Reviewer’s report

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

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Reviewer: Lea Smircic Duvnjak

Reviewer's report:

This is an excellent study investigating the association between age and A1c in nondiabetic Caucasian population and providing age-dependent reference intervals for A1c. The epidemiological studies performed so far that has formed the basis for recommending A1C to diagnose diabetes included adult populations in general. While some studies have shown increase in A1c in elderly nondiabetic population, these reports have not been recognized by current guidelines leading to overtreatment of diabetes in elderly population. That's why the present results may have important implications for everyday clinical practice.

I have some minor suggestion:

It should be clearly stated that for diagnosis of Diabetes it is recommended to perform A1C test using a method that is certified by the NGSP (www.ngsp.org) and standardized or traceable to the Diabetes Control and Complications Trial (DCCT) reference assay. The advantages of A1c in comparison with fasting plasma glucose and OGTT include less day to day variability during acute illness and greater convenience as fasting is not required. However, it is important to emphasize that A1C is an indirect measure of average blood glucose levels and that other factors that may impact hemoglobin glycation independently of glycemia need to be taken into consideration. In addition to age and ethnicity, the interpretation of A1c level in the presence of anemia and hemoglobinopathies should be discussed (in patients with an abnormal hemoglobin but normal red blood cell turnover - the sickle cell trait - an A1C assay without interference from abnormal hemoglobins should be used). In this context in the patients section - all above mentioned conditions need to be included in the exclusion criteria.

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

Yes

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?  
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Yes

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I am able to assess the statistics

Quality of written English
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