PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Protocol for establishing an Adaptive Diseases control Expert Programme in Tanzania (ADEPT) for integrating care of communicable and non-communicable diseases using tuberculosis and diabetes as a case study.
AUTHORS	Mpagama, Stellah; Ramaiya, Kaushik; Lillebæk, Troels; mmbaga, blandina; Sumari-de Boer, Marion; Ntinginya, Nyanda; Alffenaar, Jan-Willem; Heysell, Scott; Bygbjerg, Ib; Christensen, Dirk L.

VERSION 1 – REVIEW

REVIEWER	Giulia Segafredo Doctors with Africa, CUAMM
REVIEW RETURNED	31-Aug-2020

GENERAL COMMENTS	The topic is extremely relevant and research on this field is highly needed both from a global health perspective and from a national perspective. I am attaching a few comments to try to improve the quality of the manuscript. I recommend a better clarification between the implementation component and the research component of the project. It is clear that the research component is nested in a health service delivery program, probably to evaluate its feasibility and effectiveness, but it is not clear yet. The implementation program and the operational research component need to have two different objectives and this does not result clear from the manuscript. I suggest to review the paper trying to clarifying better the scope of the research component of the project. Few more detailed comments: In the abstract where there is a reference to qualitative methods but are not explained, also the research question is missing. I suggest to clearly state what is the objective of the study. Which needs to be different from the objective of the pure health care delivery model. Line 160 - 183 As they are stated, these objectives are not research objectives.The overall aim of the study cannot be the integration of TB/DM diagnosis. That is the aim of the health care delivery program. I suppose that the study is supposed to provide a sort of evaluation of the program. Line 164 - In order to provide the comprehension of the project, I suggest to provide an overview of the components of the delivery model, the objective can be stated in each of them.

	In the same way, line 171 and 179, the objective of a study cannot be to deliver international standards of care or to deliver a training. The research component needs to be better stated. Line 183 - acronyms need to be fully stated the first time they are mentioned. Line 235. Please specify how and why these are were selected. Even if the selection was made on purpose. Also, specify the difference among those settings and provide additional background information. E.g. population, TB and DB prevalence, rural/rural environment. Line 241, language not clear. What will be observed? 242 - 30 is the number of halter facilities that is going to be included? Please clarify. Line 261 I would suggest to repeat the test twice for confirmation. Line 276 - As it is stated it is not a research objective. What is the outcome that needs to be optimised? Line 279 - how is this best clinical practice going to be studied? Line 283 - in this study the stepped-wedge methodology should be explained. Why was this design selected? How is it going to be rolled out?

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Giulia Segafredo
Reviewer: 1
Institution and Country: Doctors with Africa, CUAMM
Reviewer: 1
Comments to the Author
The topic is extremely relevant and research on this field is highly needed both from a global health perspective and from a national perspective.
I am attaching a few comments to try to improve the quality of the manuscript.
Responses
Thank you very much the reviewer for acknowledging the importance of this research subject

I recommend a better clarification between the implementation component and the research component of the project.
It is clear that the research component is nested in a health service delivery program, probably to evaluate its feasibility and effectiveness, but it is not clear yet.
The implementation program and the operational research component need to have two different objectives and this does not result clear from the manuscript.
I suggest to review the paper trying to clarifying better the scope of the research component of the project.
Responses
We appreciate your comment enabling us to improve the manuscript. Now, we have two categories of

research questions that are being under study set as implementation research questions and operational research questions. The questions are as follows:
Implementation research

1. What patients did with dual TB and DM experience and what were their perspectives on services they received in the health facilities?
2. What is/are the most effective approach/es to de-implement health facility practices that do not support effective integration of proposed service delivery model using TB and DM as a case study?
3. What is the best approach to deliver on-job training and facilitate delivery of integration of TB and DM in a patient-centred approach?
4. What is the feasibility, acceptability and fidelity of the implemented designed models?
5. Where is the best place in the HCS system to implement (or initiate) integration of TB and DM?

Operational research in TB and DM
1. How many additional dual TB and DM patients will be identified during bi-directional screening of TB and DM services who would otherwise not have been identified?
2. What are the treatment outcomes of patients with dual TB and DM with or without HIV compared to other patients without DM?
3. What are the effects of therapeutic drug monitoring on dose adjustment and subsequently on treatment outcomes?

Few more detailed comments:
In the abstract where there is a reference to qualitative methods but are not explained, also the research question is missing. I suggest to clearly state what is the objective of the study.Which needs to be different from the objective of the pure health care delivery model.
Response
We aimed to include a qualitative research component to provide insight of the patients' experience, particularly those with dual TB and DM. The research question has now been added in the implementation research category as question which states "Qualitative approach will explore patients with dual TB/DM experiences they encountered during health care seeking in health facilities and their perspectives centering on integration" Also, now, the objective has been clearly stated in the abstract of the qualitative as follows; Qualitative approach will explore patients with dual TB/DM on experience of services they encountered in health facilities and their perspectives centring on integration.

Line 160 - 183 As they are stated, these objectives are not research objectives.The overall aim of the study cannot be the integration of TB/DM diagnosis. That is the aim of the health care delivery program. I suppose that the study is supposed to provide a sort of evaluation of the program.
Response
We appreciate your comment and have rephrased the overall aims to reflect the general processes of identifying mechanisms for shifting vertical to an adaptive approach and therefore, we have re-stated the overall aim as follows "The overall aims of developing an ADEPT model is to strengthen the health systems by shifting traditional vertical programmes to a patient-centred adaptive diseases control approach through integrating communicable and non-communicable diseases using the TB and DM dual epidemic as a case study in Tanzania."

Line 164 - In order to provide the comprehension of the project, I suggest to provide an overview of the components of the delivery model, the objective can be stated in each of them.
Response
We appreciate your comments and now accordingly provide an over-view of the models and described the components of each model. Likewise, we have included an objective in each described model.
Overview of the ADEPT Model

The ADEPT model has three components considered as vital to re-orient the health system to address dual communicable and non-communicable diseases. Each component is described as follows;

I. A Step-wise Training approach: The objective is to improve knowledge, skills and resource acquisition for the frontline health care providers to integrate communicable and NCDs at varying health system levels.
This model follows the “classical diffusions of innovation theory” described elsewhere 32 and organised on-job training in two clusters that will stepwise deliver a logically related set of internationals standards of patients with communicable and NCDs. The first cluster consisting of mentors that train to integrate communicable and non-communicable diseases. The potential mentors will be selected by the health managers at the respective health facilities, preferably working in either a general clinic or TB or DM clinic but also a minimum of undergraduate training. This cluster will also then serve as subsequent mentors. The initial training is through the e-learning methodology and pre-defined proceeding criterion (score > 80% of the online training) to the next phase which is a face-to-face workshop. The aim of the workshop is to expose individuals to acquire hands-on skills and conduct practical exercises related to clinical services focusing on algorithms of management or nursing care and new endorsed technologies. The second cluster will receive training and mentorship from the first cluster. The first cluster receives package/materials to train the second cluster working at the same level or at primary health care facilities.
II. Adaptive service delivery. The objective is to integrate communicable and NCDs at varying health system levels
Clinics delivering communicable or NCDs at varying levels of health facilities will receive training using a step-wise model. Considerations of infection prevention control will guide a service delivery approach while considering patient-centred recommendations. The first clinic will be applicable to clients with TB with or without other co-morbidities. Recognizing individuals with non-communicable lung diseases (CLDs) presenting with features akin of TB, a separate clinic may need to be organized. For the TB and CLD clinics, although potentially operating separately, it is important to maintain the link of these clinics as an important component of practical approach of lung health. The third clinic will encompass all non-TB-non-CLD with or without other comorbidities including HIV, DM, and Hypertension. A multimorbidity team within a health facility will facilitate mechanisms for screening communicable and NCDs.

III. Learning system model: The objective is to create a platform for reviewing data and information generated during implementation, and create a ‘self-repairing’ mechanism
The mentors or first cluster of trainees will have regular meetings at the Regional Medical Officer with attendance of District Medical Officers and different programme coordinators; including TB & Leprosy, NCDs, HIV, Malaria and Neglected Tropical Diseases. The meeting will review the clinical audit and quality improvement reports from health facilities focusing on health service delivery and identify the gaps for actions. Likewise, the coordinators will share on the expected national targets in their local context. The meeting report will be submitted to the higher authorities responsible for health. Currently the report will be submitted to the Ministry of Health Community Development Gender Elderly and Children and the President Office Regional Administration and Local Government Authority. The report will be included in the respective national technical working groups (TWG) for incorporation in the general provision of technical direction and advice. The relay mechanisms from the TWG to regions will also be established.
In the same way, line 171 and 179, the objective of a study cannot be to deliver international standards of care or to deliver a training. The research component needs to be better stated.
Response
Point taken, we have removed the objective and others and shaped the section based on the all comments provided. We have created an operational research question related to a technology that

we test in real settings as follows “What are the effects of therapeutic drug monitoring on dose adjustment and subsequent patient’s treatment outcomes?

Line 183 - acronyms need to be fully stated the first time they are mentioned.
Response
After addressing your previous comments, the phrase with the acronym has been removed
Line 235. Please specify how and why these are were selected. Even if the selection was made on purpose.
Response
We have explained the reasons for selecting 3-regions as follows: We selected Dar es Salaam because the region has the highest number of TB patients in Tanzania while Iringa is leading in HIV infection and Kilimanjaro has high burden of DM.

Also, specify the difference among those settings and provide additional background information. E.g. population, TB and DB prevalence, rural/rural environment.
Response
Thank you for the comment. We have added information related to the comment as follows
Dar es Salaam is largely a metropolitan while Iringa and Kilimanjaro selected areas cover rural (Kilolo and Siha), semi-urban (Mufindi and Same) and urban settings (Iringa Municipal and Moshi Municipal). Generally according to the National TB survey of 2012, the TB prevalence is high in Dar es Salaam and in rural settings. The burden of DM is generally 9% in Tanzania but is more common in urban settings.

Line 241, language not clear.
What will be observed?
Response
Thank you for observations. We have improved the statement as follows “A prospective cohort study of the health system study will be conducted to observe the effect of the step-down approach and integration of services

242 - 30 is the number of halter facilities that is going to be included? Please clarify.
Response
Thank you for providing an opportunity to clarify the matter. Yes, we will include halter facilities linking the dispensary, health center, district hospital and regional referral hospital.

Line 261 I would suggest to repeat the test twice for confirmation.
Response
We adapted to the country guideline and we opt to follow the general guideline to minimize confusion to service providers. We reserve the comment as we avoid to request the health facilities to do beyond the guideline

Line 276 - As it is stated it is not a research objective. What is the outcome that needs to be optimised?
Response
We have rephrased the statement and now reads as “Determine effect of diagnostics (HbA1c and therapeutic drug monitoring) for regimen and dosage selection for optimizing treatment outcomes of patients with dual TB/DM”

Line 279 - how is this best clinical practice going to be studied?
Response
We appreciate for observation and now the statement is phrased to be clearer “Health facilities effectively integrating dual TB/DM services will enter a next phase of using therapeutic drug

monitoring for optimizing dual TB/DM patient's management"

Line 283 - in this study the stepped-wedge methodology should be explained. Why was this design selected?
How is it going to be rolled out?
Response
Stepped-wedge methodology is a design that is preferably used when implementation and research go hand in hand. Especially with complex medical procedures this is a preferred approach.
A stepped wedge cluster randomised trial design is the most robust design that is logistically feasible whilst providing the level of evidence of efficacy and effectiveness to support further implementation in health care10,11. This design helps to minimise ethical issues related to withholding the optimized care in a traditional individual randomized trial design and can be considered of Low or Negligible risk. Each participating hospital starts with evaluation of the current practice followed by randomly timed implementation of the pharmacist-led service. To show the benefit of the pharmacist-led service we will compare treatment outcomes and costs of the current model of care with the new pharmacist-led service.
therapeutic drug monitoring is part of care and there is no rationale for randomizing patients but we take an opportunity to collect data systematically because of logistics which requires to establish systematically46

Reviewer: 1
Competing interests 1: None declared

FORMATTING AMENDMENTS (if any)
Required amendments will be listed here; please include these changes in your revised version:
● Required figure/s format
Figures can be supplied in TIFF, JPG or PDF format (figures in document, excel or powerpoint format will not be accepted), we also request that they have a resolution of at least 300 dpi and 90mm x 90mm of width.
Response
We have converted the figures into TIFF format
● Patient and Public Involvement:

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 there is no patient involved in the study, please state "No patient involved" under the sub-heading 'Patient and public involvement'.
Response
We have added the sub-heading: Patient and Public Involvement in the method section with a response that "Development of this protocol was informed by series of research studies that included

one study that examined patients experience of health services in the health facilities9. Findings from the described research objectives will be shared with patients' organizations subsequently contribute in shaping the agenda of effective integration of communicable and non-communicable diseases".

VERSION 2 – REVIEW

REVIEWER	Segafredo, Giulia Doctors with Africa, CUAMM
REVIEW RETURNED	06-Jan-2021

GENERAL COMMENTS	The ADEPT model seems a very interesting health-care protocol to explore, the need of researching over these new models of care delivery is increasing. Integrations of communicable and non-communicable services seems the most promising solution to increase public health effectiveness. This manuscript includes all the relevant information for its publication, however I suggest to reorganise some parts to increase its clarity. Below my reviews. Title - the title states that the objective of the paper is to describe the protocol for establishing the ADEPT in Tanzania. But the contents of the paper describe the operational research component of the program - not its implementation. ADEPT seems a health-care service delivery model which includes an operational research component it is not the research protocol itself. Abstract - I suggest to better explain the relationship between the implementation of the ADEPT protocol and its operational research component. ADEPT seems extremely interesting and it seems that there is a comprehensive research component among its activities, try to tell what is the delivery of the service and what is the research component. Line 64 - add a coma after TB/DM - Line 66 - the intervention of the prospective cohort design is not clear - how does it enable early disgnosis? Introduction- I think it is very well introduced the challenge of the co-epidemic. This section could be shorter, fewer data are needed to state the size of the epidemiological problem. The challenge in terms of heath care delivery in Tanzania, could be further articulated as it is the key challenge for which this program was developed. The aim of the model is stated to early, before the reader can understand what it is. I suggest to add a small description before declaring the objective to help the reader understanding. Line 97 vs line 113 - Does DM have a specific vertical program in Tanzania? DM services are offered at primary health care level integrated with other services. These two sentences seem to be contradictory Line 122 - Fig. 1 Is introduced in the test but is not helping to improve the comprehension of what is the model about. I would also suggest to review the figure as it is not clear. Line 160 - I suggest to articulate more and add a reference. Line 165 - Declaring the aim of in this way, is a bit confusing, because the reader does not know what is the model about. I suggest to add a small description before declaring the objective

	to help the reader understanding and to let him understanding how this model can reply to the research question. Line 198 - do you mean communicable or non-communcable lung disease? 242 -287 The description of how the heath-care delivery model is going to be implemented can be shortened. 289 - 302 - I suggest to better explain this part. Research questions are stated earlier. It should be explained here what are the research methods identified to reply to each set of research questions. The same for the section of Study outline (Line 315 onwards) - Identify the studies and for each studies specify the objectives and the methods. Specify the objective of the research component not the one of the health-care delivery model (e.g. Integrate TB and DM services, Screening of TB in DM are not research objectives)

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1 Comments
Dr. Giulia Segafredo, Doctors with Africa, CUAMM
Comments to the Author:
The ADEPT model seems a very interesting health-care protocol to explore, the need of researching over these new models of care delivery is increasing. Integrations of communicable and non-communicable services seems the most promising solution to increase public health effectiveness. This manuscript includes all the relevant information for its publication; however I suggest to reorganise some parts to increase its clarity.

Response
We appreciate the reviewer for recognizing the significance of this research subject. We thank the reviewer for taking time to review the manuscript and provide comments for improvement. We have reorganized some parts as suggested to increase clarity. We hope now the manuscript will be clearer to readers.

Below my reviews.
Title - the title states that the objective of the paper is to describe the protocol for establishing the ADEPT in Tanzania. But the contents of the paper describe the operational research component of the program - not its implementation.
ADEPT seems a health-care service delivery model which includes an operational research component it is not the research protocol itself.

Response
Thank you for the comment. Accordingly, we have made effort to detach ADEPT implementation and describe action research (implementation and operation) components separately

Abstract – I suggest to better explain the relationship between the implementation of the ADEPT protocol and its operational research component. ADEPT seems extremely interesting and it seems that there is a comprehensive research component among its activities, try to tell what is the delivery of the service and what is the research component.

Response
We appreciate for the comment and observation. Accordingly, the abstract has now been revised to reflect the changes suggested in the main manuscript. Thus, the abstract links the implementation of

the ADEPT protocol delivery and research components; both implementation and operational.

Line 64 - add a coma after TB/DM –
Line 66 - the intervention of the prospective cohort design is not clear - how does it enable early disgnosis?

Response
After addressing the comment provided in the abstract that explains the implementation of the ADEPT and research component as suggested, both line 64 and line 66 have been removed.

Introduction- I think it is very well introduced the challenge of the co-epidemic. This section could be shorter, fewer data are needed to state the size of the epidemiological problem. The challenge in terms of health care delivery in Tanzania, could be further articulated as it is the key challenge for which this program was developed.

Response
Thank you for this relevant suggestion. We have shortened the introduction section. The initial section had 82 lines (1037 words) and has now been shortened to 48 lines (607 words. We have also added data on HIV to complement the TB data and stated the size of the dual communicable and NCD epidemiological problem focusing in Tanzania and references 13 and 14

The aim of the model is stated to early, before the reader can understand what it is. I suggest to add a small description before declaring the objective to help the reader understanding.

Response
As suggested, we have now added as small description before declaring the objectives as follows:
“The ADEPT model is likely to pioneer the systems thinking methodology described by Swanson and colleagues to guide integrative changes in the health system [21], and it includes three interdependent domains; (i) step-wise training approach for knowledge and skills improvement of the frontline health care providers, (ii) adaptive service delivery through integration of communicable and NCD and (iii) continuous learning and integration of dual communicable and NCD (Figure 1).”

Line 97 vs line 113 - Does DM have a specific vertical program in Tanzania? DM services are offered at primary health care level integrated with other services. These two sentences seem to be contradictory

Response
The country has established a non-communicable programme. Now, the statements in line 97 and line 113 have been removed when shortening the introduction section as suggested.

Line 122 - Fig. 1 Is introduced in the test but is not helping to improve the comprehension of what is the model about. I would also suggest to review the figure as it is not clear.

Response
We appreciate the comment. Now the figure has been reviewed and simplified to improve the comprehension of the model. Please see Figure 1 attached:

Figure 1: The ADEPT model includes three essential domains. The performance domain is identified as integration of communicable and non-communicable diseases. For effective delivery of adaptive service, the performance domain requires support by the second and third domains called a stepwise

training approach and learning systems. The stepwise training approach will ensure the frontline health care providers acquire knowledge and skills necessary for integrating communicable and NCDs. The learning system domain should be continuously operating by including processes like implementation research and clinical audits which serves as a system lens to continuously inform the operation of the performance domain. Information flow including clinical guidelines and new practices will go through the stepwise training approach. The three functioning domains create an adaptive service delivery model for the health system.

Line 160 - I suggest to articulate more and add a reference.

Response
During the revision of this section the prior line 160 has been removed.

Line 165 - Declaring the aim of in this way, is a bit confusing, because the reader does not know what is the model about. I suggest to add a small description before declaring the objective to help the reader understanding and to let him understanding how this model can reply to the research question.
Response
We have added a brief description of the model before declaring the objectives described in the model as shown in query requiring to describe the aim. The description is: “ADEPT model is likely to pioneer the systems thinking methodology described by Swanson and colleagues to guide integrative changes in the health system [21] and includes three interdependent domains; (i) step-wise training approach for knowledge and skills improvement of the frontline health care providers, (ii) adaptive service delivery through integration of communicable and NCD and (iii) continuous learning and integration of dual communicable and NCD (Figure 1).”

Line 198 - do you mean communicable or non-communcable lung disease?

Response
We meant non-communicable lung diseases. Now, we have added an example of chronic obstructive pulmonary diseases to differentiate with communicable lung diseases such as TB.

242 -287 The description of how the health-care delivery model is going to be implemented can be shortened.

Response
We welcome this recommendation and have shortened the section considerably.

289 - 302 - I suggest to better explain this part. Research questions are stated earlier. It should be explained here what are the research methods identified to reply to each set of research questions.

Response
Point taken. The section has been articulated to reflect the research questions stated earlier. We have added the study design for both the implementation research questions set and the operational research question set.

The same for the section of Study outline (Line 315 onwards) - Identify the studies and for each studies specify the objectives and the methods. Specify the objective of the research component not the one of the health-care delivery model (e.g. Integrate TB and DM services, Screening of TB in DM are not research objectives)

Response
Likewise, as shown in the study design, the section flow has been changed to match with the

research question described. The study outline, data collection and analysis and outcomes have been divided into sub-categories reflective of the implementation and operation research questions.