADS-COMP items ($\alpha=0.833$) selected after asking three independent experts to rate the relevance of CBCL items to independently rate the irritability construct (Ellen Leibenluft, M.D., Philip Shaw, B.M.B.Ch., Ph.D., Argyris Stringaris, M.D., Ph.D., FRCPsych). All included items were rated as either definite or possible symptoms of irritability by all three expert raters and all were rated as definite by at least one rater (See [online Supplement](#) p. S7) for item content and latent variable and split half validation).

DBD dimension scores. A disruptive behavior disorder dimension was also created. The teacher ODD/CD composite utilized four BPM items while the internalizing mood composite utilized six BPM items. See the online supplement (p. S7) for details and relation to related variables in the ABCD data set.

Cognitive measures. Scores for general cognitive ability (GA), executive function (EF), and learning and memory were computed as reported in ¹⁷ and summarized in the online supplement (p. S7). The association between predictors and the dimensional ADHD latent variables were evaluated by creating latent variables for these factors.

External correlates: Polygenic score. The final external correlate was polygenic risk for ADHD. Saliva samples were collected at the baseline visit and sent to the Rutgers University Cell and DNA Repository for DNA isolation.¹⁸ Genotyping^{19,20} was performed using the Smokescreen Array.²¹ For the present study, processed genotypes were downloaded from the NIMH Data Archive (dx.doi.org/10.15154/1503209), and standard QC checks were performed. Details are provided in the online supplement. For analyses involving the PRS scores, the first three genomic principal components were covaried to control for ancestry stratification.

The polygenic risks score (PRS) was constructed using the 2016-2017 PGC+iPSYCH ADHD GWAS meta-analysis²² as the discovery data set (20,183 ADHD cases; 35,191 controls). For the primary analysis, the PRS was calculated using the LDpred method.²³ Only SNPs with INFO (imputation quality) score ≥ 0.8 in both the PGC meta-analysis and the ABCD data were considered. SNPs were further limited to the ~1.2 million HapMap SNPs as suggested for LDpred.²³ Linkage disequilibrium was estimated using all unrelated individuals in the ABCD cohort, and the PRS was created with the proportion of causal SNPs set to 0.3. For supplemental analysis, we also computed and examined a PRS constructed using standard methods as reported previously²⁴ and checked results relying only on the majority (European-ancestry) discovery set (see online supplement p. S8 for more details).

Data Sharing: The critically important ABCD data security measures, included in the data use agreement (<https://nda.nih.gov/ndapublicweb/Documents/NDA+Data+Access+Request+DUC+FINAL.pdf>) provide investigators access to the ABCD data, but prevent them from sharing any individual-specific derived measures outside of the National Data Archive (NDA).²⁵ Thus, currently the only mechanism to share subject specific ABCD-derived data is through the NDA. These

necessary restrictions on lateral data sharing greatly limit the risks of irresponsible data usage, such as participant re-identification, but limit collaboration within the research community.

We created an additional community share for the easier distribution of ABCD-derived data.¹⁶ The *ABCD BIDS Community Collection* (ABCC, ABCD-3165) enables community contributions and usage, with standardized formatting, a governance structure to maintain compliance with the NDA's important data usage standards,^{26,27} and analytic utilities to improve data accessibility and ease of use. All of the derived categorical and dimensional variables of ADHD, along with derived PRS scores, are provided through the ABCC.

Data Handling: Complex sampling corrections

All analyses were completed on data from ABCD release 2.0 (accessed 12/2018). While conceptually the analyses were not complex, the complex sampling design required special handling, which we take time to explain here. All SEM analyses were completed in Mplus²⁸ (vers. 8.3) or R²⁹ (vers. 3.6.1) as noted.

Missing Data. The proportion of missingness for the variables utilized in this report ranged from 0.0% to 70.1% ($M = 8.1\%$, $SD = 17.7\%$). In general, parent measures (KSADS, CBCL) had minimal missing data, but teacher ratings on the BPM were missing for over half the baseline sample. Multiple imputation was used to obtain unbiased parameter estimates from the full sample. In cases where data are not missing completely at random (MCAR) like this one, a substantial and robust literature has demonstrated that missingness must be modeled to achieve unbiased results and that older methods of handling missing data are biased, including methods such as listwise deletion, mean substitution, regression estimation, pairwise deletion, last observation carried forward, and single imputation.³⁰ For readers unfamiliar with the advantages of new methods such as multiple imputation, the online supplement provides brief additional

background (page S-10). All analyses were run for each of 100 imputed datasets and combined using the TYPE = MI setting in Mplus, which averages the parameter estimates per Rubin's rules.³¹ Data and results were transferred between R and Mplus using the Mplus Automation package³² (vers. 0.7-3). More details are provided in the online supplement.

Population and Nesting Adjustments.³³ To address sampling bias propensity scores³³ developed and recommended for ABCD^{34,35} were utilized to align the parameter estimates with the American Communities Survey. Propensity weights are a well-recognized method that can reduce bias introduced by unequal likelihood of selection in observational studies, such as ABCD, utilizing participant characteristics to calculate the weights^{34,36}. See supplement for additional details (page S10).

Other adjustments. Standard errors were adjusted for family and within site nesting using the TYPE = COMPLEX setting in Mplus.

Data analysis

ADHD prevalence. For ADHD, the proportion of the entire sample that met each set of criteria was calculated and weighted as described above.

Comorbidity. We evaluated the prevalence of individuals meeting each ADHD criterion and major comorbidities in the ABCD sample. To accomplish this, we used the Y ON syntax in Mplus and exponentiated the resulting logit coefficients and confidence intervals to produce proportion estimates. Separate analyses were conducted for each ADHD criterion subset, the full sample, and individuals categorized as non-ADHD. For comorbidities the prevalence was calculated within each ADHD subset. Yet, many children with ADHD present with multiple comorbidities. To adjust the within-ADHD prevalence rates to account for this, we conducted another set of logistic regressions in Mplus utilizing the binary diagnostic variables. The

outcomes for these models were the major comorbidities categories (any anxiety or fear disorder, any mood disorder, and any disruptive behavior disorder). For each ADHD criterion-major comorbidity pair, we ran two models. In the unadjusted, pairwise model, the binary ADHD criterion variable was the only predictor (along with sex and age). In the second, adjusted model, the ADHD variable and the remaining comorbidity variables were entered into the model. Thus, the second model provided the pairwise relationship adjusting for the relationships among all major comorbidities. The results of the logistic regression were then converted to prevalence estimates.

External correlates. We conducted an initial assessment of external correlates as an estimate of construct validity of the ADHD criterion definitions. We did so via a series of logistic regression analyses with the binary ADHD variable as the outcome and, respectively, cognitive principal components (executive function, general cognitive ability, and learning and memory),¹⁷ WISC matrix reasoning scale score, and ADHD PRS score as the individual predictor in each model, with sex and age as covariates. Separate models were assessed for each ADHD criterion-predictor pair. Then, to probe the differences in these associations between ADHD criterion groups, the equivalence of predictor means for non-overlapping groups of individuals from each criterion were assessed using a series of Wald tests.³⁷

External correlates of dimensional measure of ADHD. To enable an initial estimate of the construct or convergent validity of the dimensional ADHD score, we conducted a series of linear regression models in Mplus, with ADHD dimensional composite scores as the outcome and cognitive principal components (executive function, general cognitive ability, and learning and memory), WISC, and PRS scores, as well as irritability, ODD/CD, and internalizing/mood composites as the individual predictors, controlling for age and sex. As before, separate analyses

were conducted for each ADHD outcome-predictor pair for each of interpretation.

RESULTS

Characteristics of ADHD after phenotype refinement. Table 1 provides descriptive and clinical data for ADHD as defined by refined phenotypes (the four Tiers) here. Dimensional assessment of ADHD is discussed subsequently (similar information using alternative inclusion criteria are presented in Tables S1 and S1b).

ADHD Prevalence after phenotype refinement and propensity weighting. The ABCD KSADS-COMP estimates current ADHD at 9.17% (8.54% after rule outs). Prevalence was 5.41% when teacher convergence was required, and 3.53% when parent standardized ratings in the clinical range were also required. Their characteristics are summarized in Table 1. See the online supplement Table S1a for description of the groups if they are treated as non-overlapping (Table S1a). An important consideration is the children who are past ADHD but currently treated—they may be true cases but were excluded here. The results if they are included are presented in Table S1b including scores for all of the measures reported in the results here. The children excluded due to rule outs did have elevated ADHD symptoms and details on their scores on all the variables reported below are in Table S1c.

ADHD Comorbidity. Table S2a shows the weighted estimated binary comorbid disorders of ADHD. The baseline prevalence of any disorder in the ABCD sample was estimated at 22.97% (Baseline.) The rate of overall co-occurring disorders for those with ADHD (ADHD-1) was 62.74%, and 61.04% when excluding for rule-outs (ADHD-2). When teacher confirmation was required in a refined phenotype (ADHD-3), total cases with at least one comorbid condition was estimated at 63.92%; it was 70.20% with parent questionnaire elevation added (ADHD-4). Raw calculations without weighting are presented in Table S2b, with the exhaustive set of all constituent data in Table S2c.

Conditional prevalence and conditional comorbidity of ADHD. After removing comorbid schizophrenia, bipolar disorder, and IDD, total ADHD comorbidity increased slightly as diagnosis became more restrictive. This pattern also held for each of the three major disorder groups discussed here (anxiety, disruptive behavior, and mood) (see **Tables S2a and S3**). As expected, comorbidity rates decreased slightly when overlapping comorbidities were adjusted for. The adjusted comorbidities within each ADHD tier remained notable, ranging from an adjusted 28.9%-31.5% for disruptive behavior disorders and from 23.8%-27.4% for anxiety/fear disorders. Mood disorders displayed relatively low estimated prevalence within the ADHD tiers at this age range at 2.1%-2.9%.

Correlates of ADHD Tiers. **Table 1** provides the mean scores on the external validators, and **Table S4a** provides the parameters comparing each of the phenotype definitions to the non-ADHD population and to one another. The cases with psychosis and/or IDD (ADHD-1) present obvious confounds for the cognitive measures, and also presented with elevated ADHD polygenic scores (Table S-1). When they are removed, then Tier-2, Tier 3, and Tier 4 present a clear pattern of results shown in **Figure 1 and Figure 2**.

Figure 1 shows relative risk of ADHD based on polygenic score for each of the phenotype refinements defined as the top decile of PRS risk (“high risk”) compared to the bottom 50% of PRS risk (“low to average risk”). It shows that the ADHD definitions have similarly weak genetic signal. Only ADHD-4, the most restrictive, yields a sharply increased genetic signal. When ADHD is defined by Tier 4, then those in the top decile of polygenic risk have a near doubling of probability for ADHD versus low to average risk individuals. (The specific parameters associated with this figure are in Tables S4a and S4b).

Figure 2 shows that the mean scores for all three PCs (PC1 - General Ability, PC 2 -

Executive Function, PC3 - Working Memory) and WISC-V Matrix Reasoning scores decrease as the ADHD tiers increase from non-ADHD to Tier 4 (ADHD Tier 1 excluded for WISC-V confound). It also includes the PRS scores in standardized form.

Figure 3 shows that the magnitude of the effect size for all of the external neuropsychological correlates and for the PRS score of ADHD group versus non-ADHD. It shows that in relative terms, the effect parameter increases dramatically using the more restrictive definitions of ADHD.

External correlates of ADHD dimensional score. As expected, all of the convergent validity measures were significant predictors of ADHD composite scores using parent, teacher, and combined indicators (See **Table S5**) The Parent Irritability Composite, Teacher ODD/CD Composite, and Teacher Internalizing/Mood Composite provided the strongest associations with ADHD across all ADHD composites, again as expected. The association between the cognitive latent variables and the ADHD composites were also significant, with increased performance on the cognitive outcomes associated with lower scores on the ADHD variables (see Figure S2). Although the associations between the external correlates and the ADHD latent variables were all significant, they were not numerically consistent across the different ADHD outcomes (see Table S5), with some measures (e.g., the cognitive measures) more closely associated with teacher report data and others (e.g., parent irritability) more closely associated with parent report data. Thus, although the parent CBCL attention t score appears the most sensitive single measure overall, the composite ADHD factor, which utilizes both parent and teacher informants, was reported in the primary results here.

DISCUSSION

Results here provide three major findings. First, the prevalence of ADHD in the

important national ABCD study depends crucially on how ADHD is operationalized, and a best estimate using a restrictive definition that best fits the DSM-definition is 3.5-4% for current ADHD, and 6% for lifetime ADHD if children who had ADHD before and are now treated are included. This estimate, beyond the limitations noted later, improves on many prior estimates by capitalizing on the national ABCD study with a multi-method, multi-information assessment of ADHD. Propensity weighting was used to correct for sampling bias. Helpfully, the estimates here can be reconciled well with other estimates. For the US National Survey of Children's Health, a re-analysis of the 2012 survey³⁸ suggests that if the available questions about severity and duration within that survey are incorporated to estimate false positives and true positives, the prevalence of ADHD would be considerably lower (4 to 5%) than the more commonly cited 9%, and in line with findings here. Similarly, the estimates here are in line with major meta-analytic results as noted in the introduction, helping to further bolster these estimates.

Second, within the limitations noted below, the results suggest that a refined phenotype that augments computerized structured interview and key rule outs with parent and teacher standardized ratings, sharply increases the detection of biological signal, represented here by the ADHD polygenic score—and was the only categorical definition able to detect a polygenic effect.

The third, related finding is that this same story holds although somewhat less sharply for executive functioning and learning and memory. These findings are important for efforts to relate ABCD data to studies that involve examination of ADHD cases in other settings. While they may be partially explained by assuming that the more restrictive definitions are closer to the severe end of the ADHD spectrum, the method here does provide a useful categorical approach.

In fact, the signal sharply increased for polygenic risk and was only detectable here for

ADHD using the restrictive ADHD-Tier-4. Thus, when ADHD is to be considered as a category and conceptualized as a polygenic, neurodevelopmental disorder, as defined in DSM-5 for clinical purposes, then the restrictive definition has the most validity for study in the ABCD sample. Nonetheless, it is important to note again that many children who are below threshold for this definition are still impaired by ADHD symptoms and may require clinical care or educational programming.

The findings confirm substantial ADHD comorbidity. In the most restrictive phenotypes with the greatest construct validity here, fully 70% of children with ADHD have at least one comorbid condition (including OCD) (Table S2, Tier 4). The most common comorbidity, as expected, was disruptive behavior disorders. However, excepting an unusually high estimate for OCD, anxiety and mood overlaps at this age were quite low. It is likely that these ratios will increase as the sample ages into adolescence and the peak age of onset for the internalizing disorders.³⁹

This latter point is critically important to prevention, and is part of the reason it is important not to treat mood and anxiety disorders as automatic rule outs for ADHD. Indeed, recent studies provide evidence that ADHD is on the causal pathway for comorbid cases of anxiety and mood disorders.^{1,2}

The finding of cognitive score effect sizes associated with ADHD at modest effect sizes is consistent with the literature. The sample size here will add valuable information to efforts to arrive both at overall estimates of population associations with ADHD of these cognitive measures, as well as further work to identify which children are most affected by these features to characterize ADHD heterogeneity.⁴⁰

While these findings have many unique strengths and provide crucial new information at

the national level for the US, results still have to be viewed in light of several remaining limitations. First, the propensity weighting here should largely correct demographic sampling bias, but we cannot rule out other unmeasured sampling bias. Relatedly, while race and ethnicity were included in the imputation and propensity weighing models so they are not biased by race or ethnic variation, race and ethnic differences in ADHD prevalence and comorbidity remain of considerable interest and potential importance.^{41,42} Yet, cell sizes were too small to make meaningful statements in that regard here, and this remains a topic for future study. We lacked robust measures of impairment outside of the parent KSAD here⁴³ (which only required impairment in one setting) or of direct clinician evaluation of the children. Third, comorbid disorders were not as refined by consideration of rating scales or other measures the way we did with ADHD, thus comorbidities may be over- or under-estimated, although we did examine effects when youth report was considered for key disorders.

Substantial data support the idea that ADHD may also be considered like a trait dimension. The latent variable validation supplied here, and the correlates demonstrated, suggest that utilization of the composite or latent variables proposed should be productive as a means of evaluation ADHD correlations in neuroimaging and other studies. The observed correlations with executive functioning, general cognitive ability, and polygenic risk are consistent with the literature and lend support to the utility of this highly reliable composite. However, for investigators wishing to use a single simple dimensional measure of ADHD liability in the ABCD data set, the data presented here suggest that the parent CBCL attention scale T score is the most useful—and is as useful as the composite dimensional score. That result supports the extensive work done on evaluating problem dimensions in children over the past several decades⁴⁴ as useful for detection of polygenic risk and other ADHD features.

Similarly, the new irritability composite here has strong face validity via expert consensus ratings and internal validity on latent variable validation. For all composites, fit and validity replicated in a matched split-half sample within the ABCD, providing strong support for their validity and utility.

In conclusion, the ABCD study provides a valuable resource for estimation of population needs for ADHD. The analysis here suggests that the most dependable findings will benefit from utilization of a refined categorical phenotype for ADHD cases, and the use of composite dimensional scores for dimensional analysis.

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Table 1*Demographics and Group Description.*

Variable	Full Sample (N = 11875)	Non-ADHD (n = 10784)	ADHD 1 (n = 1091)	ADHD 2 (n = 1029)	ADHD 3 (n = 642)	ADHD 4 (n = 420)
%Male	52.11%	50.41%	68.92%	68.63%	64.90%	67.10%
Race:						
% White Non-Hispanic	60.10%	59.73%	63.82%	65.46%	62.88%	61.36%
% Black	15.94%	15.76%	17.71%	16.62%	17.28%	18.40%
% Asian	2.49%	2.65%	0.83%	0.88%	0.61%	0.62%
% Native American/AK Native	0.55%	0.55%	0.56%	0.50%	0.79%	0.98%
% Native Hawaiian/Pacific Is.	0.14%	0.16%	0.01%	0.01%	0.01%	0.01%
% More than one race	12.58%	12.34%	14.94%	14.79%	14.53%	16.18%
Ethnicity: % Latinx/Hispanic	20.68%	21.09%	16.59%	15.86%	18.12%	18.86%
% Prescribed ADHD Medication	8.05%	5.39%	34.28%	34.00%	39.84%	44.65%
M Age (months)	118.94 (0.07)	118.98 (0.07)	118.58 (0.22)	118.53 (0.23)	118.23 (0.30)	118.12 (0.37)
M Income Group (1-10)	7.12 (0.02)	7.13 (0.02)	7.02 (0.07)	7.15 (0.07)	6.93 (0.10)	6.70 (0.12)
M CBCL Externalizing T-score	45.72 (0.09)	44.60 (0.09)	56.82 (0.33)	56.44 (0.34)	58.60 (0.41)	61.40 (0.48)
M CBCL Internalizing T-score	48.43 (0.10)	47.55 (0.10)	57.09 (0.33)	56.76 (0.33)	57.48 (0.42)	60.21 (0.48)
M CBCL Attention T-score	53.87 (0.06)	52.74 (0.04)	65.0 (0.27)	64.70 (0.27)	66.63 (0.33)	70.76 (0.36)
M Executive Function PC2	-0.006 (0.007)	0.012 (0.007)	-0.189 (0.024)	-0.167 (0.025)	-0.20 (0.032)	-0.216 (0.041)
M General Cognitive Ability PC1	-0.008 (0.007)	0.007 (0.007)	-0.155 (0.024)	-0.125 (0.024)	-0.207 (0.031)	-0.237 (0.038)
M Learning and Memory PC3	-0.003 (0.006)	0.016 (0.007)	-0.187 (0.021)	-0.164 (0.022)	-0.222 (0.027)	-0.284 (0.033)
M WISC-V Matrix Reasoning	9.85 (0.03)	9.90 (0.03)	9.31 (0.09)	9.53 (0.09)	9.43 (0.12)	9.30 (0.15)
M PRS (standardized)	0.024 (0.009)	0.013 (0.010)	0.133 (0.030)	0.116 (0.031)	0.156 (0.039)	0.234 (0.048)
M PRS LD Pred (standardized)	0.027 (0.009)	0.013 (0.010)	0.160 (0.031)	0.140 (0.032)	0.184 (0.039)	0.259 (0.048)

Note. Values are pooled estimates of mean and standard error across all imputation sets. PC = principal component; PRS=polygenic risk score. See text for methods and definitions. N is estimated after imputation. Matrix reasoning=scaled score. For race codes, the ABCD variable codes were combined as follows: White Non-Hispanic utilized the White category, excluding anyone that met the Hispanic/Latinx ethnic variable; Asian included Asian Indian, Chinese, Filipino, Japanese, Korean, Vietnamese, and Other Asian; Native Hawaiian/Pacific Islander included Native Hawaiian, Guamanian, Samoan, and Other Pacific Islander.

Table 2

Estimated Rate within ADHD Population of Three Classes of Comorbid Psychiatric Disorder before and After Adjusting for Other Comorbidity Classes

Criterion	Covariate Inclusion Status	Any Disruptive Behavior Disorder			Any Mood Disorder			Any Anxiety Disorder		
		Est.	Lower CI	Upper CI	Est.	Lower CI	Upper CI	Est.	Lower CI	Upper CI
ADHD1 (n = 1091)	Unadjusted	36.1%	32.1%	40.2%	5.4%	3.6%	7.9%	33.0%	29.4%	36.8%
	Adjusted	31.5%	27.7%	35.6%	2.9%	1.8%	4.4%	26.3%	22.8%	30.1%
ADHD2 (n = 1029)	Unadjusted	33.1%	29.2%	37.2%	4.6%	3.0%	6.9%	30.4%	26.9%	34.2%
	Adjusted	28.9%	25.2%	32.9%	2.4%	1.5%	7.8%	23.8%	20.5%	27.5%
ADHD3 (n = 642)	Unadjusted	34.8%	30.2%	39.8%	4.7%	2.9%	7.6%	32.2%	27.8%	37.0%
	Adjusted	30.0%	25.4%	35.0%	2.3%	1.3%	3.9%	24.2%	20.1%	28.9%
ADHD4 (n = 420)	Unadjusted	36.9%	31.5%	42.7%	4.9%	2.9%	8.2%	36.8%	31.3%	42.6%
	Adjusted	30.9%	25.7%	36.7%	2.1%	1.2%	3.8%	27.4%	22.3%	33.1%

Note. Prevalence was estimated using the risk ratio (converted from the logistic regression odds ratio) with the control group as the baseline. Adjusted prevalence represents the likelihood of demonstrating the comorbidity given the ADHD criterion diagnosis controlling for other comorbidities, sex, and age. Unadjusted only controlled for sex and age. N is estimated after imputation. Any disruptive includes ODD and CD and ADHD. Any anxiety includes agoraphobia, GAD, panic disorder, specific phobia, PTSD, unspecified anxiety disorder, separation anxiety, and social anxiety. Any mood includes MDD, DMDD, and unspecified depressive disorder. See Table S2a for a breakdown of specific major disorder comorbidities in the prevalence estimates, Table S2b for values prior to imputation and weighting, Table S2c for an extended and exhaustive detail of all the constituents of this summary, and Table S3 for odds ratio results from this same analyses.

Figure 1. Risk Ratio for ADHD by PRS Score in the Top 10% vs. Bottom 50% of Scores.

Note to Figure 1. Each ADHD tier is increasingly restrictive. Figure excludes cases of schizophrenia, bipolar disorder, and intellectual development disorder (hence, excludes “ADHD-1”) for clarity. The percentages represent odds ratios that have been converted to percentage of increased risk. Thus, an $OR=1.33$ is represented here as 33%. It represents the increased risk of being in the top 10% of PRS scores based on meeting criteria for each ADHD tier for overlapping groups: ADHD-2 (KSAD only after rule outs, $n = 1029$); ADHD-3 (requires teacher BPM $T \geq 65$, $n = 642$); ADHD-4 (also requires parent CBCL attention problems T score ≥ 65 ; $n = 420$.) Error bars represent standard error for the risk ratio. PRS=LD pred polygenic risk for ADHD. Figure demonstrates that the restrictive phenotype more clearly detects polygenic risk.

Figure 2. Distribution of Values for External Variables by ADHD Tier excluding rule out cases

Note to Figure 2. For clarity of presentation, cases of schizophrenia, bipolar disorder, or intellectual development disorder are excluded (“ADHD-1”). Values represent the standardized mean within non-ADHD and ADHD Tiers 2, 3, and 4, for General Ability, Executive Function, and Learning/Memory. WISC-V Matrix reasoning is the total scaled score. PRS is polygenic risk for ADHD computed by the LD-pred method.

Figure 3.

Wald Test Statistic for Difference in Estimated Means Between Non-ADHD and ADHD Tier Groups scaled by relative effect magnitude.

Note. Values represent Wald test statistics comparing each ADHD phenotype definition to non-ADHD cases, with larger numbers representing a larger effect size. Color scale represents the difference in magnitude of the effect between the ADHD-Tier 2 comparison to non-ADHD, and the effect for ADHD-3 and ADHD-4 respectively versus non-ADHD. Thus, the effect for PRS detection is 7x as great for ADHD-4 as ADHD-2 or ADHD, whereas the effect for executive function (EF) for Tier 4 is roughly double the other tiers.