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Study protocol for developing a novel approach for improving supply chain management for SARS-CoV-2 point-of-care diagnostic services in resource-limited settings: a case study of Mopani District in Limpopo province, South Africa

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ABSTRACT

Introduction Recent evidence shows that point-of-care (POC) testing is a more feasible alternative for diagnosis of COVID-19 in settings that have poor access to laboratory diagnostic services. Equitable access to POC testing can be optimised through well-established supply chain management (SCM) systems. The proposed study aims to develop a novel approach for improving SCM for COVID-19 POC diagnostic services in resource-limited settings with poor access to laboratory diagnostic services, using Mopani District in Limpopo Province, South Africa as a study setting.

Methods and analysis This study was guided by results of the scoping review. Following the scoping review, we propose a mixed-methods study, which will be implemented in three phases. First, we will perform a geospatial analysis to investigate the spatial distribution of COVID-19 testing services. Second, we will perform an audit of POC diagnostic services including its supply chain to evaluate the effect of SCM on accessibility of COVID-19 POC diagnostic services and reveal SCM barriers and enablers of accessibility of COVID-19 POC diagnostic services. Third, we will perform a nominal group technique to collaborate with key stakeholders in co-creation of a novel approach for improving SCM systems for COVID-19 POC diagnostic services. For the geospatial analysis, we will employ the ArcGIS Software. For the analysis of quantitative and qualitative data that will be generated from the audit and nominal group discussion, we will employ Stata software and NVivo software, respectively.

Ethics and dissemination This study has been ethically reviewed and approved by two institutional review boards: University of Pretoria Faculty of Health Sciences Research Ethics Committee (approval number 655/2021) and Limpopo Department of Health Research Ethics Committee (approval number LP-2021-12-007). The results of this study will be disseminated through national and international presentations and peer-reviewed publications.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study was informed by results of a scoping review, which found limited published research on supply chain management (SCM) of COVID-19 point-of-care (POC) diagnostic services in resource-limited settings.
⇒ It is a multiphase mixed-methods study to improve SCM for COVID-19 POC diagnostic services in resource-limited settings.
⇒ Geographical information system will be used to visualise the spatial distribution of COVID-19 diagnostic services.
⇒ A nominal group technique will be used to collaborate with key stakeholders in co-creation of a novel SCM approach for improving COVID-19 POC diagnostic services.
⇒ Data will be collected from key stakeholders involved in SCM of COVID-19 POC diagnostic services.

INTRODUCTION

Although sub-Saharan Africa (SSA) was the last continent to be hit by COVID-19 pandemic, it has experienced the most devastating effects. According to the global coronavirus surveillance data, among SSA countries, South Africa was the most affected country with over 3.6 million COVID-19 confirmed cases as at 28 February 2022.1 Poor health infrastructure has been reported as one of the major hurdles in the control of COVID-19 pandemic.2 In Limpopo Province, South Africa, the control of COVID-19 has been negatively impacted by limited laboratory infrastructure. The available laboratory services were overwhelmed due to the exponential rise in COVID-19 cases and resulted in a backlog that caused a delay in receiving...
the results. Resource-limited settings, such as Limpopo Province, which are characterised by limited access to hospitals and diagnostic laboratories, rapid point-of-care (POC) tests, are beneficial to help improve access to diseases diagnosis, monitoring as well as help prevent the spread of infectious diseases. In this study, POC tests are defined as rapid diagnostic tests that are performed near or close to the patient with instant availability of results to guide immediate informed clinical decisions about disease management and patient care. COVID-19 is a highly transmissible disease; therefore, rapid and timely diagnosis is important in the control and management of the virus. The healthcare system must remain uninterrupted to ensure availability and accessibility of POC tests that are needed on a large scale for efficient control and management of COVID-19. The availability and accessibility of POC tests are dependent on numerous factors including an efficient supply chain management (SCM) system. SCM is a vehicle that ensures that POC tests reach the end-user on time. The SCM of POC diagnostic services is a complex and fragmented process that is controlled by four main links, namely, producers, purchasers, providers and patients, who contribute to creating cost-effective opportunities across the healthcare sector. SCM involves obtaining resources, managing supplies, and delivering goods and services to providers and patients. For an effective and complete SCM system, it is essential to accurately forecast and prevent stock-outs of POC test in order to improve the health outcomes. Diagnosis is key to surveillance and management of pandemics such as COVID-19. POC testing has been shown to help improve access to disease diagnosis in settings that have poor access to laboratory infrastructure. Based on the critical role that SCM has on the availability and accessibility of POC tests, there is an urgent need to develop a tailored novel approach to improve the SCM systems for COVID-19 POC diagnostic services, particularly in settings that have poor access to laboratory services such as Limpopo Province, South Africa. The main aim of this study is to develop a novel approach to improve the SCM systems for COVID-19 POC diagnostic services for resource-limited settings, using Mopani District in Limpopo province as a study setting. We anticipate that the findings of the study will guide future research on SCM for POC diagnostic testing and provide useful information to guide implementers of POC diagnostics in resource-limited settings. The study findings are likely to provide sustainable solutions to improve SCM systems for POC diagnostic services not only in Mopani District in Limpopo province, South Africa but also in similar resource-limited settings with poor access to laboratory diagnostic services.

METHODS
Study design
This study was guided by results of a scoping review. Following the scoping review, we propose a multiphase mixed-method study, which will be implemented in three phases. The results of the scoping review revealed that for the continuum of POC diagnostic services, POC diagnostic tests must be available and accessible to all who need them through a sustainable SCM system which is a multi-faceted system influenced by several factors. The scoping review also revealed that there is limited published research on SCM of POC diagnostic services in resource-limited settings and that there are currently no primary studies on the SCM systems of COVID-19 POC diagnostic services. In phase 1, we will perform a geospatial analysis to investigate the spatial distribution of COVID-19 testing services. In phase 2, we will perform an audit of POC diagnostic services including its supply chain to evaluate the effect of SCM on accessibility of COVID-19 POC diagnostics services and reveal SCM barriers and enablers of accessibility of COVID-19 POC diagnostic services. In phase 3, we will perform a nominal group technique to collaborate with key stakeholders in co-creation of a novel approach for improving SCM systems for COVID-19 POC diagnostic services.
lean SCM framework is an approach that does more with less and at the same time offer customers exactly what they want. This means using less human effort, equipment, time and space to increase the value and minimise waste simultaneously. The agile SCM framework is an approach designed to create the ability to respond rapidly and cost-effectively to unpredictable changes in the health system such as in a case of a pandemic like COVID-19. The lean and agile frameworks both strive to reduce costs but in different ways. The lean framework addresses the economies of scale (economy in relation to each product), while the agile framework addresses the economies of scope, that is the economy in relation to the organisation as a whole. While the lean strategy focuses on eliminating non-value adding activities to achieve high levels of efficiency, profitability and flexibility within the value stream in the supply chain, the agile strategy focuses on market sensitiveness, using market knowledge to respond to real demand.

**Study setting**

The study will use Mopani District as a study setting, one of the five districts in Limpopo Province, South Africa. The district is confronted by service delivery challenges recording lower averages than the national averages with regards to the provision of basic services. Mopani comprises five subdistricts/local municipalities as depicted in figure 2; namely, Greater Giyani, Ba-Phalaborwa, Greater Letaba, Greater Tzaneen and Maruleng. The seat of Mopani is Giyani. Mopani District covers an area of 20,011 km² and is made up of 16 urban areas (towns and townships) and 354 villages (rural settlements). It has a population of 1,167,598 as of the 2016 community survey.

The study population includes primary healthcare clinics (PHC) involved in the management of COVID-19. The district has a total of 97 clinics as shown in table 1; 26 in Greater Giyani, 9 in Ba-Phalaborwa, 11 in Maruleng, 31 in Greater Tzaneen and 20 in Greater Letaba. According to an area-specific live geographical information system (GIS) vulnerability mapping conducted by the Council for Science and Industrial Research (CSIR) in 2020, it showed that the areas that show higher vulnerability to COVID-19 are those that are more densely populated and with higher poverty. These are the areas surrounding Greater Giyani, Greater Letaba, Greater Tzaneen and the mining areas in Ba-Phalaborwa.

**Phase 1: geospatial analysis**

**Objective**

To investigate the spatial distribution of COVID-19 testing services.

**Design**

A cross-sectional study will be used and a GIS will be used for mapping the spatial distribution of COVID-19 diagnostic services. Geospatial analysis is pivotal in public health because it allows us to use geographical techniques
such as mapping to establish the impact of a person’s surroundings on their health outcome.\textsuperscript{22} Geospatial analysis will help us establish the proximity of COVID-19 diagnostic services to the population. We will employ GIS mapping to estimate the geographical distribution of COVID-19 diagnostic services to the population density. We will show and demonstrate access to COVID-19 diagnostic services. We will also identify areas with large populations but poor availability of diagnostic services.

Data source
A list of all PHC clinics in Mopani District Municipality.

Analysis
To determine the spatial distribution or the distance from the place of residence to nearest PHC clinic, a Moran’s Index (MI) will be run on the ArcMap software. The MI, z-scores and p values for the distance between the place of residence and the PHC clinic will be reported. The MI values will be interpreted as follows: An MI>0 will be interpreted as spatially clustered, an MI<0 will be interpreted as spatially dispersed and an MI=0 will be interpreted as spatial random distribution. The estimated distances will be computed in Microsoft Excel and imported to Stata Software for analysis. Means, SD and 95% CI will be generated for the distances.

Outcome measures
The primary outcome of geospatial analysis is the accessibility of COVID-19 diagnostic services from the place of residence. In this study, accessibility to COVID-19 diagnostic services will be measured as the distance travelled from the place of residence to the nearest PHC clinic. A <5 km will be interpreted as high accessibility, 5–10 km will be interpreted as moderate accessibility and >10 km will be interpreted as poor accessibility based on the CSIR guidelines for the provision of social facilities in South Africa.\textsuperscript{23} Another outcome for geospatial analysis is to map PHC clinics that serve a large population but have poor accessibility of COVID-19 diagnostic services.

Table 1 Vulnerability to COVID-19 per subdistrict

<table>
<thead>
<tr>
<th>Subdistrict</th>
<th>Population</th>
<th>No of PHC clinics</th>
<th>Least vulnerable</th>
<th>Slightly vulnerable</th>
<th>Vulnerable</th>
<th>Highly vulnerable</th>
<th>Extremely vulnerable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>1 167 598</td>
<td>97</td>
<td>12.51%</td>
<td>20.18%</td>
<td>37.99%</td>
<td>29.21%</td>
<td>0.12%</td>
</tr>
<tr>
<td>Ba-Phalaborwa</td>
<td>149 463</td>
<td>9</td>
<td>40.61%</td>
<td>36.78%</td>
<td>18.85%</td>
<td>3.73%</td>
<td>0.04%</td>
</tr>
<tr>
<td>Greater Giyani</td>
<td>281 667</td>
<td>26</td>
<td>8.24%</td>
<td>13.01%</td>
<td>44.46%</td>
<td>33.93%</td>
<td>0.36%</td>
</tr>
<tr>
<td>Greater Letaba</td>
<td>226 558</td>
<td>20</td>
<td>5.54%</td>
<td>20.48%</td>
<td>39.06%</td>
<td>34.79%</td>
<td>0.13%</td>
</tr>
<tr>
<td>Greater Tzaneen</td>
<td>404 375</td>
<td>31</td>
<td>9.43%</td>
<td>17.81%</td>
<td>39.05%</td>
<td>33.7%</td>
<td>–</td>
</tr>
<tr>
<td>Maruleng</td>
<td>105 535</td>
<td>11</td>
<td>10.85%</td>
<td>24.2%</td>
<td>41.48%</td>
<td>23.47%</td>
<td>–</td>
</tr>
</tbody>
</table>

PHC, primary healthcare clinic.
Phase 2: an audit of PHC providing POC diagnostic services

Objectives
- To evaluate the effect of SCM on accessibility of COVID-19 POC diagnostics services in Mopani District.
- To reveal SCM barriers and enablers of accessibility of COVID-19 POC diagnostic services in Mopani District.

Design
A cross-sectional mixed-methods study will be utilised, and data will be collected using an audit. Purposive sampling will be used to sample the largest PHC clinics with COVID-19 diagnostic services and sample large PHC clinics without COVID-19 diagnostic services. The number of PHC clinics sampled will be guided by the results of the geospatial analysis conducted to address objective 1, investigate the spatial distribution of COVID-19 testing services. We will conduct an audit on the sampled clinics. We have put together an adopted audit tool (online supplemental material 1) guided by the WHO guidelines for improving the quality of POC testing and the Management Science for Health (MSH) laboratory diagnostic supply chain guideline. To perform the audits, we will visit the PHC clinics sampled and ask the set of questions prepared. The audit tool will be piloted in five non-participating PHC clinics prior to data collection and the audit tool will be adjusted based on the assessor’s feedback. The participants of the audit will be briefed about the purpose of the audit and given information on how to complete the questionnaire.

Recruitment strategy
We will write to the PHC clinic managers and request for their participation in the study. On approval from the PHC clinic manager, we will request participation from all the PHC clinic staff who are involved in the SCM system to complete the audit tool.

Data source
An audit tool consisting of questions aimed at assessing aspects of the supply chain namely: selection, quantification, storage, procurement, quality assurance, distribution and redistribution, inventory management and human resource capacity.

Analysis
The data collected will be captured into an excel file, cleaned, validated and exported to Stata statistical software for analysis. Descriptive statistics, such as frequencies and percentages for categorical data and means (SD) or medians for numerical data, will be used to summarise audit scores. The Pearson correlation coefficient will be used to show the relationship between numerical variables. Linear regression will be used to model the relationship between the correlates. The results will be statistically significant at p≤0.05. The main themes that will arise from probing further the causes of non-compliance from the individual interviews will be analysed as themes.

Outcome measures
To evaluate the effect of SCM on accessibility of COVID-19 POC diagnostic services, we will summarise the audit scores. The audit scores will be summarised through rating the audit scores. We will sum the scores for each component to obtain the overall percentage rating. To measure SCM a point will be allocated for each question. The overall percentage score will be calculated from each audit questionnaire. Compliance to SCM will be interpreted as follows: ratings between 90% and 100% will indicate compliant SCM and ratings <90% will indicate non-compliant SCM. These ratings are based on the stipulated WHO guidelines for improving the quality of POC testing and MSH diagnostic laboratory diagnostic supply chain guideline.

To reveal SCM barriers and enablers of accessibility of COVID-19 POC diagnostic services, the sections deemed compliant after the audit will be the enablers of accessibility of COVID-19 POC diagnostic services and sections deemed non-compliant will be the barriers of accessibility of COVID-19 POC diagnostic services. We will discuss the causes of the non-compliance with the participants in order to ascertain the causes for this non-compliance.

Phase 3: nominal group discussion

Objective
To collaborate with key stakeholders in cocreation of a novel approach for improving SCM systems of COVID-19 POC diagnostic services.

Design
A mixed-methods approach will be used, and a nominal group technique will be used to collect the data. Purposive sampling will be used to obtain a representative sample of relevant key stakeholders who will help to develop a novel approach for improving SCM systems for COVID-19 POC diagnostic services. We intend to conduct one online nominal group discussion using Zoom platform. We will ensure that the nominal group discussion consists of at least one participant from the identified key stakeholders from each of the five sub-districts in Mopani District municipality.

The following key stakeholders have been identified:
- PHC district manager; oversees all the five subdistricts.
- PHC subdistrict managers; oversee the subdistrict.
- Pharmaceutical depot manager; distribution of POC tests to the districts from the provincial office.
- SCM, procurement of POC tests at provincial and district levels.
- Pharmacy assistants; inventory management at PHC clinics.
- Clinic managers, oversee the PHC clinic.
- Professional nurses; use the POC tests to test patients.
- Drivers; transport POC tests from district hospitals to PHC clinics.
Recruitment strategy
We will write to the identified key stakeholders and request for their participation in the nominal group technique.

Data source
We will use a nominal group technique to collaborate with key stakeholders in co-creation of a novel SCM approach for improving COVID-POC diagnostic services. This data collection method was selected to promote group participation in the decision-making processes. It will involve a collaboration of a small group of relevant people to reach a consensus on the identification of key issues in the supply chain process.25

The principal investigator (PI), with the help of a research assistant, will facilitate the online nominal group discussion. The identified participants will be invited to participate in the stakeholder engagement. The invitation will include a summary of the purpose of creating a platform for key stakeholders to discuss innovative approaches to improving SCM of COVID-19 POC diagnostic services.

Data collection
The nominal group technique will be conducted in four phases, as illustrated in figure 3.

Phase 1 activities:
► Introduction of participants and purpose of the workshop (15–30 min): The discussion will start with brief introductions by the participants. The PI will give a background of the workshop and share the programme of the day. The participants will be asked to complete and sign the consent form.
► Creating of groups (10 min): The participants will be divided into two or three groups. Each group will consist of at least one participant from each of the stakeholders represented.
► Silent brainstorming by each participant and noting down relevant ideas (15–20 min): A question will be posed to initiate the discussion: What are the challenges faced in the supply chain of COVID-19 POC diagnostic services in Mopani District? A follow-up question will be asked: What are the possible strategies that can be implemented to address these barriers? There will be a break-away session where each participant will be given some time for silent brainstorming and to write down all the ideas that come to mind. This process will allow key stakeholders to reflect on the barriers that prevent a seamless supply chain system. Discussions will not be allowed at this stage however participants will be able to seek clarity from the facilitators.

Phase 2 activities:
► Groups reconvene and share ideas (30–45 min): The groups will reconvene, and the participants will be given an opportunity to share their main ideas with the other group members before grouping them according to themes on a flip chart. There will be no debate about items at this stage and participants are encouraged to write down any new ideas that may arise from what others share. This process will ensure that all participants get an opportunity to make an equal contribution and provide a written record of all ideas generated by the group.
► Group discussion (20–30 min): Participants will be given an opportunity to probe further and seek clarity about any of the ideas that their fellow group members have discussed. The PI will ensure that each person can contribute, and that discussion of all ideas is thorough without spending too much time on one idea. We will ensure that the process is as neutral as possible, avoiding judgement and criticism. The group may suggest new items for discussion and combine items into categories, but no ideas will be discarded.

Phase 3 activities:
► Presentations to the whole team and removal of duplicates (45–60 min): Each team will be asked to present their group ideas to the workshop participants. Following the discussion, questions and discussions will be encouraged. As the participants are presenting, the facilitators will write down the emerging themes on a chart sheet. After the discussion, the facilitators
will group similar themes and duplicate themes will be removed. The results of the discussion will be presented by the facilitators to the group as priority areas to be ranked during the next phase.

Phase 4 activities:

- Ranking of ideas (45–60 min): This phase involves ranking of ideas, assigning a value to an idea according to its priority. A Google form will be used. The top five priority themes will be ranked using a Likert scale of 1–5, with 1 representing a very low priority and 5 representing the highest priority. The participants will complete the Google form independently.
- Collate and analyse results (45–60 min): The results will be collated and analysed by the facilitators. All recorded data and written information recorded in flip charts will be collected and saved securely for further analysis.

Analysis

Two types of data, quantitative and qualitative, will be collected from the nominal group discussions. The qualitative data will be recorded using a voice recorder and a chart sheet during the nominal group discussion for analysis at a later stage. Quantitative data will be obtained from the ranking tool created on Google form. The use of a ranking tool allows facilitators to provide feedback of the results during the workshop and probe further on the ranking data presented.

Data analysis will start with consolidating all the ideas raised by the participants of the nominal group discussion during the silent brainstorming stage. A similar group of ideas will be grouped together according to the emerging themes.

Quantitative data analysis

The quantitative data will be analysed by summing the votes allocated to each idea to determine the overall priority score. The participants will rank the ideas on a scale of 1–5 on Google form and the overall priority score will be calculated. The results of the summation of scores will be shared with the group.

Stata statistical software will be used for analysis. We will calculate the descriptive statistics, means and distributions. We will further perform a Friedman test, which is used to analyse ranked data. We will conclude the analysis by performing a post hoc test, Bonferroni Correction.

Qualitative data analysis

We will conduct a qualitative thematic analysis of the top five overall priority scores. Qualitative research analysis software NVivo will be used to conduct a conceptual analysis and code the interviews by grouping common topics and issues and categorising them under labels which represent themes that will emerge. A relational analysis will then be conducted using NVivo to examine relationships between the themes that will be derived from the data.

Outcome measures: To establish the challenges faced in the supply chain of COVID-19 POC diagnostic services in Mopani District Municipality and come up with sustainable solutions to overcome these challenges.

Patient and public involvement

No patients or members of the public were involved in the design or conduct of this study.

Data security

The study will be conducted in accordance with the protection of personal information act. The study will abide by the national COVID-19 regulations, guidelines and protocols in order to protect the health of the investigators and participants throughout the duration of the study. The participants will be briefed about the purpose of the study, issues around confidentiality of their information and written informed consent will be sought prior to participation. The participants will be provided with a copy of the signed informed consent for future reference. All the data that will be collected from the participants, both written and voice recorded, will be handled with strict confidentiality. All the data will be stored in a password protected server with access limited only to the members of the internal research team. Backup data will be saved on a password protected Google cloud storage. Transfer of data between members of the research team will be through a secure file transfer. Data collected during the study will be kept confidential in a storage for a maximum 2 years poststudy. The PI will deidentify the records in a way that will prevent reconstruction after the 2-year period. No personal identifiers will be shared with the public during the dissemination of results. It will be the responsibility of the PI and the research team to ensure that the source is unidentifiable, and the source cannot be linked to any statements made or discussed during data collection.

DISCUSSION

The aim of this study is to develop a novel approach for improving SCM for COVID-19 POC diagnostic services in resource-limited settings. To the best of our knowledge, this study is the first to assess and reveal barriers of SCM for COVID-19 diagnostic services in resource-limited settings. This study is in line with the WHO recommendation for scaling up testing programmes for COVID-19 by testing all suspected cases. This recommendation led to an increased demand for POC diagnostic services, especially in high-burden areas where there is poor access to healthcare facilities and laboratory services.

To ensure equitable accessibility and availability of POC tests, it is important that COVID-19 testing is optimised through well-established SCM systems. Currently, the Foundation for Innovative New Diagnostics in collaboration with WHO and other organisations, are playing a pivotal role in scaling up the development and delivery
of COVID-19 tests through its Access to COVID-19 Tools Accelerator and provide sustainable solutions beyond the COVID-19 pandemic.28 To provide sustainable solutions in providing POC diagnostic tests and to avoid past uncoordinated procurement issues, various stakeholders have joined forces to speed up the end of the pandemic by supporting the development and equitable distribution of tests, treatments and vaccines the world needs to reduce mortality and severe disease, restoring full societal and economic activity globally in the near term, and facilitating high-level control of COVID-19 in the medium term.29 The collaboration supports coordinated, uninter rupted provision of timely, high-quality diagnostic tests in resource limited settings.29 The collaboration serves as a platform for information exchange as well as alignment on procurement principles, planning and addressing key SCM issues.29 They also ensure that there are adequate funds to purchase projected POC diagnostic tests to make them available for use at the POC in a timeous manner.

An insufficient SCM prevents a rapid and specific diagnostic approach that is essential in identifying COVID-19 cases not only at an individual patient management level but at a population level as a public health measure to control the pandemic.30 Therefore, this study aims to investigate COVID-19 POC tests SCM in order to reveal barriers and enablers of SCM systems for COVID-19 POC diagnostic services in settings that have poor access to laboratory diagnostic services. The study also aims to provide sustainable and evidence-based solutions for policymakers and implementers of POC diagnostic services.

There are several anticipated limitations for this study. Geospatial analysis uses secondary data and it may be difficult to obtain information specific to the objective. We have applied for ethical approval from the Limpopo Department of Health which will allow us access to the District Health Information System where essential data for health services is stored. The audit and the nominal group technique will be carried out at the PHC facilities, which is the place of work for the participants. There is a high possibility that this can affect the daily operations and duties at the health facility. To mitigate this limitation, the research team will prepare the participants well in advance. We will inform them of the estimated time to complete the questionnaire and to engage in the focus group discussions. The research team will ensure that the time limits are adhered to and if exceeded for any reason, the participants will be allowed to terminate completion of the questionnaire and participation in the focus group discussion so that they can go back and resume their daily duties.

Ethical considerations
This study has been ethically reviewed and approved by two institutional review boards: University of Pretoria Faculty of Health Sciences Research Ethics Committee (approval number 655/2021) and Limpopo Department of Health Research Ethics Committee (approval number LP-2021-12-007). All participants will sign an informed consent form (online supplemental material 2) prior to participation in the study.

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Contributors KM conceptualised and wrote the draft manuscript under the supervision of TPM-T and AM. TPM-T and AM critically reviewed and provided input to revise the manuscript. All authors have read and agreed to the published version of the manuscript.

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