Reviewer’s report

Title: Exploration of knowledge and understanding in patients with primary adrenal insufficiency: A mixed methods study.

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Reviewer: Gregory A. Kline

Reviewer’s report:

In this paper, the authors report the results of their personal interviews with 10 highly selected people, (known to the primary interviewer) living with Addison's disease. This paper is hampered by the unfortunate reality that the scientific literature around adrenal crisis (not including at diagnosis) is very poor and clinical practice is largely based upon dogma derived from theoretical considerations or historical understanding. Thus, the present manuscript does become somewhat of an audit of patients' own knowledge of clinical dogma, rather than of objectively verified diagnoses, practices and outcomes.

1. The introduction of this manuscript makes a lot of references to general review articles or position statements. 10 out of 15 references are not linked to primary data. This diminishes the scientific rigour of the logical arguments that supposed to support the research question. If possible, the authors should try to build their introductory position using references to primary research data rather than summary opinion papers.

2. As an example of the above, where did the figure estimating the worldwide prevalence of PAI come from? It is not referenced. There are 5 references cited pertaining to prevalence or incidence of PAI and 3 of those references are not primary data sources. The two references that are primary data sources pertain to prevalence/incidence figures in European populations and so how do the authors arrive at a global figure, especially since the etiology and therefore prevalence of PAI may be very different in other parts of the world?

3. The authors state that psychological distress is an important cause of adrenal crisis. However, the supporting data referenced is a paper that reports selected patients' self-reported visits to a care centre for IV fluids which is not the same as a diagnosis of adrenal crisis. Even if we allow for the errors inherent in self-reporting, the paper in question (ref 10) cites 1% of adrenal crises as being due to psychological stress. Therefore, this very low and unjustified figure does not belong in the introductory arguments.

4. The authors state a 50% lifetime risk of adrenal crisis but again, the cited papers do not support this figure nor is it clear whether this excludes adrenal crisis at first diagnosis (an obviously different situation than one occurring during chronic care). When I look at the cited paper, it only shows a 33% risk of ever having a (self reported) crisis among those with PAI for 50+ years.
5. The subjects' medical records were apparently reviewed but no medical data is reported in the manuscript to support either the diagnosis or reported episodes of crisis.

6. The study design lacks any kind of controls - i.e. patients with PAI from other clinical practices or living in other parts of UK.

7. The bulk of the manuscript uses the subjects' own words to describe their experience of living with the disease. Many of the statements are fairly generic and could equally be heard from subjects living with other chronic diseases thus are not necessarily informative for PAI care.

8. The conclusions are also fairly generic - disease knowledge is important for health care providers and patient's social supporters, rare diseases are often missed, patients need help adapting to chronic disease etc. Thus, as a whole, the discussion is really more reflective of the difficulties of living with a chronic disease, not specific to PAI.

9. Any conclusions about the overall health system's knowledge and treatment of PAI are essentially impossible to interpret since the "data" is really just the subjective experience of 10 people in a local catchment area.

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

Unable to assess

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

No

**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.

Not relevant to this manuscript

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Please indicate the quality of language in the manuscript:

Acceptable
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