Reviewer's report

Title: European Consensus Statement on Diagnosis and Treatment of Adult ADHD

Version: 1 Date: 9 June 2010

Reviewer: David W Goodman

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Major Revisions-
Background section:
1st paragraph, last sentence: I'd make note that "partial remission" is a symptom count and that these patients still retain functional impairments, per Faraone paper, I believe.

2nd paragraph, last sentence: not sure I agree with this. A lot of inattentive subtype have persistent symptoms as the inattention sxs seem to persist with greater impact in adulthood than the hyperactivity/impulsivity

4th paragraph, 1st sentence: Persistence rate should be reflected in a range as papers support 30% plus.

5th paragraph: an additional reason for underdiagnosis in Europe may be the ICD 10 criteria for both inattention and hyperactivity/impulsivity symptoms leaving no entity for inattentive subtype without H/I. This is in contrast to DSM-IV. If so, it might to helpful to mention.

Stigma in general-
2nd paragraph 11th line: as in "and psychiatric residencies" as there is very little if any teaching on adult ADHD in these residency programs.

Gene, environment...-
1st paragraph, line 9: This 30-40% may be a self-reporting bias in patients whose insight into symptoms is limited, and not an accurate rate of persistence. R. Barkley's longtutinal study shows that some ADHD adult don't even recall being diagnosed with ADHD as a child. Should be noted

1st paragraph, line 10 to end: This section is unclear. Are you trying to say that symptoms in first degree relatives are poor matched and therefore the genetic implication is questionable? Needs to be clearer.

2nd paragraph, line 4: "remits" may be a function of symptom count threshold or functional level. Subthreshold symptoms doesn't mean the disorder went away and much as it has changed with neurodevelopment and/or behavioral accommodation. These conceptual distinctions should be noted somewhere.

Definition of ADHD-
End of first paragraph: you may want to consider adding a short discussion of potential modifications in diagnostic criteria proposed for DSM-5 to be published
2013, same year for ICD-11. You can find this information at www.dsm5.org under childhood disorders.

How to properly diagnosis ADHD-

2nd paragraph, line 9: this is currently the threshold proposed by DSM-5, however specificity needs to be assess in clinical settings as other acute psychiatric disorders would reach this symptoms count threshold

Last paragraph: I would suggest adding a brief mention "that based on the high heritability, the likelihood that a parent has ADHD if the child has it, is 30%. If a child has ADHD, the likelihood that one of the parents has it is 50%. The presence of ADHD in a first degree relative increases the likelihood of ADHD's presence in the patient." or something like this. I find in clinical practice that this information adds weight to the accuracy of the diagnosis.

Assessment process-

1st paragraph, last sentence: I'm unaware of any reliable soft neurologic signs seen in adults with pure ADHD. If so, this needs to be specifically referenced for adults with ADHD.

Instruments for screening and diagnosis:

1st paragraph, line 5: I'd add the sensitivity and specificity on this scale to the manuscript.

4th paragraph: I think this paragraph can be expanded to delineate the Biederman/Seidman research on EF in adult ADHD defined by neuropsychological testing vs Barkley's recent publication on the EF symptoms being more predictive of impairments.

Treatment focus in comorbid ADHD-

1st paragraph, line 4: this position will be challenged by bipolar experts who will tell you a bipolar patient may be in a quiet phase of illness and that doesn't mean it gets discounted in the treatment algorithm. The "treat the most severe comorbidity first" is a carryover from child psychiatry. In addition, there is no good quality study that offers clinical guidance on this issue so clinicians have to make the best judgement to treat one condition without worsen another. It has been proposed to diagnostically prioritize comorbidity: first SUD/alcohol abuse, then severe mood disorders, then severe anxiety disorders, then ADHD. Milder depressive or anxious symptoms might be deferred until after treatment of ADHD. I think this section needs to be more instructive to adult clinicians.

2nd paragraph, line 5: the collective work of Fran Levin in New York has not shown appreciable improvement in ADHD with it's treatment in the presence of SUD. The severity of ADHD may play a role in deciding treatment but the patient needs the SUD treated as a primary disorder.

Pharmacotherapy for adult ADHD in Europe-

2nd paragraph, line 11: mention breastfeeding as well; clarify epilepsy as untreated epilepsy (recent review suggests stimulant have little effect on seizure threshold)
4th paragraph, line 4: delete "yet" as it seems like the next part distinguishes MPH from AMPH. I'd also suggest a sentence setting this up: The abuse potential according to N. Volkow's studies relates to the rate of serum rise. Therefore, agents injected or snorted which cause rapid elevations in dopamine levels are highly abusable." then go into your next sentence. In this way, you help the reader understand that abuse potential in based on route of adminstration and not the compound (MPH v AMPH)

4th paragraph, last line: suggest text change "Therefore, medications, usually once daily dose, that have slow rate of serum rise are preferable in treatment to reduce potential for abuse and diversion." or something like this.

Types of stimulants-
1st paragraph: missing dexmethylphenidate XR approved in children, adol and adults.

2nd paragraph, line 1: lisdexamfetamine package insert recently changed to 14 hour duration in adults

2nd paragraph, line 6: I'd be reluctant to use a weight base measure here as there is no clinically relevant concept in adult psychiatry for ADHD (with the exception atomoxetine)

3rd paragraph, line 4: is this an XR preparation? if so, mention it. If not, this preparation is good for 4-6 hours, not long acting, not indicated in adult ADHD in US.

Second line psychotherapeutic agents-
1st paragraph, line 4: two studies in adults with effect sizes .35 and .4 The .6 must be the child study but I thought the effect size was .7. check this and clarify.

Also in this line, strattera duration was this duration in child or adult study? clarify.

line 8: check this. I'm only aware of the Desipramine trial in adults, not an Imipramine trial.

last line needs clarification: and they are not approved to treat ADHD, except guanfacine extended release in children in US.

2nd paragraph, line 2: Given that polypharm in the order of the day with adults with comorbidities, it may be helpful to mention the absence of inhibitory effects of MPH and AMPH on P450 enzymes. That's not to say there may not be pharmacodynamic interactions.

last sentence: I'd clarify this sentence and mentioned the RCTs have not shown consistent support for the use of complementary and alternative nutriceuticals.

Coaching and CBT-
4th paragraph: It is worth noting that there are controlled trials with CBT (Safren) and Meta-cognitive therapy (Solanto) that have been positive. This shows the field is moving to demonstrate efficacy of specific therapies. also very good recent reference on psychotherapies in adult ADHD by M Weiss et al. can be added.
Prognosis-
1st paragraph, line 5: "The poor long term prognosis of untreated ADHD..."

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

Research Grants: Forest Labs, Shire Inc, McNeil, Cephalon, New River Pharmaceuticals, Lilly and Company


Speakers Bureau: Forest Labs, Shire Inc, McNeil Pediatrics, Wyeth


Royalties: MBL Communications

Shareholder: none

Patent Holder: none

Spouse/partner: no financial support or investments with pharmaceutical companies

Activity within the past 3 years and anticipated for the next one year.

Effective July 1, 2009, Dr. David W. Goodman has not participated as a speaker in company-sponsored programs.