Short Communication - Lessons learnt during the implementation of Unity-aligned SARS-CoV-2 seroprevalence studies in Africa

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Abstract

The WHO Unity Studies initiative engaged low- and middle-income countries in the implementation of standardized SARS-CoV-2 sero-epidemiological investigation protocols and timely sharing of comparable results for evidence-based action. To gain a deeper understanding of the methodological challenges faced when conducting seroprevalence studies in the Africa region, we conducted unstructured interviews with key study teams in five countries. We discuss the challenges identified: participant recruitment and retention, sample frame, sample and data management, data analysis and presentation to policy makers. Potential solutions to aid future implementation include preparedness actions such as the development of new tools, robust planning and practice.

Introduction

To enable the rapid implementation of early COVID-19 sero-epidemiological investigations to guide policy decision-making [1], WHO developed new, or adapted existing,[2] standardized generic protocols branded as the 'Unity Studies', a key focus was supporting low- and middle-income countries to implement these studies [1]. Unity-aligned studies meet criteria including aspects of study design, study population, sampling, recruitment and using well performing serological tests [1]. The most frequently implemented studies in the Africa region were seroprevalence, transmission and vaccine effectiveness [3]. As of the 24th February 2023, 179 Unity-aligned SARS-CoV-2 seroprevalence studies were identified in the WHO African region[4].

The main methodological challenges reported in a 2022 external evaluation of the Unity Studies were delays caused by protocol finalisation, ethical approval and gaining access to funding and test kits [5]. Gaps were also reported in human resources in laboratory science, data analytics and communications[5].

To gain a deeper understanding of the methodological challenges faced when conducting seroprevalence studies in Africa, we conducted unstructured interviews with purposively sampled study teams that had implemented at least one seroprevalence Unity-aligned Study (Burkina Faso (NFK), Ghana (IOD), Mali (SB), South Africa (JK) and South Sudan (JFW)). We present four key reoccurring methodological challenges identified during these interviews and potential solutions to aid future implementation.

Recruitment and retention

Seroprevalence studies require the inclusion of a predetermined minimum number of participants to estimate the population prevalence with good precision [6]. Teams faced challenges with recruitment and retention of participants and therefore, their ability to meet their minimum sample size.

"People were reluctant to participate because of fear and stigma." (Ghana) "When initially enrolling participants into the study, we informed them that we would provide them with their test results as soon as they were available. However, there were delays with the delivery of the test kits provided by WHO, as such, we were unable to get the results to participants before the next round of follow-up visits. People didn't want to continue with the study and give a new sample before they received their results." (Burkina Faso)

These examples add weight to the well documented importance of risk communication and community engagement in surveillance and operational research [7–9]. Community engagement should be implemented as a routine activity of enhanced surveillance. Engagement opportunities include identifying people that the community trusts and building relationships with them and involving them in decision-making, utilising human resources from the community, and importantly, disseminating study findings with all stakeholders[7,9,10].

The Malian team reported that one of the main successes of their study was that:

"We were able to build a young, dynamic, multidisciplinary team capable of implementing future studies, with involvement of stakeholders at all levels including policy makers, community leaders, epidemiologists, immunologists, biologists, data mangers, sociologists and anthropologists." (Mali)

Engagement with and continual support of teams such as these is an important way to ensure timely community-based investigations during future pandemics.

Sampling frame

In an idealized setting, a perfect sampling frame (study population from which the sample is selected in order to adequately address study objectives and extrapolate conclusions appropriately to the broader target population) would be a list where each person with known characteristics (e.g. age) is listed once [2,11]. Often this does not exist in real-world settings. At the outset of the investigation, the Burkina Faso team did not have enough information about the population they were going to sample as there was no recent census data. As such:

"We were obliged to conduct a census before we could sample. The last population census was conducted in 2006 and the data needed to be updated. After randomly sampling the enumeration areas (the smallest geographic statistical unit), we visited the households in these areas and gathered information on the sociodemographic characteristics and sizes of the households. In this way we did a small census to find out about our sample and better establish our sampling frame." (Burkina Faso)

This process was time and resource intensive and delayed the start of the study.

Sampling issues also affected the South Sudan team:

"We used satellite imagery to randomly select shelters for inclusion in the study, some of the sampled households could not be located in the community due to poor internet access in some remote locations which affected the use of GPS to locate the shelters, some households were also empty when study teams arrived, hence the need for supplementary sampling." (South Sudan)

Before implementation, partners need to check if an ad-hoc census is required and feasible based on available resources.

Sample and data management

Sample and data management was noted as a key area that could be improved for future studies.

Using easy-to-collect samples like dried blood spots (DBS) significantly decreases the complexity around sample management. However, prior validation of serological tests using an appropriate panel of paired samples, and a sufficient number of samples, to study test accuracy when using DBS samples is required. Validation of both serological tests and using DBS samples was challenging at the start of the SARS-CoV-2 pandemic which meant that the robustness of non-validated study results was unknown. As such, it is recommended to use well validated serological tests and sample types where possible and that results are adjusted for test performance (see below).

Manual capturing of participant identifiers on collection forms and samples lead to errors, which further resulted in delays while these discrepancies were resolved. A possible solution suggested by several teams was the development of sample collection SOPs including how samples will be linked through unique identifiers to epidemiological data collected such as through the use of barcodes.

Respondents noted that having access to and training on offline electronic data collection tools is necessary.

"We used web-based data collection forms on a platform the team was familiar with as we didn't have time to learn a new software. We had several challenges with connectivity due to limited cell phone network connections in our sampling areas. A better tool would have been a reliable, user-friendly application that you can capture data with offline." (South Africa)

To overcome connectivity issues, some teams used offline mobile data collection tools. They suggested that trainings on how to set-up and use these tools should be done in the preparation phase, so that when studies need to be implemented, they are familiar to study teams and ready for deployment.

Data analysis and presentation

The WHO Unity team collaborated with SeroTracker [4] to provided online workshops and tailored support by producing code and analysis instruction across several analysis tools. Post-hoc adjustment support was concentrated on population and clustering adjustment to control for selection bias in participant sampling, and test adjustment to account for potential biases in estimates introduced by serological assay performance (sensitivity and specificity values).

One of the main aims of the Unity Studies is to provide robust evidence for rapid policy decision making [1]. To be effective in this aim, findings need to be presented in a clear and concise manner. Teams requested assistance with data visualization and advice on how to best present findings to policy makers [12].

Tools to address challenges

Tools (some similar to those identified during the Unity Studies evaluation [5]) to aid future study implementation were identified during the interviews (Figure 1), along with more detail on how such tools can be tailored for the African context. These included risk communication and community engagement (RCCE) guidance and tools, sample collection standard operating procedures (SOPs) and access and training in a customizable electronic offline data collection tool. For data management and analysis, having access to software in which the team is already trained, a draft plan of analysis and data visualization tools are required. In addition to updating study protocols for respiratory pathogens of pandemic potential, the Unity Studies initiative intends to generate and distribute such tools with input from partners. Countries in the African region have unique public health challenges, as such the tools created for global application, will need to

be adapted to fit the context of each study population. Trainings and site visits to implement these tools should be encouraged.

Conclusion

Conducting enhanced surveillance and operational research on a novel pathogen at the start of a pandemic is challenging yet important. The SARS-CoV-2 Unity Studies conducted in the African region have proven that these studies are possible to implement at short notice in a robust manner including in low resource settings, and that the resulting information garnered from them is crucial for shaping policy and practice [5,13].

Investigators should consider the lessons learnt during the SARS-CoV-2 pandemic fur future surveillance efforts and operational research. Several of the methodological challenges faced can be overcome through preparedness actions such as the development of new tools, robust planning and practice. Countries need to develop resilient well-coordinated and fit-for-purpose surveillance approaches that address priority surveillance objectives not met by current systems for respiratory viruses of epidemic and pandemic potential, that can be sustained or adapted during an event for pandemic preparedness and effective response [14].

Figure 1: Tools to develop for use in future sero-epidemiological study and investigation implementation

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