Reviewer’s report

Title: Melatonin and health: an umbrella review of health outcomes and biological mechanisms of action

Version: 0 Date: 29 Sep 2017

Reviewer: Evangelos Evangelou

Reviewer’s report:

The authors have performed an exhaustive search of the field, using various databases. However, I have several concerns and comments that should be addressed.

1. The authors need to better support their search start date. As it stands, it is just backed up from authors’ intuition that they will capture most if not all the reviews and studies into the field.

2. It is unclear why even though the authors' main goal is to study the impact on melatonin in human health, they consider animal and other in vitro studies as eligible. Is this a typo?

3. Having performed several systematic reviews it is difficult to believe that all 5 authors independently extracted information from eligible studies. If true, how this group reached consensus in case of disagreements? Do any metrics measuring rating agreement were used?

4. The approach by Bellou et al. incorporates an evaluation of excess of significance, which has not been performed at this particular study.

5. The criteria for the evaluation of the evidence are clearly missing. The authors need to define upfront what are the thresholds for sample size, p-values, I2 values, prediction intervals etc that they are using to consider an association as significant.

6. Please fix the typo of I2 in line 24 pg.7

7. The test to which the authors refer at line 34 is Cochran's Q statistic, which is a chi-squared based test. As it is written now could be misleading. Typo in line 24

8. The authors do not mention how they select systematic reviews that have been performed for the same associations through out their search period.

9. Line 22, pg.8: A narrative review cannot be synthesized

10. Could you please further comment on systematic reviews with 0 primary studies? Even though weird, there are some Cochrane reviews that have not been able to identify any studies for the research question they were designed for. Please elaborate if this is the case.
11. It is unclear what these overlapping studies are.

12. It is difficult to believe that in 60% of the reviews it was not possible to retrieve the number of the participants or the primary studies included. The authors should reconsider their data extraction strategy.

13. Studies such as case-series or case-studies are placed pretty low in the pyramid of evidence based medicine, I would not consider them at all in order to evaluate the evidence in a field.

13. I wouldn't call the section in pg 10 as effectiveness. I would use another term such as "evaluation of the evidence".

14. The authors do not seem to reach a specific conclusion for association with strong evidence of association.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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