RESEARCH ARTICLE

REVISED A pilot study to explore utility of electronic informed consent in a low- income setting; the case of a Controlled human infection study in Blantyre, Malawi

[version 2; peer review: 2 approved, 3 approved with reservations]

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v2 **First published:** 29 Apr 2024, **9**:233
https://doi.org/10.12688/wellcomeopenres.20770.1
Latest published: 05 Feb 2025, **9**:233
https://doi.org/10.12688/wellcomeopenres.20770.2

Abstract

Background

Electronic informed consent can improve accuracy, workflow, and overall patient experience in clinical research but has not been used in Malawi, owing to uncertainty about availability, utility, patient data security and technical support.

Objectives

We aimed to explore the utility of electronic consent (e-consent) in an ongoing human infection study in Blantyre, Malawi.

Methods

The approved paper consent forms were digitized using Open Data Kit (ODK). Following participant information giving by the research staff,

Open Peer Review

Approval Status ? ✓ ? ? ✓

	1	2	3	4	5
version 2 (revision) 05 Feb 2025		✓ view		? view	✓ view
version 1 29 Apr 2024	? view	? view	? view	? view	

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2. **Evelyne Kestelyn**, Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam
3. **Dr. Muhammed Afolabi**, London School of Hygiene and Tropical Medicine, London,

healthy literate adult participants with no audio-visual impairments completed a self-administered e-consent and provided an electronic signature. We dual-consented participants by both paper-based and electronic-consenting. Signed e-consent forms were uploaded to a secure study server. Utility of e-consenting was observed by participation rate, user-friendliness, documentation error rate, and staff perception of the overall consenting process.

Results

All 109 participants offered e-consenting accepted participation. E-consenting was user-friendly, had no identifiable documentation errors as compared to 43.1% (n 47/109) error rate with paper-based consenting, and ensured data safety, and unravelled areas for consideration. Challenges with e-consenting included difficult digitization of ethics stamped documents, as well as present but infrequent delays of retrieval of e-consent forms.

Conclusion

E-consenting is feasible, has a utility benefit in a controlled human infection study in Malawi; a low-income country, and can supplement paper-based consenting. Its usefulness can improve the consenting process in research conducted in such settings. Additionally, success of e-consenting requires a careful consideration.

Plain Language Summary

Informed consent involves educating a patient or participant about the risks, benefits and alternatives of a procedure or clinical research in a format and language that they can understand to achieve voluntary participation. Traditionally paper-based consent has been used but it is not without its limitations thus the need to introduce electronic consent. Electronic consent involves the use of electronic devices to deliver a variety of media including video as well as written words to convey the study details and then secure digital recording to save the informed consent.

We piloted electronic consent in an ongoing human infection study to assess feasibility in Malawi. The approved paper consent forms were digitized and uploaded to an electronic platform. Participants completed dual consent of paper and electronic consent in that order. We then compared issues arising from using both methods.

We found that e-consent was feasible. It proved to be reliable, and minimized documentation errors. We noted, however, that electronic consent could not be done in technologically challenged settings as it required internet connection to help upload forms to secure servers. In addition, researchers are still required to provide printed proof of consent and so current practice would also require a printer to be available. When infrastructure limitations are overcome, e-consent

UK

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Any reports and responses or comments on the article can be found at the end of the article.

offers improved participant experience and increased data reliability.

Keywords
Electronic informed consent, Open Data Kit, clinical trial, Streptococcus pneumoniae, randomized control trial.

This article is included in the Malawi-Liverpool Wellcome Trust Clinical Research Programme gateway.

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Competing interests: No competing interests were disclosed.

Grant information: This work was supported by Wellcome (211433).
The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

How to cite this article: Ngoliwa C, Chakwiya C, Gondwe J *et al.* **A pilot study to explore utility of electronic informed consent in a low- income setting; the case of a Controlled human infection study in Blantyre, Malawi [version 2; peer review: 2 approved, 3 approved with reservations]** Wellcome Open Research 2025, **9**:233 https://doi.org/10.12688/wellcomeopenres.20770.2

First published: 29 Apr 2024, **9**:233 https://doi.org/10.12688/wellcomeopenres.20770.1

REVISED **Amendments from Version 1**

The revised manuscript reflects the intention of a carefully conducted pilot. The revised manuscript responds well to reviewers' observations and concerns of the previous version. We have carefully reframed the title, built a strong background and clearly stated the problem and aims of the pilot. Additionally, we have detailed and clarified the methodology of the pilot, changed the approach to presentation of results, and have strengthened the discussion based on the results.

Provides useful detail and clarity. We have included new definitions, clarified the different consenting methods and how the pilot sub-study relates to the main study. We have also clarified on the methods, how data was handled, the usefulness of the pilot, strengths, and limitations of the pilot.

Easy to read and follow, and interesting. The new version is an improved narrative and unpicks difficulties and complexity of the previous write-up. We have provided adequate and necessary detail.

Strikes the right context of the paper. In the new version of the manuscript, we have deliberately emphasised that the pilot was conducted in the first pneumococcal vaccine trial using a human infection model in Malawi; a low- income setting. We have clarified the pilot is feasible and useful in a human infection study in Malawi; but the methods can be transferable, and the experience, observations made, and considerations proposed can be applicable to other low-income settings in Africa.

Good finishing off, proposes considerations and future steps. This new version concludes with a good synthesis of the pilot, its relevance and proposes next steps for future similar studies.

Any further responses from the reviewers can be found at the end of the article

Introduction

Informed consent; an integral part of the ethical conduct of any study, is a process that involves explaining to a patient or study participant the risks, benefits or alternatives of a procedure or clinical research in a format and language that is comprehensible, in order to ensure voluntary participation[1]. Obtaining an informed consent from a study participant can be verbal or written. The written consent has two main modalities: the traditional paper-based consenting process followed by a participant signature on a paper-consent form or an electronic consenting process followed by an electronic signature in the consent form (also called an e-consent)[2].

The traditional paper-based consent; despite its usefulness has some challenges including high documentation errors as high as 50%. These errors for example, include incomplete forms due to missing information, wrong spellings, and lack of legibility in some circumstances[3]. Additionally, paper-based consent requires physical storage which can be challenging and make remote access limited and physical retrieval of consent documents cumbersome, and usually requires physical presence of both the participant and the consenter[4–6].

E-consenting can be done physically in the presence of the study participant and the consenter (usually a nurse or clinician in the case of clinical research or medical procedure or any other trained staff), or remotely. This method of consenting uses electronic devices such as mobile phone or tablets containing study information for the potential volunteer, who demonstrates an informed consent by providing an electronic signature or thumbprint. E-consenting therefore provides a versatile alternative to the paper-based consent and can be useful in enhancing the consenting process through audio-visual and interactive components for participants requiring such[2,5]. Additionally, e-consenting allows several flexibility advantages: can be time saving especially when done remotely hence cutting time spent on travel, can provide appropriate user-friendly interface, forms can be easily accessible remotely, and mitigates the need for physical storage space[6,7].

However, e-consenting is not without limitations. These include cost of developing the initial infrastructure and technology to manage and validate electronic consenting documents[8] including the participant information and e-consent forms, need for a reliable Wi-Fi network for consenting data upload, retrieval and updates, security risks including corrupted or deleted forms, and its usability in limited resource settings[8,9].

Although e-consenting has been successfully utilised in different studies and settings, as well as ethical issues explored[10], there is no study that has explored the role of e-consenting in a human infection study conducted in a low-and middle income setting (LMIC). We therefore designed a sub-study to pilot the utility and explore considerations for e-consenting in participants enrolled in an ongoing Controlled Human Infection Study (CHIS) in Malawi, a low-income country.

Methods

Ethics consultation and approval

In October 2021, through the Data Management Support Unit at Malawi-Liverpool Wellcome Programme in Malawi, we engaged the National Health Sciences Research Committee and proposed to test the usability of e-consenting in a human infection study. NHSRC approved the proposal on 29 October 2021, pilot of e-consenting was conducted from 8th February 2022 to 9th May 2022.

Study design

We conducted an observational pilot study nested in a large cohort longitudinal trial investigating the efficacy of Pneumococcal conjugate vaccine using a Human Infection Study[11,12]. The main trial, conducted at Queen Elizabeth Central Hospital in Malawi, was approved by NHSRC (protocol 16/07/2519) and was registered in the Pan African Clinical Trials Registry (REF: PACTR202008503507113). The e-consenting pilot aimed at exploring the utility of e-consenting in a Human infection study in Malawi, in a low-income setting.

Study participants, consenting methods and procedures

E-consenting pilot recruited all willing participants enrolled in the main trial[12]. Recruited participants were healthy literate adults aged 18–40 years, had no physical disability including audio-visual deficiencies, and had access to a mobile phone.

We offered dual consenting (paper-based consenting followed by e-consenting) to all study participants recruited to the pilot.

Consenting for all participants recruited to the main trial[12] was physical paper-based consenting. The process had two main steps: firstly, study staff (a nurse or a doctor) providing study information to participants using the participant information leaflet (PIL), and secondly completion of the consent form. The consent form contained two sections: *1)* a ten-item comprehension checklist (participant wrote initials) to ensure participant understanding and agreement to adequacy of study information and voluntariness of study participation, *2)* name and signature the participant and study staff, and finally date and participant identification number (PID). Paper based PIL and consent form were filed and stored in locked cabinets within the research room.

Upon completion of paper-based consenting, all participants were offered e-consenting. This procedure was conducted in the presence of both the participant and the consenter. We allowed a "cooling off" period (approximately 5 minutes) before initiating e-consenting. The process and rationale for e-consenting was explained to study participants *apriori* including a brief demonstration of how to navigate through the e-consent forms. E-consenting adapted all ethics approved documents from the paper-based consenting. These included scanned PIL and consent forms in PDF format and the ten-item comprehension checklist in ODK format. Of note, because of the timing of the e-consenting, we did not require repetition of providing study information- the PIL was not repeated.

Study personnel first linked the electronic consent form to a PID by scanning the PID barcode. The form prompted the participant to write their name. We allowed participants to skip the PIL as this discussion had already been done. Next was the consent form containing the ten-item comprehension list. Instead of initialling, the e-consent form prompted participants to select "I agree" by a single tap at the end of each statement to demonstrate comprehension and agreement to the study information, procedures and voluntariness of participation. Using a stylus, both the participant and the study personnel signed the consent form. We exported the consent form to a secure study data server using an internet connection. We printed a copy of the completed e-consent for the study participant.

We explored several observations in both e-consenting and paper-consenting for comparability. We observed ease of navigating and completing the two consenting methods (e-consent versus paper-based consent), user-friendliness, ease of uploading and retrieving the e-consent including producing print-out copies, as well as reliability of internet connectivity. Additionally, we assessed presence of any documentation errors in both e-consent and paper-based consents based on completeness, accuracy and legibility. We categorised documentation errors into two: writing mistakes (such as inaccurate date, time, spellings, misplaced information, lack of legibility) and missing information (incompleteness). We defined *error rate* in documentation as number of participant forms, of the total consent forms, with any amount of observed errors. We sought feedback on time taken to complete e-consent and paper-based consent forms (and not time taken for the consenting process as e-consent did not require repetition of going through the PIL) from study staff. Through unstructured interviews with the study staff, we explored pros/cons of e-consenting and paper-based consenting.

Setting up e-consenting in Open Data Kit (ODK)

ODK is an open-source suite of tools designed to help users build information services[13]. Electronic forms, same as the approved paper-based consenting forms were designed using XLSForm syntax which is an intuitive language. This involved defining the questions or consent statement, response options and other relevant information like signature fields. Once the form was designed, it was converted into XML format using the XLSForm converter tool. The XML files were then uploaded to the ODK server or directly to a mobile device using the mobile app for data collection called ODK collect. Following approval from NHSRC, an identical copy of the NHSRC ethical approval stamp was affixed to the electronic CRF in ODK.

Results

A total of 109 HIS participants (male 67%, n=73) were recruited in the e-consenting sub-study (Table 1). All the 109 participants were consented using both paper-based and electronic consenting. All participants were able to navigate through the e-consent and required minimal support. Of note, 63.6% (n= 70) of the participants in this pilot were college students with prior experience of using computers and tablet devices. All recruited participants had prior experience of operating a mobile phone.

100% (n=109) e-consent forms were successfully uploaded, retrieved and printed out for copies on the same day of clinic visit. There were no missing forms or reports of breach of data security. Study staff reported experiencing delays on some days (not quantified) largely due to poor internet connectivity but were resolved during the period of the enrolment study visit (this visit took approximately 2 hours), nevertheless, the delays were not as frequent. Though unsolicited, none of the 109 participants who were offered e-consenting refused or raised any concerns with e-consenting.

There was 0% error rate (0 of 109 forms) identified in the e-consent; compared to 43.1% error rate (47/109 forms had errors) in the paper-based consent. Of these, 29.4% (n=32) were writing mistakes by both study personnel and participants, and 13.8% (n=15) were missing information. All study staff involved in the consenting process (a total of 10) consistently reported that completing the e-consent took less time than the paper-based consent. However, this was not objectively measured.

Unstructured interviews with study staff on the pros and cons of e-consenting showed that e-consenting supplemented paper-based consenting and further revealed areas of consideration[5] related to staff, participants and the e-consenting infrastructure (Table 2).

Table 1. Demographic characteristics of e-consent pilot study participants.

	Male	Female	Total
n (%)	73 (67.0%)	36 (33.0%)	109 (100%)
Age (mean)	27	27.8	27.3
Previous computer experience n(%)	63 (57.3%)	23 (20.9%)	86 (78.2%)
Education level (Primary) n(%)	6 (5.5%)	10 (9.1%)	16 (14.5)
Secondary n(%)	17 (15.5%)	7 (6.4%)	24 (21.8%)
Tertiary n(%)	50 (46.0%)	19 (17.3%)	69 (63.3%)

Table 2. Pros and cons of electronic consenting.

Category	Pros	Cons	Categorical considerations
Staff and participant operations	- Reduced documentation errors - Easy to access consent forms, including remotely	- There was need for dual consenting (paper and electronic) as a hybrid method was adopted	- Accessibility - Impact on study teams - User-friendliness and user-comprehension
e-consent infrastructure	- Easy to navigate - Faster to complete	- Need for considerations for participants with audio-visual deficiencies	- Participant familiarity and preference of consenting method - Community acceptability of technology - Complexity of the design of electronic forms - Data security
Internet facility	- Enhanced data safety as documents were immediately saved to secure server thus preventing them from loss due to misfiling or misplacement especially if there was more than one study happening at a site	- Difficult upload and retrieval of ethics stamped documents - Could not be done if internet was not available	- Availability and reliability of the internet - infrastructure
Storage facility	- Reduced the burden of filing as all forms are stored on data server	- Difficult to access - data when the - internet is unavailable	- Accessibility

Discussion

This study explored the utility of e-consenting in the first human infection study in Africa investigating the protective effect of PCV13 against experimental pneumococcal carriage[12]. We showed in this study that e-consenting is feasible in Malawi, a low–income setting, and can be used in participants with different literacy levels. All study participants engaged accepted e-consenting and completed both paper-based and e-consents. This observation; 100% participation and completion of e-consenting has been made elsewhere[5,14].

Furthermore, we observed additional usefulness of e-consenting mainly through massive reduction in documentation errors (zero-identifiable errors), as opposed to the traditional paper-based consenting (43.1% error rate). This observation, much that e-consenting immediately followed paper-based consenting (providing elucidation of the consenting process due to prior-experience/exposure), might have contributed to the observed improvement in errors, is still consistent with lower error rates as low as 1% versus 32% (e-consenting versus paper-based) observed in other studies[3,15].

Additionally, e-consenting enhanced ease of form search and retrieval from the database as well as remote access by the investigators. This advantage has shown some utility benefits in studies obtaining remote consenting, eliminating the cost

and time-burden of travel for consenting, as well as in situations where face-to-face physical consenting was deemed unsafe and disadvantageous[5]. Of note, we did not objectively quantify duration of e-consenting versus paper-based consenting. Nevertheless, study staff reported that e-consenting took less time to complete, and form upload to the server was instant. This could increase efficiency by reducing the burden of physical filing especially in settings where keeping a copy of paper-based consent form is optional. Data safety was also enhanced with electronic consenting as consent forms were immediately exported to secure servers. There were no missing forms and no reported or identified breach of participant privacy.

The strength about this study is that to our knowledge, it is the first study of a large cohort of participants in a low-income setting to explore the usability of e-consenting in a controlled human infection model. Additionally, based on 100% participation rate and successful completion, upload, retrieval and issuance of a physical printed copy of the e-consent form to all study participants approached and recruited to the e-consenting study, not only reaffirms feasibility of e-consenting but also strongly suggests acceptability of the e-consenting process in Malawi. Additionally, at the time of writing this article, the Malawi Ministry of Health did not have guidelines for electronic informed consenting. The pilot therefore provides enthusiasm to further explore participant and staff experiences, considerations for e-consenting including infrastructure set-up, ethical and cultural concerns, as well as participant factors including considerations for the illiterate, and those requiring audio-visual enhancements.

The study had some limitations. Dual consenting was offered serially to all recruited participants hence the study lacked random allocation of the consenting method which would have otherwise enhanced comparability of outcomes of the two consenting methods. We made several observations surrounding e-consenting but did not explore participants' experience and perceptions of e-consenting. Additionally, the pilot was conducted in an urban setting, at a site with access to internet and electricity hence the observation would not apply to studies done in remote areas. Since e-consenting is a new concept in Malawi, the ethics review boards did not have digital stamps thus it was initially difficult to digitize consent forms.

In conclusion, e-consenting has a utility benefit in research in Malawi, has a role in improving the consenting process and can supplement the traditional paper-based consenting. Success of e-consenting is multifactorial and its adoption requires a consultative and careful consideration.

Data availability

Underlying data

Figshare: Piloting electronic informed consent: A Pneumococcal Human Infection Study in Blantyre, Malawi. https://doi.org/10.6084/m9.figshare.24321655[16].

This project contains the following underlying data:

- Data file 1 (The attached file contains the following information: Data of participants: Age, Sex, Education level and computer literacy)

Software availability

Data was collected using the Open Data Kit (ODK) application on an android device. To complement to ODK functionality, an additional in-house application was used called ODK lookup updater application, which helped to enforce data validation.

Acknowledgements

Malawi Accelerated Research in Vaccines, Experimental Laboratory Systems consortium: **Laboratory team**: Tarsizio Chikaonda, Kondwani Jambo, Simon Sichone, Christopher Mkandawire, Raphael Kamn'gona, Percy Mwenechanya, Godwin Tembo, Mphatso Mayuni, Bridgette Galafa, Lorensio Chigoneka; **Field worker:** Tina Harawa; **Pharmacy**: John Ndaferankhande.

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16. **Econsent_pids20240403**.

Open Peer Review

Current Peer Review Status: ? ✓ ? ? ✓

Version 2

Reviewer Report 06 March 2025

https://doi.org/10.21956/wellcomeopenres.26056.r118699

✓ **Melissa McCradden**
The University of Adelaide, Adelaide, South Australia, Australia

This paper describes a pilot study primarily of the feasibility of e-consent processes in Malawi.

This reviewer has rated the conclusions as not being fully justified by the data.
"We showed in this study that e-consenting is feasible in Malawi, a low–income setting, and can be used in participants with different literacy levels."
I'm not sure that this conclusion is entirely warranted based on the data. This is a high proportion of "college students" (63%) which represent only a subset of the total population.

I find Table 1 a bit confusing. It is suggested to use a range for the age (not just the mean) and to indicate whether the education levels are highest completed or otherwise? It's also not clear if the proportion stated is the Yes or No answer to the associated question. For global readers, 'primary', 'secondary', and 'tertiary' should be defined.

Presumably, the system prompts the user to complete each field and has a set of accepted values? If true, then the low error rate (while a good thing!) is not particularly remarkable. Similarly (and related to the second point, below), if it forces a decision on particular items, how is it ascertained that users are not just clicking through to completion? Might the effect of a study team member being beside them for this process affect the generalizability of the results beyond situations where personnel are in parallel to e-consent?

A more substantial concern upon reviewing the paper is the validity of the consent itself. Not to say that paper-based consent is perfect (we know it is not), but one might expect an evaluation of the feasibility of e-consent to also assess whether the digitized process offers similar (or better) understanding of the research process, the benefits and risks, the procedures, etc. This would need to involve verification that the participant understood and appreciated the information contained in the e-consent, not just whether they completed the form without missing anything. Perhaps this is a future study for the team, and I think the paper does not over-extend what work is described herein, but it's worth a consideration.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Not applicable

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: research ethics, pediatric ethics, artificial intelligence, healthcare evaluations

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 25 February 2025

https://doi.org/10.21956/wellcomeopenres.26056.r118171

Evelyne Kestelyn
Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam

The authors have addressed all my comments satisfactory so I am happy to approve this new version without any further questions or comments.

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?
Partly

Are all the source data underlying the results available to ensure full reproducibility?
Partly

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Clinical trial conduct, ethics, data management

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 12 February 2025

https://doi.org/10.21956/wellcomeopenres.26056.r118168

?

Erisa Sabakaki Mwaka
School of Biomedical Sciences, College of Health Sciences, Makerere University, Kampala, Central Region, Uganda

I have a few more minor comments for the authors:

1. The rationale for recruiting only literate people should be included in the methods.

2. How was the unstructured interview data analysed? Content analysis? Thematic analysis? Were these unstructured interviews guided or were respondents just volunteered information? This has to be clear.

3. A part from College students, who else participated in the study? This information is not included in Table 1.

Discussion

4. In paragraph 1 of the discussion, it is stated *"We showed in this study that e-consenting is feasible in Malawi, a low–income setting, and can be used in participants with different literacy levels"*. I find this statement problematic. The findings of this study cannot be generalized to Malawi because a greater majority of the participants were literate, the sample size was small, and the

sampling was non-probability! That statement should be revised.

5. There are two contradicting responses:

· "*Thank you very much. Both consents were self-administered with supervision by the study staff, we also maintained the same nurses and clinicians during the study. We however did not explore the reason for the errors".*
and, *"The errors are due to human mistakes (both study staff and participants) quality control was done at the end of the screening visit*".

Since it is indicated in the rebuttal that these were human errors, this should be discussed in the paper. There seem to be issues with quality assurance in the trial, particularly with the documentation of informed consent. Even if participants were randomly selected (the sampling method is missing and should be included), that means, there is likelihood that a sizable proportion of the entire cohort has consenting issues. This should not happen in a trial that has good quality assurance protocols. Further, much as this paper is trying to advocate for e-consenting, it would add value to discuss how these errors can be addressed and their occurrence reduced.

6. *"Additionally, e-consenting enhanced ease of form search and retrieval from the database as well as remote access by the investigators".* How was "ease of form search" assessed? Were the nurses and doctors asked to comment on this or this is the authors' opinion? The discussion should be informed by the study findings.

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
Partly

Are all the source data underlying the results available to ensure full reproducibility?
Partly

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Version 1

Reviewer Report 01 September 2024

https://doi.org/10.21956/wellcomeopenres.22987.r90963

?

Erisa Sabakaki Mwaka
School of Biomedical Sciences, College of Health Sciences, Makerere University, Kampala, Central Region, Uganda

1. The study sought to investigate the utility of e-consenting in an ongoing clinical trial. Both paper-based and electronic consenting were done, and the error rates were compared. The participants of the study were mainly college students and community members in Blantyre however, it is not mentioned whether these were trial participants. If so, why were college students enrolled in a clinical trial? The mean age was 27 years, which is higher for average college students. It is difficult to believe that college students can have a mean age of 27 years. This should be explained.

2. This is an important study that investigated the transition from paper-based to digital consenting, however, the methods, result presentation, and discussion are weak and need major revisions if this paper is to be accepted for Indexing.

3. The title mentions “pneumococcal human infection study”. yet the manuscript does not address this topic. It might be helpful to revise the title to better reflect the content of the study.

4. The problem under study is not clearly articulated in the introduction. The objective of the study is also not stated.

5. The description of "Recruitment to the study of consenting methods" doesn't read well, it should be copy-edited. The description of the methods under the heading "Procedure for comparing consent methods in the Human Infection Study (HIS)" appears to be unclear and somewhat difficult to follow. This section should be recast and copy-edited.

6. I am not sure whether what is referred to as e-consenting is just signing an electronic form. It is stated on Page 4 "Following completion of paper-based consenting, electronic consenting process was initiated. Study personnel first linked the consent form to a study-assigned participant identification (PID) by scanning the barcodes. The form would then prompt the study personnel to write participant name and their name exactly as written on the paper-based consent form". The elements of consent are well known; the declaration/ signing of the consent document is the final step after someone has understood the consent information and voluntarily agrees to participate in research. Did the e-consenting include all the elements? I.e, disclosure, understanding, and voluntary decision-making, or people were just told to sign an e-form?

7. It is stated on page 5, that "E-consenting proved to be feasible; it was reliable as it reduced the error rate to 0% (n 0/109) compared to 43.1% (n 47/109) ..." What do the authors mean by "error rate"?

8. Is it fair to infer that e-consenting is feasible with a small sample size and biased population? The authors should justify this. Reduction in the error rate is not synonymous with feasibility!

9. Was the paper-based consent self-administered, assisted or both? Might the errors be related to the level of experience of the research assistants?

10. Might the errors be due to the lack of a quality control person or data manager?

11. How were the pros and cons of e-consenting determined? Was it through interviews? Group discussions? Written short answers? Debriefing meetings? How many staff participated in this activity? Basically, there is not enough details.

12. Page 6 states, "The use of electronic consent was noted to have improved consent form accessibility and reduced the burden of the need to print all consent and information documents. It also helped in promoting data safety and reduced the risk of data breach". What do the authors mean by improved consent form accessibility? They have indicated that the consent forms are difficult to access when there is poor internet connectivity, however, in the discussion they mention something to the contrary. This should be elaborated

13. The strengths and limitations should be presented at the end of the discussion.

14. The authors conclude that e-consenting is feasible but, they recruited a biased population of only literate participants, yet it is well documented that in much of sub-Saharan Africa, it is mainly illiterate individuals who participate in research. The authors explored the feasibility of e-consenting however, they seem to have a biased population that affects the credibility of their findings.

15. Page 6, "Though e-consenting showed to be a reliable tool when conducting research, it also proved that it will be almost impossible to use it in remote areas as it always required a working internet connection to upload the form to allow it to be in a printable pdf format and a printer for printing the participant consent forms as not all areas in Malawi have easy access to electricity and internet." Statistics on reliability are not presented, how did the authors determine that e-consenting is a reliable tool? How can it be reliable when it is not available in many areas of Malawi that neither have electricity nor internet connectivity?

16. The authors have several factual statements and inferences in the discussion and conclusion that are not supported by their findings. They should discuss their findings.

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
Not applicable

Are all the source data underlying the results available to ensure full reproducibility?
No

Are the conclusions drawn adequately supported by the results?
No

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 21 Jan 2025

Clara Ngoliwa

The study sought to investigate the utility of e-consenting in an ongoing clinical trial. Both paper-based and electronic consenting were done, and the error rates were compared. The participants of the study were mainly college students and community members in Blantyre however, it is not mentioned whether these were trial participants. If so, why were college students enrolled in a clinical trial? The mean age was 27 years, which is higher for average college students. It is difficult to believe that college students can have a mean age of 27 years. This should be explained.

- Thank you very much. Our study was a sub study under a clinical trial thus all our participants were enrolled in the trial. The mean age of 27 reflects the age for both college students and community members, please refer to the underlying data to see the detailed age for our participants. The main trial under which our study was conducted required that participants be literate. Healthy adults- aged 18 to 40 years including College students, were eligible to participate. We deliberately involved college students to increase likelihood of recruiting literate participants. This has also been the case in our sister CHIMs in Liverpool, UK.

This is an important study that investigated the transition from paper-based to digital consenting, however, the methods, result presentation, and discussion are weak and need major revisions if this paper is to be accepted for Indexing.

- Thank you. This has been agreed and considered. We have extensively revised the paper, re-written all sections and made them stronger.

The title mentions “pneumococcal human infection study”. yet the manuscript does not address this topic. It might be helpful to revise the title to better reflect the content of the study.

- Thank you. We agree and have revised the title.

The problem under study is not clearly articulated in the introduction. The objective of the

study is also not stated.

- Thank you. We have revised the introduction, stated the problem, and objectives of the study. The aim has been included in the introduction.

The description of "Recruitment to the study of consenting methods" doesn't read well, it should be copy-edited. The description of the methods under the heading "Procedure for comparing consent methods in the Human Infection Study (HIS)" appears to be unclear and somewhat difficult to follow. This section should be recast and copy-edited.

- Thank you. These sections have been revised.

I am not sure whether what is referred to as e-consenting is just signing an electronic form. It is stated on Page 4 "Following completion of paper-based consenting, electronic consenting process was initiated. Study personnel first linked the consent form to a study-assigned participant identification (PID) by scanning the barcodes. The form would then prompt the study personnel to write participant name and their name exactly as written on the paper-based consent form". The elements of consent are well known; the declaration/ signing of the consent document is the final step after someone has understood the consent information and voluntarily agrees to participate in research. Did the e-consenting include all the elements? i.e, disclosure, understanding, and voluntary decision-making, or people were just told to sign an e-form?

- Thank you very much. Our electronic consent included all elements of informed consent according to ICHGCP standards. E-consenting included participant information sheet, a 10 statement form outlining critical areas of the study, and a signature section for signing. We read the information sheet on physical papers, then asked participants to undergo e-consenting and then sign off. This is clarified more in the paper.

It is stated on page 5, that "E-consenting proved to be feasible; it was reliable as it reduced the error rate to 0% (n 0/109) compared to 43.1% (n 47/109) ..." What do the authors mean by "error rate"?

- Error rate was defined as number of participant forms with any amount of observed errors such as wrong spelling, overwriting, missing participant ID, unfilled sections, wrongly filled sections etc of the total filled consent forms. This definition has been included in the paper.

Is it fair to infer that e-consenting is feasible with a small sample size and biased population? The authors should justify this. Reduction in the error rate is not synonymous with feasibility!

- Thank you. We tested e-consent in a relatively smaller cohort of literate participants. Nevertheless, the numbers tested are not unusual for some observations and interventional studies hence the study still provides useful information to learn from.

Was the paper-based consent self-administered, assisted or both? Might the errors be related to the level of experience of the research assistants?

- Thank you very much. Both consents were self-administered with supervision by the study staff, we also maintained the same nurses and clinicians during the study. We however did not explore the reason for the errors.

Might the errors be due to the lack of a quality control person or data manager?

- The errors are due to human mistakes (both study staff and participants) quality control was done at the end of the screening visit.

How were the pros and cons of e-consenting determined? Was it through interviews? Group

discussions? Written short answers? Debriefing meetings? How many staff participated in this activity? Basically, there is not enough details.

- Thank you. This data was determined by both observation and unstructured feedback from study staff (nurses and clinicians) testing e-consent. This is described in the methods section.

Page 6 states, "The use of electronic consent was noted to have improved consent form accessibility and reduced the burden of the need to print all consent and information documents. It also helped in promoting data safety and reduced the risk of data breach". What do the authors mean by improved consent form accessibility? They have indicated that the consent forms are difficult to access when there is poor internet connectivity, however, in the discussion they mention something to the contrary. This should be elaborated

- Thank you. Our study was conducted in a technologically able setting with good internet availability. Instances of not having internet were rare and as such compared to paper based consent accessing the forms was easier than going through large physical folders.

The strengths and limitations should be presented at the end of the discussion.

- Thank you for this, we have revised this in the article.

The authors conclude that e-consenting is feasible but, they recruited a biased population of only literate participants, yet it is well documented that in much of sub-Saharan Africa, it is mainly illiterate individuals who participate in research. The authors explored the feasibility of e-consenting however, they seem to have a biased population that affects the credibility of their findings.

- Thank you. We agree with this observation. However, largely, CHIMs have involved literate participants, both in high-income and low-income settings. The pilot was a sub-study and involved literate participants of an ongoing trial. We agree that future studies should explore utility of e-consent in illiterate participants.

Page 6, "Though e-consenting showed to be a reliable tool when conducting research, it also proved that it will be almost impossible to use it in remote areas as it always required a working internet connection to upload the form to allow it to be in a printable pdf format and a printer for printing the participant consent forms as not all areas in Malawi have easy access to electricity and internet." Statistics on reliability are not presented, how did the authors determine that e-consenting is a reliable tool? How can it be reliable when it is not available in many areas of Malawi that neither have electricity nor internet connectivity?

- Thank you very much, we have rephrased this statement in the article.

The authors have several factual statements and inferences in the discussion and conclusion that are not supported by their findings. They should discuss their findings.

- Thank you. Major revisions to the article have been done.

Competing Interests: No competing interests were disclosed.

Reviewer Report 12 August 2024

https://doi.org/10.21956/wellcomeopenres.22987.r90965

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Dr. Muhammed Afolabi
London School of Hygiene and Tropical Medicine, London, UK

The authors reported the findings of their pilot study on the feasibility and usefulness of e-consenting among research participants enrolled in a parent trial in Malawi, a low-income country with an adult literacy level of 68%, according to the 2024 World Bank/UNESCO report [1]. Given this relatively high literacy level among adult population in Malawi, the authors did NOT support their exclusion of study participants who were not literate in English, with empirical evidence. This selection bias is a major methodological flaw that might have impacted the study findings adversely, as the findings could not be generalised to the adult population in Malawi. Similarly, the inclusion of a large number of students in the study further underscored the skewness and non-generaliseability of the study findings.

Also, objective comparisons could not be undertaken with the study design adopted by the authors, as the study participants had already undergone the traditional paper consenting before requesting them to repeat the same process using electronic consenting. This introduced a procedural bias into the process. An individually randomised controlled trial would have minimimised this bias and could have generated reliable findings that might have shaped future research or implementation of e-consenting in Malawi.

The authors did not indicate in their manuscript whether they provided some basic information about e-consenting to the study participants before requesting them to undertake the electronic procedure. The authors' statement that *'Participants were required to simply select I AGREE with a single tap'* suggests an over-simplification of the process and procedures involved in e-consenting. Therefore, this might not have wholly captured the process of e-consenting.

I was also expecting to see in the results factors that might have shaped the positive results on e-consenting reported by the authors. Could factors such as age, gender, education levels, previous computer experience, ownership of a smartphone, etc, have affected the participant's ability or performance to undertake e-consenting without errors?

References

1. 2024 World Bank/UNESCO report. 2024. Reference Source

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
No

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
No

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Clinical trials, vaccine research, bioethics, global public health

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 21 Jan 2025

Clara Ngoliwa

The authors reported the findings of their pilot study on the feasibility and usefulness of e-consenting among research participants enrolled in a parent trial in Malawi, a low-income country with an adult literacy level of 68%, according to the 2024 World Bank/UNESCO report (1). Given this relatively high literacy level among adult population in Malawi, the authors did NOT support their exclusion of study participants who were not literate in English, with empirical evidence. This selection bias is a major methodological flaw that might have impacted the study findings adversely, as the findings could not be generalised to the adult population in Malawi. Similarly, the inclusion of a large number of students in the study further underscored the skewness and non-generaliseability of the study findings.

- Thank you very much. Traditionally most CHIMs have been done in HICs and are recently expanding into low and middle income countries. One ethical concern for conducting CHIMs in LMICs is the challenge of obtaining voluntary informed consent especially in participants who are not literate, who may thus be considered as vulnerable (Informed consent for Controlled Human Infection Studies in low- and middle income countries: Ethical challenges ad proposed solutions (doi: 10.1111/bioe.12795. Epub 2020 Aug 10) The transferred protocols included only the literate. The pilot was a sub-study, the main trial under which the pilot was conducted was the first CHIM in Malawi and it excluded illiterate participants. We agree this method excludes a population which would have otherwise been included. Future CHIMs should conduct prior community consultation on inclusion of illiterate participants. We Agree with the reviewer and we have clarified in paper that this was a sub-study of an ongoing trial that involved only literate participants

Also, objective comparisons could not be undertaken with the study design adopted by the authors, as the study participants had already undergone the traditional paper consenting before requesting them to repeat the same process using electronic consenting. This introduced a procedural bias into the process. An individually randomised controlled trial

would have minimised this bias and could have generated reliable findings that might have shaped future research or implementation of e-consenting in Malawi.

- Thank you. We agree that prior paper based consenting might have improved observations seen in e-consenting. This has been clarified in the findings of the paper.

The authors did not indicate in their manuscript whether they provided some basic information about e-consenting to the study participants before requesting them to undertake the electronic procedure. The authors' statement that 'Participants were required to simply select I AGREE with a single tap' suggests an over-simplification of the process and procedures involved in e-consenting. Therefore, this might not have wholly captured the process of e-consenting.

- Information was given verbally. The select option was to make the process easier and faster but participants had to go through each step/ question prior to selecting I AGREE. This has been revised in the paper.

I was also expecting to see in the results factors that might have shaped the positive results on e-consenting reported by the authors. Could factors such as age, gender, education levels, previous computer experience, ownership of a smartphone, etc, have affected the participant's ability or performance to undertake e-consenting without errors?

- Thank you very much. We agree but unfortunately we did not explore these factors.

Competing Interests: No competing interests were disclosed.

Reviewer Report 07 August 2024

https://doi.org/10.21956/wellcomeopenres.22987.r87017

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Evelyne Kestelyn
Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam

The potential of using electronic consent in LMIC research settings is an exciting development and I read this article with great interest. I would propose a few changes to make this publication's outputs clearer and stronger.

Introduction.

- (Para 1) Educating a patient (in my view) sounds a bit condescending and other words like explaining, detailing might be considered.

- (Para 2) No mention is made about limitations from the patient's side, it only seems to focus on the research centre staff and storage.

- (Para 4) No mention is made about the considerable challenges of keeping digital data secure and protected once it's collected. Given this is all non- anonymised data, keeping in line with current applicable guidelines and maintaining long term data security are challenging.

Methods.

- (Ethics) I would like a bit more clarity about the 'proposal' that was approved. Was this submitted as a separate study within a trial? The study design is categorised as a cross-sectional observational study so this should get separate ethics approval from the clinical trial. This might have been obtained but is not clear from the text.

Results.

Your result section makes statements that I don't feel are supported by the data presented.

- The authors mention e-consenting is feasible but they should note that this is only the case for participants that have no (visual or hearing) impairments. No mention is made about illiterate participants or how e-consenting might be a help in this population.

- The authors mention it was reliable and mention a 0% mistake rate for the e-consenting. In my opinion, the data presented cannot be interpreted as meaning e-consenting is more reliable as the participant had already gone through a (written) consent procedure. There is no mention of how this could have affected the second consent procedure. Repeating the same actions usually leads to a lower error rate.

- (Documentation errors analysis) It might be better to clearly detail all errors so the reader can understand whether the errors were solely related to spelling, overwriting etc and not to more structural errors and understanding. This section can be broadened.

Discussion.

- (Para 1) Again I think the claim that e-consenting had a 0% error rate compared to paper-based consenting cannot be made based on this study design and results.

Previous studies.

- Did your study look at staff satisfaction or participant usability and satisfaction? Claiming e-consenting is feasible without including any data on the patients' experiences is challenging.

Study limitations.

- The authors rightly point out the lack of randomisation of the two different consent methods. For future studies, they might consider changing the order of obtaining the consent in different groups allowing for a more accurate understanding of the errors and challenges of obtaining e-consent (first and paper-based consent second).

Advantages.

- 'Data safety was enhanced'. This is not supported by any data. Challenges with maintaining this type of data (E- consents) in a long term secure way is not easy and data breaches do occur. Does the site have data about how many forms are lost or where privacy breaches have occurred with paper-based consenting?

Challenges.

- The authors mention that this pilot study was conducted to identify gaps that need to be addressed for streamlining e-consent in future studies. I am unsure what these gaps are and if they are reported in this paper.

Conclusions.

- I think the authors cannot draw the conclusion that e-consenting is feasible in a Malawian

setting. It has shown to be feasible in a very specific context only and has not taken into account the participants' perspective.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Not applicable

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
No

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Clinical trial conduct, ethics, data management

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 22 Jan 2025

Clara Ngoliwa

Introduction. (Para 1) Educating a patient (in my view) sounds a bit condescending and other words like explaining, detailing might be considered.

- Thank you very much for this input. This has been revised and the word "educating" has been replaced with "explaining" in the paper.

(Para 2) No mention is made about limitations from the patient's side, it only seems to focus on the research centre staff and storage.

- Thank you. We did not explore limitations regarding Participants as it was an observation study. This has been added as a limitation in the discussion section.

(Para 4) No mention is made about the considerable challenges of keeping digital data secure and protected once it's collected. Given this is all non- anonymised data, keeping in line with current applicable guidelines and maintaining long term data security are challenging.

- Thank you very much we have revised this paragraph to indicate this and other queries have also been clarifiy.

Methods. (Ethics) I would like a bit more clarity about the 'proposal' that was approved. Was this submitted as a separate study within a trial? The study design is categorised as a cross-sectional observational study so this should get separate ethics approval from the clinical trial. This might have been obtained but is not clear from the text.

- Thank you. This was a Sub study and approval to do a pilot was sought in an amendment. The Study is a product of a review meeting with NHSRC. We have clarified this in the paper and have provided a protocol reference number.

Results. The authors mention e-consenting is feasible but they should note that this is only the case for participants that have no (visual or hearing) impairments. No mention is made about illiterate participants or how e-consenting might be a help in this population.

- Thank you for this observation, we have revised and clarified this statement. We propose that this could be translated into other research studies. The result section has been thoroughly revised.

The authors mention it was reliable and mention a 0% mistake rate for the e-consenting. In my opinion, the data presented cannot be interpreted as meaning e-consenting is more reliable as the participant had already gone through a (written) consent procedure. There is no mention of how this could have affected the second consent procedure. Repeating the same actions usually leads to a lower error rate.

- Agreed. We have revised that statement by adding that our study did not identify any errors. This improvement could be a result of prior paper-based consent process. We have also removed the word etc. from the article.

Documentation errors analysis) It might be better to clearly detail all errors so the reader can understand whether the errors were solely related to spelling, overwriting etc and not to more structural errors and understanding. This section can be broadened.

- Thank you. We have revised this section to be more precise. We have also defined documentation errors to clarified this,

Discussion. (Para 1) Again I think the claim that e-consenting had a 0% error rate compared to paper-based consenting cannot be made based on this study design and results.

- We agree with this. Admittedly no errors were identified with electronic consent because of the choice of study design, this could have been improved with participants already being familiar with the paper-based consent. We have revised the wording in the article.

Previous studies. Did your study look at staff satisfaction or participant usability and satisfaction? Claiming e-consenting is feasible without including any data on the patients' experiences is challenging.

- Thank you very much. The pilot did not explore staff or participant satisfaction. However we sought staff feedback on e-consenting.

Study limitations. The authors rightly point out the lack of randomisation of the two different consent methods. For future studies, they might consider changing the order of obtaining the consent in different groups allowing for a more accurate understanding of the errors and challenges of obtaining e-consent (first and paper-based consent second).

- Thank you, excellent observation. We agree.

Advantages. 'Data safety was enhanced'. This is not supported by any data. Challenges with maintaining this type of data (E- consents) in a long-term secure way is not easy and data breaches do occur. Does the site have data about how many forms are lost or where privacy breaches have occurred with paper-based consenting?

- Thank you so much. The study file is kept in the institutional database. Our study did not have missing E-Consent forms. No data breaches were identified during this study. We have consulted and confirmed that there were no data breache. We have revised the wording of the article.

Challenges. The authors mention that this pilot study was conducted to identify gaps that need to be addressed for streamlining e-consent in future studies. I am unsure what these gaps are and if they are reported in this paper.

- The paper demonstrates feasibility of e-consent in Human Infection Studies. The study set up had required facilities to support use of an e- consent. The pilot serves as a reference to studies requiring to set up and demonstrate usability by participants. We have Rephrased the sentence from “identify gaps” to “propose considerations.

Conclusions. I think the authors cannot draw the conclusion that e-consenting is feasible in a Malawian setting. It has shown to be feasible in a very specific context only and has not taken into account the participants' perspective.

- Agreed! We suggest studies considering e- consent should have a similar set up and explore participant experiences in detail. We have Revised the wording. And have included statements such as “usefulness, unique advantages, and enthusiasm for utility is studies recruiting large cohorts of participants.

Competing Interests: No competing interests were disclosed.

Reviewer Report 08 June 2024

https://doi.org/10.21956/wellcomeopenres.22987.r82476

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Dr. Francis Masiye
Malawi University of Science and Technology, Limbe, Southern Region, Malawi

This paper presents exciting results of a study piloted by e-consent/digital consent. It is well-written and presented. However, the following issues need to be addressed by the authors:
1. Please provide the NHSRC reference number for the study in the methods section under "Ethics".
2. There are discrepancies in how potential participants provided consent during their recruitment into the study; under the section on "Recruitment to the study of consenting methods", it is stated that verbal consent was obtained from participants, and yet under the section on "Procedure for comparing consent methods in the HIS", it states that both participants and study staff signed the consent form respectively. Please confirm whether verbal consent or written consent was obtained from participants. If verbal consent was obtained from potential participants, please justify why verbal consent was sought.
3. Under the section on "Procedure for comparing consent methods in the HIS", it is stated that

participants were quizzed with 10 questions to assess understanding, please explain how the data collected from the 10 questions was analyzed.
4. Under the section on "Setting up e-consenting in ODK", it is explained that data was collected using the ODK application, please explain how data collected via the ODK platform was analyzed and how the results were arrived at.
5. Please clarify why none of the authors declares any conflict of competing interests or lack of it.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
Partly

Are all the source data underlying the results available to ensure full reproducibility?
No source data required

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: My areas of research interest are informed consent, post-trial access, fair resource allocation, clinical trial monitoring, and regulatory aspects of clinical research.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 21 Jan 2025

Clara Ngoliwa

This paper presents exciting results of a study piloted by e-consent/digital consent. It is well-written and presented. However, the following issues need to be addressed by the authors:
1. Please provide the NHSRC reference number for the study in the methods section under "Ethics"

- Thank you very much. The NHSRC reference number has been added to the article.

There are discrepancies in how potential participants provided consent during their recruitment into the study; under the section on "Recruitment to the study of consenting methods", it is stated that verbal consent was obtained from participants, and yet under the section on "Procedure for comparing consent methods in the HIS", it states that both

participants and study staff signed the consent form respectively. Please confirm whether verbal consent or written consent was obtained from participants. If verbal consent was obtained from potential participants, please justify why verbal consent was sought.

- Thank you. We agree that this indeed is a discrepancy we have revised the sentence under “Recruitment to the study of consenting methods” to read “Participants underwent dual consenting (paper-based and electronic consenting in that order)." to clarify how the consenting processes went.

Under the section on "Procedure for comparing consent methods in the HIS", it is stated that participants were quizzed with 10 questions to assess understanding, please explain how the data collected from the 10 questions was analysed.

- Thank you. The quiz was in relation to the CHIM study as stated that this was a sub study, the quiz was marked in real time to assess participant comprehension. Pass mark was at least 80%. This data was not analysed.

Under the section on "Setting up e-consenting in ODK", it is explained that data was collected using the ODK application, please explain how data collected via the ODK platform was analyzed and how the results were arrived at.

- Thank you very much. This data was not analysed. The electronic consent form included all components of the physical paper- based consent. We checked for any missing consents, incomplete consents and documentation errors. These have been defined and clarified in the new version of the revised manuscript.

Please clarify why none of the authors declares any conflict of competing interests or lack of it.

- Thank you very much. It was a pilot to inform feasibility of e-consenting in an LMIC setting. This was a sub study conducted by same investigators. The pilot was not designed for any commercialisation.

Competing Interests: No competing interests were disclosed.