Reviewer’s report

Title: Preventing misdiagnosis of diabetes in the elderly: Age-dependent HbA1c reference intervals derived from two population-based study cohorts

Version: 0 Date: 12 Oct 2018

Reviewer: Baqiyah Conway

Reviewer's report:

This was a very enlightening article on the age-dependency of HbA1C, with important clinical implications. I have only a few minor comments and some concerns that need clarification.

1. The Background section was quite informative, but missing was whether the RBC lifespan changes with age. While the authors provide some information about change in RBC lifespan with age, this needs to be included in the introduction as well as it is important to the rationale of why HbA1c-changes with age should be considered (otherwise the So What? is missing-people may simply have a deterioration of metabolic glycemic homeostasis with age).

2. In the Methods section, please provide more information about the SHIP and SHIP-Trend cohort studies. What were/are the purposes of those cohort studies.

3. Why were there different exclusion criteria for the SHIP and SHIP-Trend (Figure 1)?

4. First paragraph of the Discussion section and Table 1: related to the previous question, it is not clear whether obese subjects were included in the current study. The methods section says they were excluded, Figure 1 says they were excluded from the SHIP-0 study, but Table 1 indicates they were included in both cohorts where approximately 25% of the subjects were obese. Please make this much clearer in the manuscript.

5. Page 11, lines 254-255: the authors imply that HbA1C is the only biomarker being used for the diagnosis of diabetes. This is not the case.

6. Page 11, line 266: insert "age-related" before "increase" where it says "...the increase in HbA1C..."

7. Figure 2. This figure needs to be better labeled. There appears to be four panels, not two. So labeling the panes "a" "b" "c" "d" might be more appropriate than simply "A" "B". Also, the figure legend for this figure should also clearly specify all four figures, otherwise the reader is left to guess that the two top figures belong together and the two bottom figures belong together.
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.

Yes

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