

**An umbrella review of evidence syntheses to inform vaccination practices  
and policies for the COVID-19 pandemic in Africa**



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## PREAMBLE

## DECLARATION

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Also, thanks, mom, and dad.

And the Cape Town wineries.

## THESIS ABSTRACT

**Background:** Since 2020, the world has experienced uncertainty due to the COVID-19 pandemic. The pandemic period is compounded by emergent of new SARS-CoV-2 variants requiring adjustments to the public health control measures. Globally, as of July 2022, there were about 600 million cases of SARS-CoV-2 and around 6.5 million deaths caused by the virus. The morbidity and mortality rates associated with the SARS-COV-2 continue to rise, albeit at a slower pace than in the earlier phases of the pandemic. Beyond the morbidity and mortality associated with the SARS-CoV-2, the pandemic has disrupted healthcare systems, particularly in Africa. The public health response to the pandemic is characterized by several interventions and innovations, including development of COVID-19 vaccines. To contain the pandemic, rapid deployment of COVID-19 vaccines is critical. However, COVID-19 vaccines rollout in Africa has been slow and often poor. Locally relevant evidence can be used to accelerate the rollout of COVID-19 vaccines in Africa. Diverse evidence on COVID-19 vaccines is rapidly accumulating. This study aimed to identify, analyze, and characterize the evidence syntheses that is available and has the potential to inform COVID-19 vaccination practices and policies in Africa.

**Methodology:** We conducted an umbrella review. This type of review is ideal to describe a diverse range of evidence-based topics. The diverse range of evidence accessed was COVID-19 disease burden, SARS-CoV-2 variants, COVID-19 vaccines safety and efficacy in HIV infected persons on the continent, prevalence of COVID-19 vaccines hesitancy and acceptability as well as communication strategies to generate COVID-19 vaccines demand, promote uptake of vaccines and mitigate vaccine hesitancy. We searched for the evidence from PubMed/Medline, Web of Science, Scopus (EMBASE), Epistemonikos and The Cochrane Library. Search filters were used to identify study types of interest: systematic reviews, rapid reviews, meta-analysis. The search period was between December 2019 and August 2021. Search outputs were exported to Rayyan software for screening and thereafter, predefined outcomes were extracted from the included studies. Study characteristics, number and types of evidence syntheses were reported. Pooled results from the included studies were reported, including the statistical methods used. Where pooling of reported results had not been done and was feasible to do so, we conducted our own data pooling.

**Results and conclusions:** A total of 1111 papers were retrieved from all the databases. After screening, 15 papers were included: systematic reviews (n=4), systematic reviews and meta-

analysis (n=7), meta-analysis alone (n=2), rapid review and meta-analysis (n=1), and a review of surveys (n=1). Results from the included studies were from 36 (66%) out of 55 African countries. The most abundant evidence was related to the COVID-19 burden and specifically, seroprevalence of antibodies against SARS-CoV-2 which ranged from 8.2% (95% CI: 0.8-22.3%) to 22% (95% CI 14%-31%) during the study period. Evidence syntheses gaps included incidence and severity of COVID-19 related outcomes such as hospitalization and mortality, as well as for vaccine hesitancy and acceptance rates. There is paucity of systematized evidence on the continent for the diverse evidence to guide COVID-19 vaccines rollout.

## LIST OF ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
COVID-19	Coronavirus Disease 2019
DCI	Daily Cumulative Index
DRC	Democratic Republic of Congo
ES	Evidence Synthesis
HCWs	Healthcare Workers
HIV	Human Immunodeficiency Virus
HR	Hazard Ratio
OR	Odds Ratio
PLWHA	People Living with HIV and AIDS
RR	Risk Ratio
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus-2
TB	Tuberculosis
VOC	Variants of Concern
WHO	World Health Organization

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# STUDY PROTOCOL

## **An umbrella review protocol of the evidence syntheses to inform vaccination practices and policies for COVID-19 pandemic in Africa**

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## ABSTRACT

In Africa, the rollout of COVID-19 vaccines has been slower than in high income settings. Furthermore, in Africa, the rollout started in the first quarter of 2021 compared with earlier periods (December 2020 and January 2021) in high income settings. Optimal COVID-19 vaccination rollout in Africa should be guided by context-specific and up to date available evidence. This is an umbrella review protocol that will identify and characterize the evidence syntheses that is available and can inform COVID-19 vaccination practices and policies in Africa. We will search for the relevant evidence synthesis from multiple databases. Prespecified data will be extracted from the relevant evidence synthesis and summarized. Findings from the proposed umbrella review will be important in two ways. First, available, and up to date evidence on COVID-19 vaccines and immunization in Africa will be accessed and summarized- this will be relevant to policy makers in the continent who has limited access to systematically collated local evidence. Second, priority evidence gaps on the topic will be identified. The gaps will enable evidence producers and consumers to focus their efforts and resources on key evidence gaps. This protocol will be registered in Open Science Framework.

## INTRODUCTION

### *BACKGROUND*

Since the World Health Organization (WHO) declared Coronavirus Disease 2019 (COVID-19) a pandemic in March 2020 [1], global research output on the pandemic rapidly expanded [2]. The COVID-19 pandemic has demanded rapid use of existing evidence as well as rapid identification of evidence gaps, generation of new evidence and its application thereof. Available literature on different COVID-19 pandemic topics is playing a critical role in the response to the COVID-19 pandemic by guiding the best use of available, up to date evidence as well as reducing waste through duplication of research. The introduction and rollout of COVID-19 vaccines can be guided by available and relevant context specific literature.

Despite extensive interventions and implementation of various control measures such as usage of masks, sanitizing and washing of hands, as well as the use of appropriate personal protective equipment, the COVID-19 pandemic is still a global public health priority [3–6]. A vaccine to prevent infection or severe COVID-19 is the best hope for bringing the pandemic to an end. Safe and effective COVID-19 vaccines are crucial, particularly for healthcare workers (HCWs) on the front line of the pandemic response and other vulnerable individuals of the population who have a higher risk of severe disease after infection [5]. As at the time of writing this protocol, several vaccines had been approved for emergency use against the pandemic [7]. The optimal use and rollout of the new vaccines against COVID-19 should be guided by available and up to date evidence. Routinely, evidence on disease burden, vaccine efficacy and safety as well as potential impact of the intervention is used to guide vaccine introduction [8]. For COVID-19 vaccine introduction, there are many other relevant considerations such as prioritization of target groups, vaccination strategies, programmatic and equity considerations, acceptability as well as circulating SARS-CoV-2 variants.

Evidence syntheses (ES) is a rapidly growing field [9]. Of interest in ES, is its application in

response to public health emergencies, such as outbreaks and pandemics. Evidence syntheses includes systematic reviews and meta-analyses, widely considered as the pinnacle in the hierarchy of evidence [9]. Then there are scoping reviews which share several characteristics with systematic reviews, but a key difference is that the purpose of the scoping review is to map the body of the literature on a topic area [10]. Rapid reviews are newer forms of ES in response to policymakers' needs for quality evidence summarized in an effective and urgent way, especially during an emergency as is the case with COVID-19 pandemic. Rapid reviews are a truncated form of a systematic review wherein certain components have been omitted or simplified to generate information in a short period of time [11]. Due to the increasing demand for timely, summarized and quality evidence, and with the increasing numbers of published systematic reviews, a novel development is the umbrella reviews, or simply, overviews or reviews [12–14]. Taken together, these different types of reviews are central to the field of ES. Application of ES is critical in informing vaccination practices and policies that are context specific.

Evidence synthesis plays a vital role to improve and strengthen national vaccines decision-making, more so with regards to new vaccine introductions [8]. In the period of COVID-19 pandemic, large number of systematic reviews and research evidence continue to be generated. These ES are to inform diverse public health interventions against the disease in general and more specifically, vaccination. The ES to inform COVID-19 vaccination practices and policies hinges on a broad scope of issues such as disease burden, vaccine efficacy and safety, prioritization of target groups for vaccination, acceptability of vaccines and vaccine cost effectiveness among others. Against this background, umbrella reviews provide a unique opportunity to describe the evidence base relevant for COVID-19 vaccination rollout, identify gaps and guide policy makers in making use of the best available evidence in a timeous manner.

Our study will identify and characterize the ES that is available and can inform COVID-19 vaccination practices and policies in Africa. The study will be restricted to specific issues that can be used to inform the guidelines issued by the World Health Organization (WHO) on assessing countries' readiness to introduce and deliver COVID-19 vaccines [15].

The WHO guidelines emphasize on the following issues in preparation for COVID-19 vaccines roll out:

- Planning and co-ordination
- Resources and funding
- Regulatory
- Prioritization, targeting and COVID-19 surveillance
- Service delivery
- Training and supervision
- Monitoring and evaluation
- Vaccines, cold chain, and logistics
- Safety and surveillance
- Demand generation and communication

Whereas all the above issues are important, we will not focus on all of them in this study. Instead, we will choose a few of them which are: prioritization, targeting and COVID-19 surveillance; vaccines; demand generation and communication. The choice of these areas of focus is driven by existing knowledge of essential elements that are routinely considered when recommending introduction of new vaccines using evidence-based approaches (5).

### *PROBLEM STATEMENT & RATIONALE*

In high income countries (HICs), rollout of vaccines against COVID-19 started as early as December 2020. For African countries, the rollout of COVID-19 vaccines has been slow and started in the first quarter of 2021. Successful rollout of the vaccines in Africa can be guided by the latest ES. Specifically, this study aims to characterize the ES generated in Africa to inform some of the WHO guidelines which in turn, guides optimal rollout of COVID-19 vaccines on the continent. Characterization of ES will focus on the following areas, each with own literature search strategy:

- a) Prioritization, targeting and COVID-19 surveillance (including SARS-CoV-2 variants), highlighting the COVID-19 disease burden in terms of morbidity and mortality associated with different risk factors.
- b) COVID-19 vaccine safety and efficacy in HIV infected populations. HIV population is chosen given the high burden of HIV in Sub-Saharan Africa and the potential impact of this high burden on vaccine effectiveness.
- c) Cost effectiveness of COVID-19 vaccines.
- d) COVID-19 vaccines demand generation, communication, and vaccine hesitancy.

### *REVIEW QUESTIONS*

- What is the quantity of ES (based on the study focus areas) generated in Africa to guide the rollout of vaccines against COVID-19?
- What are the types of ES (based on the study focus areas) generated in Africa to guide the rollout of vaccines against COVID-19?
- What are the key gaps in the available ES (based on the study focus areas) to guide the rollout of vaccines against COVID-19?

### *REVIEW OBJECTIVES*

- To quantify ES that can guide the roll out of vaccines against COVID-19 in Africa.
- To describe the types of ES to guide the rollout of vaccines against COVID-19 in Africa.
- To describe the key gaps in the available ES to guide the roll out of vaccines against COVID-19.

## METHODS

### *Literature search*

To search for the relevant literature required to address the review questions and objectives, we will apply the PI/ECO (Population, Intervention or Exposure, Comparison and Outcome) approach to each review question which will guide in the development of literature search strategies. The approach is ideal for the search strategy development as the topics of interest for the ES in this review are many and diverse. We will conduct a comprehensive search of the relevant literature from the following databases: PubMed, Google Scholar, Web of Science, Scopus (includes EMBASE), Cochrane Library and Epistemonikos.

To identify the relevant literature from each of the databases, we will develop a systematic Boolean search strategy that will utilize key words such as: “COVID-19 [MeSH]”; “SARS-CoV-2”; “COVID-19 Vaccines [MeSH]”; “SARS-CoV-2 Vaccines”; “Coronavirus Disease 2019 Vaccine”; “Africa [MeSH]”; “COVID-19 surveillance”; vaccine cost-effectiveness”; “COVID-19 vaccine hesitancy”. A detailed search strategy for each of the review question is provided in *Supplementary Tables 1 to 4*.

### *Study inclusion criteria*

The following types of peer-reviewed ES will be eligible for inclusion: scoping reviews, rapid reviews, systematic reviews and, meta-analyses. In addition, ES will be included if published between December 2019 and August 2021, reports data from any African country and is published in English, French or Portuguese. The August 2021 period was chosen as it was the month when the protocol and search was completed.

### *Study exclusion criteria*

Primary studies, narrative reviews and opinion pieces will be excluded. In addition, ES published outside the period of the review interest and in languages other than English, French and Portuguese will be excluded.

### *Study screening*

The retrieved literature will be exported to Rayyan Intelligent Systematic Review [16]. The Rayyan software will be used for the screening of the search results. Prior to screening, duplicates will be identified and removed. Thereafter, screening will be done using titles and abstracts to decide if the literature merits inclusion based on the pre-defined criterion. Screened articles will be assigned to three categories: “included”, “excluded”, and, “maybe”. Full texts of articles in the “included” and “maybe” categories will be sourced. Further screening of the “maybe” category will be conducted by two authors to identify articles for inclusion. Disagreements will be resolved by discussions and consensus, failure to which the third author will arbitrate. The reference lists of the included articles will also be screened to identify any missed articles that merits inclusion.

### *Data extraction*

One author (KE) will independently extract the data. A second author (BMK) will verify the extracted data. Quality check of the data extraction will be done by a third author (ED). Information to be abstracted from the included studies will include:

- Study characteristics (author details, title of the review, publication details such as the type of ES, date of publication and countries where data was collected from).
- Review questions and objectives.
- Outcomes of interests that relates to the questions of this umbrella review as described below.

### *Review outcomes*

The outcomes of interest are as follows:

- COVID-19 disease burden stratified by risk categories/groups.
- SARS-COV-2 variants stratified by countries or regions.
- Vaccine efficacy in HIV infected persons.
- Vaccine safety in HIV infected persons.
- Cost-effectiveness data on COVID-19 vaccines currently (as of August 2021) in use among African countries.
- Prevalence of hesitancy and acceptability.
- COVID-19 vaccines sentiments analyses.
- Communication strategies to generate COVID-19 vaccines demand, promote uptake of vaccines and mitigate vaccine hesitancy against COVID-19 vaccines.

### *Assessment of summary effects*

Summary results from the ES will be extracted and reported, including the statistical methods used. Where pooling of reported results has not be done and it is feasible to do so, we will conduct our own analyses based on the reported results and any other relevant information provided by the authors of the included studies. For quantitative outcomes, fixed and random effects meta-analysis methods will be applied where applicable. The study heterogeneity will be assessed using the  $\chi^2$ -based Cochran's Q test and the  $I^2$  heterogeneity. The  $I^2$  values of 25%, 50%, and 75% indicate low, moderate, and large heterogeneities, respectively. For all the meta-analytic outcome measures, 95% CI will be reported. Statistical analysis will be performed in MS Excel and RevMan software.

Qualitative outcomes will be narratively summarized. Where thematic analysis has been reported, a summary of the key themes will be reported.

### *Quality of the included studies*

To assess the methodological quality of the included reviews, we will record the quality assessments of each review, including publication bias and heterogeneity, in table format. We will report on the tools the authors used and the results of the quality assessments to verify the methodological quality of the reviews.

### *Ethical considerations*

Ethical approval and clearance will not be required for this study as no human subjects will be directly involved. All the literature sources that will be used in this review are already available on the public domain and all other work and help from other investigators will be acknowledged.

### *Discussion*

Timely and high-quality evidence is needed to guide the response to the COVID-19 pandemic by health authorities in Africa to mitigate the negative impacts caused by the disease. Globally, COVID-19 research evidence is accumulating rapidly. Whereas some of the global evidence can be used in Africa to inform the response to the pandemic, COVID-19 vaccination rollout in Africa should be best guided by context-specific and up to date available evidence. Africa's COVID-19 research evidence is also rapidly increasing, like the trend observed globally.

To our knowledge and at the time of conducting this study, COVID-19 research evidence in Africa is not well characterized. As our study interest in ES characterization is broad, we will conduct an umbrella review to address this knowledge gap. This umbrella review will identify and characterize the ES that is available and can inform COVID-19 vaccination practices and policies in Africa. The review will evaluate the quality of the available evidence and identify the gaps in ES that can be prioritized by evidence producers in Africa.

### *Timeline of study activities*

For the purposes of the study management, different research activities and estimated timelines to conduct the study are shown in *Table 1*

Table 1. Timeline of research activities

Task	Timeline																	
	March – July 2021				August-October 2021			November 2021	December 2021	January – June 2022						July 2022	August 2022	September 2022
Protocol development	■	■	■	■														
Literature Search					■	■	■	■										
Data extraction								■	■	■								
Data analysis										■	■	■	■	■	■			
Journal manuscript										■	■	■	■	■	■			
Write up manuscript										■	■	■	■	■	■	■	■	
Finalization of manuscript														■	■	■	■	
Submission																	■	

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# JOURNAL MANUSCRIPT

*The manuscript is formatted for the Vaccine journal. Guidelines for a review article in the journal are shown in Appendix C.*

## **An umbrella review of evidence syntheses to inform vaccination practices and policies for the COVID-19 pandemic in Africa**

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### **Authors' contributions:**

**KE** implemented the study that included search of articles, screening of articles, data extraction and analysis and wrote the first draft.

**EAD** supervised the implementation of the study, quality checked data extraction and reviewed the manuscript drafts.

**RM** conceived the study and reviewed the final draft.

**BMK** conceived and supervised the study, quality checked data extraction and data analysis as well as review of the manuscript drafts.

## ABSTRACT

**Background:** In Africa, the rollout of COVID-19 vaccines lags other continents. The rollout in Africa started in the latter part of the first quarter of 2021 compared with earlier periods in high income settings. Optimal COVID-19 vaccination rollout in Africa should be guided by context-specific and up to date evidence. We conducted an umbrella review to identify, analyze and characterize the evidence syntheses that is available and has the potential to inform COVID-19 vaccination practices and policies in Africa.

**Methods:** A systematic search for scoping reviews, systematic reviews, rapid reviews, and meta-analyses was performed in PubMed/Medline, Web of Science, Scopus (EMBASE), Epistemonikos and The Cochrane Library. Search outputs were exported to Rayyan software for screening. From the included studies, predefined outcomes were extracted and recorded on a data extraction form. Study characteristics, number and types of evidence syntheses were reported. Pooled results from the included studies were reported, including the statistical methods used. Where pooling of reported results had not been done and was feasible to do so, we conducted our own data pooling.

**Results:** A total of 1111 papers were retrieved from all the databases. After removing duplicates and screening for inclusion, 15 papers were included: systematic reviews (n=4), systematic reviews and meta-analysis (n=7), meta-analysis alone (n=2), rapid review and meta-analysis (n=1), and a review of surveys (n=1). Results from the included studies were from 36 (66%) out of 55 African countries. The most abundant evidence was on the seroprevalence of antibodies against SARS-CoV-2 which ranged from 8.2% (95% CI: 0.8-22.3%) to 22% (95% CI 14%-31%).

**Conclusions:** At the time of conducting this study, there was paucity of systematized evidence from majority of the African countries. Evidence syntheses gaps were evident for the incidence and severity of COVID-19 related outcomes, including hospitalization and mortality, as well as vaccine acceptance rates.

**Open Science Framework Registration:** [10.17605/OSF.IO/PTB9W](https://doi.org/10.17605/OSF.IO/PTB9W)

**Keywords:** COVID-19 disease, SARS-CoV-2 infection, Africa, COVID-19 vaccine, evidence synthesis, systematic reviews

## INTRODUCTION

In December 2019, an outbreak of pneumonia-like illness of unknown origin was reported in Wuhan, China [1]. Subsequently and after laboratory evaluations of the patients, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was reported to be the seventh human coronavirus to be discovered [1–3]. Since then, SARS-COV-2 has spread rapidly. Globally, as of July 2022, there were about 600 million cases of SARS-CoV-2 and around 6.5 million deaths caused by the virus [4,5]. The number of SARS-COV-2-associated infections and deaths continue to increase albeit at a slower rate than in 2021. Regardless, the pandemic continues to threaten communities and global public health security.

The COVID-19 pandemic has put enormous pressure on health systems, leaving some African countries more vulnerable to health and social economic challenges than pre-pandemic period [6,7]. The suboptimal performance of health systems across the continent, coupled with the high prevalence of diseases such as HIV/AIDS and tuberculosis (TB), as well as weak economies was thought to make Africa more vulnerable to the pandemic than other continents [7,8]. On the upside, the continent has a large proportion of young population, and as of 2021, around 40% of the population was aged 15 years or younger [9]. Upon infection with SARS-COV-2, younger age groups are less likely to develop severe disease compared with the older age groups [10,11]. Globally, rapid rollout of COVID-19 vaccines is advocated to mitigate the risks associated with the pandemic.

Public health efforts in response to the pandemic are compounded by factors such as continuous emergence of SARS-COV-2 variants of concern (VOC), suboptimal vaccine confidence and waning of immunity following vaccination or natural infection [12]. The epidemiology of COVID-19 pandemic varies across different countries and regions [6]. Although studies have reported the African region has experienced a relatively lower burden of the pandemic compared to other regions, the infection rates, number of cases and mortality rates remain high [7]. In July 2022, Africa's reported disease burden accounted for 2% and 4% of global cases and deaths respectively [13]. Of concern, as of July 2022, the proportion of at least one dose of COVID-19 vaccine coverage in high income settings was estimated at 80% compared to 21% in low-income settings [14]. Majority of countries in Africa fall under the low-income

settings category. COVID-19 vaccination coverage rates in Africa are suboptimal despite improved access to the much-needed vaccines [14].

The epidemiology of COVID-19 pandemic in Africa has been variable across countries and generally, less severe than was initially expected [15,16]. It is hypothesized that the continent's large proportion of young population as well as cross reactive immunity from seasonal coronaviruses may have blunted the impacts of the pandemic [11,16,17]. Comprehensive testing and timely reporting of COVID-19 burden remains a challenge in many African countries. Systematic evidence on the epidemiology of the pandemic in Africa is however slowly accumulating. An evidence-informed and robust COVID-19 public health response is critical to guide policy makers in the response to the pandemic, especially with vaccination rollout [7].

Globally, vaccination against COVID-19 is a key public health intervention to control the pandemic. As of July 2022, several vaccines had been approved for use against the pandemic [18]. The optimal use and rollout of the new vaccines against COVID-19 should be guided by available and up to date evidence. Routinely, evidence on disease burden, vaccine efficacy and safety as well as potential impact of the intervention is used to guide vaccine introduction [18]. For COVID-19 vaccine introduction, other relevant considerations include circulating SARS-COV-2 variants, programmatic and equity considerations as well as acceptability and vaccines confidence [18].

As the rollout of the COVID-19 vaccines gain momentum, there are growing hinderances, such as supply-related challenges, vaccine nationalism, and inequitable vaccine access both within and across countries [12,19,20]. Another emerging problem is that of low vaccines confidence resulting to suboptimal uptake of COVID-19 vaccines in many settings [12,21–24]. There is a need for health authorities and all key stakeholders in Africa to rely on high quality and timely evidence that will inform context-specific COVID-19 vaccination rollout plans, convenient to the local populations.

Overviews of systematic reviews (umbrella reviews) are an increasingly popular method of evidence synthesis, that attempts to systematically retrieve and summarize the results of multiple systematic reviews [25,26]. We conducted an umbrella review to summarize the

available evidence that is generated in Africa and can inform COVID-19 vaccination policies on the continent.

## METHODOLOGY

### *Study design*

We conducted an umbrella review. This type of review is ideal to summarize a diverse range of evidence-based research. We utilized this method to summarize the relevant evidence-base available and with potential to inform practices and policies for COVID-19 vaccines rollout in Africa.

### *Review questions*

- What is the quantity of evidence synthesis (ES) (based on the study focus areas) generated in Africa to guide the rollout of vaccines against COVID-19?
- What are the types of ES (based on the study focus areas) generated in Africa to guide the rollout of vaccines against COVID-19?
- What are the key gaps in the available ES (based on the study focus areas) to guide the rollout of vaccines against COVID-19?

### *Review objectives*

- To quantify ES that can guide the rollout of vaccines against COVID-19 in Africa.
- To describe the types of ES to guide the rollout of vaccines against COVID-19 in Africa.
- To describe the key gaps in the available ES to guide the roll out of vaccines against COVID-19.

### *Review outcomes*

- COVID-19 disease burden stratified by reported SARS-CoV-2 variants.
- SARS-COV-2 variants stratified by countries or regions.
- COVID-19 vaccines safety and efficacy in HIV infected persons.
- Cost-effectiveness of COVID-19 vaccines.
- Prevalence of COVID-19 vaccines hesitancy and acceptability.
- COVID-19 vaccines sentiments.
- Communication strategies to generate COVID-19 vaccines demand, promote uptake of vaccines and mitigate vaccine hesitancy against COVID-19 vaccines.

### *Search strategy*

We used a PI/ECO (Population, Intervention or Exposure, Comparison and Outcome) approach to conduct a literature search. The approach is ideal for the search strategy development as the topics of interest for the review are diverse. Detailed search strategy was used to retrieve literature sources from PubMed, Web of Science, Scopus (EMBASE), Epistemonikos and the Cochrane Library databases.

To identify the relevant literature from each of the databases, a systematic Boolean search strategy was developed utilizing key words such as: “COVID-19 [MeSH]”; “SARS-CoV-2”; “COVID-19 Vaccines [MeSH]”; “SARS-CoV-2 Vaccines”; “Coronavirus Disease 2019 Vaccine”; “Africa [MeSH]”; “COVID-19 surveillance”; “vaccine cost-effectiveness”; “COVID-19 vaccine hesitancy”. The detailed search strategy is provided in Supplementary Tables 1-4 (*Part C*).

### *Inclusion and exclusion criteria*

For reviews to be eligible for inclusion, the following types of peer-reviewed ES were included: scoping reviews, systematic reviews, rapid reviews, and meta-analyses. Observational and interventional studies, narrative reviews, and opinion pieces were excluded. Evidence synthesis reviews that reported data from multiple countries were included as long as African countries were represented. From such reviews, only data from the African countries was extracted. The reviews that did not include any studies from Africa were excluded. Reviews that were conducted in any other language other than English, French or Portuguese, were excluded. Reviews that conducted their search between December 2019 and August 2021 were included as this was the period for this MPH study.

### *Study screening, data extraction and quality assessment*

For screening, ES retrieved from all the databases were exported to Rayyan Intelligent Systematic Review [27]. The entire screening, data extraction and quality assessment process was conducted by one author (KE) then verified by two authors (BMK and EAD). Prior screening, duplicates were identified and removed in Rayyan. Thereafter, screening was done first by reading titles and abstracts to decide if the literature merits inclusion. Screened articles were assigned to three categories: “included”, “excluded”, and, “maybe”. Full texts of articles in the “included” and “maybe” categories were retrieved. Further screening of the “maybe”

category was conducted on the full text papers. Disagreements were resolved by discussions and consensus between KE and BMK, failure to which EAD arbitrated. The reference lists of the included articles were screened to identify any missed articles that merits inclusion. Quality assessment of the included reviews that were conducted by the authors of the reviews were summarized and tabulated.

### *Data analysis*

A data analysis plan aligned with the review questions and the study objectives was developed (*Figure S1: Data Analysis Plan*). For quantitative outcomes, pooled summary results were reported from the included articles. Where pooled results were not available and was feasible to do, we did own pooling. For all the meta-analytic outcome measures, 95% CI were reported. For qualitative outcomes, thematic summaries from the included articles were narratively reported. This umbrella review is guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) diagram [28].

## RESULTS

### *Search Results*

The literature search yielded a total of 1111 articles: 323 from PubMed, 63 from Scopus, 583 from Web of Science, 65 from Epistemonikos and 77 from The Cochrane Library. All the articles were exported to Rayyan for screening. Of these total, 210 articles were duplicates that were removed leaving a total of 901 articles for subsequent screening (*Figure 1*). Titles and abstracts of the 901 articles were screened independently by KE and BMK with discrepancies being resolved by discussions and consensus. In total, 786 articles were excluded leaving 115 articles for full text screening. The two authors (KE and BMK) independently screened the 115 full text articles and excluded 100 articles. Reasons for exclusions included wrong study design wrong population, and wrong outcomes of interest. Where discrepancies and consensus were not possible, a third author (EAD) arbitrated. The remaining 15 articles [29,30,39–42,31– 38] were included for data extraction, analyses, and reporting (*Figure 1*).

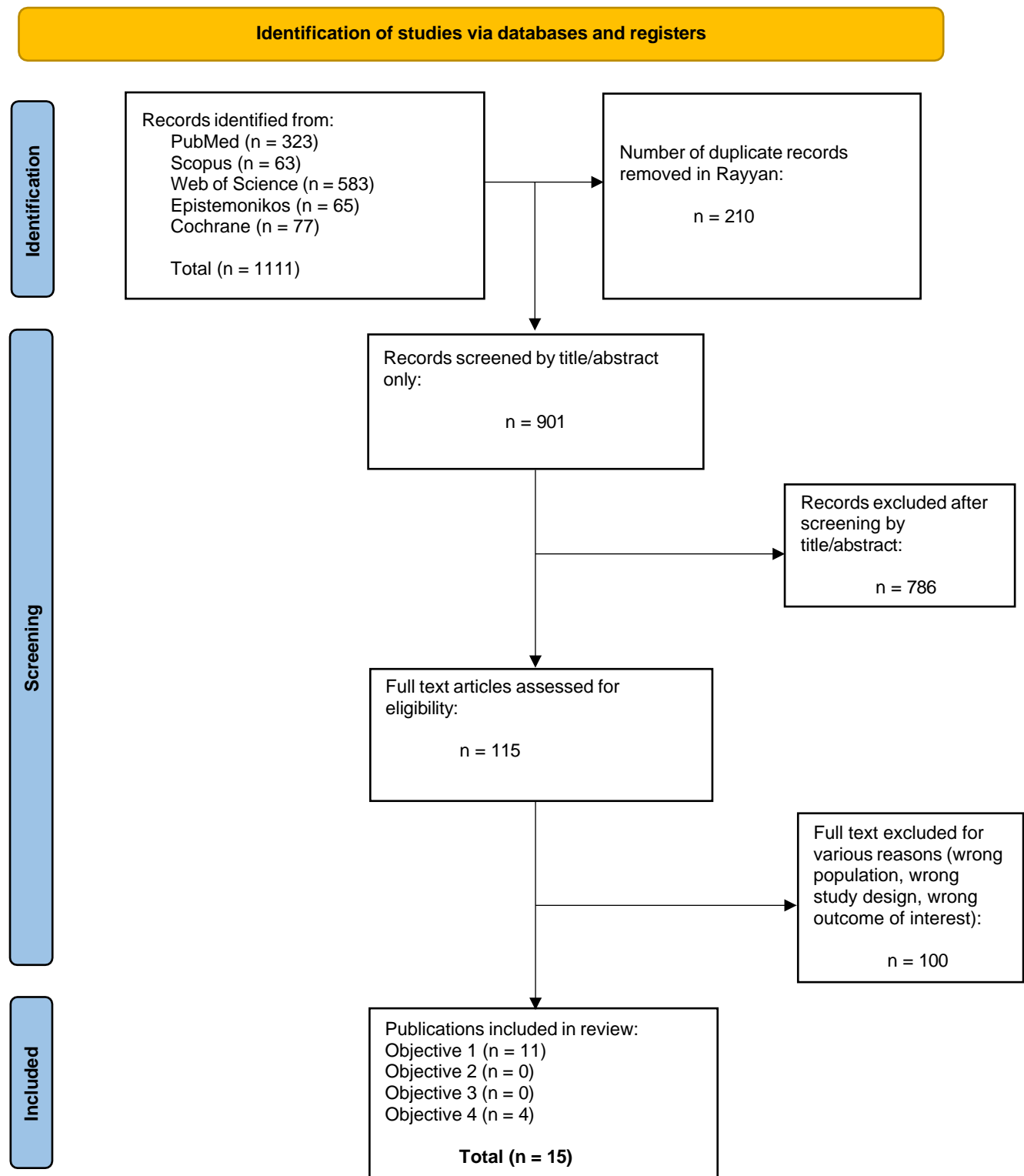


Figure 1: PRISMA flow diagram of the identification, screening, and inclusion of studies

### *Characteristics of the included articles*

The types of ES included in this study were: systematic reviews (n=4), systematic reviews and meta-analysis (n=7), meta-analysis (n=2), scoping review and meta-analysis (n=1), and a review of surveys (n=1).

Outcomes related to COVID-19 disease burden were reported by 12 studies: systematic reviews (n=2), systematic reviews and meta-analysis (n=7), meta-analysis (n=2) and scoping review and meta-analysis (n=1).

Outcomes related to COVID-19 vaccines demand generation, communication, vaccine hesitancy and sentiments or willingness to receive vaccines were reported by 4 studies: systematic reviews (n=2), systematic reviews and meta-analyses (n=1) and a scoping review of surveys wherein results are narratively reported (n=1).

Outcomes on safety and efficacy of COVID-19 vaccines in people living with HIV and AIDS (PLWHA) as well as on cost-effectiveness of COVID-19 vaccines were not reported by any of the included studies. Similarly, there were no included studies reporting the SARS-COV-2 variants.

The primary studies included in the ES were from 36 (66%) out of the 55 African countries representing all the regions on the continent (*Table 1*). Primary studies from Nigeria (n=13) and South Africa (n=8) constituted most evidence per country contributing to the ES included in this review. Unsurprisingly, most of the primary studies were focused on the COVID-19 burden as the outcome of interest.

*Table 1.* List of countries, number of primary studies included by the 15 reviews, and the outcomes of interest that were reported

<b>Region of Africa</b>	<b>Country</b>	<b>Number of primary studies included in the review.</b>	<b>Outcome measurement</b>
<b>Northern Africa</b>	Egypt	6	Seroprevalence of antibodies against COVID-19, mortality rate, vaccine acceptance rate
	Libya	4	Seroprevalence of antibodies against SARS-CoV-2; mortality rate
	Sudan	1	Seroprevalence of antibodies against SARS-CoV-2
	Morocco	2	Mortality rate; recovery rate

Tunisia

1

Mortality rate

	Chad	1	Death count
<b>Eastern Africa</b>	Djibouti	1	Mortality rate
	Kenya	4	Seroprevalence of antibodies against SARS-CoV-2; Mortality risk; Prevalence of HIV/SARS-CoV-2 co-infection
	Ethiopia	5	Seroprevalence of antibodies against SARS-CoV-2; mortality rate; Prevalence of HIV/SARS-CoV-2 co-infection; Level of willingness to receive vaccine
	Malawi	2	Seroprevalence of antibodies against SARS-CoV-2
	Rwanda	1	Acceptance levels and factors associated with vaccine acceptance rate
	South Sudan	1	Seroprevalence of antibodies against SARS-CoV-2
	Uganda	4	Seroprevalence of antibodies against SARS-CoV-2; Prevalence of HIV/SARS-CoV-2 co-infection; level of willingness to receive vaccine
	Mozambique	1	Vaccine acceptance rate
	Somalia	1	Mortality rate
	Sudan	1	Mortality rate
	Zambia	1	Seroprevalence of antibodies against SARS-CoV-2
<b>Central Africa</b>	Cameroon	3	Seroprevalence of antibodies against SARS-CoV-2; Vaccine acceptance rate
	DRC	3	Seroprevalence of antibodies against SARS-CoV-2; Vaccine acceptance rate
	Congo		Seroprevalence of antibodies against SARS-CoV-2; mortality rate; Prevalence of HIV/SARS-CoV-2 co-infection; Vaccine acceptance rate
	Gabon	1	Seroprevalence of antibodies against SARS-CoV-2
<b>Southern Africa</b>	South Africa	8	Seroprevalence of antibodies against SARS-CoV-2; Mortality rate; Mortality risk; Prevalence of HIV/SARS-CoV-2 co-infection; Vaccine acceptance rate
<b>Western Africa</b>	Benin	1	Death count
	Burkina Faso	2	Death count; Vaccine acceptance rate
	Côte D'Ivoire (Ivory Coast)	2	Seroprevalence of antibodies against SARS-CoV-2; death count
	Gambia	1	Death count
	Ghana	1	Death Count
	Guinea	1	Death Count
	Guinea-Bissau	1	Death Count
	Liberia	1	Death Count
	Mauritania	1	Death Count
	Niger	1	Death count

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Nigeria	13	Seroprevalence of antibodies against SARS-CoV-2; mortality rate; death count; prevalence of HIV/COVID-19 co-infection
Senegal	1	Death count
Sierra Leone	1	Death count
Togo	1	Death count

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The COVID-19 burden reported in 5 reviews included the mortality rate associated with SARS-CoV-2 (2–6). Five reviews reported the seroprevalence of antibodies against SARS-CoV-2 [29,32,36,38,44]. Other COVID-19 burden related outcome measures reported included severity [31], the prevalence of HIV/SARS-CoV-2 infection [36], the incidence of COVID-19 [34], and the recovery rate [33]. The characteristics of the outcome measurements are shown in *Tables 2-6*.

Four reviews (all systematic reviews and meta-analyses) reported seroprevalence of antibodies against SARS-CoV-2 (*Table 2*). Chisale *et al.*, reported seroprevalence data from 19 African countries, between December 2020 and April 2021, and included different population groups with a sample size of 27,735. Variables of interest in this study were age, gender, comorbidities, marital status, level of education, and three population groups: healthcare workers (HCWs), general population and blood donors. The seroprevalence of antibodies against SARS-CoV-2 at the period of the study ranged from 8.2% (95% CI: 0.8-22.3%) to 22% (95% CI 14%-31%) [29,36,44]. Chisale *et al.*, reported the most significant factors affecting the seroprevalence being the number of days between the first reported COVID-19 case and the date the study was conducted. Among population groups, blood donors had higher levels of antibodies against SARS-CoV-2 (33%, 95% CI 10%-50%) when compared to HCWs (18%, 95% CI 10%-50%) [29].

Galanis *et al.*, reported seroprevalence data from 3 African countries, between December 2019 and August 2021, and included a sample size of 651, all of whom were HCWs. The seroprevalence of antibodies against SARS-CoV-2 ranged from 8.2% (95%CI 0.8-22.3%).

Bobrovitz *et al.*, reported seroprevalence data from 9 African countries, between January 2020 and December 2020 with a sample size of 14, 652. The seroprevalence of antibodies ranged from 8.2% (95% CI 0.1-17.7%) in North Africa to 19.5% (95% CI 9.0 - 26.0%) in sub-Saharan Africa. The Democratic Republic of Congo (DRC) and Nigeria had the highest seroprevalence rates of 40.8% and 41.0%, respectively [38].

He *et al.*, reported seroprevalence data from 3 African countries, between December 2019 and February 2021, with a sample of 144 representing HCWs. The seroprevalence rates for both Nigeria and Congo were 48% (95% CI 39.2%-57.3%), and 11% (95% CI 0.0%-22%) for Egypt [32].

Table 2. Characteristics of the reviews measuring the seroprevalence rate of antibodies against SARS-CoV-2

Authors, Year	Type of Review	Countries included	Factors Assessed	Sample Size (min-max)	Summary Statistics (%)	Period of when data was collected
Chisale et al., 2021 <sup>22</sup>	Systematic Review and Meta-Analysis	South Africa; Libya; Ethiopia; Kenya; DRC; Nigeria; Malawi; Togo; Ivory Coast; Zambia; Egypt; Gabon; Congo Brazzaville; South Sudan; Cameroon; Guinea Bissau	Age, sex, comorbidities, marital status, level of education, HCWs, general population, blood donors	27, 735 (99 - 4585)	22% (95%CI: 14-31)	December 2020 – April 2021
Galanis et al., 2021	Systematic Review and Meta-Analysis	Libya; Egypt; Malawi	Age, sex, HCWs	651 (74- 500)	8.2% (95%CI 0.8-22.3%)	December 2019 – April 2020
Bobrovitz et al., 2021	Systematic Review and Meta-Analysis	Congo, Nigeria, Ethiopia, Kenya, South Africa, Libya	COVID-19 cases, HCWs, race and ethnicity, sex, age	14,652 (99- 9922)	<b>Sub-Saharan Africa:</b> (19.5%, 9.0 - 26.0%). <b>North Africa &amp; Middle East:</b> (8.2%, 0.1-17.7%)	January 2020 – December 2020
He et al., 2021	Systematic Review and Meta-Analysis	Egypt, Nigeria, Congo	COVID-19 infection, nurses	144 (28-83)	<b>African region:</b> (48.2%, 95% CI 39.2% - 57.3%). <b>Egypt:</b> (11%, 95%CI 0.00-22)	December 2019 – February 2021

A systematic review by Gesesew *et al.*, investigated the risk factors for COVID-19 infection, disease severity and related deaths in Africa and globally, between April 2020 and August 2020. Data from 4 African countries was included by the Gesesew *et al.*, study that assessed the following risk factors: sociodemographic, lifestyle and behavioral, climate variables and chronic comorbidity characteristics. There were no odds ratios reported for the risk factors assessed.

In a meta-analysis investigating the clinical characteristics of COVID-19 cases in Africa between January and October 2020, Olumade and Uzairue reported data from 5 countries Morocco, Nigeria, Senegal, Congo, and Uganda with a total sample size of 4499 (*Table 3*). Of the cases, 69% were males. Overall, the most prevalent symptoms were fever (43%), cough (33%), headache (11%), and breathing problems (17%) while fatality rate was reported to be 5.6%.

In a scoping review that included meta-analysis, BaHammam *et al.*, reported COVID-19 recovery from 22 countries in the WHO EMR region during the first 4 months of the pandemic (*Table 3*). A subset of the data used to perform the meta-analysis was from 7 African countries: Djibouti, Egypt, Libya, Morocco, Somalia, Sudan, and Tunisia) [33]. The average recovery rate from the 7 countries was 43% with the lowest recovery rate of COVID-19 reported in Sudan (13%) while the highest recovery rate was reported in Tunisia (87%). The low recovery rate during early period of the pandemic is possibly due to limited testing and potentially restricted to severe cases at the time when the management of the severe COVID-19 cases was not fully understood.

The same study (BaHammam *et al.*,) reported COVID-19 death rates. The average COVID-19 death rate for the 7 African countries was 3.5% [33]. Death rate was lowest in Djibouti (0.6%) and highest in Tunisia (4.6%). It needs to be pointed out the sample sizes of the COVID-19 cases among the 7 countries in the study ranged from (n=75) in Libya to (n=17967) in Egypt. These variable sample sizes points to issues on data quality for the reported outcomes (recovery and death rates). Unsurprisingly, the  $I^2$  reported in the meta-analysis was at maximum (100%).

Phannajit *et al.*, reported the incidence of COVID-19 disease and included countries from all continents among which the following were from Africa: Congo, Nigeria, Ethiopia, Kenya, South Africa, and Libya. Unfortunately, summary results from the individual African countries were not provided in the review (*Table 3*). When compared to the continents of Americas, Europe and Asia, the study found that African countries had the lowest pooled Daily Cumulative Index (DCI) at 193.09 cases/day on the day (March 28<sup>th</sup>, 2021) the authors conducted the search [34]. The 193.09 cases/day is about three COVID-19 cases per 100 persons population. Interestingly and for the same period, the pooled DCI of COVID-19 was the highest among high-income countries (2096.5 cases/day) compared to middle- and lower-income countries (1168.91 cases/day) [34]. Phannajit *et al.*, reported the mortality rate of COVID-19 disease in Southern Africa and included a sample size of 125,704,789. The percentage of cases that died was reported to be 1.71% (95% CI 1.48%-1.97%).

Tinto *et al.*, reported absolute number of cases and death counts of COVID-19 in West Africa (comprising of 17 countries) between March and July 2020 (*Table 3*). Of the 17 countries, Nigeria had the highest number of cases (n=41,804) while the Gambia had the least cases (n=326). Similarly, death counts were highest in Nigeria (n=868) and lowest in the Gambia (n=18). However, in absence of denominated cases and death counts to compute the prevalence or incidence in these countries, these absolute numbers are of little public health value as a measure of disease burden.

Table 3. Characteristics of the reviews measuring the mortality or fatality rate of COVID-19, and the risk factors and groups that were assessed.

Authors, Year	Type of Review	Countries included	Factors Assessed	Sample Size (min-max)	Summary Statistics (% , OR count)	Period of data collected of included studies
<b>Olumade &amp; Uzairue 2021</b>	Meta-Analysis	Morocco, Nigeria, Senegal, Congo, Uganda	Clinical symptoms; fever, cough, headache, breathing problem; COVID-19 cases	4 499 (9 - 3467)	5.6% (95CI 2.7%-8.6%).	January 2020 – October 2020
<b>BaHamman et al., 2021</b>	Scoping Review, Meta-Analysis	Djibouti, Egypt, Libya, Morocco, Somalia, Sudan and Tunisia	General population	34578 (75- 17967)	<b>Djibouti</b> (0.006, 95%CI 0.003-0.010). <b>Egypt</b> (0.044, 95% CI 0.041-0.047). <b>Libya</b> (0.040, 95% CI 0.013-0.117). <b>Morocco</b> (0.027, 95% CI 0.023-0.030). <b>Somalia</b> (0.039, 95% CI 0.031-0.049). <b>Sudan</b> (0.043, 95% CI 0.037-0.050). <b>Tunisia</b> (0.046, 95% CI 0.035-0.060)	January 2020 – May 2020
<b>Phannajit et al., 2021</b>	Meta-Analysis	Congo, Nigeria, Ethiopia, Kenya, South Africa, Libya	Geographic regions; economic status, current health expenditure; and healthcare performance; general population	125,704,789	1.71%; 95CI 1.48-1.97	28 March 2021
<b>Tinto et al., 2021</b>	Systematic Review and Meta-Analysis	Benin, Burkina Faso, Cape Verde, Côte D'Ivoire, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone, Togo.	Death Count	131 049 (326-41804)	18 – 868 deaths	March 2020 to July 2020

It has been reported that people living with HIV and AIDS could be at a higher risk of developing severe COVID-19 disease which in turn increases the odds for hospitalization or death [36,37]. Hariyanto *et al.* investigated the impact of HIV and SARS-CoV-2 co-infection on the mortality outcomes of COVID-19 disease between December 2019 and January 2021. A subgroup analysis from studies conducted in Kenya and South Africa showed a positive association between HIV and mortality from COVID-19 [OR = 1.13 (95% CI = 1.04 –1.23) (*Table 4*). Additionally, the authors reported no association with age, gender, CD4 count of <200 cells / $\mu$ l or antiretroviral therapy [37].

Raya *et al.* reported the prevalence of HIV/SARS-CoV-2 co-infection and the potential risk of severe illness and death in PLWHA, in 6 African countries and included a sample size of 22, 212 COVID-19 cases, between December 2019 and July 2021. An increase of 14% in risk of severe COVID-19 disease for PLWHA in Africa was reported, however, there was no significant increase in mortality rate due to COVID-19 in PLWHA (1.915, 95% CI 0.992-3.696).

*Table 4.* Characteristics of the reviews measuring the co-infection prevalence of COVID-19 cases among HIV-infected populations and the death count

<b>Authors, Year</b>	<b>Type of Review</b>	<b>Countries included</b>	<b>Measure</b>	<b>Factors Assessed</b>	<b>Sample Size (min-max)</b>	<b>Summary Statistics</b>	<b>Period of data collection</b>
<b>Raya et al., 2021</b>	Systematic Review and Meta-Analysis	South Africa, Nigeria, Kenya, Uganda, Ethiopia, Congo	Prevalence of HIV/SARS-CoV-2 co-infection	COVID-19 clinical outcomes; PLWHA	25 212 (54 - 22308)	RR 1.138 (95% CI 1.048 - 1.235)	December 2019 to July 2021
<b>Hariyanto et al., 2021</b>	Systematic Review and Meta-Analysis	South Africa, Kenya	COVID-19 disease; PLWHA	SARS-CoV-2/HIV co-infection	7132 (24-3978)	OR 1.13 (95% CI 1.04 – 1.23)	December 2019 – January 2021

Table 5 describes the characteristics of vaccine demand generation, communication, and vaccine hesitancy. The measurement of vaccine acceptance was mainly reported as the vaccine acceptance rate, willingness to receive a vaccine or intention to vaccinate. The population assessed amongst the reviews included: HCWs [41,42,45], the general population [41,42,45] and population not defined [40].

Sallam reported vaccine hesitancy worldwide and included 3 countries from Africa with a sample size of 1 902 consisting of HCWs and the general population, on the 25<sup>th</sup> of December 2020. The study reported the percentages of people that would be willing to receive the COVID-19 vaccine to be: 27.7% of HCWs in the DRC, and 81.6% and 65.2% of general populations in South Africa and Nigeria respectively [40-53].

Mahmud *et al.*, reported the acceptance of the COVID-19 vaccine and included 4 countries from Africa with a sample size of 11 253 consisting of both members of the general population and HCWs on the 25<sup>th</sup> of April 2020. Amongst HCWs, 27.7% agreed to the COVID-19 vaccine (95% CI 24.2-31.2%) and 42.5% members of the general population would receive the COVID-19 vaccine (95% CI 23.1%-61.8%). The highest acceptance rate was reported in Nigeria, and the lowest in Cameroon, and the general population were more willing to receive the vaccine compared to HCWs [45].

Wake *et al.*, investigated the willingness to receive the COVID-19 vaccine and the associated factors from 4 African countries, between December 2019 and January 2021. The study had a sample size of 2 851 that consisted of HCWs, adults (>18 years) and medical students. Across the four African countries, Ethiopia reported the highest level of willingness (80.9%), compared to the Congo (27.7%), Uganda (37.3%), and Nigeria (50.2%). In Congo, being male and having a positive attitude towards COVID-19 vaccine were associated with higher acceptance of the vaccine. In Uganda, being female, single, having a perceived risk of getting COVID-19 in the future, and having received any vaccine in the past 5 years, were associated with the acceptance of the COVID-19 vaccine [47].

Arce *et al.*, conducted a review of surveys on the COVID-19 vaccine acceptance and hesitancy in low- and middle-income countries including 6 African countries with a sample size of 8 525, between June 2020 and January 2021. From the study, Mozambique had the highest levels of

willingness to accept the COVID-19 vaccine (89.1%), and Burkina Faso had the lowest acceptance levels (66.5%).

Table 5. Characterization of COVID-19 vaccines demand generation, communication and vaccine hesitancy, and the factors that affected the acceptance rate

Authors, Year	Type of Review	Countries included	Population (min-max)	Factors and groups assessed	Summary Statistics	Period of data collected
<b>Sallam 2021</b>	Systematic Review	South Africa, Nigeria	1902 (613-670)	HCWs; general population; age	<b>DRC:</b> 27.7%. <b>South Africa:</b> 81.6%. <b>Nigeria:</b> 65.2%	25 <sup>th</sup> December 2020
<b>Mahmud et al., 2021</b>	Systematic Review and Meta-Analysis	Egypt; Nigeria; Congo; Cameroon	11 235 (613-4131)	HCWs; general population	<b>Egypt:</b> 45.9 (95%CI 41.51-50.29); 34.9 (95%CI 32.88-36.92). <b>Nigeria:</b> 40.5 (35.48-45.52). <b>Congo:</b> 55.9 (95%CI 54.39-57.41); 27.7 (24.16-31.24). <b>Cameroon:</b> 15.4 (95%CI 13.99-16.81)	25th April 2020
<b>Wake et al., 2021</b>	Systematic Review	Congo; Ethiopia; Uganda; Nigeria	2851 (409-1228)	HCWs; age;	<b>Congo:</b> 27.7%. <b>Ethiopia:</b> 80.9%. <b>Uganda:</b> 37.3%. <b>Nigeria:</b> 50.2%	December 2019 – May 2021
<b>Arce et al., 2021</b>	Review of surveys	Burkina Faso; Mozambique; Nigeria; Sierra Leone; Uganda	8525 (976-2109)	HCWs, age and education	<b>Burkina Faso:</b> 66.5%, 95%CI (63.5-69.5). <b>Mozambique:</b> 89.1, 95%CI (86.5-91.7). <b>Nigeria:</b> 76.2%, 95%CI (74.3-78.2). <b>Rwanda:</b> 84.9%, 95%CI (82.9-86.8). <b>Sierra Leone (1):</b> 78.0%, 95%CI (75.5-80.5); <b>Sierra Leone (2):</b> 87.9%, 95%CI (86.2-89.6). <b>Uganda (1):</b> 85.8%, 95%CI (84.4-87.2); <b>Uganda (2):</b> 76.5%, 95%CI (74.3-78.7)	June 2020 – January 2021

*Quality assessment as reported by the authors of the included reviews.*

Quality assessments of ES is important in guiding evidence users on the reliability of the generated evidence. We were therefore interested in assessing how each of the reviews conducted a risk of bias assessment as well as rated the quality of evidence. Reported quality assessments from each review was extracted and has been displayed in Table 6.

Publication bias assessment was performed in 8 reviews, 3 reviews did not perform the assessment, and 2 reviews did not report on whether they performed publication bias assessment. Heterogeneity assessments were reported in 8 reviews.

The quality assessment tools used in the 10 reviews that conducted quality assessment were: Joana Briggs Institute (JBI) prevalence appraisal tool (5/12), British National Institute for Clinical Excellence (BNICE) appraisal tool (1/12), Newcastle-Ottawa Scale (4/12), MASTER Scale (1/12) and STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) (1/12).

Table 6. Characteristics of quality assessments of the included studies conducted by the authors of the reviews.

Author, Year	Publication Bias Assessment		Quality Assessment		Heterogeneity
<b>Characteristic 1</b>					
Chisale et al., 2021	Yes	Egger's test	JBI	High and Low	$I^2$
Olumade et al, 2021	Yes	Egger's test p	BNICE	Quality score of between 5-7	$I^2$
Gesesew et al., 2021	Yes	NR	JBI	NR	No
Galanis et al., 2021	Yes	Egger's test	JBI	NR	$I^2$
BaHamman et al., 2021	No	NR	NR	NR	$I^2$
Tinto et al., 2021	No	NR	NR	NR	NR
Phannajit et al., 2021	No	NR	No	NR	NR
Bobrovitz et al., 2021	No	NR	JBI	High, Moderate and Low	NR
Hariyanto et al., 2021	Yes	NR	Newcastle-Ottawa Scale	NR	NR
He et al., 2021	Yes	NR	JBI	High and Moderate	$I^2$
Raya et al., 2021	Yes	Egger's test	Newcastle-Ottawa Scale	NR	NR
<b>Characteristic 4</b>					
Sallam 2021	No	NR	NR	NR	NR
Mahmud et al., 2021	Yes	Z -test	STROBE		$I^2$
Wake 2021	NR	NR	Newcastle-Ottawa Scale	NR	NR
Arce et al., 2021	NR	NR	NR	NR	NR

## DISCUSSION

We successfully conducted an umbrella review that identified and characterized policy-relevant evidence syntheses that can guide decision makers in strengthening evidence-based COVID-19 vaccination rollout programs in Africa. The policy-relevant evidence syntheses identified were from 15 studies and consisted of systematic reviews, meta-analyses, a scoping review, and a review of surveys. The most reported outcomes from the identified ES were related to COVID-19 burden. Evidence syntheses related to the risk of HIV infection on COVID-19 prognosis was limited and conflicting, whereas evidence syntheses on COVID-19 vaccines demand generation, communication, and vaccine hesitancy was highly variable across countries and limited. There was paucity of evidence syntheses on outcomes related to the SARS-COV-2 variants, COVID-19 vaccines safety and efficacy among PLWHA, as well as cost effectiveness of COVID-19 vaccines for the continent. Overall, the ES that we identified represented studies conducted from 36 out of the 55 African countries.

Globally, COVID-19 vaccines rollout started at the peak of the pandemic. Given the initial limited supply of vaccines relative to high demand, a global values framework for fair allocation and prioritization was developed and supported by WHO's Strategic Advisory Group of Experts on Immunization (SAGE) [48]. One key element of the framework is the prioritization of at-risk population groups. These population groups included HCWs, older populations and those with co-morbidities such as diabetes, and other severe co-morbidities such as HIV/AIDS [28,33,39]. When most African countries started the rollout of COVID-19 vaccines, they adhered to this prioritization criteria as the continent had limited to no access of the vaccines [49]. Interestingly and in our study, we did not find many reviews that had documented evidence on the risk groups within the African continent. The African continent has other potential COVID-19 risk factors such as HIV/AIDS, TB, Malaria, and malnutrition that could inform allocation and prioritization, contextually. As an example, no review from the included studies solely investigated the risk of COVID-19 in TB diseased populations. Findings from this umbrella review showed limited evidence on the disease burden that goes beyond the global allocation and prioritization framework.

Findings from our umbrella review showed seroprevalence of SARS-COV-2 antibodies was the most frequently reported outcome of COVID-19 disease burden. The seroprevalence of SARS- CoV-2 antibodies were most often studied amongst HCWs, and results indicate HCWs within Africa tend to have higher seropositivity rates to SARS-COV-2 than the general population. The seroprevalence of SARS-COV-2 antibodies has a strong association with time

post the reporting of the first COVID-19 case. Seroprevalence of SARS-COV-2 antibodies has increase with time in all settings. Given the abundance of the outcome, it may be worthwhile to conduct a living systematic review of the seroprevalence of SARS-COV-2 antibodies in Africa with the intention of getting a clearer picture of how hybrid immunity could inform future COVID-19 vaccination policies. In addition, such data could give a better insight into the natural immunity status of the continent as the world slowly transition from pandemic to COVID-19 endemicity [50,51].

As of July 2022, Africa lags other continents with respect to COVID-19 vaccination coverage [52,53]. The reasons for lagging are many, among which is access to vaccines. Evidence from our umbrella review showed that vaccine confidence on the continent is highly variable, and somewhat lacking. The results indicate that vaccine hesitancy is comparatively higher to other countries [40,45]. The driving factors are safety, side effects and efficacy [54]. Even amongst the HCWs, the acceptancy was low. This is not beneficial to the COVID-19 vaccination rollout, as those that trust the knowledge and experience of the HCWs, will reject the vaccine as well. It is not new knowledge that among African countries, there is a mistrust of vaccines developed in the Western countries, but this needs to be addressed and constantly monitored to develop consistent and effective communication strategies to challenge the potential rise of new variants and conflicting views on COVID-19 vaccines which continue to plague Africa [54].

Integration of the COVID-19 vaccine into routine immunization programs is under consideration, and the WHO is urging African countries to follow those countries that have integrated COVID-19 vaccination into routine vaccination programs. Policymakers are being encouraged to identify robust and context-specific strategies to speed-up routine immunization to mitigate the impact of COVID-19 on the performance of their national immunization programs (55). Nigeria has been successful at integrating COVID-19 vaccines into the national vaccination schedule; children from 9-59 months are being vaccinated against all childhood diseases and the COVID-19 vaccine is being given to persons aged 18 years and older (56). In South Africa, the Mamello Health Clinic in the Free State has integrated the COVID-19 vaccine into patients' routine health checkup as well as when they bring their children in for their immunizations (57). Coupled with the national electronic vaccination data system, this has proved beneficial. It has become possible to remind patients about their vaccinations and routine health checkups and has helped the district officials to identify clusters of patients that have fallen behind with their COVID-19 vaccinations (57).

The 15 studies included in this umbrella review rank on top of the pyramid of the hierarchy of evidence. Authors of most of the included studies conducted a quality assessment as well as risk of bias assessment. Majority of the reviews were those of systematic reviews and meta-analysis. The studies provide a rigorous and transparent evidence base, from which policy makers can draw locally relevant data to inform immunization practices and policies during the period of public health emergency [58,59]. Nevertheless, the evidence base is still highly limited in terms of quantity of data as well as the breadth (evidence on diverse topics). As an example, evidence on the SARS-COV-2 variants of concerns was not available.

It is important to highlight that the COVID-19 pandemic has introduced novel infrastructure like advanced laboratory and surveillance systems. These infrastructures can be leveraged to enhance public health responses to existing epidemics and disease outbreaks in Africa, such as those caused by HIV, TB, and Ebola virus (EBV). Global partnership plays an integral role in overcoming public health challenges and requires government coordination and collaborative efforts [60]. During the COVID-19 pandemic, the African Union Commission, Africa CDC, and the WHO, in partnership with African countries established the Africa Taskforce for Coronavirus Preparedness and Response (AFTCOR) [60,63]. This partnership, along with the Africa CDC and the WHO, was able to capacitate African countries with resources to accurately diagnose COVID-19 infection along with other public health measures such as surveillance, screening, prevention and control facilities, clinical management of infected people, risk communication, supply-chain management, and stockpiles [62]. This highlights the importance of collaboration and interdependence, coordinated coherent responses, and what can be achieved by working together. It is time that the leadership of African countries become more proactive and learn from the successes and failures during the pandemic, reshape their response to capitalize on the successes and utilize them to stabilize other public health challenges, such as those caused by HIV, TB and EBV. The partnerships have been developed, there is now the requirement to mobilize the necessary public health measures to stabilize the threats, such as containment measures, prevention, and screening, prioritizing vulnerable and high-risk groups and ensuring effective and efficient healthcare delivery. To avoid resistance from the people, and to implement the measures effectively, governments need to appeal to the people's understanding and co-operation. The only way to do this is through community engagement, social awareness, and effective communication to fight widespread misleading information and incorrect facts that would complicate social learning [60]. People need to be fully educated on the diseases, how they are spread, and what to do when someone becomes symptomatic. Lack of trust in governmental agencies and resistance to interventions contribute to the spread of the

disease and the weakening of already fragile health systems.

Additionally, the COVID-19 pandemic has forced us to address and assess our health infrastructures. To increase the resilience of our infrastructures across multiple dimensions such as physical, operational, financial and governance, changes need to be made to legislation, policies, and practices regarding our response to public health threats. Maintenance of hospitals, clinics, healthcare delivery, immunization schedules, especially to the remote areas where access to water, food and sanitation are scarce, are crucial to stabilizing Africa's healthcare systems. These changes, on national, regional, local, and programmatic levels, need to be solely based on evidence syntheses to avoid the implications for the economy and society when the decisions are made in the absence of facts. All informed decisions regarding all aspects of society need to be based on the best evidence available at the time. As such, the leaders of Africa need to reshape their governance, and co-operate with one another because global health is a shared responsibility, and it is the responsibility of every African country to prioritize public health and to hold each other accountable for the benefit of the continent.

The limitations of this review included lack of comprehensive datasets in the included reviews. Also, there was lack of reviews that assessed the safety and efficacy of the COVID-19 vaccines in PLWHA, the cost-effectiveness of the COVID-19 vaccines in PLWHA as well as SARS-COV-2 variants. Some of the primary studies were included in more than one review and this is reported in Supporting Information (S7).

In summary, at the time of this study there was limited systematized local data to guide contextually relevant COVID-19 vaccines rollout in Africa. Given the time periods wherein the data reported in our umbrella review was collected (between 2019 and 2021), the findings of our review do not represent the most current evidence. However, the vaccination coverage remains low across Africa, reflecting the need to continue producing and advocating for use of the available evidence to guide COVID-19 vaccines rollout in Africa.

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## APPENDIX

APPENDIX A. *Supporting Information*

*S1 Table.* Literature search strategy: prioritization; targeting and COVID-19 surveillance (including SARS-COV-2 variants), highlighting the COVID-19 disease burden in terms of morbidity and mortality.

No.	Category	Query	Search
#1	Population	Africa	Africa OR African OR Algeria OR Angola OR Benin OR Botswana OR "Burkina Faso" OR Burundi OR "Cabo Verde" OR Cameroon OR Cameroun OR "Canary Islands" OR "Cape Verde" OR "Central African Republic" OR Chad OR Comoros OR Congo OR "Cote d'Ivoire" OR "Democratic Republic of Congo" OR Djibouti OR Egypt OR Eritrea OR eSwatini OR Ethiopia OR Gabon OR Gambia OR Ghana OR Guinea OR Guinea- Bissau OR "Ivory Coast" OR Jamahiriya OR Kenya OR Lesotho OR Liberia OR Libya OR Madagascar OR Malawi OR Mali OR Mauritania OR Mauritius OR Mayotte OR Morocco OR Mozambique OR Namibia OR Niger OR Nigeria OR Principe OR Reunion OR Rwanda OR "Saint Helena" OR "Sao Tome" OR Senegal OR Seychelles OR "Sierra Leone" OR Somalia OR "St Helena" OR Sudan OR Swaziland OR Tanzania OR Togo OR Tunisia OR Uganda OR "Western Sahara" OR Zaire OR Zambia OR Zimbabwe
#2	Event	COVID-19	COVID-19 OR "SARS Coronavirus 2" OR SARS-CoV-2 OR SARS-coronavirus-2 OR nSARS-COV-2 OR "SARS-CoV-2 variants" OR "Variants of Concern" OR VOC OR "Variants of Interest" OR VOIs OR 20I/501Y.V1 OR B.1.1.7 OR Alpha OR 20H/501Y.V2 OR B.1.351 OR B.1.351.2 OR B.1.351.3 OR Beta OR P1 OR P1.1 OR P1.2 OR Gamma OR B1.617.2 OR AY.1 OR AY.2 OR Delta OR Delta plus OR Lambda "SARS-CoV-2 variants" OR "B.1.1.7 variant" OR "Alpha variant" OR "B1.351 variant" OR "beta variant" OR "B.1617.2 variant" OR "Delta variant" OR "P.1 variant" OR "Gamma variant"
#3	Outcome	Various outcomes	Seroprevalence OR prevalence OR morbidity OR mortality OR incidence OR hospitalization OR "case fatality" OR severity OR "Risk groups" OR "Risk factors"
#4			#1 AND #2 AND #3
Filters			Years: 2019-2021; Meta-analysis OR Systematic reviews OR Reviews Language: English, French, Portuguese

S2 Table. Literature search strategy: vaccine safety and efficacy in HIV infected populations

No.	Category	Query	Search
#1	Population	HIV	PLWHA OR Immunosuppressed OR “Human Immunodeficiency Virus” OR HIV OR AIDS OR “HIV positive” OR HIV+ OR “acquired immune deficiency syndrome virus”
#2	Event	Vaccination Immunization	OR Sinovac COVID-19 vaccine OR SARS-CoV-2 vaccine OR CoronaVac OR Pfizer-BioNTech OR BNT162b2 COVID-19 vaccine OR Vaxzevria OR Oxford-AstraZeneca COVID-19 vaccine OR AZD1222 OR ChAdOx1 nCoV-19 vaccine OR mRNA-1273 Moderna vaccine OR <b>Johnson &amp; Johnson’s Janssen OR J&amp;J/Janssen COVID-19 Vaccine OR JNJ-78436735</b> OR Sputnik V COVID-19 vaccine OR COVID-19 vaccine BIBP OR Sinopharm vaccine OR Covishield vaccine OR Covaxin
#3	Outcome	Various outcomes	Safety profile OR safety signals OR safety assessments OR Adverse Events OR Severe Adverse Reaction OR AEs OR SAEs OR Pain OR Redness OR Swelling Tiredness OR Headache OR Muscle pain OR Chills OR Fever OR Nausea OR thrombosis OR thrombocytopenia OR vaccine-induced immune thrombotic thrombocytopenia OR VITT OR Myocarditis OR Pericarditis OR Guillain-Barré syndrome OR Seizure OR anaphylactic shock OR efficacy OR effectiveness OR pooled efficacy
#4			#1 AND #2 AND #3
Filters			Years: 2019-2021; Meta-analysis OR Systematic reviews OR Reviews Language: English, French, Portuguese

S3 Table. Literature search strategy: Cost effectiveness of COVID-19 vaccines

No.	Category	Query	Search
#1	Population	Africa	Africa OR African OR Algeria OR Angola OR Benin OR Botswana OR "Burkina Faso" OR Burundi OR "Cabo Verde" OR Cameroon OR Cameroun OR "Canary Islands" OR "Cape Verde" OR "Central African Republic" OR Chad OR Comoros OR Congo OR "Cote d'Ivoire" OR "Democratic Republic of Congo" OR Djibouti OR Egypt OR Eritrea OR eSwatini OR Ethiopia OR Gabon OR Gambia OR Ghana OR Guinea OR Guinea- Bissau OR "Ivory Coast" OR Jamahiriya OR Kenya OR Lesotho OR Liberia OR Libya OR Madagascar OR Malawi OR Mali OR Mauritania OR Mauritius OR Mayotte OR Morocco OR Mozambique OR Namibia OR Niger OR Nigeria OR Principe OR Reunion OR Rwanda OR "Saint Helena" OR "Sao Tome" OR Senegal OR Seychelles OR "Sierra Leone" OR Somalia OR "St Helena" OR Sudan OR Swaziland OR Tanzania OR Togo OR Tunisia OR Uganda OR "Western Sahara" OR Zaire OR Zambia OR Zimbabwe
#2	Event	Vaccination OR Immunization with COVID-19 vaccines	Sinovac COVID-19 vaccine OR SARS-CoV-2 vaccine OR CoronaVac OR Pfizer-BioNTech OR BNT162b2 COVID-19 vaccine OR Vaxzevria OR Oxford-AstraZeneca COVID-19 vaccine OR AZD1222 OR ChAdOx1 nCoV-19 vaccine OR mRNA-1273 Moderna vaccine OR <b>Johnson &amp; Johnson's Janssen OR J&amp;J/Janssen COVID-19 Vaccine OR JNJ-78436735</b> OR Sputnik V COVID-19 vaccine OR COVID-19 vaccine BIBP OR Sinopharm vaccine OR Covishield vaccine OR Covaxin
#3	Outcome	Various outcomes	Cost effectiveness OR cost utility OR cost-efficient OR cost benefits OR economic evaluation OR economics
#4			#1 AND #2 AND #3
Filters			Years: 2019-2021; Meta-analysis OR Systematic reviews OR Reviews Language: English, French, Portuguese

S4 Table. Literature search strategy: COVID-19 vaccines demand generation, risk communication, and vaccine hesitancy

No.	Category	Query	Search
#1	Population	Africa	Africa OR African OR Algeria OR Angola OR Benin OR Botswana OR "Burkina Faso" OR Burundi OR "Cabo Verde" OR Cameroon OR Cameroun OR "Canary Islands" OR "Cape Verde" OR "Central African Republic" OR Chad OR Comoros OR Congo OR "Cote d'Ivoire" OR "Democratic Republic of Congo" OR Djibouti OR Egypt OR Eritrea OR eSwatini OR Ethiopia OR Gabon OR Gambia OR Ghana OR Guinea OR Guinea- Bissau OR "Ivory Coast" OR Jamahiriya OR Kenya OR Lesotho OR Liberia OR Libya OR Madagascar OR Malawi OR Mali OR Mauritania OR Mauritius OR Mayotte OR Morocco OR Mozambique OR Namibia OR Niger OR Nigeria OR Principe OR Reunion OR Rwanda OR "Saint Helena" OR "Sao Tome" OR Senegal OR Seychelles OR "Sierra Leone" OR Somalia OR "St Helena" OR Sudan OR Swaziland OR Tanzania OR Togo OR Tunisia OR Uganda OR "Western Sahara" OR Zaire OR Zambia OR Zimbabwe
#2	Event	Vaccination OR Immunization with COVID-19 vaccines	Sinovac COVID-19 vaccine OR SARS-CoV-2 vaccine OR CoronaVac OR Pfizer-BioNTech OR BNT162b2 COVID-19 vaccine OR Vaxzevria OR Oxford-AstraZeneca COVID-19 vaccine OR AZD1222 OR ChAdOx1 nCoV-19 vaccine OR mRNA-1273 Moderna vaccine OR <b>Johnson &amp; Johnson's Janssen OR J&amp;J/Janssen COVID-19 Vaccine OR JNJ-78436735</b> OR Sputnik V COVID-19 vaccine OR COVID-19 vaccine BIBP OR Sinopharm vaccine OR Covishield vaccine OR Covaxin
#3	Outcome	Various outcomes	Demand generation OR vaccines demand OR risk communication OR vaccine hesitancy OR community engagements OR public education OR sentiment analysis OR communication strategies
#4			#1 AND #2 AND #3
Filters			Years: 2019-2021; Meta-analysis OR Systematic reviews OR Reviews Language: English, French, Portuguese

S5 Table. Data extraction form

Study Details												
Study No	Author	Year of Publication	Title of article	Journal	Country(ries) and n (number of studies included)	Regions	Type of Review	Sample Size	Total population included in the pooled analysis (min - max)	Number of included studies	Databases searched	Search Period

S5a Table . Data extraction specifics for characteristic of COVID-19 burden.

Measure of COVID-19 burden	Seroprevalence/Prevalence	Incidence	Fatality/Morbidity/Mortality/Death Rate	Infection of severe COVID-19	Hospitalisation	Recovery rate	TB co-infection	Co-morbidities	Risk Factors assessed	Risk Groups Assessed	Outcomes
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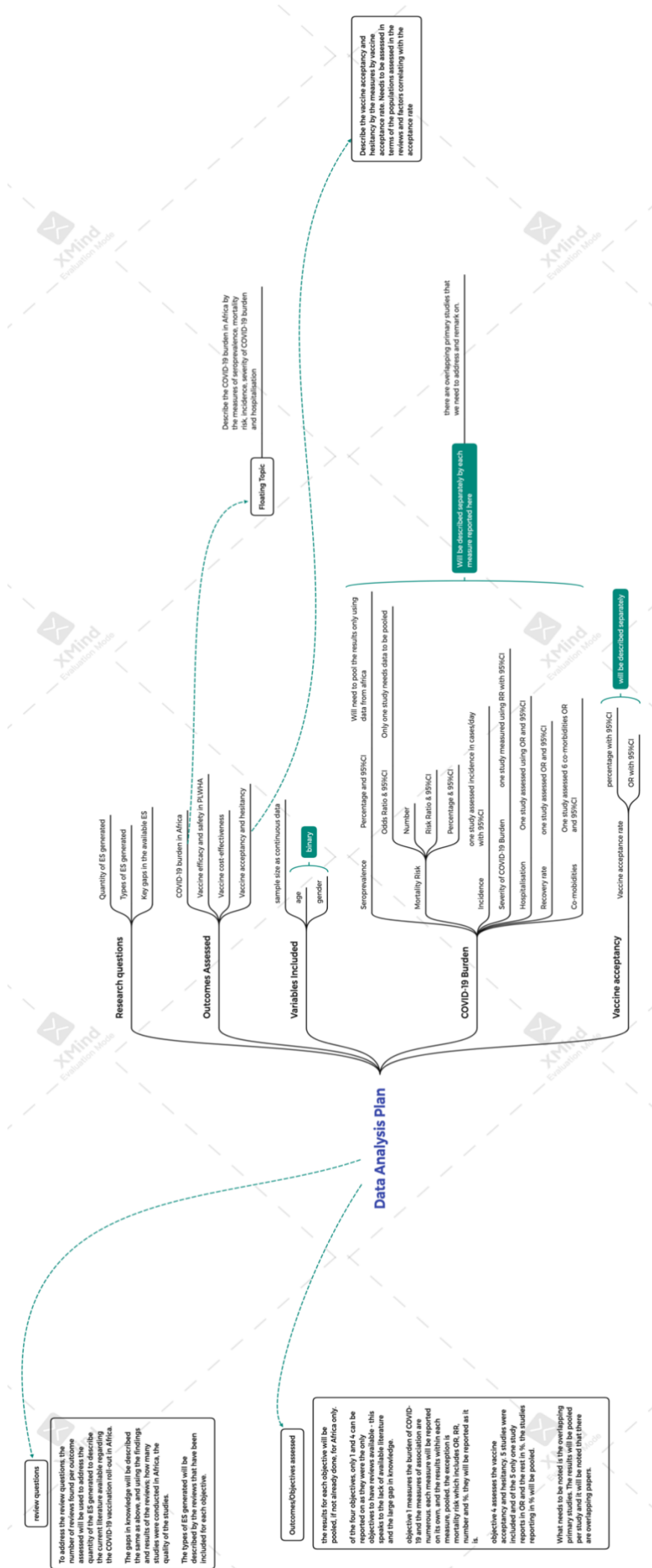
S5b Table. Data extraction specifics for the characterization of the vaccine acceptance rate

Outcome measured	Vaccine Acceptance Rate	Population Assessed	Factors correlating with vaccine acceptancy	Results	Outcomes
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For both characterizations, we also assessed:

Publication Bias assessment	Heterogeniety	Meta-analysis	Quality Assessment	Results of Quality Assessment
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Figure S1. Data analysis plan



*S6a Table.* Characteristics of included reviews characterizing the prioritizing, targeting and surveillance of COVID-19 burden including mortality and hospitalization.

<b>Authors, Year</b>	<b>Type of Review</b>	<b>Countries included</b>	<b>Population (min-max)</b>	<b>Measure of COVID-19 burden</b>	<b>Risk factors assessed</b>	<b>Risk groups assessed</b>
<b>Chisale et al., 2021</b>	Systematic Review and Meta-Analysis	South Africa, Nigeria, Libya, Egypt, Ethiopia, Kenya, DRC, Malawi, Togo, Ivory Coast, Zambia, Gabon, Congo Brazzaville, South Sudan, Cameroon, Guinea Bissau	27, 735 (99 – 4585)	Seroprevalence of antibodies against COVID-19	Age, sex, co-morbidities, level of education, smoking	HCW, general population, blood donors,
<b>Olumade &amp; Uzairue 2021</b>	Meta-Analysis	Morocco, Nigeria, Senegal, Congo, Uganda	4 499 (9 – 3467)	Mortality Rate	Clinical symptoms; fever, cough, headache, breathing problem	General population of the African countries; any persons positive for SARS-CoV-2
<b>Gesese et al., 2021</b>	Systematic Review	Congo; Ethiopia; Uganda; Nigeria	NR	Severity of COVID-19 related outcomes based on risk factors assessed	Sociodemographic, lifestyle and behavioral, climate variables and chronic comorbid characteristics	General population
<b>Galanis et al., 2021</b>	Systematic Review and Meta-Analysis	Libya, Egypt, Malawi	651 (74- 500)	Seroprevalence of antibodies against COVID-19	Age, sex, occupation	HCWs
<b>BaHamman et al., 2021</b>	Scoping review, Meta-Analysis	Djibouti, Egypt, Libya, Morocco, Somalia, Sudan, Tunisia	34578 (75- 17967)	Mortality and Recovery rate	NR	General population
<b>Tinto et al., 2021</b>	Systematic Review	Benin, Burkina Faso, Cape Verde, Côte D'Ivoire, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone, Togo	131 049 (326-41804)	Death Count	HIV, Diabetes Mellitus, high blood pressure	General population
<b>Phannajit et al., 2021</b>	Meta-Analysis	NR	125,704,789	Incidence and mortality rate	Geographic regions; economic status, such as country income and GDP; current health expenditure; and healthcare performance	General population
<b>Bobrovitz et al., 2021</b>	Systematic Review and Meta-Analysis	Congo, Nigeria, Ethiopia, Kenya, South Africa, Libya	14,652 (99-9922)	Seroprevalence of antibodies against COVID-19	Race and ethnicity, sex, age, HCW status	COVID-19 cases

<b>Hariyanto et al., 2021</b>	Systematic Review and Meta-Analysis	South Africa, Kenya	65 085 (113 – 41877)	Mortality risk	COVID-19/HIV co-infection	PLWHA
<b>He et al., 2021</b>	Systematic Review and Meta-Analysis	Egypt, Nigeria, Congo	144 (28-83)	Seroprevalence of antibodies against COVID-19	COVID-19 infection	Nurses
<b>Mapahla et al., 2021</b>	Systematic Review and Meta-Analysis	South Africa	22 421 (113-22308)	Mortality rate, Hospitalization (including the need for intensive care services)	COVID-19 infection	PLWH
<b>Raya et al., 2021</b>	Systematic Review and Meta-Analysis	South Africa, Nigeria, Kenya, Uganda, Ethiopia, Congo	25 212 (54 – 22308)	Prevalence of HIV/SARS-CoV-2 co-infection	COVID-19 infection clinical outcome	PLWHA

*S6b Table.* Characterization of COVID-19 vaccine acceptance rate in Africa.

<b>Authors, Year</b>	<b>Type of Review</b>	<b>Countries included</b>	<b>Population (min-max)</b>	<b>Measure of vaccine demand, hesitancy</b>	<b>Risk factors assessed</b>	<b>Risk groups assessed</b>
<b>Sallam et al., 2021</b>	Systematic Review	South Africa, Nigeria, DRC	1902 (613-670)	Vaccine acceptance rate	Age	HCWs; general population; age
<b>Mahmud et al., 2021</b>	Systematic Review and Meta-Analysis	Egypt; Nigeria; Congo; Cameroon	11 235 (613-4131)	Vaccine acceptance rate	NR	HCWs; general population
<b>Wake et al., 2021</b>	Systematic Review	Congo; Ethiopia; Uganda; Nigeria	2851 (409-1228)	Level of willingness to receive vaccine		HCWs; age;
<b>Arce et al., 2021</b>	Review of surveys	Burkina Faso; Mozambique; Nigeria; Sierra Leone; Uganda	8525 (976-2109)	Acceptance levels and factors associated with acceptance		General population sampled for the survey
<b>Shamshirsaz et al., 2021</b>	Systematic Review and Meta-Analysis	South Africa	346	Intention to vaccine		Pregnant women

S7 Table. Table of primary studies being repeated between reviews.

<b>Author (primary study)</b>	<b>Number of times being repeated</b>	<b>Country</b>	<b>Outcome of interest</b>
<b>Abdelghffar et al., 2020</b>	2	Libya	Seroprevalence of antibodies against SARS-CoV-2
<b>Batchi-Bouyou et al.,</b>	2	Congo	Seroprevalence of antibodies against SARS-CoV-2
<b>Boulle et al., 2021</b>	2	South Africa	Mortality rate; Hospitalization; prevalence of HIV/SARS-CoV-2
<b>Chibwana 2020</b>	2	Malawi	Seroprevalence of antibodies against SARS-CoV-2
<b>Kagucia et al., 2021</b>	2	Kenya	Seroprevalence of antibodies against SARS-CoV-2; mortality rate
<b>Kaseem et al., 2020</b>	3	Egypt	Seroprevalence of antibodies against SARS-CoV-2
<b>Kempen et al.,</b>		Ethiopia	Seroprevalence of antibodies against SARS-CoV-2; mortality rate
<b>Kirenga et al. 2020</b>	2	Uganda	Mortality rate; prevalence of HIV/SARS-CoV-2 infection
<b>Majiya et al. (2021)</b>	2	Nigeria (incl. Niger)	Seroprevalence of antibodies against SARS-CoV-2
<b>Mostafa</b>	2	Egypt	Seroprevalence of antibodies against SARS-CoV-2; Vaccine acceptance rate
<b>Mukwege et al., 2020</b>	2	DRC	Seroprevalence of antibodies against SARS-CoV-2
<b>Nachega et al., 2020</b>	2	Congo	Mortality rate; prevalence of HIV/SARS-CoV-2 co-infection
<b>Nzaji et al. 2020</b>	3	DRC	Vaccine acceptance rate
<b>Olayanju et al., 2020</b>	2	Nigeria	Seroprevalence of antibodies against SARS-CoV-2
<b>Parker et al., 2021</b>	3	South Africa	Mortality rate; Hospitalization; prevalence of HIV/SARS-CoV-2

## APPENDIX B. *PRISMA checklist*



### PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
<b>TITLE</b>			
Title	1	Identify the report as a systematic review.	Cover page
<b>ABSTRACT</b>			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	1
<b>INTRODUCTION</b>			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	4
<b>METHODS</b>			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	5
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	5
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	6
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	6
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	6
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	N/A
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	15
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	14
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	14
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	N/A
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	N/A
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A



## PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
<b>RESULTS</b>			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	6
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	6
Study characteristics	17	Cite each included study and present its characteristics.	11,13,14,16,18,19
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	N/A
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	12,15,17,20
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	20,21
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	20,21
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A
<b>DISCUSSION</b>			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	23
	23b	Discuss any limitations of the evidence included in the review.	24
	23c	Discuss any limitations of the review processes used.	24
	23d	Discuss implications of the results for practice, policy, and future research.	25
<b>OTHER INFORMATION</b>			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	1
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	1
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	N/A
Competing interests	26	Declare any competing interests of review authors.	N/A
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	N/A

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71

## APPENDIX C. Article type guidelines – Vaccine

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Submission Checklist

Please:

1. read the Aims & Scope to gain an overview and assess if your manuscript is suitable for this journal;
2. use the Microsoft Word template or LaTeX template or Free Format Submission to prepare your manuscript;
3. make sure that issues about publication ethics, research ethics, copyright, authorship, figure formats, data and references format have been appropriately considered;
4. Ensure that all authors have approved the content of the submitted manuscript.
5. Authors are encouraged to add a biography (optional) to the submission and publish it.

Manuscript Submission Overview

Types of Publications

Vaccines has no restrictions on the length of manuscripts, provided that the text is concise and comprehensive. Full experimental details must be provided so that the results can be reproduced. Vaccines requires that authors publish all experimental controls and make full datasets available where possible (see the guidelines on Supplementary Materials and references to unpublished data).

Manuscripts submitted to Vaccines should neither be published previously nor be under consideration for publication in another journal. The main article types are as follows:

Articles: Original research manuscripts. The journal considers all original research manuscripts provided that the work reports scientifically sound experiments and provides a substantial amount of new information. Authors should not unnecessarily divide their work into several related manuscripts, although short Communications of preliminary, but significant, results will be considered. The quality and impact of the study will be considered during peer review.

Reviews: These provide concise and precise updates on the latest progress made in a given area of research. Systematic reviews should follow the PRISMA guidelines.

Case reports: Case reports present detailed information on the symptoms, signs, diagnosis, treatment (including all types of interventions), and outcomes of an individual patient. Case

reports usually describe new or uncommon conditions that serve to enhance medical care or highlight diagnostic approaches.

### Submission Process

Manuscripts for Vaccines should be submitted online at [susy.mdpi.com](https://susy.mdpi.com). The submitting author, who is generally the corresponding author, is responsible for the manuscript during the submission and peer-review process. The submitting author must ensure that all eligible co-authors have been included in the author list (read the criteria to qualify for authorship) and that they have all read and approved the submitted version of the manuscript. To submit your manuscript, register and log in to the submission website. Once you have registered, click here to go to the submission form for Vaccines. All co-authors can see the manuscript details in the submission system, if they register and log in using the e-mail address provided during manuscript submission.

### Accepted File Formats

Authors must use the Microsoft Word template or LaTeX template to prepare their manuscript. Using the template file will substantially shorten the time to complete copy-editing and publication of accepted manuscripts. The total amount of data for all files must not exceed 120 MB. If this is a problem, please contact the Editorial Office [vaccines@mdpi.com](mailto:vaccines@mdpi.com). Accepted file formats are:

**Microsoft Word:** Manuscripts prepared in Microsoft Word must be converted into a single file before submission. When preparing manuscripts in Microsoft Word, the Vaccines Microsoft Word template file must be used. Please insert your graphics (schemes, figures, etc.) in the main text after the paragraph of its first citation.

**LaTeX:** Manuscripts prepared in LaTeX must be collated into one ZIP folder (including all source files and images, so that the Editorial Office can recompile the submitted PDF). When preparing manuscripts in LaTeX, please use the Vaccines LaTeX template files. You can now also use the online application [writeLaTeX](https://www.latexstudio.net/) to submit articles directly to Vaccines. The MDPI LaTeX template file should be selected from the [writeLaTeX](https://www.latexstudio.net/) template gallery.

**Supplementary files:** May be any format, but it is recommended that you use common, non-proprietary formats where possible (see below for further details).

**Disclaimer:** Usage of these templates is exclusively intended for submission to the journal for peer-review, and strictly limited to this purpose and it cannot be used for posting online on preprint servers or other websites.

### Free Format Submission

Vaccines now accepts free format submission:

We do not have strict formatting requirements, but all manuscripts must contain the required sections: Author Information, Abstract, Keywords, Introduction, Materials & Methods, Results, Conclusions, Figures and Tables with Captions, Funding Information, Author Contributions, Conflict of Interest and other Ethics Statements. Check the Journal Instructions for Authors for more details.

Your references may be in any style, provided that you use the consistent formatting throughout. It is essential to include author(s) name(s), journal or book title, article or chapter title (where required), year of publication, volume and issue (where appropriate) and

pagination. DOI numbers (Digital Object Identifier) are not mandatory but highly encouraged. The bibliography software package EndNote, Zotero, Mendeley, Reference Manager are recommended.

When your manuscript reaches the revision stage, you will be requested to format the manuscript according to the journal guidelines.

### Cover Letter

A cover letter must be included with each manuscript submission. It should be concise and explain why the content of the paper is significant, placing the findings in the context of existing work. It should explain why the manuscript fits the scope of the journal.

Any prior submissions of the manuscript to MDPI journals must be acknowledged. If this is the case, it is strongly recommended that the previous manuscript ID is provided in the submission system, which will ease your current submission process. The names of proposed and excluded reviewers should be provided in the submission system, not in the cover letter. All cover letters are required to include the statements:

We confirm that neither the manuscript nor any parts of its content are currently under consideration or published in another journal. All authors have approved the manuscript and agree with its submission to (journal name).

### Author Biography

Authors are encouraged to add a biography (maximum 150 words) to the submission and publish it. This should be a single paragraph and should contain the following points:

1. Authors' full names followed by current positions;
2. Education background including institution information and year of graduation (type and level of degree received);
3. Work experience;
4. Current and previous research interests;
5. Memberships of professional societies and awards received.

### Note for Authors Funded by the National Institutes of Health (NIH)

This journal automatically deposits papers to PubMed Central after publication of an issue. Authors do not need to separately submit their papers through the NIH Manuscript Submission System (NIHMS, <http://nihms.nih.gov/>).

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### Manuscript Preparation

#### General Considerations

Research manuscripts should comprise:

Front matter: Title, Author list, Affiliations, Abstract, Keywords

Research manuscript sections: Introduction, Materials and Methods, Results, Discussion, Conclusions (optional).

Back matter: Supplementary Materials, Acknowledgments, Author Contributions, Conflicts of Interest, References.

Review manuscripts should comprise the front matter, literature review sections and the back matter. The template file can also be used to prepare the front and back matter of your review

manuscript. It is not necessary to follow the remaining structure. Structured reviews and meta-analyses should use the same structure as research articles and ensure they conform to the PRISMA guidelines.

Research Data and supplementary materials: Note that publication of your manuscript implies that you must make all materials, data, and protocols associated with the publication available to readers. Disclose at the submission stage any restrictions on the availability of materials or information. Read the information about Supplementary Materials and Data Deposit for additional guidelines.

Preregistration: Where authors have preregistered studies or analysis plans, links to the preregistration must be provided in the manuscript.

Guidelines and standards: MDPI follows standards and guidelines for certain types of research. See [https://www.mdpi.com/editorial\\_process](https://www.mdpi.com/editorial_process) for further information.

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## Front Matter

These sections should appear in all manuscript types

**Title:** The title of your manuscript should be concise, specific and relevant. It should identify if the study reports (human or animal) trial data, or is a systematic review, meta-analysis or replication study. When gene or protein names are included, the abbreviated name rather than full name should be used. Please do not include abbreviated or short forms of the title, such as a running title or head. These will be removed by our Editorial Office.

**Author List and Affiliations:** Authors' full first and last names must be provided. The initials of any middle names can be added. The

PubMed/MEDLINE standard format is used for affiliations: complete address information including city, zip code, state/province, and country. At least one author should be designated as corresponding author, and his or her email address and other details should be included at the end of the affiliation section. Please read the criteria to qualify for authorship.

**Abstract:** The abstract should be a total of about 200 words maximum. The abstract should be a single paragraph and should follow the style of structured abstracts, but without headings: 1) **Background:** Place the question addressed in a broad context and highlight the purpose of the study; 2) **Methods:** Describe briefly the main methods or treatments applied. Include any relevant preregistration numbers, and species and strains of any animals used. 3) **Results:** Summarize the article's main findings; and 4) **Conclusion:** Indicate the main conclusions or interpretations. The abstract should be an objective representation of the article: it must not contain results which are not presented and substantiated in the main text and should not exaggerate the main conclusions.

**Keywords:** Three to ten pertinent keywords need to be added after the abstract. We recommend that the keywords are specific to the article, yet reasonably common within the subject discipline.

## Research Manuscript Sections

**Introduction:** The introduction should briefly place the study in a broad context and highlight why it is important. It should define the purpose of the work and its significance, including specific hypotheses being tested. The current state of the research field should be reviewed carefully and key publications cited. Please highlight controversial and diverging hypotheses when necessary. Finally, briefly mention the main aim of the work and highlight the main conclusions. Keep the introduction comprehensible to scientists working outside the topic of

the paper.

**Materials and Methods:** They should be described with sufficient detail to allow others to replicate and build on published results. New methods and protocols should be described in detail while well-established methods can be briefly described and appropriately cited. Give the name and version of any software used and make clear whether computer code used is available. Include any pre-registration codes.

**Results:** Provide a concise and precise description of the experimental results, their interpretation as well as the experimental conclusions that can be drawn.

**Discussion:** Authors should discuss the results and how they can be interpreted in perspective of previous studies and of the working hypotheses. The findings and their implications should be discussed in the broadest context possible and limitations of the work highlighted. Future research directions may also be mentioned. This section may be combined with Results.

**Conclusions:** This section is not mandatory but can be added to the manuscript if the discussion is unusually long or complex.

**Patents:** This section is not mandatory but may be added if there are patents resulting from the work reported in this manuscript.

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#### Back Matter

**Supplementary Materials:** Describe any supplementary material published online alongside the manuscript (figure, tables, video, spreadsheets, etc.). Please indicate the name and title of each element as follows Figure S1: title, Table S1: title, etc.

**Acknowledgments:** In this section you can acknowledge any support given which is not covered by the author contribution or funding sections. This may include administrative and technical support, or donations in kind (e.g., materials used for experiments).

**Author Contributions:** Each author is expected to have made substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data; or the creation of new software used in the work; or have drafted the work or substantively revised it; AND has approved the submitted version (and version substantially edited by journal staff that involves the author's contribution to the study); AND agrees to be personally accountable for the author's own contributions and for ensuring that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and documented in the literature.

For research articles with several authors, a short paragraph specifying their individual contributions must be provided. The following statements should be used "Conceptualization, X.X. and Y.Y.; Methodology, X.X.; Software, X.X.; Validation, X.X., Y.Y. and Z.Z.; Formal Analysis, X.X.; Investigation, X.X.; Resources, X.X.; Data Curation, X.X.; Writing – Original Draft Preparation, X.X.; Writing – Review & Editing, X.X.; Visualization, X.X.; Supervision, X.X.; Project Administration, X.X.; Funding Acquisition, Y.Y.", please turn to the CRediT taxonomy for the term explanation. For more background on CRediT, see here. "Authorship must include and be limited to those who have contributed substantially to the work. Please read the section concerning the criteria to qualify for authorship carefully".

**References:** References must be numbered in order of appearance in the text (including table captions and figure legends) and listed individually at the end of the manuscript. We recommend preparing the references with a bibliography software package, such as EndNote, ReferenceManager or Zotero to avoid typing mistakes and duplicated references. We encourage citations to data, computer code and other citable research material. If available online, you may use reference style 9. below.

Citations and References in Supplementary files are permitted provided that they also appear in the main text and in the reference list.

In the text, reference numbers should be placed in square brackets [ ], and placed before the punctuation; for example [1], [1–3] or [1,3]. For embedded citations in the text with pagination, use both parentheses and brackets to indicate the reference number and page numbers; for example [5] (p. 10). or [6] (pp. 101–105).

The reference list should include the full title, as recommended by the ACS style guide. Style files for Endnote and Zotero are available. References should be described as follows, depending on the type of work:

Journal Articles:

1. Author 1, A.B.; Author 2, C.D. Title of the article. Abbreviated Journal Name Year, Volume, page range. Books and Book Chapters:

2. Author 1, A.; Author 2, B. Book Title, 3rd ed.; Publisher: Publisher Location, Country, Year; pp. 154–196.

3. Author 1, A.; Author 2, B. Title of the chapter. In Book Title, 2nd ed.; Editor 1, A., Editor 2, B., Eds.; Publisher: Publisher Location, Country, Year; Volume 3, pp. 154–196.

Unpublished materials intended for publication:

4. Author 1, A.B.; Author 2, C. Title of Unpublished Work (optional). Correspondence Affiliation, City, State, Country. year, status (manuscript in preparation; to be submitted).

5. Author 1, A.B.; Author 2, C. Title of Unpublished Work. Abbreviated Journal Name year, phrase indicating stage of publication (submitted; accepted; in press).

Unpublished materials not intended for publication:

6. Author 1, A.B. (Affiliation, City, State, Country); Author 2, C. (Affiliation, City, State, Country). Phase describing the material, year. (phase: Personal communication; Private communication; Unpublished work; etc.)

Conference Proceedings:

7. Author 1, A.B.; Author 2, C.D.; Author 3, E.F. Title of Presentation. In Title of the Collected Work (if available), Proceedings of the Name of the Conference, Location of Conference, Country, Date of Conference; Editor 1, Editor 2, Eds. (if available); Publisher: City, Country, Year (if available); Abstract Number (optional), Pagination (optional).

Thesis:

8. Author 1, A.B. Title of Thesis. Level of Thesis, Degree-Granting University, Location of University, Date of Completion. Websites:

9. Title of Site. Available online: URL (accessed on Day Month Year).

Unlike published works, websites may change over time or disappear, so we encourage you create an archive of the cited website using a service such as WebCite. Archived websites should be cited using the link provided as follows:

10. Title of Site. URL (archived on Day Month Year).

See the Reference List and Citations Guide for more detailed information.

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## Preparing Figures, Schemes and Tables

File for Figures and Schemes must be provided during submission in a single zip archive and at a sufficiently high resolution (minimum 1000 pixels width/height, or a resolution of 300 dpi or higher). Common formats are accepted, however, TIFF, JPEG, EPS and PDF are preferred. Vaccines can publish multimedia files in articles or as supplementary materials. Please contact the editorial office for further information.

All Figures, Schemes and Tables should be inserted into the main text close to their first citation and must be numbered following their number of appearance (Figure 1, Scheme I, Figure 2, Scheme II, Table 1, etc.).

All Figures, Schemes and Tables should have a short explanatory title and caption.

All table columns should have an explanatory heading. To facilitate the copy-editing of larger tables, smaller fonts may be used, but no less than 8 pt. in size. Authors should use the Table option of Microsoft Word to create tables.

Authors are encouraged to prepare figures and schemes in color (RGB at 8-bit per channel). There is no additional cost for publishing full color graphics.

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## Publication Ethics Statement

Vaccines is a member of the Committee on Publication Ethics (COPE). We fully adhere to its Code of Conduct and to its Best Practice Guidelines.

The editors of this journal enforce a rigorous peer-review process together with strict ethical policies and standards to ensure to add high quality scientific works to the field of scholarly publication. Unfortunately, cases of plagiarism, data falsification, image manipulation, inappropriate authorship credit, and the like, do arise. The editors of Vaccines take such publishing ethics issues very seriously and are trained to proceed in such cases with a zero tolerance policy.

Authors wishing to publish their papers in Vaccines must abide to the following:

Any facts that might be perceived as a possible conflict of interest of the author(s) must be disclosed in the paper prior to submission. Authors should accurately present their research findings and include an objective discussion of the significance of their findings.

Data and methods used in the research need to be presented in sufficient detail in the paper, so that other researchers can replicate the work.

Raw data should preferably be publicly deposited by the authors before submission of their manuscript. Authors need to at least have the raw data readily available for presentation to the referees and the editors of the journal, if requested. Authors need to ensure appropriate measures are taken so that raw data is retained in full for a reasonable time after publication. Simultaneous submission of manuscripts to more than one journal is not tolerated.

The journal accepts exact translations of previously published work. All submissions of translations must conform with our policies on translations.

If errors and inaccuracies are found by the authors after publication of their paper, they need to be promptly communicated to the editors of this journal so that appropriate actions can be taken. Please refer to our policy regarding Updating Published Papers.

Your manuscript should not contain any information that has already been published. If you include already published figures or images, please obtain the necessary permission from the copyright holder to publish under the CC-BY license. For further information, see the Rights and

Permissions page.

Plagiarism, data fabrication and image manipulation are not tolerated.

Plagiarism is not acceptable in Vaccines submissions.

Plagiarism includes copying text, ideas, images, or data from another source, even from your own publications, without giving any credit to the original source.

Reuse of text that is copied from another source must be between quotes and the original source must be cited. If a study's design or the manuscript's structure or language has been inspired by previous works, these works must be explicitly cited.

All MDPI submissions are checked for plagiarism using the industry standard software iThenticate. If plagiarism is detected during the peer review process, the manuscript may be rejected. If plagiarism is detected after publication, an investigation will take place and action taken in accordance with our policies.

Image files must not be manipulated or adjusted in any way that could lead to misinterpretation of the information provided by the original image.

Irregular manipulation includes: 1) introduction, enhancement, moving, or removing features from the original image; 2) grouping of images that should obviously be presented separately (e.g., from different parts of the same gel, or from different gels); or 3) modifying the contrast, brightness or color balance to obscure, eliminate or enhance some information.

If irregular image manipulation is identified and confirmed during the peer review process, we may reject the manuscript. If irregular image manipulation is identified and confirmed after publication, we may correct or retract the paper.

Our in-house editors will investigate any allegations of publication misconduct and may contact the authors' institutions or funders if necessary. If evidence of misconduct is found, appropriate action will be taken to correct or retract the publication. Authors are expected to comply with the best ethical publication practices when publishing with MDPI.

### Citation Policy

Authors should ensure that where material is taken from other sources (including their own published writing) the source is clearly cited and that where appropriate permission is obtained. Authors should not engage in excessive self-citation of their own work.

Authors should not copy references from other publications if they have not read the cited work.

Authors should not preferentially cite their own or their friends', peers', or institution's publications. Authors should not cite advertisements or advertorial material.

In accordance with COPE guidelines, we expect that "original wording taken directly from publications by other researchers should appear in quotation marks with the appropriate citations." This condition also applies to an author's own work. COPE have produced a discussion document on citation manipulation with recommendations for best practice.

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### Reviewer Suggestions

During the submission process, please suggest three potential reviewers with the appropriate expertise to review the manuscript. The editors will not necessarily approach these referees. Please provide detailed contact information (address, homepage, phone, e-mail address). The proposed referees should neither be current collaborators of the co-authors nor have published with any of the co-authors of the manuscript within the last five years. Proposed reviewers should be from different institutions to the authors. You may identify appropriate Editorial Board members of the journal as potential reviewers. You may suggest reviewers from among the authors that you frequently cite in your paper.

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### English Corrections

To facilitate proper peer-reviewing of your manuscript, it is essential that it is submitted in grammatically correct English. Advice on some specific language points can be found here.

If you are not a native English speaker, we recommend that you have your manuscript professionally edited before submission or read by a native English-speaking colleague. This can be carried out by MDPI's English editing service. Professional editing will enable reviewers and future readers to more easily read and assess the content of submitted manuscripts. All

accepted manuscripts undergo language editing, however an additional fee will be charged to authors if very extensive English corrections must be made by the Editorial Office: pricing is according to the service here.

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### Authorship

MDPI follows the International Committee of Medical Journal Editors (ICMJE) guidelines which state that, in order to qualify for authorship of a manuscript, the following criteria should be observed:

Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND Drafting the work or revising it critically for important intellectual content; AND

Final approval of the version to be published; AND

Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Those who contributed to the work but do not qualify for authorship should be listed in the acknowledgments. More detailed guidance on authorship is given by the International Council of Medical Journal Editors (ICMJE).

Any change to the author list should be approved by all authors including any who have been removed from the list. The corresponding author should act as a point of contact between the editor and the other authors and should keep co-authors informed and involve them in major decisions about the publication. We reserve the right to request confirmation that all authors meet the authorship conditions.

For more details about authorship please check MDPI ethics website.

### Reviewers Recommendation

Authors can recommend potential reviewers. Journal editors will check to make sure there are no conflicts of interest before contacting those reviewers, and will not consider those with competing interests. Reviewers are asked to declare any conflicts of interest. Authors can also enter the names of potential peer reviewers they wish to exclude from consideration in the peer review of their manuscript, during the initial submission progress. The editorial team will respect these requests so long as this does not interfere with the objective and thorough assessment of the submission.

### Editorial Independence

#### Lack of Interference With Editorial Decisions

Editorial independence is of utmost importance and MDPI does not interfere with editorial decisions. All articles published by MDPI are peer reviewed and assessed by our independent editorial boards, and MDPI staff are not involved in decisions to accept manuscripts. When making an editorial decision, we expect the academic editor to make their decision based only upon:

The suitability of selected reviewers;

Adequacy of reviewer comments and author response; Overall scientific quality of the paper.

In all of our journals, in every aspect of operation, MDPI policies are informed by the mission

to make science and research findings open and accessible as widely and rapidly as possible.

## Editors and Editorial Staff as Authors

Editorial staff or editors shall not be involved in processing their own academic work. Submissions authored by editorial staff/editors will be assigned to at least two independent outside reviewers. Decisions will be made by other Editorial Board Members who do not have a conflict of interest with the author. Journal staff are not involved in the processing of their own work submitted to any MDPI journals.

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## Editorial Procedures and Peer-Review

### Initial Checks

All submitted manuscripts received by the Editorial Office will be checked by a professional in-house Managing Editor to determine whether they are properly prepared and whether they follow the ethical policies of the journal, including those for human and animal experimentation.

Manuscripts that do not fit the journal's ethics policy or do not meet the standards of the journal will be rejected before peer-review. Manuscripts

that are not properly prepared will be returned to the authors for revision and resubmission.

After these checks, the Managing Editor will consult the journals' Editor-in-Chief or Associate Editors to determine whether the manuscript fits the scope of the journal and whether it is scientifically sound. No judgment on the potential impact of the work will be made at this stage. Reject decisions at this stage will be verified by the Editor-in- Chief.

### Peer-Review

Once a manuscript passes the initial checks, it will be assigned to at least two independent experts for peer-review. A single-blind review is applied, where authors' identities are known to reviewers. Peer review comments are confidential and will only be disclosed with the express agreement of the reviewer.

In the case of regular submissions, in-house assistant editors will invite experts, including recommendations by an academic editor. These experts may also include Editorial Board Members and Guest Editors of the journal. Potential reviewers suggested by the authors may also be considered. Reviewers should not have published with any of the co-authors during the past five years and should not currently work or collaborate with any of the institutions of the co-authors of the submitted manuscript.

### Optional Open Peer-Review

The journal operates optional open peer-review: Authors are given the option for all review reports and editorial decisions to be published alongside their manuscript. In addition, reviewers can sign their review, i.e., identify themselves in the published review reports. Authors can alter their choice for open review at any time before publication, but once the paper has been published changes will only be made at the discretion of the Publisher and Editor-in-Chief. We encourage authors to take advantage of this opportunity as proof of the rigorous process employed in publishing their research. To guarantee impartial refereeing, the names of referees will be revealed only if the referees agree to do so, and after a paper has been accepted for publication.

## Editorial Decision and Revision

All the articles, reviews and communications published in MDPI journals go through the peer-review process and receive at least two reviews. The in-house editor will communicate the decision of the academic editor, which will be one of the following:

### Accept after Minor Revisions:

The paper is in principle accepted after revision based on the reviewer's comments. Authors are given five days for minor revisions.

### Reconsider after Major Revisions:

The acceptance of the manuscript would depend on the revisions. The author needs to provide a point by point response or provide a rebuttal if some of the reviewer's comments cannot be revised. Usually, only one round of major revisions is allowed. Authors will be asked to resubmit the revised paper within a suitable time frame, and the revised version will be returned to the reviewer for further comments.

### Reject and Encourage Resubmission:

If additional experiments are needed to support the conclusions, the manuscript will be rejected and the authors will be encouraged to re-submit the paper once further experiments have been conducted.

### Reject:

The article has serious flaws, and/or makes no original significant contribution. No offer of resubmission to the journal is provided.

All reviewer comments should be responded to in a point-by-point fashion. Where the authors disagree with a reviewer, they must provide a clear response.

## Author Appeals

Authors may appeal a rejection by sending an e-mail to the Editorial Office of the journal. The appeal must provide a detailed justification, including point-by-point responses to the reviewers' and/or Editor's comments. The Managing Editor of the journal will forward the manuscript and related information (including the identities of the referees) to the Editor-in-Chief, Associate Editor, or Editorial Board member. The academic Editor being consulted will be asked to give an advisory recommendation on the manuscript and may recommend acceptance, further peer-review, or uphold the original rejection decision. A reject decision at this stage is final and cannot be reversed.

In the case of a special issue, the Managing Editor of the journal will forward the manuscript and related information (including the identities of the referees) to the Editor-in-Chief who will be asked to give an advisory recommendation on the manuscript and may recommend acceptance, further peer-review, or uphold the original rejection decision. A reject decision at this stage will be final and cannot be reversed.

## Production and Publication

Once accepted, the manuscript will undergo professional copy-editing, English editing, proofreading by the authors, final corrections, pagination, and, publication on the [www.mdpi.com](http://www.mdpi.com) website.