Reviewer’s report

Title: Clinical and cost-effectiveness of oral sodium bicarbonate therapy for older patients with chronic kidney disease and low-grade acidosis (BiCARB): a pragmatic randomised, double blind, placebo-controlled trial

Version: 1  Date: 05 Feb 2020

Reviewer: Claudine Jurkovitz

Reviewer's report:

The authors have addressed all the comments and revised accordingly their manuscript: "Clinical and cost-effectiveness of oral sodium bicarbonate therapy for older patients with chronic kidney disease and low-grade acidosis (BiCARB): a pragmatic randomised, double-blind, placebo-controlled trial".

A few points however remain to be considered:

1. In the weaknesses section of the discussion (page 16), the authors emphasize that the small increase in bicarbonate concentration relative to the placebo may explain the absence of improvement in physical function and rate of CKD progression. However, according to figure 2, the bicarbonate serum concentration in the intervention group seems constant after the initial increase, whereas the bicarbonate concentration in the placebo group increases over the months to reach the level of the intervention arm at 24 months. This increase in serum bicarbonate in the placebo group should also be mentioned and discussed as a weakness. It can certainly be explained by several factors including the fact that this study was designed as a pragmatic trial so no recommendations were given to physicians on the management of low serum bicarbonate concentrations and that 18 patients from the placebo group crossed over.

2. Regarding the time-frame for the secondary outcomes, I understand that the secondary outcomes were analyzed over the 24 months of the study using all available time-points. In the methods section, page 9 line 47, could "this time" be replaced by "24 months"?

3. I thank the authors for providing the information regarding the 187 patients who completed the SPPB (primary outcome) compared to those who did not complete the SPPB (page 11, lines 42-49). Could the comparison between those who completed the SPPB at one year versus those who did not, be provided for each treatment group?

4. Would it be possible to increase the font of the number of patients at each time point in figure 2 or improve the contrast?
5. In table 1, could the symbol for percentage (%) be added to each variable (Ethnicity, Cause of renal dysfunction, Cardiovascular comorbidity) for consistency?

6. In table 2, the asterisk beside the title does not seem to match the asterisk in the footnote

**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

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