Reviewer's report

Title: Algorithms for the diagnosis and treatment of restless legs syndrome in primary care

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Reviewer: Richard Allen

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This is a much-needed paper to help advance better identification and treatment of RLS.

There are some problems that you should consider. Some of these are careless and others represent a lack of critical thought that dampens enthusiasm for the manuscript.

These are all major compulsory revision requests

1) In the introduction, point a, the reference for 50% with sleep less than 5 hours is very poor study using a simple questionnaire to identify RLS patients that had at its best 50% positive predictive value. There are now studies with physician diagnosed RLS that show this estimate is far too extreme. Those with physician judged medically significant RLS have an average self-reported sleep time of about 5.2-5.4 hours and milder RLS has sleep times of about 6.5 hours (Allen, Sleep Med, 2010). The 5-hour statement here is an example of exaggeration that produces skepticism about the real significance of RLS. Even some of the PSG data with moderately severe clinical cases of RLS show higher sleep times (e.g. Saletu, 326 mins). You should either reference better studies with a more honest statement about the sleep loss or be more vague. Hopefully you have been careful not to exaggerate your case too much. You don’t need to do that, but when you do such as this effort to cherry pick to make an incorrect point you loose credibility before anyone bothers to read the rest of the paper. In this regard the issue of daytime drowsiness is not well documented except in some mild RLS patients, so if you emphasize this and the clinician is looking at his patient who despite reporting significant sleep loss is conspicuously alert in the office the clinician will start to doubt the patient’s report of poor sleep. Precision and accuracy is very important.

2) You are inconsistent on what you report as the range of lifetime prevalence of RLS…. 3 – 10% in the abstract and 5 – 10% in the introduction. This is confusing to readers, better to be consistent. 3 – 10% is probably more accurate.

3) In discussing the underdiagnosis you ignore the problem of the questionnaire approach with about a 50% false positive identification. The underdiagnosis may represent an artifact of too many in these studies who do not have RLS or have only such mild RLS that diagnosis makes no sense. How do you know that the doctors were not right rather than your questionnaires. There is one study with physician diagnosis that you do not even reference. I am bothered by the lack of
critical thought with this part of the manuscript, especially if you are striving for credibility. This needs to be rewritten. As written it has limited credibility.

4) The estimate of 35 – 66% of RLS as having moderate to severe disease is certainly unlikely and again would cause readers to wonder why their clinical experience differs from this. This might be true if you talk about only those with symptoms twice a week or more, but the 66% figure again seems likely to represent problems with the questionnaire data approach. This could be removed. The physician diagnosed RLS had a population prevalence of less than 1% for clearly medically significant RLS and less than 3% for severe to moderate medical significance. These are likely to be more realistic estimates – and reflect considerably less than expected from your presentation here. Telling doctors that they are missing so many patients creates a disconnect with their clinical experience and is likely to turn them off, especially when it is probably much exaggerated here. Again take a look at the results of the physician diagnosed study.

5) The argument for not using the algorithm from the MAYO clinic publication seems a bit weak. It is not clear the European guidelines should differ from American ones. The added data is helpful and newer treatment options need to be considered. I wonder if this should be reworded to emphasize the newer treatment options.

6) You have misstated the first diagnostic criteria.
   It is an urge to move USUALLY accompanied or caused by … You left out this important usually … but state it correctly below the criteria.
   The urge or sensations BEGIN or worsen with rest… and not as you state increase or worsen with rest the begin with rest is a critical concept.
   The symptoms become worse in the evening or night, not as you state in the night. The night is too restrictive and not accurate.

7) The high rate of RLS with PD may reflect the medication effect more than problems with diagnosis, I am not certain that it is correct to suggest that the experienced clinician such as Ondo who reports somewhat high rate of RLS with PD would not make an accurate differential diagnosis.

8) Statements like “many physicians are unaware that …. doses required” should be avoided without any supporting evidence. There is no need to talk about physician ignorance if that is the group you want to influence and certainly not good to be so critical here.

9) There is a very awkward sentence “Treatment for RLS should only be initiated when the symptoms impair the patient’s quality of life, daytime functioning, social functioning or sleep to be impaired.” Please clean this up.

10) I went to the web site to see the recommended diary and could not find it there. It certainly is not easy to find if it is there at all. Please correct this problem.

11) For intermittent treatment would you not also consider a GABA active hypnotic if it mostly disturbs sleep.

12) When evaluating iron status from blood samples the transferrin measure is
expensive and not very helpful. I wonder if they meant this to be transferrin saturation.

13) What is meant by the phrase “Frequently intravenous iron therapy is necessary.” What makes this necessary???

14) The phrase “simultaneously to symptomatic treatment” is confusing presumably this was meant to say concurrent with other treatments....

15) Why painful forms of RLS .... “should” be treated with alpha-2 drugs. This is a strong statement. What about opioids? In some cases the dopaminergic drug may also work.

16) The recommendation of follow up every 6 months seems a bit extreme. Yearly follow up is likely to work better, but there are certainly no basis for making this rather strong statement about follow up every 6 months. This will be difficult for many primary care doctors. Could this be more flexible? I worry it feels you are out of contact with the scheduling demands in primary care.

17) Why is the RLS diagnostic index included without any reference to its use or data supporting its utility? It is unlikely primary care doctors will use this sort of scale or interview process. This will take much too long for most doctors. I have trouble imagining it ever being used in primary care setting.

18) The recommended laboratory evaluation differs in the table from that described for iron status in the text. Serum iron may not be very helpful and the critical criteria for ferritin should be consistent.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests