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Primer

Attention-deficit/hyperactivity disorder

In the format provided by the authors and unedited

Update on Attention-Deficit/Hyperactivity Disorder

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Supplementary Box 1. Free Tools for Assessing ADHD in Childhood and Adulthood

Clinical Interviews for ADHD in Youth

Schedule for Affective Disorders and Schizophrenia in School- Age Children (K-SADS)

Semi-structured diagnostic interview. Evaluates past and current psychopathology in children and adolescents. Translations available in many languages. The K-SADS-PL is compatible with DSM-5.

https://www.pediatricbipolar.pitt.edu/sites/default/files/KSADS_DSM_5_SCREEN_Final.pdf

Child and Adolescent Psychiatric Assessment (CAPA)

Semi-structured interview that evaluates current symptomatology of in children and adolescent, based on DSM-5 criteria. Versions for youth and preschoolers with Spanish & Portuguese translations are available. The interview is free, but one must pay for training https://devepi.duhs.duke.edu/capa.html

Development and Well-Being Assessment (DAWBA)

Designed for trained non-clinicians as well as clinicians, using a prespecified set of questions, along with probes for impairment. Translations available in many languages. The DAWBA generates ICD-10 and DSM-5 diagnoses. https://www.dawba.info/py/dawbainfo/f1euk.py

Parent Interview for Child Symptoms (PICS)

Semi-structured interview that focuses on diagnostic criteria for ADHD, ODD, and CD in children and adolescents, along with probes for impairment, but also addresses symptoms of other psychiatric disorders. It has now been updated for DSM-5 criteria.

A companion semi-structured, telephone-based interview for teachers (Teacher Telephone Interview; TTI) focuses on symptoms of ADHD, ODD, CD in the school setting, with screening questions to assess

other psychopathologies. Dutch translation of each is available. https://lab.research.sickkids.ca/wp-content/uploads/sites/79/2020/05/PICS-Mini-2_May-2019-1.pdf

Rating Scales for ADHD in Youth

Vanderbilt ADHD Rating Scales

The teacher version assesses symptoms and performance impairment at school; the parent/caregiver version assesses perceptions of school performance and social functioning. Both are incorporated into the American Academy of Pediatrics ADHD Toolkit, Spanish translation available. https://www.nichq.org/sites/default/files/resource-file/NICHQ-Vanderbilt-Assessment-Scales.pdf

SNAP-IV

Rating scale focusing on symptoms of ADHD and ODD for teachers or parents/caregivers. It is sensitive to the changes related to treatment. Has been translated into several languages (e.g., Portuguese, Spanish, French). Assesses the severity of symptoms but has not been revised for DSM-5

Short Scale (26-item) available from: http://www.caddra.ca/pdfs/caddraGuidelines2011SNAP.pdf

Full Scale [90-item] with scoring instructions available from: http://www.shared-care.ca/files/SNAP_IV_Long_with_Scoring.pdf

Strengths and Difficulties Questionnaire (SDQ)

A brief broad-band standardized rating scale assessing selected symptoms of multiple disorders, with items pertaining to inattention and hyperactivity/impulsivity, as well as probes for impairment. Does not cover all DSM criteria. Parallel versions available for parent/caregiver, teacher, and self-report. Translations available in numerous languages. PDF versions of the SDQ and scoring instructions are available online at: http://sdqinfo.org

Clinical Interviews for ADHD in Adults

Diagnostic Interview for Adult ADHD, (DIVA-5)

DIVA-5 is a structured Diagnostic Interview for Adult ADHD based on DSM-5. Available in many languages. http://www.divacenter.eu/DIVA.aspx

Rating Scales for ADHD in Adults

Adult ADHD Self-Report Scale (ASRS-5)

The ASRS-5 assesses DSM 5 symptoms of ADHD in adults. It is a self-report questionnaire available here: https://www.hcp.med.harvard.edu/ncs/ftpdir/adhd/ASRS-5_English.pdf

There are 2 options for scoring. First, you can use simple scoring the link is on the site. (i.e., score each item in the range 0-4 and give everyone a summary score of 0-24) and use the resulting 0-24 continuous score as a predictor without having a clinical threshold. Anyone can do this without asking permission. This approach is used in the vast majority of other screening scales.

Second, you can contact Lenard Adler at NYU (Lenard.Adler@nyumc.org) to get permission to use the proprietary scoring rules for the DSM-5 version. If the intended use is for academic purposes and not part of an industry sponsored trial, there will be no charge for use of the scale, but your institution will need to sign a use agreement prior to our sending the scoring instructions. This inter-institutional agreement is fairly standard. Requests for commercial uses of the screener will require a license, which can also be arranged by contacting Dr. Adler.

Wender Utah Rating Scale (WURS)

The WURS was developed to retrospectively diagnosis childhood ADHD in adults using DSM-IV criteria. It is a self-report questionnaire.

http://neurosciencecme.com/library/rating_scales/adhd_wender.pdf

Supplementary Table 1: Diagnostic Challenges and Recommendations	
Challenge	Recommendation
Disentangling normative from pathological behavior in preschool children	• Use measures designed for assessment of preschool ADHD such as the Preschool Age Psychiatric Assessment (PAPA; https://devepi.duhs.duke.edu/measures/the-preschool-age-psychiatric-assessment-papa/) ○ Obtain teacher report and behavioral observations in the preschool setting ○ Provide provisional diagnosis as needed and continue to monitor over time. Most preschoolers with subthreshold ADHD later meet full criteria for the disorder.[208]
Full diagnostic interview and collection of informant ratings is too time consuming for my practice	• In adults: screen for ADHD using a self-report scale such as the Adult ADHD Self-Report Scale (ASRS; https://adhdscreeneronline.com/) ○ For children/adolescents: screen for ADHD using a parent rating scale such as the Vanderbilt ADHD Diagnostic Rating System (http://www.nichq.org/childrens-health/adhd/resources/vanderbilt-assessment-scales) or the SNAP rating scales (http://www.caddra.ca/pdfs/caddraGuidelines2011SNAP.pdf) ○ Follow-up with a brief patient/parent interview to assess impairment, chronicity, cross-situational expression, and possible alternative explanations for symptoms. If information gathered appears consistent for ADHD, refer to a specialist for a full diagnostic assessment.
I'm not sure if a patient should be diagnosed with ADHD, another disorder or both?	• Although symptoms of ADHD are present in other disorders, most symptoms of other disorders do not occur in ADHD and overlapping symptoms do not account for comorbidity[209]. Applying DSM/ICD criteria for each disorder resolves issues of differential diagnosis, keeping in mind that the symptoms of ADHD are chronic and occur in multiple settings.

Patient reports significant ADHD symptoms but is generally successful in most domains of life	• Define impairment as relative to the patient's potential (e.g., IQ) • Assess the impact of ADHD symptoms on many domains (e.g., relationships with loved ones, education/career, household responsibilities, friendships, parenting, driving, health behaviors) • Consider the patient's functioning relative to individuals with similar intellectual or other gifts.
Can I trust an ADHD evaluation done via telehealth?	• All standard and most auxiliary diagnostic tasks can be completed using telehealth methods (exceptions: vital sign monitoring and psychoeducational testing) o Telehealth assessments should follow the same gold standard practices as in-person assessments. o Learn more about the procedures used in the telehealth assessment to determine its integrity/safety
Information gathered from two reporters are contradictory	• Consider the impact of context on symptom expression—does the discrepancy reflect true cross-situational differences in behavior? o Discrepancies may be influenced by the time of day being rated, whether symptoms are being rated on or off medication, and which symptoms are most likely to be visible to the informant o Use an "or rule" to combine symptoms across raters, counting a symptom as valid if reported by any rater ➢ Ask informants to share perceived reasons for discrepancies with other raters and discuss rater differences in diagnostic summaries: ➢ Self-<u>under-reporting</u> is most frequently explained by self-awareness challenges, though <u>informant over-reporting</u> can emerge due to negative biases toward the patient ➢ <u>Self</u>-<u>over-reporting</u> may emerge when individuals seek a diagnosis as a means to an end or misperceive normative cognitive variations as clinically meaningful; however, <u>informant under-reporting</u> can occur when

	symptoms are internally experienced and not observable to others

I suspect that a patient may be feigning or exaggerating their symptoms	• Assess the patient's motives for diagnosis
	  ○ Obtain multiple informant reports, particularly from parents
	  ○ Make extra efforts to document childhood and current impairment (e.g., consulting school records, asking for concrete examples of impairment)

An individual has multiple comorbidities and differential diagnosis is challenging	• Conduct a full psychiatric interview that includes probes querying examples of symptoms and their onset, duration, and relative severity for each candidate diagnosis; consider whether ADHD symptoms are only present in the context of another condition o Diagnosing two or more psychiatric disorders is to be expected o Query the interplay of symptoms from each candidate diagnosis o Review a full recent physical examination and consult with primary care providers as needed to understand physical conditions that may contribute to symptoms o Refer for specialized testing if deeper assessment is not possible
The patient has subclinical ADHD-like traits and am not sure if I should give an ADHD diagnosis	• Assess whether full breadth of ADHD has ever been present (and can be diagnosed with a partial remission specifier) or was never present o If never present, the DSM-5-TR allows for "314.01/F90.8: Other Specified ADHD" or "314.01/F90.9: Unspecified ADHD" to be diagnosed when distress or impairment is present but other criteria for ADHD are not met o If impairment or distress is not present, the diagnosis should not be given
The patient's ADHD emerged after age 12 and am not sure if I should give an ADHD diagnosis	• Ensure that childhood ADHD has been assessed to the best possible degree with informant reports, history taking and record gathering o Assess mitigating factors that may have masked childhood ADHD (e.g., scaffolding from parents) o Consider alternative explanations (i.e., psychiatric, or physical disorders) for late-onset symptoms o The DSM-5-TR allows for "314.01/F90.8: Other Specified ADHD" or "314.01/F90.9: Unspecified ADHD" to be diagnosed when all criteria except age of onset are met

Supplementary Table 2: Directions for Future Research

Topics / methods	Challenges and/or pertinent questions
Clinical phenotype	
Gender issues	What characterizes the ADHD phenotype in women? How does the clinical presentation in women change over development? Should there be a separate ADHD diagnostic algorithm for women and for men? What drives the on average later age of diagnosis in women, and the underdiagnosis in women? How can we understand the changing gender ratio over development? What is the impact of hormonal changes (use of oral contraceptives, puberty, menstrual cycle, menopause, pregnancy, post-partum) on core symptoms and co-occurring problems in women?
Deficient Emotional Self Rregulation (DESR)	Should DESR become part of the definition of the ADHD clinical phenotype? Is DESR a clinical subtype of ADHD, a specifier of ADHD, or a cross-disorder construct?
Cognitive Disengagement Syndrome (CDS) (formerly named Sluggish Cognitive Tempo)	Is CDS a clinical subtype of ADHD, a specifier of ADHD, a cross-disorder construct, or a stand-alone condition?
Digital phenotyping	Will digital phenotyping using smart phones deliver new digital markers to characterize or subgroup ADHD, for example by temporal variability of behavior, or response to environmental cues?
Impairment – Assessment of functioning	Develop better and more precise criteria for assessing functional impairments and implement these in clinical practice and research
(Self-)stigma	Study the extent and impact of (self-)stigma in ADHD and develop strategies to avoid (self-)stigma and minimize its impact. Which factors contribute to prejudice, stereotyping, and discrimination? Does a diagnosis of ADHD per se increases (self-)stigma and if so, under which circumstances?
Co-occurring somatic conditions	What mechanisms underlie the associations with co-occurring somatic conditions? What is the role of shared genetic factors, shared environmental factors, lifestyle factors, adherence to medical recommendations, and treatment factors?

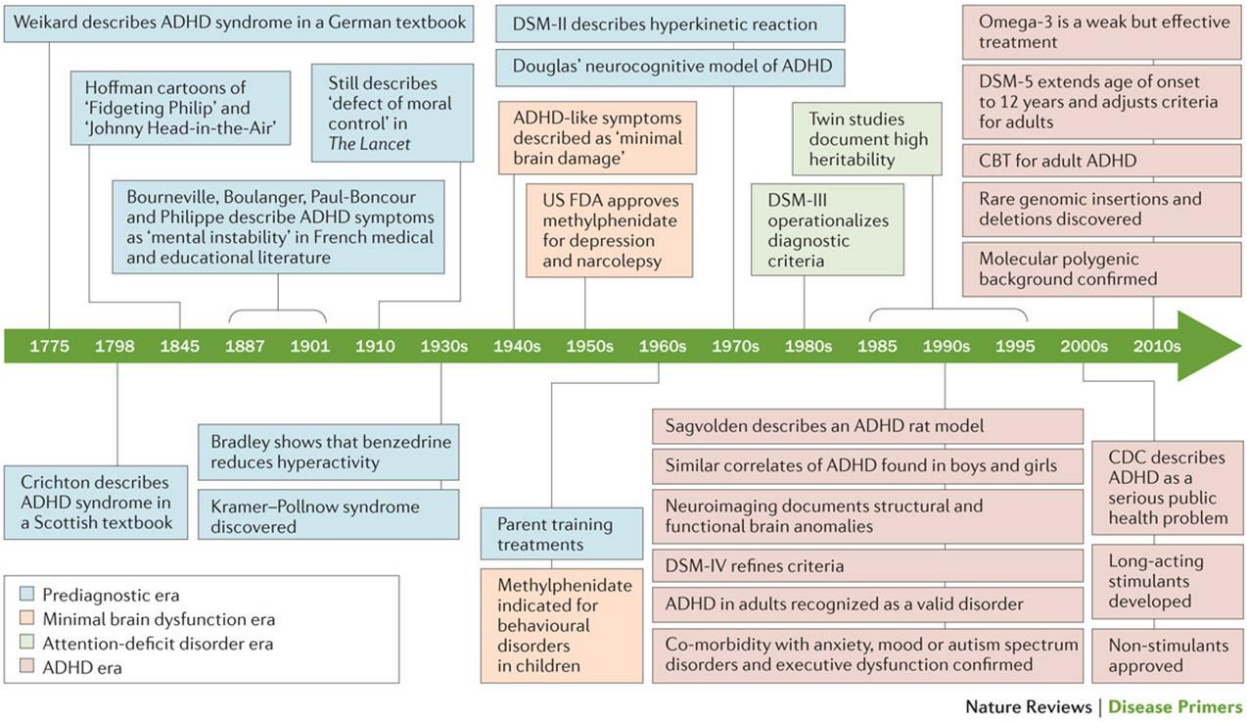
Co-occurring mental problems / conditions	Clarify the associations between ADHD and sleep problems. Are sleep problems a cause or a consequence of ADHD symptoms? What is the association with / overlap with borderline personality disorder? Is ADHD associated with later risk for mild cognitive impairment and dementia, and if so, what are the underlying mechanisms?
Course	
Early manifestations of ADHD	Using prospective high-risk fetus/infant and sibling-control designs, can we identify early manifestations and precursors of ADHD, and document (diversity in) early developmental pathways? Can we establish early pre-diagnostic biomarkers?
Late-onset ADHD	Is ADHD always a neurodevelopmental condition? Is late-onset ADHD a developmental subtype of ADHD, or a separate condition?
Remittance versus persistence	What are the (epi)genetic, brain, environmental, and cognitive mechanisms that drive variation in the course of ADHD (remittance, persistence, escalation)?
Positive factors	
Positive outcomes	What predicts a positive and successful developmental outcome of ADHD, in terms of functioning, wellbeing and quality of life?
Strengths	What are the strengths and assets of ADHD? How can we build on this in prevention and intervention efforts?
Resilience and protective factors	What makes individuals with ADHD resilient against adversity and stress? What are the protective factors at all levels of analysis: genetics, personal traits and endowments, family and school environments, neighborhood, society?
Public health	
Social and health disparity	What are causes and mechanisms that underlie differences in access to care for disadvantaged populations? How can this be remediated?
Country and cultural differences	Conduct a comparative analysis of healthcare accessibility and ADHD prevalence and outcomes across diverse countries with varying cultural backgrounds, resources, healthcare systems, and health insurance structures.

Biology	
Induced pluripotent stem cells (iPSC) and organoids	Establish in vitro ADHD neuronal / brain tissue models and examine their molecular, cellular, and physiological properties. Screen and test these models for new molecular targets and for gene-environment interactions.
Post-mortem brain tissue	Intensify efforts and improve infrastructure to collect and conserve post-mortem brain tissue from ADHD patients and build brain bank repositories.
Genetics	Improve biological relevance and predictive power of polygenic and gene set scores. Study the pleiotropic effects of ADHD and other neurodevelopmental conditions genes. Try to "find" the missing heritability (gap between phenotypic variance explained by behavioral genetics and molecular genetics). How does the genetic architecture change over development? Which genetic factors are stable and which pop-up in specific periods?
Epigenetics	Conduct large, prospective pediatric cohorts with repeated measures of DNA methylation, environment, behavior, and brain measures to identify developmentally sensitive epigenetic signals, and analyse the direction of effect. Does DNA methylation predict course or outcome, is it mediating the effect of genes and environmental factors, and/or conversely, is it the result of the changes in the phenotype? Do epigenetic signals provide stratification markers?
Gut-brain axis	Explore the role of the gut microbiota in calibrating the gut-brain axis and modulating neurocognitive development and neurodevelopmental risk. Do microbiota mediate or moderate the effect of lifestyle on ADHD severity, course, and outcome? Do microbiota deliver stratification markers for ADHD?
Immune system, inflammation	Examine the role of the immune system and neuro-inflammation in ADHD. Is there an immune subtype of ADHD? What is the role of maternal immune activation during pregnancy on neurodevelopmental risk?
Brain imaging	Will use of well characterized clinical samples, prospective multisite protocols, pre-registration, and standardization of preprocessing pipelines resolve inconsistencies of imaging findings?
Environment	

Exposures during pregnancy	Assess impact of exposures during pregnancy of medications, drugs, toxins, smoking, alcohol on neurodevelopment using genetically informed designs. Assess impact of perturbations of pregnancy, use of vitamins and nutrition during pregnancy.
Social environment	Develop more precise measures of the family environment, parent-child interactions and parenting behavior and assess their associations with ADHD symptoms in longitudinal designs. Examine the influence of school factors (school climate, school culture, teacher behavior, classroom routine) and neighborhood characteristics on ADHD symptoms.
Social media, use of smart phones	What are the positive and negative effects of social media exposure on ADHD symptoms? What is the association between smart phone use and ADHD?
Biological / physical environment	Using genetically informed designs, examine effects of exposure to environmental toxins, pollution, climate change, radiation, and urbanity on ADHD symptoms, mental health, cognition, and brain functioning.
Very prematurity (VP) – Very low birth weight (VLBW)	Using prospective longitudinal designs, what are the mediating and moderating mechanisms of the increased neurodevelopmental risk of VP and VLBW?
Statistics	
Computational modelling	Build mathematical models of experimentally observed behavior, cognitive and/or biological data to test top-down hypotheses and improve the mapping of behavior and cognition to biological and brain measures.
Normative modelling	Quantify interindividual differences of biological measures with respect to the normative range to parse heterogeneity in ADHD cohorts and provide statistical inferences at the level of individual subjects.
Artificial intelligence (AI)	Use AI to analyse complex big data sets and identify hidden patterns to generate new top-down hypotheses and to create clinically actionable predictive models.
Interventions	
Lifestyle	Conduct well-designed and controlled observational and experimental studies to examine the effect of lifestyle (food, nutrition, sleep, physical activity) on ADHD.

Study design	Improve designs of medication studies by treatment-targeted enrichment, adaptive treatment and precision measures to reach goals of precision medicine
Environmental engineering	To which extent should and can we engineer the direct physical and social environment (family, school, workplace) to accommodate individuals with ADHD's weaknesses and build on their strengths?
Skills Training and CBT	Add an improve components to enhance effectiveness. Clarify the best setting and duration for sustained therapeutic success.
Coaching	Conduct well-designed and controlled studies of coaching, a widely used but poorly studied method to help people with ADHD.
Psychopharmacology	Use computational methods to find new treatment targets for pharmacotherapy
All Treatments	Generate more data on the long-term safety and efficacy of all treatments.

Supplementary Figure 1 – History of ADHD



Adapted with permission from Ref 1.

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