Author’s response to reviews

Title: Improving Proteinuria Screening with Mailed Smartphone Urinalysis Testing in Previously Unscrened Patients with Hypertension: a Randomized Controlled Trial

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Author’s response to reviews:

Dear Editorial Committee,

We thank you and the reviewers for your careful consideration of our manuscript. We believe that we have addressed the important concerns raised, and that the manuscript is substantially improved as a result. We hope that the paper may now be acceptable for publication in BMC Nephrology.

Best regards,

Alex Chang, MD, MS, on behalf of the co-authors
Editor Comments:

1 It is stated that 'Verbal consent was obtained as written consent would have required patients to come in person, limiting generalizability'. However, please clarify whether this verbal consent procedure was approved by the ethics committee.

- Thank you for this comment. Yes, the verbal consent procedure was approved by the ethics committee. This has been clarified in the Declarations section.

2 Please state whether figure 1 is your own or taken from another source.

- Thank you for this inquiry. The figure was provided by the manufacturer of the home testing device, Healthy.io, and is not copyrighted.

Reviewer reports:

Claudio Rigatto (Reviewer 1): This lucid and very well written manuscript describes an individual level RCT of a smartphone based home urinalysis test for proteinuria screening in high risk community dwelling patients. Despite several limitations which are well discussed in the manuscript, the investigators did manage to show a ~50% increase in proteinuria screening (29% vs 18%) in the intervention group. Disappointingly, few patients testing positive were subsequently confirmed with quantitative ACR testing.

The paper has several strengths including a well-executed RCT design, relatively large N, a well written manuscript and a cogent and balanced discussion.

- We thank the reviewer for the kind comments.

I have a few thoughts for the authors, more in the spirit of intellectual dialogue than criticism/revision:

1. I would have liked to see a broader discussion on implications for future research in the discussion, as I think this study has several important lessons in this regard.
2. The first lesson is the importance of waived consent in the execution of such a study. In future every effort should be made to obtain this waiver, as the yield without it is predictably low. This may require changes to existing rules in the case of low risk interventions such as this.

3. Then second lesson is the importance of a single step testing process in this environment. It does not surprise me that the uptake of ACR screening following Dip + status was low. From the end user perspective, if a home tester, who, out of preference or necessity has gone to the trouble of mastering and doing the test, however simple, is then required to attend the lab for further testing, all perception of value invested in the home test is lost. The home test must be as definitive as possible to avoid attrition at this step. Quantitative ACR testing is a must in future endeavours of this kind.

4. Although the above points are briefly made under limitations, I would have preferred the authors to have given them more relevance, perhaps in a paragraph highlighting future research implications.

-The reviewer brings up excellent points related to the importance of waived consent in this type of trial, as well as the simplifying the process as much as possible for the end-user to maximize adherence. We wholeheartedly agree with these sentiments as we learned of these limitations during the execution of this trial. While we addressed these issues partially in the limitations section, we agree that more emphasis could be made to help others plan a trial or implementation of home testing. We have added several sentences in the discussion and conclusion to elaborate on these issues in more detail.

Visnja D. Lezaic (Reviewer 2): The objective of this randomized controlled trial was to evaluate the effectiveness of home urinalysis testing, using a smartphone urinalysis kit (Dip.io), among previously unscreened patients with hypertension receiving care at the Geisinger Health System. The authors proposed a simple technique, promises to increase testing of people at risk. The technique is applicable in different environments. Together with screening performed in general practice units, detection of people with kidney damage is likely to increase significantly. Or at least pay attention to the frequent controls of people with signs of kidney damage. The authors cite several limitations, but do not state whether false negative results are also considered.
We thank the reviewer for the comments. We have added to the limitation section that it is possible some of the results could be false negatives or false positives, which is impossible to know due to few having repeat testing.