Development of a “State of Practice” Dataset 2: Randomized Clinical Trials in Low-Resource Settings for select Global Health Diseases, 2019-2024

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1. Background

The State of Practice Dataset 2 (SOPD2) identifies randomized pharmacological intervention trials conducted in Africa and South Asia across disease areas falling under the categories of communicable, maternal, neonatal, and nutrition (CMNN) (excluding COVID-19). This dataset provides a recent evidence map that is representative of such trials and will be utilized to answer questions about trial characteristics, including methodological attributes.

Despite a trend from 1990-2019 of improving health globally, the greatest proportion of disease burden among the world's poorest billion is still communicable, maternal, neonatal, and nutrition (CMNN) diseases (65%)(1). Compared with the disease burden in high-income countries, CMNN diseases also account for the largest disparities, with age-standardized DALY rates for CMNN conditions 2,147% higher in the poorest billion. For SOPD2, CMNN disease areas were defined by the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) conducted by the Institute for Health Metrics (IHME)(2). The GBD is global in scope and provides a comprehensive list of CMNN diseases organized into a levelled hierarchy.

To find relevant treatment trials, a systematic literature search was conducted to identify trial publications that were in scope. While limited, the trial publication is likely the most accurate record of the methods used, regardless of what is recorded in the protocol. Systematic literature searches explicitly describe the methodology that will be used to undertake the search which should include clearly stated objectives, eligibility criteria for evidence, and a documented search strategy(3). The key advantages of this systematic approach are that the search results are transparent and reproducible, reducing the potential for bias. The explicit methodology increases the potential utility of the search results and contextualizes the dataset to enable appropriate use. Systematic literature searches are also easily updated over time as new evidence becomes available, reducing duplication of effort.

The first State of Practice Dataset (SOPD1), assembled in 2022, identified randomized pharmacological intervention trials conducted in sub-Saharan Africa across CMNN disease areas, and published between 2018 and October 2022. SOPD2 is an update of SOPD1 to identify trials that have been published more recently, expand the search to include an additional database, and to broaden the geographical scope. A comparison of the scope between SOPD1 and SOPD2 has been summarized in Appendix 9.1.

2. Objectives

To identify relevant recent randomized treatment trials in IHME CMNN disease areas conducted in Africa and South Asia.

To develop a dataset of primary publications from randomized controlled trials (RCTs) conducted in Africa and South Asia across CMNN disease areas (excluding COVID-19) that provides a recent record of study designs and methods used in these trials. This will provide an overview of the evidence landscape in these areas, facilitate exploratory analyses, and provide important context for decision making.

3. Methods

3.1. Criteria for considering studies for this dataset

Eligibility criteria are summarized below in table format. Further elaboration and explanation can be found in the subsections below the table.

Study and source eligibility	
Study design	☒ RCTs ☒ Cluster- RCTs
'PICOC' eligibility	
Population	All ages will be included with no restrictions on study eligibility based on population.
Intervention(s)	All pharmacological interventions aiming to treat the disease states (or symptoms) that are within scope will be included. Studies comparing different formulations, doses, schedules, of the same intervention (e.g., vaccines) will be included.
Comparator(s)	All comparators will be eligible for inclusion.
Outcome(s)	All efficacy and safety outcomes are eligible for inclusion. Studies with the main purpose of assessing adherence and acceptability outcomes will be excluded.
Context	Studies with at least one study site in African or South Asian countries according to the World Bank as of May 1, 2024.

3.1.1. Inclusion criteria

Inclusion criteria for studies and their publications are further outlined in the following sections.

3.1.1.1. Randomized assignment to intervention arms

Assignment to intervention arms was randomized or cluster-randomized and the study was conducted in humans.

3.1.1.2. Conducted in Africa or South Asia

Studies with at least one study site in a country in Africa or South Asia were included, even if other study sites were not in Africa or South Asia. The countries within Africa and South Asia were defined according to the World Bank(4). This approach was adopted as the most straightforward way to include trials dedicated to assessing interventions toward the environments of interest.

3.1.1.3. CMNN disease area

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The study was conducted in one of the disease areas defined as CMNN (excluding COVID-19) by the IHME in their Global Burden of Diseases, Injuries and Risk Factors Study (GBD) published in 2021(2).

3.1.1.4. Pharmacological interventions

The study tested the efficacy or safety of a pharmacological intervention aiming to treat or prevent the disease states (or symptoms) in scope as defined above. As nutrition diseases were in scope, food was also included where used as a dietary supplement. To be included, interventions needed to be applied directly to the participant whose health outcomes were measured. Interventions falling into the following categories were included:

- Chemicals & Drugs
- Vaccines
- Antibiotics
- Molecules, including oxygen (for oxygen rationale, see Section 3.1.1.4.1.)
- Inorganic Chemicals (e.g., Ferric Compounds / Iron)
- Dietary Supplements, usually chemicals or molecules
- Food, when used as a Dietary Supplement
- Implantable device that includes medicine (i.e., pharmacological mechanism of action)
- Plasma (see Section 3.1.1.4.2.)

3.1.1.4.1. Oxygen and other medical gases

Oxygen and other medical gas interventions were included as medical gases are classed as drugs by The Food and Drug Administration (FDA). Oxygen has an established range of effective doses and known adverse effects at high doses(5). Supplemental oxygen is also a very common intervention in neonatal care(6), so it is particularly relevant to the disease scope for this dataset. Furthermore, oxygen appears in the WHO Model List of Essential Medicines 2021(7).

3.1.1.4.2. Blood and blood products

Interventions that were providing blood or blood products to participants were included. Blood components are regulated by the FDA as licensed biologics and as drugs. Blood and blood products also appear in the WHO Model List of Essential Medicines 2021(7).

3.1.1.5. Published after 2018

Publications published between 1/1/2019 and the search date (June 21, 2024) were included. The intention was for the dataset to include at least five years of data.

3.1.2. Exclusion criteria

3.1.2.1. Non-randomized study designs

All non-randomized study designs were excluded, including observational studies, cohort studies, cross-sectional studies, modeling studies, and economic analyses.

3.1.2.2. Pilot studies

Pilot studies were excluded as they are not designed to assess efficacy and safety. They typically assess implementation and feasibility with a view to running a larger trial to properly assess efficacy and safety. A small number of publications used the term 'pilot study' but were not what the reviewers consider 'true' pilot studies. They were designed to assess efficacy or safety and powered appropriately. These were included.

3.1.2.3. Secondary publications

Publications that did not present the results for the primary outcome of a trial were excluded. Therefore, secondary analyses and other additional publications were excluded. Studies within studies or secondary analyses may include subgroup analyses, adherence or trial implementation measures, pharmacokinetic studies, effectiveness of diagnostic devices, characteristics of the disease, and many other associated questions. While these are relevant treatment questions, the purpose of this dataset is not to gather all information relating to a trial. The goal of the State of Practice Dataset is to include one record (the main trial publication) per trial that provides the most relevant and accurate account of the methodological features of the trial. Including additional publications from the same trial would lead to counting that trial multiple times. More specifically, the methods used in that trial would be counted multiple times, and the fraction or share of that method in the total pool would be overrepresented.

3.1.2.4. Unpublished/unavailable study publications

Studies that were not published as a full text publication were excluded. This included studies where an abstract appeared to reference a full text journal article, however the full text paper for that abstract could not be found or retrieved, after exhaustive search efforts, via any mechanism. As the purpose of this search is to produce a dataset for analysis that is comprised of full text publications, it is necessary to exclude studies where no such publication exists.

3.1.2.5. Non-pharmacological interventions

Studies where the main purpose was to test the following interventions were excluded:

- Care Coordination or Care Routines (see Section 3.1.2.5.1.)
- Counseling or Therapy

- Cash incentives
- Devices (including insertable or implantable devices) that did not include medicine, and therefore did not work via a pharmacological mechanism of action
- Diagnostic Tests (see Section 3.1.2.5.2.)
- Digital Apps, Smartphones, or Algorithms
- Electrical Stimulation of the brain
- Human touch / Kangaroo Care / Skin-to-skin contact
- Plant interventions when used as a medicinal agent, not as a nutritional supplement (see Section 3.1.2.5.3.)
- Reminders
- Surgical interventions, including circumcision
- Training or Education
- Water
- Water, Sanitation, and Hygiene interventions (WASH), including soap (see Sections 3.1.2.5.4. – 3.1.2.5.5.)

3.1.2.5.1. Care Coordination or Care Routines

Studies where the main purpose was to examine the impact of different care coordination interventions were excluded. These types of interventions may compare the impact of having different health care professionals administer treatment, for example midwives versus physicians, or different treatment locations, for example, community-based care versus hospital-based care. They may compare different services designed to enhance linkage to care, or different mechanisms for dispensing medication, for example community refill groups versus facility-based delivery.

3.1.2.5.2. Diagnostic Tests

Studies where the main purpose was to compare the effectiveness of different diagnostic tests were excluded, including those examining the impact of frequency or timing of testing and/or testing location, for example point-of-care versus central testing. Studies assessing test and treat approaches, or screening and treatment approaches, or universal treatment compared with targeted treatment (which may be based on level of disease as determined by a test), were included.

3.1.2.5.3. Plant interventions

Some plant interventions are where plants, cooked or raw, are ingested as food. In others, plants are applied to the outside of the body or turned into something intended to be medicine. For this dataset, when plants were used as food, those

studies were included due to the inclusion of nutrition in disease scope. When plants were used as traditional remedies, traditional medicines, or the main medicinal agent, they were excluded, as these agents typically do not have approval for medicinal use by regulatory agencies.

3.1.2.5.4. WASH interventions

Water, sanitation and hygiene interventions (WASH) were excluded. Examples of WASH interventions include, increasing access to water, well disinfection, household water treatment, source-based water treatment, providing latrines, hygiene promotion, distribution of soap and/or hygiene kits, and environmental hygiene(8). These interventions do not usually include a substance with a pharmacological mechanism of action that is administered directly to a participant. Chlorine-based household water treatment does include a molecule with a chemical mechanism of action. However, chlorine kills pathogens in the water prior to a human encountering the water. Therefore, excluding these interventions was consistent with the eligibility requirement that interventions must be directly applied to and act on/within the participant whose health outcomes are measured.

3.1.2.5.5. Soap and soap-like substances

Studies that tested regular soap as an intervention were excluded. The mechanism of action of soap is primarily mechanical (i.e., rubbing action and micelles trapping and removing dirt and germs), rather than chemical or pharmacological. For inclusion in this dataset, the intervention must have some agent with primarily a chemical action, for example, antibacterial. Studies where the intervention included a chemical agent within soap or a soap-like substance (e.g., anti-microbials, and anti-fungals) were included, provided the agent was applied to the participant whose health outcomes were measured. Therefore, studies testing interventions applied to health professionals (e.g., hand sanitizer for doctors or nurses), and not the study participants, were excluded.

3.1.2.6. Vector control

Interventions that were not applied directly to a human and assessed by measuring health outcomes in that human were excluded. Therefore, all vector control interventions, including indoor residual spraying and larviciding, were excluded. Bed nets treated with insecticide, while administered on an individual level, were excluded as the chemical component acts on an insect.

3.1.2.7. Adherence, acceptability, preferences

This dataset is designed to include trial publications where the trial is evaluating the efficacy and safety of medicinal interventions. These types of trials are likely to

provide the most relevant and accurate record of the methods utilized in pharmacological treatment trials. If the main purpose of a study was to assess adherence, cost, patient preferences, acceptability, or feasibility, it was excluded. Studies that included adherence measures as secondary outcomes, while the primary outcomes were related to effectiveness or safety, were included.

3.2. Search methods for identification of studies

<table>
<tr><td colspan="5">Search methods</td></tr>
<tr><td>Electronic databases</td><td>Database
☒ MEDLINE
☒ CENTRAL</td><td colspan="2">From:
2019</td><td>To:
June 21, 2024</td></tr>
<tr><td>Approach to ongoing and unpublished studies</td><td colspan="3">☐ Include ongoing studies
☐ Unpublished studies
☐ Studies in press
☒ Exclude all studies that are ongoing, unpublished, or in press</td><td></td></tr>
<tr><td colspan="5">Methods for screening search results</td></tr>
<tr><td>Screening methods</td><td colspan="2">Single on included decisions
Dual on excluded decisions
Dual</td><td>Abstract
☒
☒
☐</td><td>Full text
☐
☐
☒</td></tr>
<tr><td>Discrepancy resolution</td><td colspan="4">☐ Consensus
☒ Third reviewer</td></tr>
<tr><td>Excluded studies</td><td colspan="4">All excluded studies during abstract and full text screening will be documented with a reason for exclusion.</td></tr>
<tr><td>Inclusion of abstracts and conference proceedings</td><td colspan="4">☒ Exclude all
☐ Include if clearly eligible and have usable data
☐ Include if clearly eligible regardless of usable data
☐ Include if eligibility is unclear and add to section in report</td></tr>
<tr><td rowspan="2">Inclusion of non-English language studies</td><td colspan="4">☐ Include abstracts and full texts in any language
☐ Include full texts only in any language
☒ Exclude</td></tr>
<tr><td colspan="4">☐ All potentially relevant abstracts will progress to full text screen
☐ [Single/dual] title/abstract screen by foreign-language speaker(s)
☐ [Abstract/methods/full text] will be translated for abstract/full text screen
☒ Listed as non-English language and not assessed further</td></tr>
<tr><td>Software</td><td colspan="4">Rayyan(9)</td></tr>
</table>

The search was conducted in the following databases:

- PubMed
- Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library.

The search strategy was developed using PubMed MeSH terms and keywords for all included countries, combined with MeSH terms for all diseases listed under CMNN by IHME(2), except COVID-19. These terms were also combined with the PubMed format of the Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision)(10). This aspect of the search strategy was not necessary to include when translating the search strategy for CENTRAL because CENTRAL is designed to contain RCT and quasi-RCT records(11). The search was limited to papers with a publication date from 2019-present. The development of the search code is discussed in the following sections, and the final search strategy is included in Appendix 9.4.

3.2.1. Development of search code by concept

3.2.1.1. Countries

The Africa region was defined by the list of member states of the African Union (AU)(12). The countries in South Asia were defined according to the World Bank country and lending groups(4). A list of all included countries is shown in Appendix 9.2. Using MeSH headings for 'Africa' and 'Asia, Southern', incorporated all relevant countries into the search as MeSH terms, except for Mauritius, which was added as an additional MeSH heading.

To ensure that relevant studies that were not indexed to a country MeSH in PubMed were also included in the search results, additional text word searches were added for the names of the countries and their demonyms (where appropriate, truncation was used to capture both the country name and demonym using the one term).

3.2.1.2. Diseases

The disease areas in scope for this dataset were those listed under CMNN in the 2021 IHME GBD Study(2). The search code to capture the full range of these disease areas was developed by mapping each GBD disease term/category to a MeSH term in PubMed. The GBD hierarchy of CMNN disease terms (except COVID-19) and their corresponding PubMed MeSH terms are shown in table form in Appendix 9.3. The process for mapping each disease term/category to a MeSH term was as follows:

- All GBD disease terms at the lowest level (level 4) in the published hierarchy of diseases were mapped to the most appropriate PubMed MeSH term. This was determined by evaluating the GBD definition compared with the MeSH scope note.

- All level 3 GBD disease terms that did not have level 4 terms as “children” (i.e., nested underneath in the hierarchy) were also mapped to the most appropriate MeSH term.
- If there was a level 4 or childless level 3 term in GBD that was a category of diseases and was not specific (e.g., included the word “Other”), the header for that term (which was either a level 3 or level 2 term respectively) was mapped to a MeSH term instead to ensure no diseases were missed.
- If there was not an appropriate equivalent MeSH term for a GBD disease term, the GBD header for that term was mapped to a MeSH term instead to ensure no diseases were missed.
- If all the “children” terms (level 3 or level 4) of a level 2 or level 3 header term in GBD were mapped to a MeSH term, the GBD header term was not mapped.
- Due to the broad scope of the diseases included, text word searches were not used to supplement the MeSH disease terms.

3.2.1.3. Study design

To find randomized trials, the search code was developed as follows:

- Use the PubMed format of the Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision)(10).
- The Cochrane Highly Sensitive Search Strategy includes an exclusion term for animals. This was supplemented in our search with additional animal specific exclusion terms to increase search precision.
- Additional exclusion terms were added to automatically exclude papers that mentioned particular words in the title (e.g. “case study”, “observational”, “modelling/modelling”). This removed a subset of irrelevant papers and increased search precision.
- Study design terms for inclusion and exclusion were chosen based on pilot screening evaluation of search results (see Section 3.2.1.4.2.).

3.2.1.4. Limits

To ensure the feasibility of conducting and maintaining this dataset with current trial information, certain limits were introduced to the search. This was to reduce the volume and maximize the relevance of studies retrieved.

3.2.1.4.1. Date restriction

In terms of study design, more recent studies will be most useful to inform questions about contemporary or recent trial design methods and trends, in part toward predicting future trial design approaches. The search was limited to

papers published from 2019 onwards. Publication date is defined as when the article was published in a journal, not when the article became available in PubMed.

3.2.1.4.2. Exclusion terms

Studies on COVID-19 were out of scope and were excluded using the NOT Boolean operator.

Additional publication type exclusion terms were added as follows:

- **Publication type terms**
    - protocol
    - editorial
    - comment
    - letter
    - case study or case studies or case report or case reports
    - congress or conference
    - systematic review or meta analysis or narrative review or literature review

An earlier iteration of the search was piloted, revealing many excluded publications due to the wrong study design (not randomized) or due to being a secondary analysis/publication of a trial. The following exclusion terms were added to the search using the NOT Boolean operator:

- **Study design terms**
    - observational
    - modeling OR modelling
    - cross-sectional
    - qualitative
- **Secondary analysis/additional publication terms**
    - nested
    - sub-study
    - secondary analysis/analyses
    - post-hoc analysis

To be conservative in excluding, the study design terms and secondary analysis/additional publication terms were required to appear in the title of a paper for that paper to be excluded. The effect of adding these terms was tested to confirm that adding them increased the precision of the search with minimal loss in terms of sensitivity.

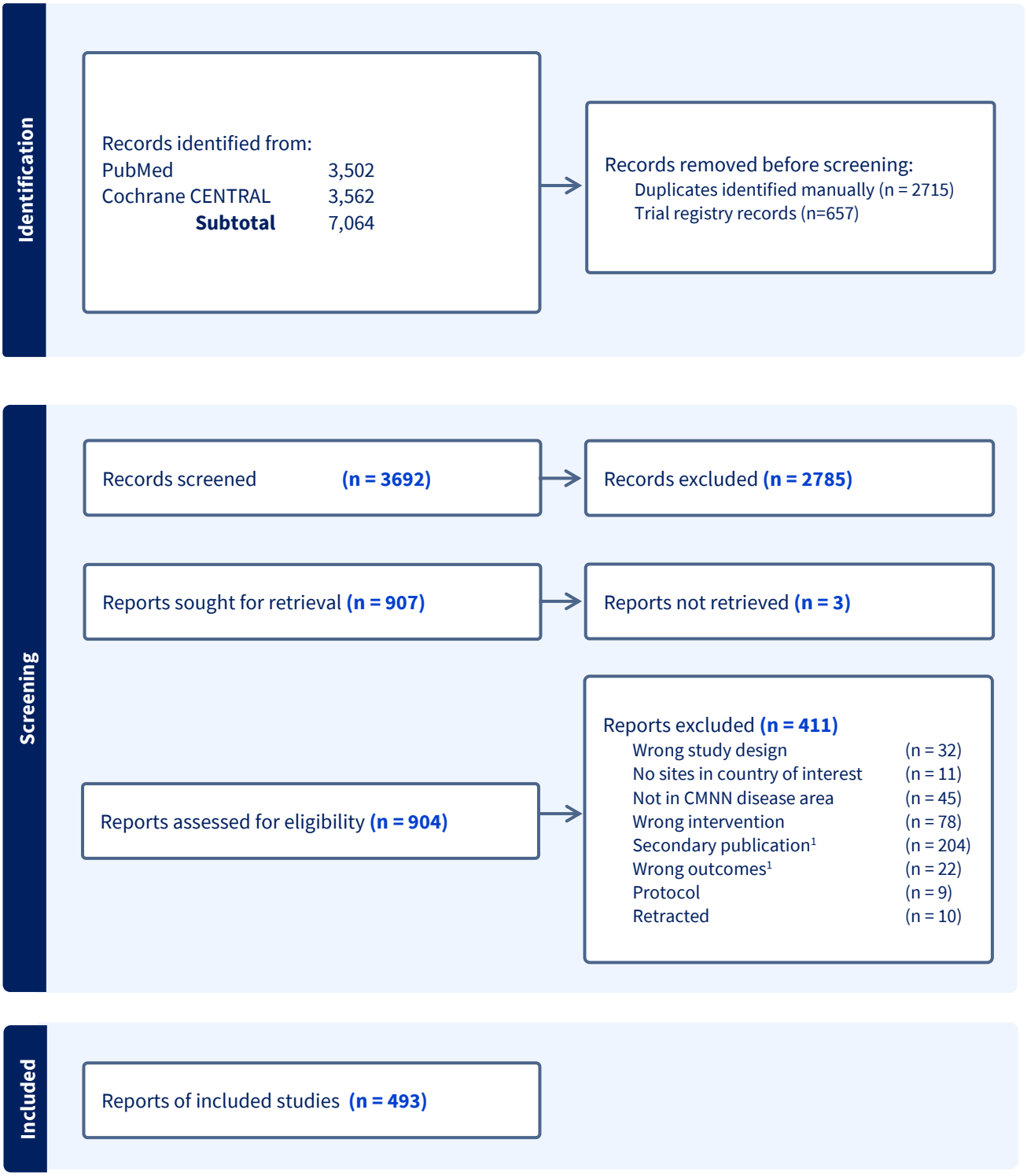
3.2.2. Selection of studies

An initial single screen of all titles and abstracts was conducted to identify publications that were candidates for full text screening. Any articles that received a single vote for inclusion progressed to the full text screening stage. Articles were excluded during the initial screen if the reviewer could determine from the title and abstract that it did not meet the inclusion criteria. To reduce error, all abstracts that were excluded by a single reviewer were then screened for inclusion by a different second reviewer, and any abstracts that received a single vote for inclusion after duplicate screening were progressed to the full text screening stage. Full text copies of all publications identified for potential inclusion were obtained and screened independently for final inclusion by two reviewers. Disagreements in screening decisions were resolved by a third reviewer with previous experience designing and conducting the search for SOPD1. Contacting study authors for further information was out of scope due to limited time and resources.

4. Search Results

The results identified from PubMed (n=3,502) and CENTRAL (n=3,562) were combined and duplicates (n=2715) removed. Trial registry records (n=657) were also removed since publication of primary results was the unit of inclusion for each trial in this dataset. The PRISMA flow diagram in Figure 1 depicts how the citations identified were processed for this dataset. During full text screening, three articles were not available via any mechanism. The remaining 904 full text articles were retrieved and independently evaluated against the inclusion criteria by at least two reviewers, resulting in 503 articles for inclusion. An additional 10 articles were excluded during the data extraction phase for the reasons noted in Figure 1, leaving a final number of 493 publications for inclusion.

Figure 1: PRISMA Flow Diagram



[1]Ten publications were excluded during the data extraction phase for the following reasons: secondary publication (n=9); wrong outcomes (n=1).

5. Limitations

5.1. Limits to comprehensiveness of the search strategy

An important aspect of a systematic search is comprehensiveness in order to minimize publication bias. Searches are designed, tested, and refined to try to find every study relevant to the question of interest, while minimizing the number of irrelevant results. This is particularly important for answering effectiveness questions. SOPD2 is not designed to answer questions related to the effectiveness of interventions. Due to the very broad scope of the disease categories and time included in this dataset, the level of comprehensiveness of the searching process needed to be reduced to meet budget limitations. It was not feasible to find every single paper meeting the inclusion criteria. However, an effort was made to search in a systematic and unbiased way across all disease categories. This means the dataset should be representative of the trials that have been conducted in African and South Asian countries across these disease categories (excluding COVID-19) and published from 2019 – mid-2024. The following limits to the comprehensiveness of the search were applied to ensure a manageable number of relevant results were retrieved for screening:

- Date limits, particularly because more recent trials provide the most relevant information about study design and methodological features that are likely to be used in future studies.
- English language only
- Limited to Africa and South Asia
- Search conducted in two databases (PubMed and CENTRAL), while not including Embase, F1000, Web of Science, or other databases
- MESH disease categories were used exclusively for disease terms. This means studies not indexed to a disease MESH term would be missed. Supplementing with text word searches for the large number of diseases was not practical to do in a systematic way.

These limits were appropriate given the intended purpose of this dataset. Perhaps most importantly, all decisions regarding the searching and screening process have been documented. This is in agreement with global guidance for the development of rapid systematic reviews (13,14). This ensures reproducibility, maximizes transparency, and helps provide guidance for the appropriate use of this dataset.

5.2 IHME CMNN diseases may exist in MESH hierarchies not included in our search strategy

The approach used for mapping individual IHME CMNN diseases to MESH hierarchies was one where IHME pre-aggregated, at times, a number of diseases to a group, without specifying the detail. These pre-aggregations were not common. It could be true that one of the pre-aggregated diseases within a CMNN hierarchy was decided by the National Library of Medicine PUBMED organization to be assigned to a widely different, and not included in SOPD, hierarchy. If this did occur, there would be no way to know that the CMNN disease was left out of the

SOPD MESH hierarchies, unless the general knowledge and spot-checking of the authors identified such. While it is not seen by the authors as likely, it could be that some rare condition was treated in this way and not identified.

5.3 The dataset repository does not include all supplemental materials

The data files (trial publication .pdf files) collected were the main publication, and it could be that some methods are delineated in finer detail in that paper's supplements. Identifying and collecting these additional trial publications was beyond the scope of the project.

6. Future updates

It is anticipated that SOPD2 may be updated to maintain a relatively recent dataset of trial publications. Future updates of the searching process could include searching of trial registries for completed trials or incorporating an additional literature database. The geographical focus could be further expanded to include additional countries where low-resource trials are conducted. However, increasing comprehensiveness will need to be balanced with the time and resources required to collate and maintain the dataset. Further improvements could be made to the sensitivity or precision of the search. Over eighty percent of papers that were found in the search for SOPD2 were excluded during the screening phase. There may be further opportunities for optimizing the search precision and also reducing the burden of manual screening, perhaps by incorporating artificial intelligence (AI) tools and approaches in the screening process(15–17). While somewhat limited by the ability to identify the main trial paper in an automated way either via the search strategy or by screening, these opportunities could be explored.

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9. Appendices

9.1. SOPD Version Scope Comparison

SOPD1	SOPD2
Database(s) searched: PubMed	Database(s) searched: PubMed CENTRAL
One-stage screening process: • Abstract screening with access of full text papers only when eligibility could not be determined by the abstract alone.	Two-stage screening process: • Abstract screening • All citations included at abstract stage progressed to full text screening.
Included: • Published between Jan 2018 and the search date (October 24, 2022) • At least one study site in sub-Saharan Africa • CMNN disease area (excluding COVID) as defined by IHME GBD Study, 2019 • Randomized assignment to intervention arms • Studies testing efficacy/safety of pharmacological interventions applied directly to the participant whose health outcomes were measured. Due to nutrition scope, food was included where used as a dietary supplement.	Included: • Published between Jan 2019 and the search date (June 21, 2024) • At least one study site in Africa or South Asia • CMNN disease area (excluding COVID) as defined by IHME GBD Study, 2021 • Randomized assignment to intervention arms • Studies testing efficacy/safety of pharmacological interventions applied directly to the participant whose health outcomes were measured. Due to nutrition scope, food was included where used as a dietary supplement.
Excluded: • Secondary publications from the same trial (only one main publication per trial was included) • Pilot studies • Studies that included non-pharmacological interventions in any of the study arms • Vector control interventions • Studies where the main purpose was to assess adherence, cost, patient preferences, acceptability, or feasibility • Studies where the main purpose was to test a strategy of distribution for an intervention	Excluded: • Secondary publications from the same trial (only one main publication per trial was included) • Pilot studies • Studies where the main purpose was to assess a non-pharmacological intervention • Vector control interventions • Studies where the main purpose was to assess adherence, cost, patient preferences, acceptability, or feasibility

9.2. Table of included countries

Africa		South Asia
Angola	Morocco	Afghanistan
Burundi	Madagascar	Bangladesh
Benin	Mali	Bhutan
Burkina Faso	Mozambique	India
Botswana	Mauritania	Sri Lanka
Central African Republic	Mauritius	Maldives
Côte d'Ivoire	Malawi	Nepal
Cameroon	Namibia	Pakistan
Congo, Dem. Rep.	Niger	
Congo, Rep.	Nigeria	
Comoros	Rwanda	
Cabo Verde	Sudan	
Djibouti	Senegal	
Algeria	Sierra Leone	
Egypt, Arab Rep.	Somalia	
Eritrea	South Sudan	
Ethiopia	São Tomé and Príncipe	
Gabon	Eswatini	
Ghana	Seychelles	
Guinea	Chad	
Gambia, The	Togo	
Guinea-Bissau	Tunisia	
Equatorial Guinea	Tanzania	
Kenya	Uganda	
Liberia	South Africa	
Libya	Zambia	
Lesotho	Zimbabwe	

9.3. Table of CMNN disease categories and matching MeSH terms

The table below shows the levelled hierarchy for all CMNN disease categories published in IHME GBD(18) and the corresponding MeSH term from PubMed that was used to include that disease category in the search code.

Cause	Level	PubMed MeSH Term
Communicable, maternal, neonatal, and nutritional diseases	1	-
HIV/AIDS and sexually transmitted infections	2	-
HIV/AIDS	3	HIV Infections
HIV/AIDS–drug-susceptible tuberculosis	4	To level 3
HIV/AIDS–multidrug-resistant TB without extensive drug resistance	4	To level 3
HIV/AIDS–extensively drug-resistant tuberculosis	4	To level 3
HIV/AIDS resulting in other diseases	4	To level 3
Sexually transmitted infections excluding HIV	3	Sexually Transmitted Diseases
Syphilis	4	Syphilis
Chlamydial infection	4	Chlamydia Infections
Gonococcal infection	4	Gonorrhea
Trichomoniasis	4	Trichomonas Vaginitis
Genital herpes	4	Herpes Genitalis
Other sexually transmitted infections	4	To level 3
Respiratory infections and tuberculosis	2	Respiratory Tract Infections OR Tuberculosis
Tuberculosis	3	Tuberculosis
Latent tuberculosis infection	4	Latent Tuberculosis
Drug-susceptible tuberculosis	4	to level 3
Multidrug resistant TB without extensive drug resistance	4	Tuberculosis, Multidrug-Resistant
Extensively drug-resistant tuberculosis	4	Extensively Drug-Resistant Tuberculosis
Lower respiratory infections	3	to level 2
Upper respiratory infections	3	Respiratory Tract Infections
Otitis media	3	Otitis Media
Enteric infections	2	Gastroenteritis
Diarrhoeal diseases	3	Dysentery
Typhoid and paratyphoid	3	-
Typhoid fever	4	Typhoid Fever
Paratyphoid fever	4	Paratyphoid Fever
Invasive non-typhoidal Salmonella (iNTS)	3	Salmonella Infections
Other intestinal infectious diseases	3	to level 2
Neglected tropical diseases and malaria	2	Parasitic diseases OR Vector Borne Diseases OR Waterborne Disease OR Zoonoses OR Virus Diseases
Malaria	3	Malaria
Chagas disease	3	Chagas Disease
Leishmaniasis	3	-

Visceral leishmaniasis	4	Leishmaniasis, Visceral
Cutaneous and mucocutaneous leishmaniasis	4	Leishmaniasis, Cutaneous OR Leishmaniasis, Mucocutaneous
African trypanosomiasis	3	Trypanosomiasis, African
Schistosomiasis	3	Schistosomiasis
Cysticercosis	3	Cysticercosis
Cystic echinococcosis	3	Echinococcosis
Lymphatic filariasis	3	Filariasis
Onchocerciasis	3	Onchocerciasis
Trachoma	3	Trachoma
Dengue	3	Dengue
Yellow fever	3	Yellow Fever
Rabies	3	Rabies
Intestinal nematode infections	3	-
Ascariasis	4	Ascariasis
Trichuriasis	4	Trichuriasis
Hookworm disease	4	Hookworm Infections
Food-borne trematodiases	3	Trematode Infections
Leprosy	3	Leprosy
Ebola virus disease	3	Hemorrhagic Fever, Ebola
Zika virus disease	3	Zika Virus Infection
Guinea worm disease	3	Dracunculiasis
Other neglected tropical diseases	3	to level 2
Other infectious diseases	2	Infections
Meningitis	3	Meningitis
Encephalitis	3	Encephalitis
Diphtheria	3	Diphtheria
Pertussis	3	Whooping Cough
Tetanus	3	Tetanus
Measles	3	Measles
Varicella and herpes zoster	3	Varicella Zoster Virus Infection
Acute hepatitis	3	-
Acute hepatitis A	4	Hepatitis A
Acute hepatitis B	4	Hepatitis B[1]
Acute hepatitis C	4	Hepatitis C[1]
Acute hepatitis E	4	Hepatitis E
Other unspecified infectious diseases	3	to level 2
Maternal and neonatal disorders	2	-
Maternal disorders	3	Pregnancy Complications
Maternal haemorrhage	4	Postpartum Hemorrhage
Maternal sepsis and other maternal infections	4	Pregnancy Complications, Infectious
Maternal hypertensive disorders	4	Hypertension, Pregnancy-Induced
Maternal obstructed labor and uterine rupture	4	Uterine Rupture OR Dystocia
Maternal abortion and miscarriage	4	Abortion, Spontaneous
Ectopic pregnancy	4	Pregnancy, Ectopic

Indirect maternal deaths	4	Maternal Death
Late maternal deaths	4	Maternal Death
Maternal deaths aggravated by HIV/AIDS	4	Maternal Death
Other maternal disorders	4	to level 3
Neonatal disorders	3	Pregnancy Complications OR Infant, Newborn, Diseases
Neonatal preterm birth	4	Premature Birth
Neonatal encephalopathy due to birth asphyxia and trauma	4	Asphyxia Neonatorum OR (Hypoxia, Brain AND Infant, Newborn)[2]
Neonatal sepsis and other neonatal infections	4	Neonatal Sepsis
Haemolytic disease and other neonatal jaundice	4	Jaundice, Neonatal OR Erythroblastosis, Fetal
Other neonatal disorders	4	to level 3
Nutritional deficiencies	2	Malnutrition
Protein-energy malnutrition	3	Protein-Energy Malnutrition
Iodine deficiency	3	Iodine/deficiency
Vitamin A deficiency	3	Vitamin A Deficiency
Dietary iron deficiency	3	Iron Deficiencies
Other nutritional deficiencies	3	to level 2

[1]Chronic hepatitis B and C were out of scope and were excluded in the search code using the "no explosion" modifier on the MeSH terms for Hepatitis B and Hepatitis C. This modifier means MeSH terms below those MeSH terms in the MeSH hierarchy were not included.

[2]The GBD disease term "Neonatal encephalopathy due to birth asphyxia and trauma" was mapped to the MeSH term "Asphyxia Neonatorum", however this was not an adequate match, and did not capture all the relevant results. The combination of two MeSH terms ('Hypoxia, Brain' AND 'Infant, Newborn') was added to better represent the GBD disease term.

9.4. Search strategy and results

Searches were conducted on June 21, 2024

Database	Hits
PubMed	3,502
Cochrane CENTRAL	3,562
Subtotal	**7,064**
Duplicates	*2715*
Trial records	*657*
Total	**3,692**

Pubmed Search: Accessed June 21, 2024

Search No.	Search Terms	Hits
Country		
#1	(“Africa”[mh] OR “Mauritius”[mh] OR "central africa"[tw] OR "southern africa"[tw] OR "western africa"[tw] OR "eastern africa"[tw] OR “northern africa”[tw] OR “Algeria*”[tw] OR ("Burkina Faso"[tw] OR "Burkinabe"[tw]) OR "Cameroon*"[tw] OR ("Central African Republic"[tw] OR "Central African?"[tw]) OR ("Chad"[tw] OR “Chadian”[tw]) OR ("Republic of the Congo"[tw] OR "Congolese"[tw]) OR ("Democratic Republic of the Congo"[tw] OR “Democratic Republic of Congo”[tw] OR “DR Congo”[tw]) OR “Egypt*”[tw] OR ("Equatorial Guinea*"[tw] OR "Equatoguinean?"[tw]) OR "Gabon*"[tw] OR (“Sao Tome and Principe”[tw] OR "Sao Tome*"[tw]) OR ("Burundi*"[tw] OR "Barundi"[tw]) OR ("Comoros"[tw] OR “Comorian”[tw]) OR "Djibouti*"[tw] OR "Eritrea*"[tw] OR "Ethiopia*"[tw] OR "Kenya*"[tw] OR "Madagas*"[tw] OR "Mauriti*"[tw] OR "Rwand*"[tw] OR "Seychell*"[tw] OR "Somali*"[tw] OR "South Sudan*"[tw] OR "Sudan*"[tw] OR "Tanzania*"[tw] OR "Uganda*"[tw] OR "Mauritania*"[tw] OR "Angola*" [tw] OR ("Botswana"[tw] OR "Batswana"[tw] OR "Motswana"[tw]) OR ("Eswatini"[tw] OR "Swazi*"[tw]) OR ("Lesotho"[tw] OR "Basotho"[tw] OR "Mosotho"[tw]) OR “Libya*”[tw] OR "Malawi*"[tw] OR “Morocc*”[tw] OR "Mozambi*"[tw] OR "Namibia*"[tw] OR "South Africa*"[tw] OR “Tunisia*”[tw] OR (“Western Sahara”[tw] OR “Sahrawi*”[tw]) OR "Zambia*"[tw] OR "Zimbabwe*"[tw] OR “Benin*”[tw] OR ("Cabo Verde*"[tw] OR "Cape Verde*"[tw]) OR (“Cote d’Ivoire”[tw] OR "Ivory Coast"[tw] OR "Ivorian*"[tw]) OR "Gambia*"[tw] OR	1,003,396

Search No.	Search Terms	Hits
	"Ghana*"[tw] OR ("Guinea*"[tw] NOT (“New Guinea*”[tw] OR “Guinea worm”[tw])) OR ("Guinea-Bissau*"[tw] OR "Bissau-Guinean?"[tw]) OR "Liberia*"[tw] OR ("Mali"[tw] OR “Malian?”[tw]) OR ("Niger"[tw] OR “Nigerien?”[tw]) OR "Nigeria*"[tw] OR "Senegal*"[tw] OR "Sierra Leone*"[tw] OR "Togo*"[tw] OR “Asia, Southern”[mh] OR “south asia*”[tw] OR “southern asia*”[tw] OR “Afghan*”[tw] OR “Bangladesh*”[tw] OR “Bhutan*”[tw] OR “India*”[tw] OR “Sri Lanka*”[tw] OR “Maldiv*”[tw] OR "Nepal*"[tw] OR "Pakistan*"[tw])	
Disease		
#2	(“HIV Infections”[mh] OR "Sexually Transmitted Diseases"[mh] OR “Syphilis”[mh] OR “Chlamydia Infections”[mh] OR “Gonorrhea”[mh] OR “Trichomonas Vaginitis”[mh] OR “Herpes Genitalis”[mh])	442,180
#3	(“Respiratory Tract Infections”[mh] OR "Tuberculosis"[mh] OR “Latent Tuberculosis”[mh] OR “Tuberculosis, Multidrug-Resistant”[mh] OR “Extensively Drug-Resistant Tuberculosis”[mh] OR “Otitis media”[mh])	806,115
#4	(“Gastroenteritis”[mh] OR “Dysentery”[mh] OR “Typhoid Fever”[mh] OR “Paratyphoid Fever”[mh] OR “Salmonella Infections”[mh])	290,206
#5	(“Vector Borne Diseases”[mh] OR “Parasitic Diseases”[mh] OR “Waterborne Diseases”[mh] OR “Zoonoses”[mh] OR “Virus Diseases”[mh] OR “Malaria”[mh] OR “Chagas Disease”[mh] OR “Leishmaniasis, Cutaneous”[mh] OR “Leishmaniasis, Mucocutaneous”[mh] OR “Leishmaniasis, Visceral”[mh] OR “Trypanosomiasis, African”[mh] OR “Schistosomiasis”[mh] OR “Cysticercosis”[mh] OR “Echinococcosis”[mh] OR “Filariasis”[mh] OR “Onchocerciasis”[mh] OR “Trachoma”[mh] OR “Dengue”[mh] OR “Yellow Fever”[mh] OR “Rabies”[mh] OR “Ascariasis”[mh] OR “Trichuriasis”[mh] OR “Hookworm Infections”[mh] OR “Trematode Infections”[mh] OR “Leprosy”[mh] OR “Hemorrhagic Fever, Ebola”[mh] OR “Zika Virus Infection”[mh] OR “Dracunculiasis”[mh])	1,690,564
#6	(“Infections”[mh] OR “Meningitis”[mh] OR “Encephalitis”[mh] OR “Diphtheria”[mh] OR "Whooping Cough"[mh] OR “Tetanus”[mh] OR “Measles”[mh] OR “Varicella Zoster Virus Infection”[mh] OR “Hepatitis A”[mh] OR “Hepatitis B”[mh:noexp] OR “Hepatitis C”[mh:noexp] OR “Hepatitis E”[mh])	3,192,295

Search No.	Search Terms	Hits
#7	("Pregnancy Complications"[mh] OR "Postpartum Hemorrhage"[mh] OR "Pregnancy Complications, Infectious"[mh] OR "Hypertension, Pregnancy-Induced"[mh] OR "Dystocia"[mh] OR "Uterine Rupture"[mh] OR "Abortion, Spontaneous"[mh] OR "Pregnancy, Ectopic"[mh] OR "Maternal Death"[mh] OR "Infant, Newborn, Diseases"[mh] OR "Premature Birth"[mh] OR "Asphyxia Neonatorum"[mh] OR ("Hypoxia, Brain"[mh] AND "Infant, Newborn"[mh]) OR "Neonatal Sepsis"[mh] OR "Jaundice, Neonatal"[mh] OR "Erythroblastosis, Fetal"[mh])	649,729
#8	("Malnutrition"[mh] OR "Vitamin A Deficiency"[mh] OR "Protein-Energy Malnutrition"[mh] OR "Iron Deficiencies"[mh] OR "Iodine/deficiency"[mh])	156,534
#9	("COVID-19"[mh])	266,720
#10	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	4,054,734
#11	#10 NOT #9	3,788,014
Study design (Cochrane filter)		
#12	(randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR clinical trials as topic [mesh:noexp] OR randomly [tiab] OR trial [ti])	1,621,384
Exclusions		
#13	((animals [MeSH Terms] NOT humans [MeSH Terms]) or "in vitro" [tiab] or "rat" [tiab] or "rodent*" [tiab] or "mouse" [tiab] or "mice" [tiab] or "murine" [tiab] or "dog" [tiab] or "canine" [tiab] or "pig" [tiab] or "porcine" [tiab] or "bovine" [tiab] or "cow" [tiab])	7,087,885
#14	"editorial" [pt] or "comment*" [pt] or "letter" [pt] or "case study" [tiab] or "case studies" [tiab] or "case reports" [pt] or "case stud*" [tiab] or "case report*" [tiab] or "congress" [tiab] or conference [tiab] or systematic review [tiab] or meta-analysis [tiab] or meta analysis [tiab] or narrative review [tiab] or literature review [tiab] or "protocol"[ti]	5,318,039
#15	("observational"[ti] OR "modeling"[ti] OR "modelling"[ti] OR "cross-sectional"[ti] OR "qualitative"[ti])	366,257
#16	("nested" [ti] OR "sub-study" [ti] OR "secondary analysis" [ti] OR " secondary analyses"[ti] OR "post-hoc analysis" [ti])	17,172
#17	#13 OR #14 OR #15 OR #16	12,544,126

Search No.	Search Terms	Hits
TOTAL		
#18	((#1 AND #11 AND #12) AND (2019/01/01:2024/06 [dp])) NOT #17	**3,502**

CENTRAL via Cochrane website: Accessed June 21, 2024

Search #	Terms	Result
#1	([mh Africa] OR [mh Mauritius] OR "central africa":ti,ab,kw OR "southern africa":ti,ab,kw OR "western africa":ti,ab,kw OR "eastern africa":ti,ab,kw OR "northern africa":ti,ab,kw OR Algeria*:ti,ab,kw OR ("Burkina Faso":ti,ab,kw OR Burkinabe:ti,ab,kw) OR Cameroon*:ti,ab,kw OR ("Central African Republic":ti,ab,kw OR ("Central" NEXT African?):ti,ab,kw) OR (Chad:ti,ab,kw OR Chadian:ti,ab,kw) OR ("Republic of the Congo":ti,ab,kw OR Congolese:ti,ab,kw) OR ("Democratic Republic of the Congo":ti,ab,kw OR "Democratic Republic of Congo":ti,ab,kw OR "DR Congo":ti,ab,kw) OR Egypt*:ti,ab,kw OR (("Equatorial" NEXT Guinea*):ti,ab,kw OR Equatoguinean?:ti,ab,kw) OR Gabon*:ti,ab,kw OR ("Sao Tome and Principe":ti,ab,kw OR ("Sao" NEXT Tome*):ti,ab,kw) OR (Burundi*:ti,ab,kw OR Barundi:ti,ab,kw) OR (Comoros:ti,ab,kw OR Comorian:ti,ab,kw) OR Djibouti*:ti,ab,kw OR Eritrea*:ti,ab,kw OR Ethiopia*:ti,ab,kw OR Kenya*:ti,ab,kw OR Madagas*:ti,ab,kw OR Mauriti*:ti,ab,kw OR Rwand*:ti,ab,kw OR Seychell*:ti,ab,kw OR Somali*:ti,ab,kw OR ("South" NEXT Sudan*):ti,ab,kw OR Sudan*:ti,ab,kw OR Tanzania*:ti,ab,kw OR Uganda*:ti,ab,kw OR Mauritania*:ti,ab,kw OR Angola*:ti,ab,kw OR (Botswana:ti,ab,kw OR Batswana:ti,ab,kw OR Motswana:ti,ab,kw) OR (Eswatini:ti,ab,kw OR Swazi*:ti,ab,kw) OR (Lesotho:ti,ab,kw OR Basotho:ti,ab,kw OR Mosotho:ti,ab,kw) OR Libya*:ti,ab,kw OR Malawi*:ti,ab,kw OR Morocc*:ti,ab,kw OR Mozambi*:ti,ab,kw OR Namibia*:ti,ab,kw OR ("South" NEXT Africa*):ti,ab,kw OR Tunisia*:ti,ab,kw OR ("Western Sahara":ti,ab,kw OR Sahrawi*:ti,ab,kw) OR Zambia*:ti,ab,kw OR Zimbabwe*:ti,ab,kw OR Benin*:ti,ab,kw OR (("Cabo" NEXT Verde*):ti,ab,kw OR ("Cape" NEXT Verde*):ti,ab,kw) OR ("Cote d'Ivoire":ti,ab,kw OR "Ivory Coast":ti,ab,kw OR Ivorian*:ti,ab,kw) OR Gambia*:ti,ab,kw OR Ghana*:ti,ab,kw OR (Guinea*:ti,ab,kw NOT (("New" NEXT Guinea*):ti,ab,kw OR "Guinea worm":ti,ab,kw)) OR (Guinea-Bissau*:ti,ab,kw	51878

	OR Bissau-Guinean?:ti,ab,kw) OR Liberia*:ti,ab,kw OR (Mali:ti,ab,kw OR Malian?:ti,ab,kw) OR (Niger:ti,ab,kw OR Nigerien?:ti,ab,kw) OR Nigeria*:ti,ab,kw OR Senegal*:ti,ab,kw OR ("Sierra" NEXT Leone*):ti,ab,kw OR Togo*:ti,ab,kw OR [mh "Asia, Southern"] OR ("south" NEXT asia*):ti,ab,kw OR ("southern" NEXT asia*):ti,ab,kw OR Afghan*:ti,ab,kw OR Bangladesh*:ti,ab,kw OR Bhutan*:ti,ab,kw OR India*:ti,ab,kw OR ("Sri" NEXT Lanka*):ti,ab,kw OR Maldiv*:ti,ab,kw OR Nepal*:ti,ab,kw OR Pakistan*:ti,ab,kw)	
#2	([mh "HIV Infections"] OR [mh "Sexually Transmitted Diseases"] OR [mh Syphilis] OR [mh "Chlamydia Infections"] OR [mh Gonorrhea] OR [mh "Trichomonas Vaginitis"] OR [mh "Herpes Genitalis"])	21930
#3	([mh "Respiratory Tract Infections"] OR [mh Tuberculosis] OR [mh "Latent Tuberculosis"] OR [mh "Tuberculosis, Multidrug-Resistant"] OR [mh "Extensively Drug-Resistant Tuberculosis"] OR [mh "Otitis media"])	30601
#4	([mh Gastroenteritis] OR [mh Dysentery] OR [mh "Typhoid Fever"] OR [mh "Paratyphoid Fever"] OR [mh "Salmonella Infections"])	10824
#5	([mh "Vector Borne Diseases"] OR [mh "Parasitic Diseases"] OR [mh "Waterborne Diseases"] OR [mh Zoonoses] OR [mh "Virus Diseases"] OR [mh Malaria] OR [mh "Chagas Disease"] OR [mh "Leishmaniasis, Cutaneous"] OR [mh "Leishmaniasis, Mucocutaneous"] OR [mh "Leishmaniasis, Visceral"] OR [mh "Trypanosomiasis, African"] OR [mh Schistosomiasis] OR [mh Cysticercosis] OR [mh Echinococcosis] OR [mh Filariasis] OR [mh Onchocerciasis] OR [mh Trachoma] OR [mh Dengue] OR [mh "Yellow Fever"] OR [mh Rabies] OR [mh Ascariasis] OR [mh Trichuriasis] OR [mh "Hookworm Infections"] OR [mh "Trematode Infections"] OR [mh Leprosy] OR [mh "Hemorrhagic Fever, Ebola"] OR [mh "Zika Virus Infection"] OR [mh Dracunculiasis])	55575
#6	([mh Infections] OR [mh Meningitis] OR [mh Encephalitis] OR [mh Diphtheria] OR [mh "Whooping Cough"] OR [mh Tetanus] OR [mh Measles] OR [mh "Varicella Zoster Virus Infection"] OR [mh "Hepatitis A"] OR [mh ^"Hepatitis B"] OR [mh ^"Hepatitis C"] OR [mh "Hepatitis E"])	108307

#7	([mh "Pregnancy Complications"] OR [mh "Postpartum Hemorrhage"] OR [mh "Pregnancy Complications, Infectious"] OR [mh "Hypertension, Pregnancy-Induced"] OR [mh Dystocia] OR [mh "Uterine Rupture"] OR [mh "Abortion, Spontaneous"] OR [mh "Pregnancy, Ectopic"] OR [mh "Maternal Death"] OR [mh "Infant, Newborn, Diseases"] OR [mh "Premature Birth"] OR [mh "Asphyxia Neonatorum"] OR ([mh "Hypoxia, Brain"] AND [mh "Infant, Newborn"]) OR [mh "Neonatal Sepsis"] OR [mh "Jaundice, Neonatal"] OR [mh "Erythroblastosis, Fetal"])	26637
#8	([mh "Malnutrition"] OR [mh "Vitamin A Deficiency"] OR [mh "Protein-Energy Malnutrition"] OR [mh "Iron Deficiencies"])	8064
#9	MeSH descriptor: [Iodine] explode all trees and with qualifier(s): [deficiency - DF]	129
#10	([mh "COVID-19"])	7822
#11	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9	147307
#12	#11 NOT #10	139485
#13	(([mh animals] NOT [mh humans]) OR "in vitro":ti,ab OR rat:ti,ab OR rodent*:ti,ab OR mouse:ti,ab OR mice:ti,ab OR murine:ti,ab OR dog:ti,ab OR canine:ti,ab OR pig:ti,ab OR porcine:ti,ab OR bovine:ti,ab OR cow:ti,ab)	42529
#14	editorial:pt OR comment*:pt OR letter:pt OR "case study":ti,ab OR "case studies":ti,ab OR "case reports":pt OR ("case" NEXT stud*):ti,ab OR ("case" NEXT report*):ti,ab OR congress:ti,ab OR conference:ti,ab OR "systematic review":ti,ab OR meta-analysis:ti,ab OR "meta analysis":ti,ab OR "narrative review":ti,ab OR "literature review":ti,ab OR protocol:ti	80884
#15	(observational:ti OR modeling:ti OR modelling:ti OR cross-sectional:ti OR qualitative:ti)	10737
#16	#13 OR #14 OR #15	132175

#17	#1 AND #12	14623
#18	#17 NOT #16	13069
#19	("nested" OR "sub-study" OR "secondary analysis" OR " secondary analyses" OR "post-hoc analysis"):ti	10905
#20	#18 NOT #19 with Publication Year from 2019 to 2024, in Trials	3562