Appendix e-1. *DSM-5* **criteria for ADHD**

DSM-5 Criteria for ADHD

People with ADHD show a persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development:

1. **Inattention: Six or more symptoms of inattention for children up to age 16, or five or more for adolescents 17 and older and adults; symptoms of inattention have been present for at least 6 months, and they are inappropriate for developmental level:**
   ◦ Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or with other activities.
   ◦ Often has trouble holding attention on tasks or play activities.
   ◦ Often does not seem to listen when spoken to directly.
   ◦ Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (e.g., loses focus, side-tracked).
   ◦ Often has trouble organizing tasks and activities.
   ◦ Often avoids, dislikes, or is reluctant to do tasks that require mental effort over a long period of time (such as schoolwork or homework).
   ◦ Often loses things necessary for tasks and activities (e.g. school materials, pencils, books, tools, wallets, keys, paperwork, eyeglasses, mobile telephones).
   ◦ Is often easily distracted
   ◦ Is often forgetful in daily activities.

2. **Hyperactivity and Impulsivity: Six or more symptoms of hyperactivity-impulsivity for children up to age 16, or five or more for adolescents 17 and older and adults; symptoms of hyperactivity-impulsivity have been present for at least 6 months to an extent that is disruptive and inappropriate for the person's developmental level:**
   ◦ Often fidgets with or taps hands or feet, or squirms in seat.
   ◦ Often leaves seat in situations when remaining seated is expected.
   ◦ Often runs about or climbs in situations where it is not appropriate (adolescents or adults may be limited to feeling restless).
   ◦ Often unable to play or take part in leisure activities quietly.

- ◦ Is often "on the go" acting as if "driven by a motor".
- ◦ Often talks excessively.
- ◦ Often blurts out an answer before a question has been completed.
- ◦ Often has trouble waiting his/her turn.
- ◦ Often interrupts or intrudes on others (e.g., butts into conversations or games)

In addition, the following conditions must be met:

- Several inattentive or hyperactive-impulsive symptoms were present before age 12 years.
- Several symptoms are present in two or more setting, (e.g., at home, school or work; with friends or relatives; in other activities).
- There is clear evidence that the symptoms interfere with, or reduce the quality of, social, school, or work functioning.
- The symptoms do not happen only during the course of schizophrenia or another psychotic disorder. The symptoms are not better explained by another mental disorder (e.g. Mood Disorder, Anxiety Disorder, Dissociative Disorder, or a Personality Disorder).

Based on the types of symptoms, three kinds (presentations) of ADHD can occur:

Combined Presentation: if enough symptoms of both criteria inattention and hyperactivity-impulsivity were present for the past 6 months

Predominantly Inattentive Presentation: if enough symptoms of inattention, but not hyperactivity-impulsivity, were present for the past six months

Predominantly Hyperactive-Impulsive Presentation: if enough symptoms of hyperactivity-impulsivity but not inattention were present for the past six months.

Because symptoms can change over time, the presentation may change over time as well.

Reference: Division of Human Development, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention Attention-Deficit/Hyperactivity Disorder Web page. http://www.cdc.gov/ncbddd/adhd/diagnosis.html. Updated September 29, 2014. Accessed November 20, 2014.

Appendix e-2. AAN GDDI mission

The mission of the GDDI is to develop, disseminate, and implement evidence-based systematic reviews and clinical practice guidelines related to the causation, diagnosis, treatment, and prognosis of neurologic disorders.

The GDDI is committed to using the most rigorous methods available within its budget, in collaboration with other available AAN resources, to most efficiently accomplish this mission.

Appendix e-3. AAN GDDI members 2014–2015

The AAN has structured its subcommittee overseeing guideline development in several ways in recent years. The GDDI was first formed in 2014; it existed under a previous name and structure when this practice advisory project was inaugurated. At the time this advisory was approved to advance beyond subcommittee development, the subcommittee was constituted as below.

Cynthia Harden, MD (Chair); Steven R. Messé, MD (Co-Vice-Chair); Sonja Potrebic, MD, PhD (Co-Vice-Chair); Eric J. Ashman, MD; Richard L. Barbano, MD, PhD; Brian Callaghan, MD; Jane Chan, MD; Diane Donley, MD; Richard M. Dubinsky, MD, MPH; Terry Fife, MD; Jeffrey Fletcher, MD; Michael Haboubi, DO; John J. Halperin, MD; Yolanda Holler, MD; Andres M. Kanner, MD; Annette M. Langer-Gould, MD, PhD; Jason Lazarou, MD; Nicole Licking, DO; David Michelson, MD; Pushpa Narayanaswami, MBBS, DM; Maryam Oskoui, MD; Richard Popwell, Jr., MD; Tamara Pringsheim, MD; Alejandro A. Rabinstein, MD; Alexander Rae-Grant, MD; Anant Shenoy, MD; Kevin Sheth, MD; Kelly Sullivan, PhD; Theresa A. Zesiewicz, MD; Jonathan P. Hosey, MD (Ex-Officio); Stephen Ashwal, MD (Ex-Officio); Deborah Hirtz, MD; Jacqueline French, MD (Guideline Process Historian)

Appendix e-4. Complete search strategy

Medline, EMBASE, and Central databases, without time constraints

1. ADHD
2. Attention$
3. Attention Deficit Hyperactivity Dis$
4. ADD
5. Attention Deficit Dis$
6. 1 OR 2 OR 3 OR 4 OR 5
7. EEG
8. theta
9. beta
10. beta/theta
11. 8 OR 9 OR 10
10. 6 AND 7 AND 11

Appendix e-5. AAN rules for classification of evidence for risk of bias

Diagnostic scheme

Class I

A cohort study with prospective data collection of a broad spectrum of persons with the suspected condition, using an acceptable reference standard for case definition. The diagnostic test is objective or performed and interpreted without knowledge of the patient's clinical status. Study results allow calculation of measures of diagnostic accuracy.

Class II

A case-control study of a broad spectrum of persons with the condition established by an acceptable reference standard compared to a broad spectrum of controls or a cohort study where a broad spectrum of persons with the suspected condition where the data was collected retrospectively. The diagnostic test is objective or performed and interpreted without knowledge of disease status. Study results allow calculation of measures of diagnostic accuracy.

Class III

A case-control study or cohort study where either persons with the condition or controls are of a narrow spectrum. The condition is established by an acceptable reference standard. The reference standard and diagnostic test are objective or performed and interpreted by different observers. Study results allow calculation of measures of diagnostic accuracy.

Class IV

Studies not meeting Class I, II, or III criteria, including consensus, expert opinion, or a case report.

Appendix e-6. Modified GRADE criteria applied to clinical questions

Modified GRADE criteria applied to question 1*

Diagnostic test	Outcome±	No. & class of studies	Effect	Precision	Consistency	Directness	Plausibility	Publication bias	Magnitude of effect	Dose response	Comment	Confidence in evidence
EEG theta/beta ratio and EEG frontal power	Improved diagnosis	1 Class III	Accuracy 88% (95% CI 84%–91%)	—	—	D	—	—	—	—	The examination used in the trial would rarely be available to the clinician	Very low

Abbreviation: CI = confidence interval
*For patients with attention-deficit/hyperactivity disorder (ADHD) [patient population], does the addition of EEG theta/beta ratio and EEG frontal power [diagnostic test], compared with standard clinical diagnosis [comparative intervention], lead to improved diagnosis of ADHD [outcome]?
±Includes benefits to core symptoms and associated conditions, harms, tolerability.

Modified GRADE criteria applied to question 2*

Diagnostic test	Outcome±	No. & class of studies	Effect	Precision	Consistency	Directness	Plausibility	Publication bias	Magnitude of effect	Dose response	Comment	Confidence in evidence
EEG theta/beta ratio and EEG frontal power	Accuracy	2 Class I	TPR 93.8% (87.3%–97.1%) FNR 16.4% (8.9–28.2%)	—	—	D	—	—	—	—	Downgraded for significant problems with generalizability of the studies	Moderate

Abbreviations: CI = confidence interval; FNR = false negative rate; TPR = true positive rate.

*For patients with attention-deficit/hyperactivity disorder (ADHD) [patient population], what is the accuracy of EEG theta/beta ratio and EEG frontal power [diagnostic test], compared with standard clinical diagnosis [comparative intervention]?

±Includes benefits to core symptoms and associated conditions, harms, tolerability.

Appendix e-7: Steps and rules for formulating recommendations

Constructing the recommendation and its rationale

    Rationale for recommendation summarized in the Clinical Context includes three categories of premises:
- Evidence-based conclusions for the systematic review
- Stipulated axiomatic principles of care
- Strong evidence from related conditions not systematically reviewed

    Actionable recommendations include the following mandatory elements:
- The patient population that is the subject of the recommendation

- The person performing the action of the recommendation statement

- The specific action to be performed

- The expected outcome to be attained

Assigning a level of obligation

    Modal modifiers used to indicate the final level of obligation (LOO)
- Level A: *Must*

- Level B: *Should*

- Level C: *May*

- Level U: No recommendation supported

LOO assigned by eliciting panel members' judgments regarding multiple domains, using a modified Delphi process. Goal is to attain consensus after a maximum of three rounds of voting. Consensus is defined by:
- $\geq$ 80% agreement on dichotomous judgments

- $\geq$80% agreement, within one point for ordinal judgments

- If consensus obtained, LOO assigned at the median. If not obtained, LOO assigned at the 10th percentile

Three steps used to assign final LOO:
1. Initial LOO determined by the cogency of the deductive inference supporting the recommendation on the basis of ratings within four domains. Initial LOO anchored to lowest LOO supported by any domain
    -   Confidence in evidence. LOO anchored to confidence in evidence determined by modified form of the Grading of Recommendations Assessment, Development and Evaluation process
        -   Level A: High confidence
        -   Level B: Moderate confidence
        -   Level C: Low confidence
        -   Level U: Very low confidence
    -   Soundness of inference assuming all premises are true. LOO anchored to proportion of panel members convinced of soundness of the inference
        -   Level A: 100%
        -   Level B: $\geq$80% to < 100%
        -   Level C: $\geq$50% to <80%
        -   Level U or R: <50%
    -   Acceptance of axiomatic principles: LOO anchored to proportion of panel members who accept principles
        -   Level A: 100%
        -   Level B: $\geq$80% to < 100%
        -   Level C: $\geq$50% to <80%
        -   Level U or R: <50%
    -   Belief that evidence cited from rerated conditions is strong: LOO anchored to proportion of panel members who believe the related evidence is strong
        -   Level B: $\geq$80% to 100% (recommendations dependent on inferences from nonsystematically reviewed evidence cannot be anchored to a Level A LOO)
        -   Level C: $\geq$50% to <80%
        -   Level U or R: <50%

2. LOO is modified mandatorily on the basis of the judged magnitude of benefit relative to harm expected to be derived from complying with the recommendation
    -   Magnitude relative to harm rated on 4-point ordinal scale

- Large benefit relative to harm: benefit judged large, harm judged none
- Moderate benefit relative to harm: benefit judged large, harm judged minimal; or benefit judged moderate, harm judged none
- Small benefit relative to harm: benefit judged large, harm judged moderate; or benefit judged moderate, harm judged minimal; or benefit judged small, harm judged none
- Benefit to harm judged too close to call: Benefit and harm judged to be the equivalent
  - Regardless of cogency of the recommendation the LOO can be no higher than that supported by the rating of the magnitude of benefit relative to harm
    - Level A: Large benefit relative to harm
    - Level B: Moderate benefit relative to harm
    - Level C: Small benefit relative to harm
    - Level U: Too close to call
  - LOO can be increased by one grade if LOO corresponding to benefit relative to harm greater than LOO corresponding to the cogency of the recommendation

3. LOO optionally downgraded on the basis of the following domains
   - Importance of the outcome: critical, important, mildly important, not important
   - Expected variation in patient preferences: none, minimal, moderate, large
   - Financial burden relative to benefit expected: none, minimal, moderate, large
   - Availability of intervention: universal, usually, sometimes, limited

The tables shown in appendix e-8 summarize the results of panel ratings for each domain described above. The tables also indicate the corresponding assigned LOOs. The last column in each indicates whether consensus was obtained for that domain.

Appendix e-8. Clinical contextual profile for factors considered in developing the practice recommendation

In this appendix, *EVID* refers to evidence systematically reviewed, *PRIN* to axiomatic principles of care, and *INFER* to inferences made from one or more statements in the recommendation rationale.

PRACTICE RECOMMENDATIONS

Rationale

Diagnosis with clinical examination and EEG testing

The evidence for the utility of EEG theta/beta power ratio to augment a clinician's judgment when he or she is diagnosing possible ADHD is not strong enough to make a recommendation (EVID). A test must have a demonstrated advantage over the existing reference standard to supersede that reference standard (PRIN). A research study is the proper setting in which to demonstrate that the reference standard evaluation for ADHD can be improved on (INFER).

Recommendation
Clinicians should inform patients with suspected ADHD and their families that the EEG theta/beta power should not be used to confirm an ADHD diagnosis or to support further testing after a clinical evaluation, unless such diagnostic assessments take place within the limits of a research study (Level R).
Note: Level R recommendations are ones that "the guideline authors assert should be applied only in research settings."[8]

Strength of inference

Element	Weak	Modest	Moderate	Strong	Consensus
Internal inferences	< 50%	> 50% to < 80%	> 80% to < 100%	100%	Yes
Strong related evidence	< 50%	≥ 50% to < 80%	≥ 80% to 100%	X	Yes
Acceptance of principles	< 50%	≥ 50% to < 80%	≥ 80% to < 100%	100%	Yes
Logical	< 50%	≥ 50% to <	≥ 80% to <	100%	Yes

		80%	100%		
Confidence in evidence	Very low	Low	Moderate	High	Yes

Note: The lowest of the elements—confidence in the evidence, the logic of the rationale, and the acceptance of principles, strong related evidence, or internal inferences—determines the strength of the evidence.

Strength of recommendation

Modifier	U/R	C	B	A	Consensus
Feasibility	Limited	Sometimes	Usually	Universal	Yes
Financial burden	Prohibitive	Moderate	Minimal	None	Yes
Variation in preferences	Large	Moderate	Small	Minimal	Yes
Importance of outcomes	Not important	Somewhat important	Very important	Critical	Yes
Benefit relative to harm	Too close to call	Modest	Moderate	Large	Yes
Strength of inference	Weak	Modest	Moderate	Strong	Yes

Note: The strength of the recommendation is anchored to the strength of the inference. The recommendation strength can be downgraded for any modifier. In can be upgraded only by one level for a Moderate to Large Benefit relative to Harm.
A Level R recommendation is selected when the overall benefit to risk of the intervention cannot be determined AND the intervention is known to cause harm or to be costly.

Rationale

Accuracy of EEG theta/beta power ratio

We downgraded our confidence in the evidence to moderate because of significant problems with generalizability (see table e-2) (EVID). Physicians pledge to do no harm when they take the Hippocratic Oath (PRIN). There is a risk for significant harm to people misdiagnosed with ADHD because of an unacceptably high false-positive EEG result (INFER). Because of this risk of harm, the combination of theta/beta power ratio and frontal beta power should not be used in place of a standard clinical examination (INFER).

Recommendations

Clinicians should inform patients with suspected ADHD and their families that the combination of EEG theta/beta power ratio and frontal beta power should not replace a standard clinical evaluation (Level B). There is a risk for significant harm to patients of being misdiagnosed with ADHD because of the unacceptably high false-positive diagnostic rate of EEG theta/beta power ratio and frontal beta power (Level B).

Strength of inference

Element	Weak	Modest	Moderate	Strong	Consensus
Internal inferences	< 50%	> 50% to < 80%	> 80% to < 100%	100%	Yes
Strong related evidence	< 50%	≥ 50% to < 80%	≥ 80% to 100%	X	Yes
Acceptance of principles	< 50%	≥ 50% to < 80%	≥ 80% to < 100%	100%	Yes
Logical	< 50%	≥ 50% to < 80%	≥ 80% to < 100%	100%	Yes
Confidence in evidence	Very low	Low	Moderate	High	Yes

Note: The lowest of the elements—confidence in the evidence, the logic of the rationale, and the acceptance of principles, strong related evidence, or internal inferences—determines the strength of the evidence.

Strength of recommendation

Modifier	U/R	C	B	A	Consensus
Feasibility	Limited	Sometimes	Usually	Universal	Yes
Financial burden	Prohibitive	Moderate	Minimal	None	Yes
Variation in preferences	Large	Moderate	Small	Minimal	Yes
Importance of outcomes	Not important	Somewhat important	Very important	Critical	Yes
Harm relative to benefit	Too close to call	Modest	Moderate	Large	Yes

Strength of inference	Weak	Modest	Moderate	Strong	Yes

Note: The strength of the recommendation is anchored to the strength of the inference. The recommendation strength can be downgraded for any modifier. In can be upgraded only by one level for a Moderate to Large Benefit relative to Harm.