PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Financial Incentives to Increase Uptake of Pediatric HIV Testing (FIT): Study Protocol for a Randomized Controlled Trial in Kenya
AUTHORS	Wagner, Anjuli; Njuguna, Irene; Neary, Jillian; Omondi, Vincent; Otieno, Verlinda; Babigumira, Joseph; Maleche-Obimbo, Elizabeth; Wamalwa, Dalton; John-Stewart, G; Slyker, Jennifer

VERSION 1 – REVIEW

REVIEWER	Stefan Priebe Unit for Social and Community Psychiatry, Queen Mary, University of London, United Kingdom
REVIEW RETURNED	09-Jun-2018

GENERAL COMMENTS	Before commenting I need to say that I have no experience whatsoever with services in Africa, no expertise at all in HIV treatment and only very limited expertise in screening programmes or care for children. I do have a background in studies of financial incentives and in trial methodology. I found the protocol clear and well written. One might discuss details of the design, but I understand that it has been approved by all relevant bodies and therefore cannot be changed anymore anyway. Two minor points: a) When the term financial incentives is used in the context of Western health care, it usually refers to exactly that, i.e. an incentive to motivate people. Yet, in the introduction the authors point to a potentially different effect here, i.e. that the money enables people to come and that without the money some might not be able to afford the costs of coming to the service. Did I misunderstand this? If not, how relevant is the enabling factor in relation to the different levels of incentives? Perhaps, that can be clarified for the reader. b) The study has two primary outcomes which however are not independent of each other. Are they co-primary outcomes and is the study powered appropriately for two rather than only one primary outcome? And finally just a comment: it might say something about the current state of ‘global health’ that a study conducted in Africa has as many authors based in the US (including the first, last and corresponding author) as in Kenya. Yet, this is not a specific criticism of this paper or its authors.

REVIEWER	D Tappin University of Glasgow, UK

REVIEW RETURNED	29-Jun-2018

GENERAL COMMENTS	Discussion, study limitations and concluson may not be required although they are interesting. No description of 'trial sponsor' that I can see No information on Management Committee or Steering Committee Hypothesis should be labelled Is it a superiority trial? In general I am not sure this is in the format of BMJ Open, but I will leave this to editors

VERSION 1 – AUTHOR RESPONSE

Reviewers' Reports:

Reviewer: 1
Reviewer Name: Stefan Priebe
Institution and Country: Unit for Social and Community Psychiatry, Queen Mary, University of London, United Kingdom
Please state any competing interests or state 'None declared': None declared

Before commenting I need to say that I have no experience whatsoever with services in Africa, no expertise at all in HIV treatment and only very limited expertise in screening programmes or care for children. I do have a background in studies of financial incentives and in trial methodology.

I found the protocol clear and well written. One might discuss details of the design, but I understand that it has been approved by all relevant bodies and therefore cannot be changed anymore anyway.

Two minor points:

1) When the term financial incentives is used in the context of Western health care, it usually refers to exactly that, i.e. an incentive to motivate people. Yet, in the introduction the authors point to a potentially different effect here, i.e. that the money enables people to come and that without the money some might not be able to afford the costs of coming to the service. Did I misunderstand this? If not, how relevant is the enabling factor in relation to the different levels of incentives? Perhaps, that can be clarified for the reader.

We thank the reviewer for this thoughtful comment and cross-context comparison. We agree with the reviewer's comment that a financial incentive is to motivate people to complete a desired behavior. We hypothesize that the incentive may have different possible mechanisms. One possible mechanism is that the incentive would "nudge" individuals to take action or to act more promptly; this mechanism is consistent with behavioral economics literature. The other possible mechanism is that the incentive will offset costs, enabling an individual to take action. This second mechanism is supported by formative work from our previous qualitative and quantitative studies in this population, in which direct and indirect costs were cited as a barrier to completing testing.

We have clarified this in the manuscript's Conceptual Framework section, with the revised sentence, "FI may motivate parents who are willing to test to take action to test by either offsetting costs or by motivating more prompt action."

2) The study has two primary outcomes which however are not independent of each other. Are they co-primary outcomes and is the study powered appropriately for two rather than only one primary outcome?

In response to this comment, we have reviewed the statistical considerations raised in the manuscript, "Sample size determination for clinical trials with co-primary outcomes: exponential event times" (Hamasaki Pharm Stat 2013), as well as the FDA's guidance, entitled "Multiple Endpoints in Clinical Trials". This trial has multiple endpoints; we hypothesize that increasing levels of FI may motivate more individuals to test their children (the proportion testing) or may motivate them to test their children more promptly (time to testing). This trial aims to detect a difference in either endpoint, rather than both endpoints.

Our study was powered to detect a difference in the binary outcome (proportion of individuals completing testing), as this outcome requires greater numbers of subjects than the continuous outcome (time to testing). However, our power calculations and statistical analysis plan have not taken into account the dependence of the two outcomes.

Given that this trial aims to detect a difference in either endpoint and that these outcomes are not independent, this runs the risk of increasing type I error. We also have predicted strong positive dependence in our co-primary outcomes, making some conventional approaches to controlling for multiplicity too conservative. To address this, we have added a Hochberg correction to the individual p-values (overall alpha level of 0.05). This specific example fulfills the assumptions of the Hochberg correction. We have modified the manuscript to include the sentence, "Primary outcome analyses will include a Hochberg's adjustment to p-values to address multiplicity."

3) And finally just a comment: it might say something about the current state of 'global health' that a study conducted in Africa has as many authors based in the US (including the first, last and corresponding author) as in Kenya. Yet, this is not a specific criticism of this paper or its authors.

We appreciate this important and timely comment. While the reviewer has not required a response to this comment, we wish to take the opportunity to express our agreement and share how our team has considered authorship within the context of this study. We are fortunate that our research group is part of a >30 year long collaboration between the University of Nairobi and University of Washington that has jointly invested in the training of several "generations" of research leaders. Within the current study, two junior scientists (Wagner [US epidemiologist] and Njuguna [Kenyan medical doctor]) have co-led the FIT trial under the guidance of US and Kenyan mentors (Wamalwa, Slyker). At the beginning of the pilot and trial, this team agreed on equitable authorship for Kenyan and US team members. Two manuscripts have been published from this study, one each with Kenyan and US lead author; two manuscripts (including this manuscript) are pending publication, one each with Kenyan and US lead authors. We thank the reviewer for the opportunity to address this comment.

Reviewer: 2
Reviewer Name: D Tappin
Institution and Country: University of Glasgow, UK
Please state any competing interests or state 'None declared': None

1) Discussion, study limitations and conclusion may not be required although they are interesting.

We appreciate this comment. We have elected to retain these sections in the manuscript, unless the editorial team requests removal.

2) No description of 'trial sponsor' that I can see

We have revised the section entitled “Funding”, replacing the word “funders” with “sponsors” to clarify the sponsorship of this trial.

3) No information on Management Committee or Steering Committee

We believe that the reviewer is commenting on item 5d of the SPIRIT checklist, “Roles and responsibilities”. We have modified the sentence in the “Ethical considerations” section to read, “A data monitoring committee will not be convened due to no planned interim analyses and minimal risk potential of the intervention. A steering/management committee was not deemed applicable in this trial.”

4) Hypothesis should be labelled

We have adapted the sentence in the section “Conceptual Framework” to include labeling of our hypothesis, now reading, “Hypothesis: We hypothesize that the proposed FI intervention will primarily move willing parents from “Willing to test” to “Taking action” (Figure 1).”

5) Is it a superiority trial?

Yes, this is a superiority trial. We have modified the sentence of the “Study design” section to now read, “The FIT trial is a 5-arm, unblinded, individual-level, superiority randomized controlled trial (RCT) of FI.”

6) In general I am not sure this is in the format of BMJ Open, but I will leave this to editors

We have addressed all formatting comments from the editorial office in the below comments.

FORMATTING AMENDMENTS (if any): Required amendments will be listed here; please include these changes in your revised version:

1) Please provide another copy of your figures with better qualities and please ensure that Figures are of better quality or not pix-elated when zoom in. NOTE: They can be in TIFF or JPG format and make sure that they have a resolution of at least 300 dpi and at least 90mm x 90m of width. Figures in PDF, DOCUMENT, EXCEL and POWER POINT format are not acceptable.

We have included revised figures as high quality JPG formats with >300 dpi.

2) We have implemented an additional requirement to all articles to include 'Patient and Public Involvement’ statement within the main text of your main document. Please refer below for more information regarding this new instruction: Authors must include a statement in the methods section

of the manuscript under the sub-heading 'Patient and Public Involvement'. This should provide a brief response to the following questions:

How was the development of the research question and outcome measures informed by patients' priorities, experience, and preferences?
How did you involve patients in the design of this study?
Were patients involved in the recruitment to and conduct of the study?
How will the results be disseminated to study participants?
For randomised controlled trials, was the burden of the intervention assessed by patients themselves?
Patient advisers should also be thanked in the contributorship statement/acknowledgements.
If patients and or public were not involved please state this.

We have added the following section to the manuscript in the "Methods and analysis" section:

Patient and Public Involvement:

The research intervention and outcome were informed by formative research with the patient population: the concept of FI emerged from qualitative and quantitative work with patients 19; the value and format of the FI were reviewed by patients during the pilot 23. Site specific, and overall, study results will be shared with the research facilities in closeout meetings; we do not have ethical permission to re-contact individual study participants to share study results.