## PEER REVIEW HISTORY



## ARTICLE DETAILS

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| **TITLE (PROVISIONAL)** | Adapting a club-based medication delivery strategy to a hypertension context: The CLUBMEDS Study in Nigeria |
| **AUTHORS** | Santo, Karla; ISIGUZO, Godsent; Atkins, Emily; Mishra, Shiva; Panda, Rajmohan; Mbau, Lilian; Fayomi, Samuel; Ugwu, Collins; Odili, Augustine; Virani, Salim |

## VERSION 1 - REVIEW

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| **REVIEWER** | Dr. Amjad Khan<br>Lecturer of Clinical Pharmacy, Department of Pharmacy, Quaid-i-Azam University 45320, Islamabad, Pakistan |
| **REVIEW RETURNED** | 19-Mar-2019 |

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| **GENERAL COMMENTS** | Review Report of Manuscript ID bmjopen-2019-029824 entitled "Adapting a club-based medication delivery strategy to a hypertension context: The CLUBMEDS Study in Nigeria"<br>General Comments<br>The manuscript addresses an important clinical issue. It reports the strategy of CLUBMEDS strategy for the management of hypertension in Nigeria. The findings of the instant study will minimize the barriers and risk factors for uncontrolled hypertension and will improve hypertension control in Nigerian hypertensive patients.<br>The manuscript may be accepted for publication after addressing/incorporating the following queries/suggestions.<br><br>Query # 01: The introduction section is too lengthy, should be concise.<br>Query # 02: In the recruitment and training section, the authors mentioned that they will use an automated BP monitor for BP measurements. When the blood pressure readings will be taken, is there any inclusion criteria and specific timings for BP measurement?<br>Query # 03: The dates of the pilot study to be conducted is missing in the manuscript. The authors are advised to mention the dates in the manuscript.<br>Query # 04: How the sample size is calculated for this study?<br>Query # 05: How the data will be analyzed. The authors are encouraged to mention about statistical analysis.<br>Query # 06: Every study has several study limitations. “Limitations of the study” section is missing in the manuscript. |

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| **REVIEWER** | Gertrude Nsorma Nyaaba<br>Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands |
| **REVIEW RETURNED** | 28-Mar-2019 |

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| **GENERAL COMMENTS** | The manuscript is well written and clearly addresses a topic of public health importance in a resource constrained setting. I have a few minor comments.<br>1. are the adherence clubs made up of both sexes? Given that literature indicates that some men are not adherent because of side effects such as sexual weakness and the perceptions regarding the virility of men within African societies, they may not feel comfortable discussing their challenges surrounding medication adherence. and evidence shows that within African societies, women may not feel comfortable discussing their concerns in the presence of men given the traditional structures.<br>2. evidence shows that persons with HTN often have co-morbid conditions which could potentially influence their adherence and the impact of the interventions. how would the support clubs handle the influence of other chronic condition on their HTN adherence?<br>3. Given that the facilitator will be dispensing the medication during the club meetings, thus not requiring person with HTN to go to health facilities for routine monitoring etc, how would persons developing HTN related complications be picked up if they only see the health worker once a year?<br>4. since the study is interested in improving adherence to HTN treatment, could you elaborate on why we are not recruiting known non-adherent HTN patients from the facilities but rather recruiting persons already adherent to treatment? unless we are recruiting new cases?<br>5. while there is a criteria for selecting club facilitators, the criteria for selecting research assistants is not elaborated on in the protocol. given the functions that they will be playing for the club, it appears that there is a need to know the criteria used in selecting them. kindly provide that criteria. Again, why are the patients not allowed to choose their own club facilitators? it appears that the club facilitators will be "imposed" on them and this could significantly influence adherence and impact.<br>6. drug shortages within the health system are a documented challenge to medication adherence. how will this be handled? again, financial constraints have been highlighted as a key barrier to medication adherence. how will this be handled?<br>7. It is indicated that they will be trained to identify symptoms? what kind of symptoms and for what?<br>8. again there is the indication that pharmacist or assistants will be used in handling medications. I am not sure how feasible this is given the shortages of such health professionals at the facility level.<br>9. the responsibilities of the club facilitator appears quite extensive, how will they be motivated to dedicate so much of their time to these responsibilities.<br>10. there does not seem to be dissemination to the club members and communities in which the study will be carried out in.<br>11. How will the clubs involve relatives and communities as stated in line 451? this has not been addressed in the manuscript yet at the end we indicate it will involve them. |

**VERSION 1 – AUTHOR RESPONSE**

REVIEWER #1 COMMENTS:

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1) The introduction section is too lengthy, should be concise.

We have reduced the introduction section length (pages 6-9).

2) In the recruitment and training section, the authors mentioned that they will use an automated BP monitor for BP measurements. When the blood pressure readings will be taken, is there any inclusion criteria and specific timings for BP measurement?

There are no specific inclusion criteria on BP levels and timing of BP measurements. To be eligible to participate in the study, patients will have to have a confirmed diagnosis of hypertension and be indicated for treatment with anti-hypertensive medications. We have now included a sentence in the Recruitment and training section specifying these inclusion criteria (page 12, lines 267-269).

3) The dates of the pilot study to be conducted is missing in the manuscript. The authors are advised to mention the dates in the manuscript.

We have added the recruitment period dates (page 19, lines 411-412).

4) How the sample size is calculated for this study?

There was no formal sample size calculation. As this is a pilot study evaluating the feasibility of the CLUBMEDS strategy, we chose a convenient sample of 100 patients to include in the study. We have added a sentence clarifying this (page 12, 259-260) and also added this as a study limitation (page 22, lines 486-488).

5) How the data will be analysed. The authors are encouraged to mention about statistical analysis.

A Statistical analysis section was added (page 18, lines 382-392).

6) Every study has several study limitations. “Limitations of the study” section is missing in the manuscript.

We have added a paragraph in the Discussion section addressing the limitations of the study (page 22, lines 483-498).

REVIEWER #2 COMMENTS:

1) Are the adherence clubs made up of both sexes? Given that literature indicates that some men are not adherent because of side effects such as sexual weakness and the perceptions regarding the virility of men within African societies, they may not feel comfortable discussing their challenges surrounding medication adherence. And evidence shows that within African societies, women may not feel comfortable discussing their concerns in the presence of men given the traditional structures.

Yes, the adherence clubs are for both sexes. We have clarified this in the CLUBMEDS pilot study section (page 12, line 256). We have also added a sentence in the limitations paragraph addressing the issue that some men and women might not feel comfortable sharing challenges and concerns in the presence of the opposite sex. However, we believe that this aspect can also be discussed and addressed in the post-implementation stage of the study (page 22, lines 490495).

2) Evidence shows that persons with HTN often have co-morbid conditions which could potentially influence their adherence and the impact of the interventions. How would the support clubs handle the influence of other chronic condition on their HTN adherence? The adherence clubs will support the patients in any challenges and concerns that might be related to adherence to anti-hypertensive medications, be it related to other chronic conditions or not. If the adherence clubs support is not sufficient to help the patient address one particular challenge in medication adherence related to a comorbidity, the patient may discuss this issue with the CHEWs or nurses at the primary healthcare facility. We have added a sentence about this support from the CHEWs and nurses to any adherence-related issues that may arise during the club meetings and that the role-model patients might not be able to address (page 15, lines 343-344).

3) Given that the facilitator will be dispensing the medication during the club meetings, thus not requiring person with HTN to go to health facilities for routine monitoring etc. How would persons developing HTN related complications be picked up if they only see the health worker once a year?

As part of the CLUBMEDS strategy, at each monthly club meeting, the role-model patient will identify any symptoms or alert signs of complications of uncontrolled hypertension. In addition, the role-model patients are responsible for referring the patient to the primary healthcare facility to see a CHEW or nurse for further evaluation in case a symptom or alert sign is identified or if the patient is due for a regular 6-months check-up at the facility (as described on page 15, lines 332-334). In addition, the CHEWs and nurses will still be responsible for scheduling regular return visits to the facility for club members every six months (as describe on page 16, lines 349). Therefore, the CLUBMEDS strategy will reduce the need for the patient to go to the facility to collect the anti-hypertensive medications every month; however, it will not reduce the number of regular assessment visits with CHEWs and nurses at the facility, which occur every 6 months.

4) Since the study is interested in improving adherence to HTN treatment, could you elaborate on why we are not recruiting known non-adherent HTN patients from the facilities but rather recruiting persons already adherent to treatment? Unless we are recruiting new cases?

All patients attending the primary healthcare facilities during the recruitment period with a confirmed diagnosis of hypertension and with an indication of treatment with anti-hypertensive medications are eligible, irrespective of their level of adherence at baseline (as described on page 12, lines 267-269), either new cases or old ones. We understand the reviewer's point that an intervention focussed on non-adherent patients might demonstrate greater efficacy, however we did not want adherent patients to become non-adherent in order to participate in the clubs. We have now added a sentence in the limitations paragraph addressing this issue (page 22, lines 488-490).

5) While there is a criteria for selecting club facilitators, the criteria for selecting research assistants is not elaborated on in the protocol. Given the functions that they will be playing for the club, it appears that there is a need to know the criteria used in selecting them. Kindly provide that criteria. Again, why are the patients not allowed to choose their own club facilitators? It appears that the club facilitators will be "imposed" on them and this could significantly influence adherence and impact.

The research nurses working in this study are already part of the local research team conducting the CLUBMEDS and other clinical and epidemiological studies in hypertension in Nigeria. The research team is comprised of clinicians-researchers with experience in the management of cardiovascular diseases assisted by nurses with experience in clinical research methods, such as patient consenting, data collection and data entry. As the research nurses were not selected specifically to work in this study, there are no selection criteria for selecting them. We have changed the words 'research assistant' and 'research assistants' to 'research nurse' and 'research nurses' throughout the text.

In addition, as the role-model patients have a specific set of responsibilities in the CLUBMEDS strategy, there are eligibility criteria as described on page 13, lines 278-283. These criteria restrict the pool of potential club facilitators, however, as described on page 14, lines 303-306, the research nurses will help the patients to form the adherence clubs based on the patients' domiciliary proximity. The post-implementation process evaluation will uncover if the choice of club facilitator impacts participation and adherence.

6) Drug shortages within the health system are a documented challenge to medication adherence. How will this be handled? Again, financial constraints have been highlighted as a key barrier to medication adherence. How will this be handled?

Although, we are implementing the study in sites where an affordable medicines supply has been secured for at least the study period, we agree with the reviewer that drug shortages and financial constraints might be limiting factors for this intervention and we have now added a sentence in the limitations paragraph addressing this issue (page 22, lines 495-498).

7) It is indicated that they will be trained to identify symptoms? What kind of symptoms and for what?

We have now added information on what type of symptoms the role-model patients were trained to identify (page 15, lines 328-331). These are: extremely high BP levels, severe headache, dizziness, blurred vision, nausea/vomiting, nosebleeds, chest pain/shortness of breath.

8) Again, there is the indication that pharmacist or assistants will be used in handling medications. I am not sure how feasible this is given the shortages of such health professionals at the facility level.

Due to lack of pharmacists and pharmacist assistants at the facilities, the facility nurses and the CHEWs will be responsible for pre-packing the anti-hypertensive medication refills for the adherence clubs to be collected by the role-model patients before every CLUBMEDS monthly session (page 16, lines 358-359). We understand the reviewers point about the potential lack of pharmacists, pharmacist assistants, nurses or CHEWs responsible for pre-packaging the medications in the facilities interfering with the intervention feasibility in other settings. We have now added a sentence adding this issue as a study limitation (page 22, lines 495-498).

9) The responsibilities of the club facilitator appear quite extensive, how will they be motivated to dedicate so much of their time to these responsibilities.

We agree with the reviewer that the responsibilities of the role-model patient are quite extensive; however, these patients were informed of such responsibilities before they agreed to participate in the CLUBMEDS strategy as a club facilitator. Therefore, they were aware of the time dedication they would need to spend to fulfil their responsibilities as a club facilitator. In addition, there were some incentives for these patients to assume these responsibilities. The role-model patients will be able to keep the BP monitors after the study completion and will receive financial support to purchase BP monitor batteries and for transportation to the facility.

We have added a paragraph about these incentives (page 15, lines 337-340).

10) There does not seem to be dissemination to the club members and communities in which the study will be carried out in.

This is the first pilot study of this intervention, as such the reach of the CLUBMEDS strategy is limited at this stage to be implemented in only two healthcare facilities in two locations, one urban and one rural, in Southeast Nigeria.

11) How will the clubs involve relatives and communities as stated in line 451? This has not been addressed in the manuscript yet at the end we indicate it will involve them.

The club meetings are open to participation of relatives of the club members, e.g. a wife can attend the monthly club meeting with her husband who is a club member. We have added a sentence in the manuscript making this clear (page 14, lines 311-313).