Note: This report was used to solicit feedback from WHO's Product Development for Vaccines Advisory Committee (PDVAC), and does not represent the final methodology, results, or views of any of the contributors. Final methods and results will be published in a peer-reviewed article, currently in preparation.

MCDA SURVEY PREPARATION AND LAUNCH - DRAFT FOR PDVAC

Partnering with regions and countries to identify priority pathogens for vaccines

Immunization Agenda 2030 Monitoring and Evaluation – November 2022

Abbreviations

AFRO	WHO Regional Office for Africa
AMR	Antimicrobial resistance
AMRO	WHO Regional Office for the Americas
cCMV	Congenital cytomegalovirus
CDC	US Centers for Disease Control and Prevention
CEPI	Coalition for Epidemic Preparedness Innovations
CHIK	Chikungunya virus
CMV	Cytomegalovirus
DALYs	Disability-adjusted life years
DCVMN	Developing Country Vaccine Manufacturers Network
EMRO	WHO Regional Office for the Eastern Mediterranean
EPEC	Enteropathogenic *Escherichia coli*
ETEC	Enterotoxigenic *Escherichia coli*
EURO	WHO Regional Office for Europe
ExPEC	Extra-intestinal pathogenic *E. coli*
FGS	Female genital schistosomiasis
GAS	Group A streptococcus
GBS	Group B streptococcus
GBD	Global Burden of Diseases Project
GDP	Gross domestic product
HIV-1	Human immunodeficiency virus 1
HSV	Herpes simplex virus
IA2030	Immunization Agenda 2030
ICTRP	International Clinical Trials Registry Platform
IHME	Institute for Health Metrics and Evaluation
IFPMA	International Federation of Pharmaceutical Manufacturers Associations
InPEC	Intestinal pathogenic *E. coli*
iNTS	Invasive non-typhoidal *Salmonella*
M&E	Monitoring and evaluation
MCDA	Multi-criteria decision analysis
MDA	Mass drug administration
NITAG	National immunization technical advisory group
NTD	Neglected tropical disease
NTS	Non-Typhoidal *Salmonella*
PAPRIKA	Potentially All Pairwise Rankings of All Possible Alternatives
PDVAC	Product Development for Vaccines Advisory Committee
PHEIC	Public health emergency of international concern
R&D	Research and development
RDB	R&D Blueprint
RHD	Rheumatic heart disease
RITAG	Regional immunization technical advisory group
RO	WHO Regional Office
RSV	Respiratory syncytial virus
SAGE	WHO's Strategic Advisory Group of Experts on Immunization
SEARO	WHO Regional Office for South-east Asia
SMC	Seasonal malaria chemoprevention
SP7	Strategic Priority 7 of IA2030, "Research and Innovation"
STI	Sexually transmitted infection
TB	Tuberculosis
TPP	Target product profile
USD	United States dollars
UTI	Urinary tract infection
VVP	Vaccine value profile
WHO	World Health Organization
WPRO	WHO Regional Office for the Western Pacific
YLDs	Years lived with disability
YLL	Years of life lost

I. Executive Summary

Introduction

Immunization Agenda 2030: A Global Strategy to Leave No One Behind (IA2030) is the World Health Assembly-endorsed global strategy for immunization, aimed toward maximizing the impact of vaccines. *Research and Innovation* is its seventh strategic priority, or "SP7". In the IA2030 Monitoring and Evaluation (M&E) Plan, Indicator 7.2 will monitor progress relating to a "short list" of global research and development (R&D) targets. According to this plan, "World Health Organization (WHO) headquarters and regional offices together with key partners/stakeholders are to mutually define targets and evaluate progress at the global and regional levels. This process will require a prioritization framework to align on priorities, targets, and a mechanism for monitoring and evaluation."[a] This call for mutually defined pathogen targets is in keeping with the IA2030 core principles of "people-centered, country-owned, partnership-based, and data-guided."

The Product Development for Vaccines Advisory Committee (PDVAC) has been charged with proposing the short list of pathogen targets for new vaccines (where vaccines do not yet currently exist, or where a new indication is needed), for endorsement by the WHO Strategic Advisory Group of Experts on Immunization (SAGE) in March 2023. Because global vaccine development decision makers currently do not have a robust mechanism to engage with regional or country stakeholders on priorities to guide new vaccine R&D, this will require designing and implementing a new mechanism. While the initial focus is on identifying pathogen priorities for new vaccines, this mechanism can also serve as the basis for collaboration on other important aspects of research and innovation strategies, such as priorities for implementation and operational research.

This report describes progress in creating this new mechanism to partner with regions and countries to identify priority pathogens for vaccines. It builds on preparation described in the *Landscaping and Methods Brief* for this project.

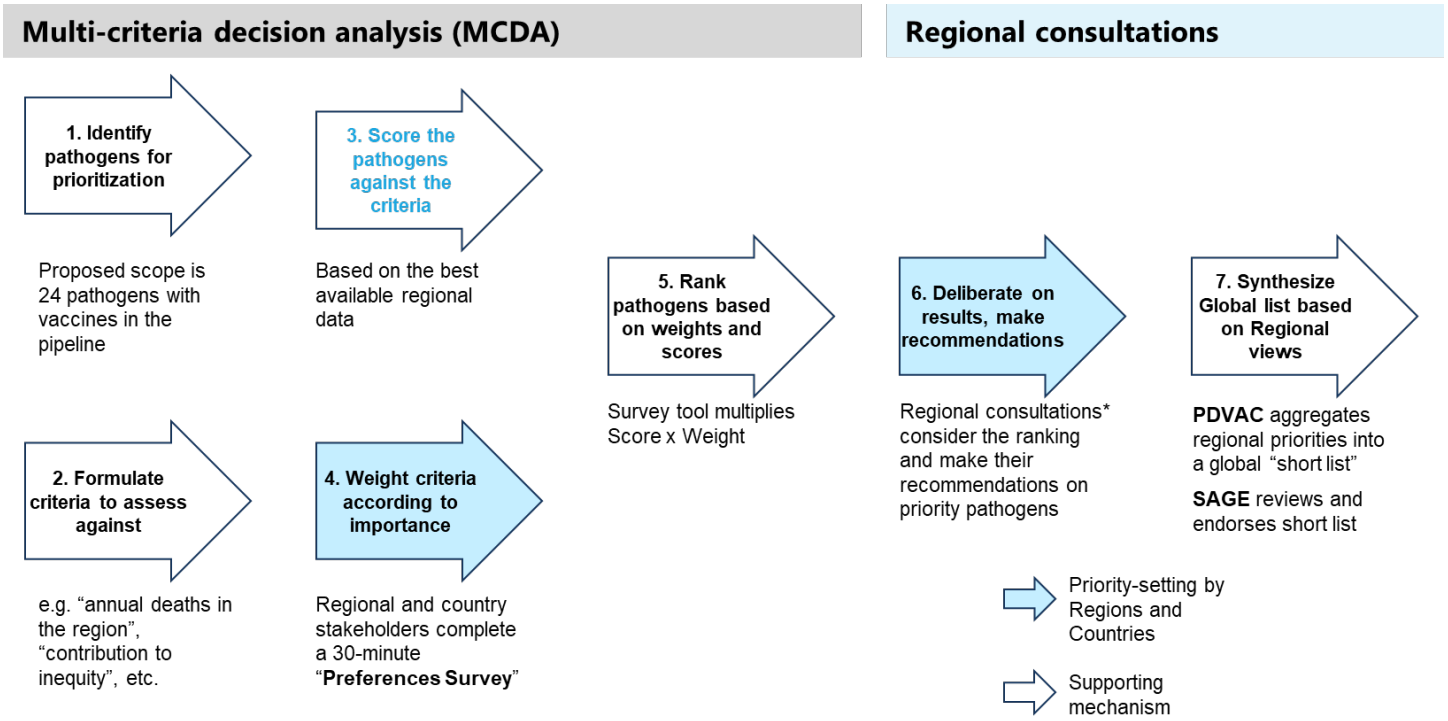
Collaborative approach

Figure 1 gives an overview of the collaborative approach to identify regional priorities, developed with advice and feedback from WHO regional offices (ROs), Regional Immunization Technical Advisory Group (RITAG) chairs, and regional representatives from PDVAC and the IA2030 SP7 Working Group. The

[a] http://www.immunizationagenda2030.org/images/documents/IA2030_Annex_FrameworkForActionv04.pdf

approach starts with multi-criteria decision analysis (MCDA) using the PAPRIKA survey tool[a] to rank pathogens in the context of each region. These results will be deliberated upon in regional consultations and inform regional recommendations for pathogen priorities.

Figure 1 Collaborative approach to identify regional priorities



Progress: MCDA survey preparation and launch

As of late November 2022, MCDA surveys are being launched in each WHO region. Stakeholders from WHO regional offices (ROs) and their associated Regional Immunization Technical Advisory Groups (RITAGs) are serving as liaisons to regional and country decision makers and experts.

These steps were taken to prepare and launch the surveys:

1. **Identify pathogens for prioritization**. The final scope of the MCDA exercise consists of 24 pathogens for which there are no licensed vaccines (or for which the licensed vaccines do not fulfill critical target product attributes); but which have vaccines in clinical development; and have been prioritized by a global mechanism or disease control strategy. Pathogens with potential for epidemics and public health emergencies of international concern (PHEICs) have been excluded

[a] PAPRIKA: "Potentially All Pairwise Rankings of All Possible Alternatives", https://www.1000minds.com/about/paprika

from the scope to avoid duplication with R&D Blueprint prioritization efforts. After the Preferences Surveys are complete, additional pathogens that have been identified through discussions with regional stakeholders, such as Hepatitis C and Chlamydia can be added during data analysis.

2. **Formulate criteria to assess against**. Eight criteria were defined based on precedents identified in the landscaping, good practices in MCDA,[a] and expert advice. The 8 final criteria are shown in Table 3. For each criterion, 5 levels—Very low, Low, Medium, High, and Very high—were defined as the basis for pathogen scoring.

3. **Score the pathogens against the criteria on a region-by-region basis**. Among the final criteria, 3 were scored quantitatively using data from the Global Burden of Diseases (GBD) project.[b] The remaining 5 criteria were scored qualitatively based on literature searches and expert advice. To make efficient use of expert time, 3 analysts conducted the literature searches and proposed scores for each combination of pathogen, region, and criterion. Pathogens were also scored in the global context. All scores were then reviewed by at least 1 pathogen expert and at least 2 regional experts, and differences were resolved by consensus within the project team. Results of the scoring are summarized below.

4. **Prepare and disseminate surveys to weight criteria according to importance**. Region-specific PAPRIKA surveys were prepared to enable regional and country stakeholders to weight the criteria. Each survey included the pathogen scores for that region, in order to display ranked lists of pathogens based on each individual's responses. To enable broader participation, surveys were translated into the major languages for each region. Invitations to complete the regional surveys are being disseminated through WHO regional and country offices, RITAGs and through stakeholder groups such as the Global NITAG Network. In parallel, a global survey has been prepared to enable comparisons between the perspectives of global and regional or country stakeholders. Global stakeholders are encouraged to complete the survey, which can be accessed at https://bit.ly/GLOBAL_EN. All surveys will remain open until December 16, 2022.

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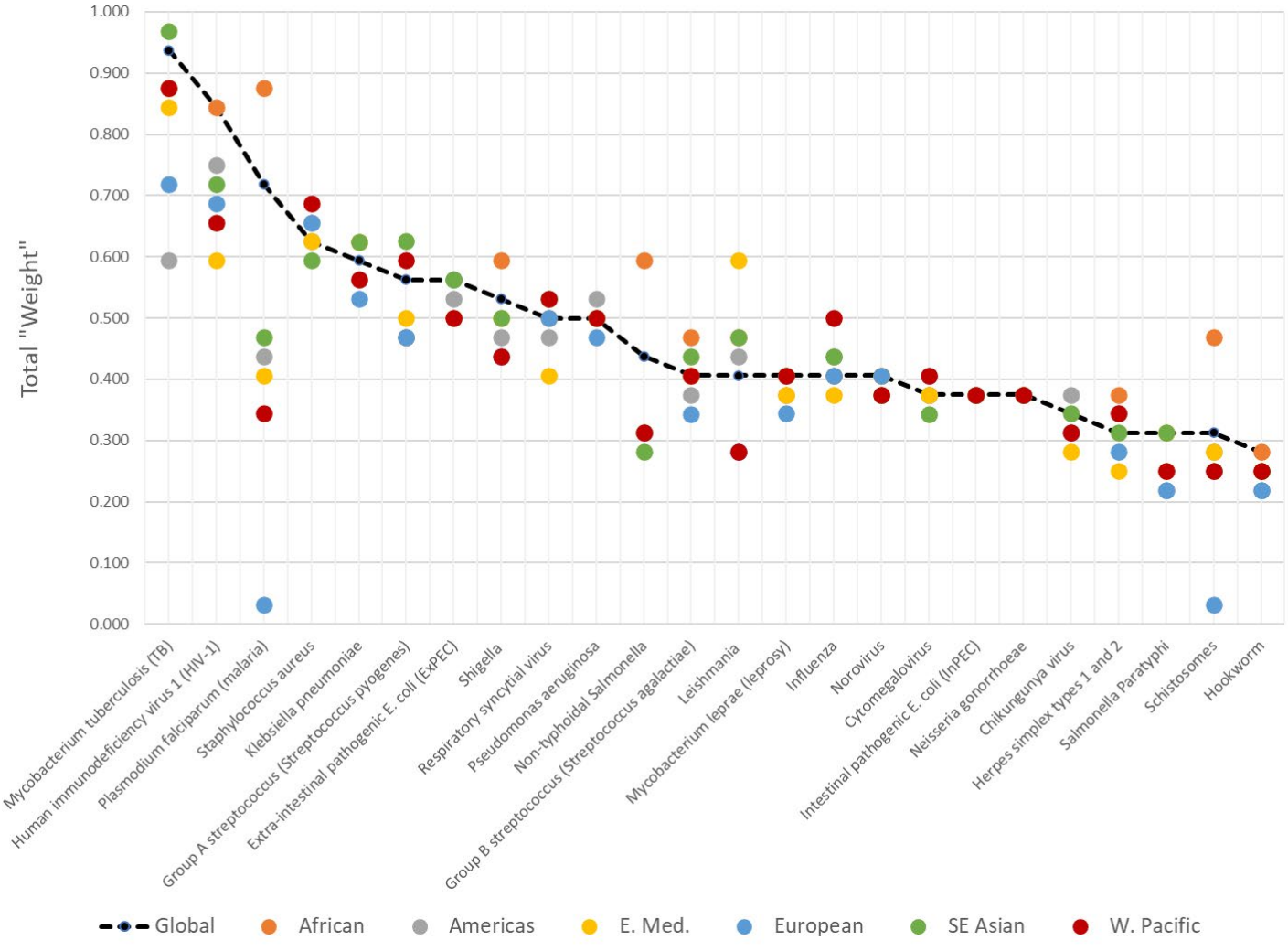
[a] Marsh K, IJzerman M, Thokala P, Baltussen R, Boysen M, Kaló Z, et al. Multiple Criteria Decision Analysis for Health Care Decision Making—Emerging Good Practices: Report 2 of the ISPOR MCDA Emerging Good Practices Task Force. Value in Health [Internet]. 2016 Mar [cited 2022 Jul 4];19(2):125–37. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1098301515300152

[b] https://ghdx.healthdata.org/gbd-2019

Scoring results

Detailed results from the pathogen scoring are given in Annex D: Pathogen Summaries. In addition, Annex E: Regional Summaries compares pathogen scores on a region-by-region basis. Figure 2 summarizes the results of the scoring *by assuming that all criteria have equal weight*. Globally and across regions, *Mycobacterium tuberculosis* was among the most heavily weighted, scoring Very high for most criteria in most regions. Conversely, hookworm generally had the lowest weight, scoring Very low or Low for most criteria in most regions. For a given pathogen, diversity in total weight reflects diversity in scores across regions. For example, both *P. falciparum* and schistosomes have very low prevalence in the European region, and therefore had lower scores and were less heavily weighted in that region.

Figure 2 "Base Case" pathogen weights



PAPRIKA results from each region will weight the criteria according to importance. This will shift these results so that they reflect regional and country perspectives, not just pathogen scores.

Lessons learned

- **Highlight the context**. For feasibility, this process is initially addressing the narrow question of priorities for new vaccine R&D and setting aside important issues such as ways to improve introduction and coverage of existing vaccines. Acknowledging such limitations and providing information on the other ways those concerns are being or can be addressed can help stakeholders understand how this prioritization fits into the greater context of immunization research and innovation. Within this process, the Preferences Surveys are the first step, and will inform regional stakeholder consultations to finalize the pathogen prioritization. These consultations will also incorporate considerations such as the probability of success and market attractiveness for new vaccines, which were too complex to include in the surveys. Contextualizing the surveys helps prepare for the consultations and strengthens understanding of the overall approach.
- **"Right-size" the scoring effort**. In conducting literature searches and scoring the pathogens, it is important to strike the right balance between rigor and practicality. For example, some practices that are essential to evidence-informed policy making (such as assessing the quality of the evidence) were not as relevant to this project, which is intended to inform product development.
- **Improve understanding of GBD data.** Because of the importance of GBD data in priority setting, it is essential to continue improving the evidence base for GBD estimates, the quality of GBD data, the broader understanding of GBD methods, and understanding of the level of standardization in burden estimation methods from pathogen to pathogen.
- **Take a more structured approach to qualitative scoring**. The considerations in Table 7 (qualitative levels for scoring) were a useful guide but could be improved in future prioritizations. The list of considerations could be more complete and include numeric thresholds rather than descriptions such as "all or most of the time". Guidance could be provided on how to score pathogens such as non-Typhoidal Salmonella with multiple disease presentations that differ in incidence and severity. Guidance could also be provided on how to address data gaps and heterogeneity within WHO regions.
- **Increase engagement of regional experts in the scoring of the qualitative criteria**. Vaccine value profiles based on extensive literature reviews were developed by groups of subject matter experts for the majority of pathogens included in the prioritization exercise. These served as sources for the scoring exercise. However, greater consultation with regional experts could enable more rigorous and context-specific scoring.

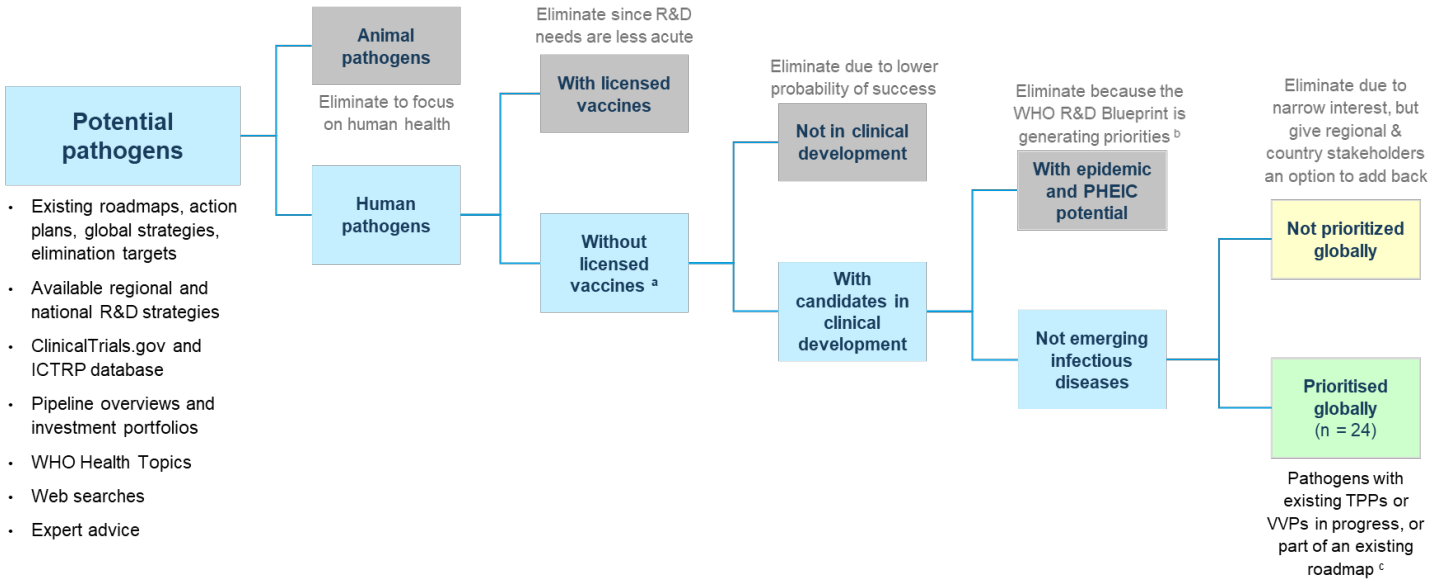
II. Report

A. Survey Preparation

1. Pathogen scope

The initial list of pathogens was compiled from a landscape of existing vaccine-related priorities identified in the published and gray literature. These included pathogens prioritized for vaccine R&D, or for research or surveillance at the global, regional or national level. Additional pathogens were identified by searching for vaccine trials on ClinicalTrials.gov[a] and the International Clinical Trials Registry Platform,[b] and from Health Topics on the WHO website,[20] an analysis of investments in global health research,[21] and Wikipedia.[22] A series of filters was applied to the pathogen list to reduce it to a more manageable number as shown in Figure 3.

Figure 3 Pathogen Filtering Scheme



a Pathogens where vaccines for new indications are needed were included.
b. PHEIC: Public health emergency of international concern. https://www.who.int/teams/blueprint/updating-the-WHO-list-of-pathogens-with-epidemic-and-PHEIC-potential
c. Roadmaps include *Vaccines to tackle drug resistant infections*, and *Roadmap for NTDs*
Abbreviations: ICTRP – International Clinical Trials Registry Platform. NTD – neglected tropical disease. TPP – target product profile. VVP – Vaccine Value proposition

Since this scope was originally presented to PDVAC in July 2022, the following changes have been made:

- **Excluded pathogens with potential for epidemics and public health emergencies of international concern**, such as SARS-CoV-1 and other pathogens addressed by the WHO R&D Blueprint project. These pathogens are difficult to compare to the other pathogens in our scope due to their emergent nature. In addition, the R&D Blueprint

[a] Search conducted on June 6, 2022 using the keyword "vaccine", and limited to phase 1, 2, and 3 trials. 7343 trials found.
[b] Search conducted on June 8, 2022 using the keyword "vaccine", and limited to phase 1, 2, and 3 trials. 6718 trials found.

project is currently engaged in a priority-setting exercise. Including these pathogens in both exercises risks causing confusion.

- **Excluded dengue and *Neisseria meningitidis* serogroup X.** Vaccines for these pathogens that fulfill critical target product attributes have recently been licensed, so they are no longer in the scope of this exercise.

The final pathogen scope is shown in Table 1. Two pathogens, Hepatitis C and *Chlamydia*, were inadvertently omitted and will be incorporated in advance of the regional consultations.

Table 1 Pathogen Scope

Chikungunya virus	*Mycobacterium leprae* (leprosy)
Cytomegalovirus	*Mycobacterium tuberculosis* (TB)
Extra-intestinal pathogenic *E. coli* (ExPEC)	*Neisseria gonorrhoeae*
Group A streptococcus (*Streptococcus pyogenes*)	Non-typhoidal *Salmonella*
Group B streptococcus (*Streptococcus agalactiae*)	Norovirus
Herpes simplex types 1 and 2	*Plasmodium falciparum* (malaria)
Hookworm	*Pseudomonas aeruginosa*
Human immunodeficiency virus 1 (HIV-1)	Respiratory syncytial virus
Influenza	*Salmonella* Paratyphi
Intestinal pathogenic *E. coli* (InPEC)	Schistosomes
Klebsiella pneumoniae	*Shigella*
Leishmania	*Staphylococcus aureus*

Note: Hepatitis C and Chlamydia will be added to the scope in advance of regional consultations

2. Expert advice

Interviews were conducted with experts in MCDA and prioritization to inform the approach. Experts were identified through literature review and interviewed in August and September 2022. Discussion topics included the proposed overall approach and stakeholder engagement, approaches to setting quantitative thresholds for MCDA criteria, definitions of qualitative criteria, and approaches for scoring pathogens against the criteria.

The list of experts and key messages from these discussions are given in Table 2. Additional detail is given in Annex A: Advice from experts in priority setting. Points relating to the design and implementation of Preferences Surveys have been addressed as described in this report.

Table 2 Expert advice on prioritization methods

Experts	
Rob Baltussen Radboud University Medical Center	**Prof. Lydia Kapiriri** McMaster University
Prof. Paul Hansen Otago University, co-founder of 1000minds	**Stacey Knobler** Sabin Vaccine Institute
Dr Maarten Jansen WHO, CAPACITI project manager	**Colin Sanderson** London School of Hygiene and Tropical Medicine
Prof. Mark Jit London School of Hygiene and Tropical Medicine, member of PDVAC	**Dr Yot Teerawattanon** Ministry of Public Health, Thailand, founder of the Health Intervention and Technology Assessment Program

Key Points

- Simplify language to reduce cognitive load on survey users.
- Consider the principles of fair processes, which include revisability, transparency, inclusion, and revisability.
- Be prepared to accept results that may not align with global perspectives and be prepared to explain to funders and developers why those results are important.
- Validity of the survey results will depend on who is surveyed, focus on identifying the right stakeholders.
- Disseminate the survey through additional channels, beyond WHO offices and ministries of health. Consider NITAGs, VACFA, APEC.
- Capture descriptive information on the respondents. This will allow us to expand data collection to fill gaps, weight based on respondent attributes, and explore differences in perspective.
- Instead of using disability-adjusted life years (DALYs) as a criterion, consider years of healthy life lost to disability (YLDs). YLD do not overlap with mortality, and statistics are available from the IHME GBD project.
- Document how pathogens are scored for each of the criteria, including who does the scoring, how they are scored, and how the scores are evaluated.
- In scoring, make the level of uncertainty more explicit. Define degrees, e.g. level inferred by data from another region / level based on minimal data from this region / level based on more data from this region.
- When data are lacking, it is ok to transparently infer levels. “That’s just how it is, if you don’t guess there is nothing.”
- Consider also taking a global perspective, for example by scoring pathogens globally rather than region-by-region.
- Sensitivity testing that focuses on criteria with the greatest weights and pathogens with most limited supporting data is reasonable.
- Regional consultations should adhere to best practices in revising priorities. For example, changes in pathogen scores should be evidence-based, and new criteria added should be non-overlapping with existing criteria.
- It will be important to give regional stakeholders an opportunity to add pathogens into the scope of prioritization. (This will be done in the regional consultations.)

3. Criteria definitions

Criteria for prioritization were developed by identifying potential criteria through a literature search, eliminating overlapping criteria, and consolidating criteria to reduce complexity and cognitive load on survey participants. Initial criteria were refined with feedback from PDVAC, experts in prioritization (including experts in MCDA), and pilot testers of the Preferences Surveys. This resulted in 8 criteria, as shown in Table 3. The qualitative criteria were further defined as shown in Table 7.

Table 3 Criteria

Criteria	Description	Scoring
1. Annual deaths in children under 5	Deaths attributable to the pathogen in both sexes, < 5 years old	Quantitative
2. Annual deaths in people 5 and older	Deaths attributable to the pathogen in both sexes, ≥ 5 years old	Quantitative
3. Years lived with disability (all ages)	Years of healthy life lost each year due to disability or ill-health caused by the pathogen	Quantitative
4. Social and economic burden per case	Reflects individual social and economic impact such as impact on education, stigma, and the costs of prevention, health care, and lost productivity. To avoid "double-counting" disease prevalence, this criterion is evaluated on a ***per case basis***	Qualitative
5. Disruption due to outbreaks	Reflects societal impact due to outbreaks, including social disruption, impact on healthcare, trade and tourism, and the cost of containment measures	Qualitative
6. Contribution to inequity	Reflects disproportionate impact on socially and economically disadvantaged groups, including women	Qualitative
7. Contribution to antimicrobial resistance (AMR)	Reflects the threat of resistance, based on current levels of resistance, contribution to antibiotic use, and designation as an AMR priority	Qualitative
8. Unmet needs for prevention and treatment	Reflects the effectiveness and suitability of alternative measures. Considers whether current measures are "deliverable" to those who need them but ***does not consider current levels of access***	Qualitative

4. Quantitative scoring

"Scoring" refers to assigning a pathogen to one of the five levels—from Very low to Very high—for each of the 8 criteria. All of the pathogens were scored on a region-by-region basis for each of the criteria. In addition, all of the pathogens were scored on a global basis using the same approach.

Criteria 1 – 3 were scored quantitatively using numeric thresholds for each measure and region. The thresholds were calculated as follows:

- **Assemble data**. For pathogens included in the Global Burden of Diseases (GBD) Project, region-specific and global values for 2019 from were downloaded from https://vizhub.healthdata.org/gbd-results/. For pathogens not included in that dataset but included in the Global Bacterial Antimicrobial Resistance Burden Estimates 2019 (https://ghdx.healthdata.org/record/ihme-data/global-bacterial-antimicrobial-resistance-burden-estimates-2019), data for 2019 summed by WHO region were obtained directly from IHME. Together, these datasets give burden estimates for most of the pathogens in the scope of this exercise. (Gaps were addressed as discussed below.) ***Because these values were calculated for 2019, the effects of the COVID-19 pandemic are not captured in this dataset.***
- **Calculate specific measures as needed**. In many instances, the GBD dataset did not include the specific age bands required for this project. In those cases, the required figures were calculated from the data available (e.g. deaths in people over 5 was calculated by subtracting deaths in children under 5 from all ages deaths). In addition, the AMR dataset did not include YLD values. YLDs were calculated by subtracting Years of Life Lost (YLLs) from DALYs.
- **Identify the working range**. For the purposes of calculating thresholds, HIV, Tuberculosis, and Malaria were excluded from the dataset to enable greater discrimination among lower-burden pathogens.
- **Divide the working range into five equal parts**. Resulting thresholds are shown in Table 4. (While two significant figures are shown in the table, thresholds were calculated and applied with the full precision available in the source data.)

These thresholds were used to score all pathogens for Criteria 1 – 3 as shown in the regional and pathogen summaries. For simplicity, these summaries give only the scores and point estimates. An excel worksheet showing calculations and uncertainty intervals is available upon request.

Table 4 Quantitative thresholds

WHO Region	Criteria	Thresholds				
		Very low	Low	Medium	High	Very high
African	1 Annual deaths in children under 5	<22,000	22,000-44,000	44,000-66,000	66,000-88,000	>88,000
	2 Annual deaths in people 5 and older	<20,000	20,000-41,000	41,000-61,000	61,000-81,000	>81,000
	3 Annual years lived with disability (all ages)	<190,000	190,000-390,000	390,000-580,000	580,000-780,000	>780,000

WHO Region	Criteria	Thresholds				
		Very low	Low	Medium	High	Very high
Americas	1 Annual deaths in children under 5	<1,500	1,500-3,000	3,000-4,500	4,500-6,100	>6,100
	2 Annual deaths in people 5 and older	<37,000	37,000-74,000	74,000-110,000	110,000-150,000	>150,000
	3 Annual years lived with disability (all ages)	<59,000	59,000-120,000	120,000-180,000	180,000-230,000	>230,000
E. Med.	1 Annual deaths in children under 5	<6,700	6,700-13,000	13,000-20,000	20,000-27,000	>27,000
	2 Annual deaths in people 5 and older	<15,000	15,000-29,000	29,000-44,000	44,000-58,000	>58,000
	3 Annual years lived with disability (all ages)	<54,000	54,000-110,000	110,000-160,000	160,000-220,000	>220,000
European	1 Annual deaths in children under 5	<680	680-1,400	1,400-2,000	2,000-2,700	>2,700
	2 Annual deaths in people 5 and older	<40,000	40,000-79,000	79,000-120,000	120,000-160,000	>160,000
	3 Annual years lived with disability (all ages)	<25,000	25,000-50,000	50,000-75,000	75,000-100,000	>100,000
SE Asian	1 Annual deaths in children under 5	<8,600	8,600-17,000	17,000-26,000	26,000-35,000	>35,000
	2 Annual deaths in people 5 and older	<37,000	37,000-74,000	74,000-110,000	110,000-150,000	>150,000
	3 Annual years lived with disability (all ages)	<130,000	130,000-260,000	260,000-390,000	390,000-520,000	>520,000
W. Pacific	1 Annual deaths in children under 5	<1,500	1,500-3,100	3,100-4,600	4,600-6,100	>6,100
	2 Annual deaths in people 5 and older	<49,000	49,000-99,000	99,000-150,000	150,000-200,000	>200,000
	3 Annual years lived with disability (all ages)	<83,000	83,000-170,000	170,000-250,000	250,000-330,000	>330,000
Global	1 Annual deaths in children under 5	<41,000	41,000-82,000	82,000-120,000	120,000-160,000	>160,000
	2 Annual deaths in people 5 and older	<190,000	190,000-380,000	380,000-570,000	570,000-760,000	>760,000
	3 Annual years lived with disability (all ages)	<450,000	450,000-910,000	910,000-1,400,000	1,400,000-1,800,000	>1,800,000

Additional calculations and data sources beyond GBD results were used to estimate measures that are not found in the GBD datasets, complement GBD results, and inform sensitivity testing. These cases are shown in Table 5. More detail on these additional calculations and data sources can be found in Annex D: Pathogen Summaries.

Table 5 Additional calculations and data sources

Pathogen	Available data	Calculations
Chikungunya virus	Not included in GBD 2019. YLDs and Deaths (all ages) from Puntasecca et al, 2021	**YLDs:** use values as reported by Puntasecca et al. **Deaths:** Use values reported by Puntasecca et al. Because median age of onset is 40 years and median age of death is 60 years, assume all deaths occur in people 5 and over
Cytomegalovirus (CMV)	Not included in GBD 2019. Congenital CMV Mortality in the US, Bristow et al 2011 Congenital CMV mortality in South Africa, Diar and Velaphi, 2014 CMV-related childhood mortality in Australia, Smithers-Sheedy 2015	**Deaths in children under 5:** Use available incidence and mortality rates to generate high and low estimates as discussed in Section III.D.2 **Deaths in people 5 and older:** score as Low. In sensitivity testing, evaluate Very low and Medium. **YLDs:** score as Low or Medium, depending on the regional context. In sensitivity testing, evaluate lower and higher scores
Extra-intestinal pathogenic *E. coli* (ExPEC)	GBD 2019 Anti-microbial resistance dataset	**Deaths and YLDs** are the totals of antibiotic resistant and susceptible forms of *E. coli*, for all of the non-diarrheal presentations included in the dataset
Group A streptococcus (GAS, *Streptococcus agalactiae*)	GBD 2019 Cause of Death dataset gives deaths and YLDs for rheumatic heart disease (RHD) GBD 2019 Anti-microbial resistance dataset give deaths and YLDs for Group A streptococcus	Calculate the total burden of GAS by summing the two measures
Herpes simplex type 1 and type 2	GBD 2019 includes YLDs but not deaths	**Deaths in children under 5:** Use available neonatal herpes incidence and case fatality rates to estimate annual deaths, as discussed in Section III.D.6. **Deaths in people 5 and older:** score as Very low. In sensitivity testing, evaluate Low.
Hookworm and *Mycobacterium leprae* (Leprosy)	GBD 2019 includes YLDs but not deaths	Score **deaths** in both age groups as Very low. In sensitivity testing, evaluate Low.

Pathogen	Available data	Calculations
Mycobacterium tuberculosis (TB)	GBD 2019 includes YLDs and Deaths for TB The Global Tuberculosis Report[a] has also estimated TB deaths on a regional basis	Use values from the Global Tuberculosis Report in the Preferences Survey. Conduct sensitivity testing for scores that differ between the two sources. For details, see Section III.D.14.
Non-typhoidal *Salmonella* (NTS)	GBD 2019 Cause of Death dataset gives deaths and YLDs for Invasive Non-typhoidal *Salmonella* (iNTS) GBD 2019 Etiology dataset give deaths and YLDs for non-typhoidal *Salmonella*	As recommended by IHME, calculate total NTS by summing the two measures
Plasmodium falciparum (malaria)	GBD 2019 includes YLDs and Deaths for malaria (not species-specific) World Malaria Report 2021 includes % *P. vivax* cases by WHO region	Estimate maximum and minimum potential Deaths and YLDs based on GBD 2019 data and % *P. vivax* **Max**: assume that all malaria deaths are *P. falciparum* **Min**: scale back the estimate by the % of *P. vivax* cases per region

For transparency, scores were coded to indicate the level of data available as shown in Table 6.

Table 6 Coding for quantitative data availability

A: Burden data from GBD 2019 or AMR dataset
B: Burden calculated by other studies
C: Data not available or gap-filling estimates have been made.

[a] https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022

5. Qualitative scoring

a) Detailed definitions for each level

Criteria 4 – 8 were scored qualitatively. For these criteria, definitions of each level were developed with advice from experts in MCDA and refined during the scoring process. As shown in Table 7, some definitions include sub-criteria that give more detail on issues to consider in scoring each pathogen.

Table 7 Qualitative Levels

Criteria / *Sub-criteria*	**Very low**	**Low**	**Medium**	**High**	**Very high**
4 Social and economic burden per case	Very low burden for each case	Low burden for each case	Moderate burden for each case	High burden for each case	Very high burden for each case
4.1 Economic burden per case	*Very low cost to treat, rarely leads to hospitalization* *Little or no losses of productivity*	*Low cost to treat, seldom requires hospitalization* *Minor losses of productivity*	*Moderate cost to treat or sometimes requires hospitalization* *Some losses of productivity*	*High cost to treat or often requires hospitalization* *Moderate losses of productivity*	*Very high cost to treat or typically requires hospitalization* *Serious losses of productivity*
4.2 Social burden per case	*Little or no impact on education or social well-being (e.g due to stigma)*	*Minor impact on education or social well-being (e.g due to stigma)*	*Some impact on education or social well-being (e.g due to stigma)*	*Moderate impact on education or social well-being (e.g due to stigma)*	*Serious impact on education or social well-being (e.g due to stigma)*
5 Disruption due to outbreaks	Little or no social disruption or impact on healthcare, trade or tourism	Slight social disruption or impact on healthcare, trade or tourism	Moderate social disruption or impact on healthcare, trade or tourism	High social disruption or impact on healthcare, trade or tourism, including due to preventive measures	Very high social disruption or impact on healthcare, trade and tourism, including due to preventive measures
6 Contribution to inequity	Affects all communities equally	Burden falls on socially and economically disadvantaged groups, including women, **slightly** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, **moderately** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, **much** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, all or most of the time

Criteria / *Sub-criteria*	Very low	Low	Medium	High	Very high
7 Contribution to antimicrobial resistance (AMR)	Not resistant to first-line drugs and not associated with antibiotic use	Little resistance to first-line drugs and little association with antibiotic use	Some resistance to first-line drugs, associated with high antibiotic use	Significant resistance to first-line drugs, associated with high antibiotic use	A global resistance threat due to widespread resistance and association with high antibiotic use
7.1 AMR Priority	*The pathogen has not been highlighted as a priority for AMR*	*The pathogen has not been highlighted as a priority for AMR*	*The pathogen has been highlighted as a country priority for AMR*	*The pathogen has been highlighted as a regional priority for AMR*	*The pathogen has been highlighted as a critical or high global priority for AMR*
7.2 Frequency of resistance	*Very few isolates are resistant to first-line antimicrobial drugs*	*A low proportion of isolates is resistant to first-line antimicrobial drugs*	*A moderate proportion of isolates is resistant to first-line antimicrobial drugs*	*A high proportion of isolates is resistant to first-line antimicrobial drugs*	*A high proportion of global isolates is resistant to first-line antimicrobial drugs*
7.3 Antibiotic use	*Low antibiotic ANTIMICROBIAL use is associated with infection by the pathogen*	*Moderate or low antibiotic use is associated with infection by the pathogen*	*High antibiotic use is associated with infection by the pathogen*	*High antibiotic use is associated with infection by the pathogen*	*High antibiotic use is associated with infection by the pathogen*
8 Unmet needs for prevention and treatment	The alternatives for prevention or treatment meet the needs of most people	The alternatives for prevention or treatment meet the needs of many people	The alternatives for prevention or treatment meet the needs of some people	The alternatives for prevention or treatment meet the needs of few people	There are no effective alternatives for prevention or treatment

b) Initial scoring by 3 analysts

To make efficient use of expert time, 3 analysts compiled data on the pathogens and proposed scores for the qualitative criteria. The analysts were:

- **Angela Hwang**, Principal consultant, Angela Hwang Consulting. Bio at: ahwang.net/about
- **Anastasia Pantelias**, Associate Partner, Bridges to Development. Bio at: bridgestodevelopment.org/who-we-are
- **Maria Dreher**, student in Infectious Diseases, London School of Hygiene and Tropical Medicine. Bio at: www.linkedin.com/in/maria-victoria-dreher-wentz/

Data were compiled from PubMed queries and internet searches in English to inform the scoring. To give a more balanced picture, PubMed queries focused on systematic reviews. In addition, WHO has commissioned Vaccine Value Profiles (VVPs) for many of these pathogens.[a] VVPs, developed by groups of subject matter experts, provide a holistic,

[a] The pathogens in scope that do not have VVP are: *Staph. Aureus*, ExPEC, Group A strep., *P. aeruginosa*, and *M. leprae*.

high-level assessment of the information that is currently available to inform value assessments for vaccines under development. When available, VVPs were used as key sources for pathogen scoring. The VVPs are undergoing peer-review and will be published as a supplement in the journal *Vaccine* in the coming months.

Using the definitions in Table 7, each analyst independently scored all pathogens on a region-by-region basis and from a global perspective. Differences among their scores were discussed to arrive at consensus scores among the three analysts. Initial scores were summarized by pathogen and by region using the format shown in Annex D: Pathogen Summaries and Annex E: Regional Summaries.

Varying levels of data were found. For transparency, scores were coded as shown in Table 8 to indicate the level of data available.

Table 8 Coding for qualitative data availability

Qualitative scoring
A: Based on data from regional sources
B: Score inferred based on sources from other regions or pathogens

6. Review of scoring by disease and regional experts

Each Regional Summary was reviewed by at least two regional experts and each Pathogen Summary was reviewed by at least one pathogen expert, as shown in Table 9. (Also see Annex B: Instructions to reviewers) Declarations of interests were collected from all non-WHO reviewers and assessed for any conflicts of interest. Any conflicts of interest were managed according to WHO's policies and procedures. (See Annex C: Declarations of Interest for relevant interests.)

Table 9 Expert review of pathogen scores

Region	**Reviewers**
African Region	• **KP Asante**, Kintampo Health Research Centre • **Michelle Groome**, National Institute for Communicable Diseases, A Division of the National Health Laboratory Service, South Africa • **Helen Rees**, Wits Reproductive Health and HIV Research Institute
Region of the Americas	• **Peter Figueroa**, University of the West Indies • **Cristiana Toscano**, Federal University of Goiás
Eastern Mediterranean	• **Ahmed Deemas Al Suwaidi**, Department of Pediatrics, College of Medicine and Health Sciences - United Arab Emirates University • **Ghassan Dbaibo**, American University of Beirut
European	• **Helena Hervius Askling**, Karolinska Institutet • **Anh Wartel**, International Vaccine Institute
South-East Asian	• **Kawser Choudhury**, Samorita Hospital Panthapath, Dhanmondi, Dhaka • **Sonali Kochhar**, University of Washington

Region	Reviewers
Western Pacific	• **David Durrheim**, University of Newcastle, Australia • **Kim Mulholland**, Murdoch Children's Research Institute
Global	• **Birgitte Giersing**, World Health Organization • **Kathleen Neuzil**, University of Maryland School of Medicine Center for Vaccine Development and Global Health

Pathogen	Reviewers
Chikungunya virus	• **Diana Rojas Alvarez**, World Health Organization • **Alan Barrett**, University of Texas Medical Branch
Cytomegalovirus	• **Hannah Clapham**, Saw Swee Hock School of Public Health, National University of Singapore
Extra-intestinal pathogenic *E. coli* (ExPEC)	• **Lou Bourgeois**, PATH
Group A streptococcus	• **Andrew Steer**, Murdoch Children's Research Institute • **Jeffrey Cannon**, Telethon Kids Institute and University of Western Australia
Group B streptococcus	• **Kirsty Le Doare**, St George's University
Herpes simplex virus (Types 1 and 2	• **Katharine Looker**, Population Health Sciences, Bristol Medical School, University of Bristol
HIV-1	• **Pat Fast**, IAVI
Hookworm	• **Julie Jacobson**, Bridges to Development
Influenza	• **Chris Chadwick**, World Health Organization
Intestinal pathogenic *E. coli* (InPEC)	• **Lou Bourgeois**, PATH
Klebsiella pneumoniae	• **Alan Cross**, Center for Vaccine Development and Global Health, U. of Maryland School of Medicine
Leishmania	• **Paul Kaye**, University of York
Mycobacterium leprae	• **Julie Jacobson**, Bridges to Development
Mycobacterium tuberculosis	• **Nebiat GEBRESELASSIE**, World Health Organization
Neisseria gonorrhoeae	• **Winston Abara**, US Centers for Disease Control and Prevention
Non-typhoidal *Salmonella*	• **Calman MacLennan**, Bill & Melinda Gates Foundation
Norovirus	• **Ben LOPMAN**, Department of Epidemiology, Rollins School of Public Health Emory University
Plasmodium falciparum	• **Muhammed Afolabi**, London School of Hygiene and Tropical Medicine • **Patricia Njuguna**, PATH
Pseudomonas aeruginosa	• **Alan Cross**, Center for Vaccine Development and Global Health, U. of Maryland School of Medicine

Pathogen	Reviewers
Respiratory syncytial virus	• **Harish Nair**, Centre for Global Health at The University of Edinburgh • **Ruth Karron**, Johns Hopkins Bloomberg School of Public Health
Salmonella Paratyphi	• **Calman MacLennan**, Bill & Melinda Gates Foundation
Schistosomes	• **Amadou Garba**, World Health Organization
Shigella	• **Bill Hausdorff**, PATH
Staphylococcus aureus	• **Jean C. Lee**, Harvard Medical School

7. Final scores

Due to time constraints, pathogen and regional reviews proceeded in parallel and it was not possible to conduct a consensus-building process. Instead, reviewer feedback was synthesized and final scores were agreed-upon by the IVB project team. These decisions prioritized the perspectives of regional reviewers and considered consistency across pathogens and regions. Final scores for each pathogen are given in Annex D: Pathogen Summaries and Annex E: Regional Summaries.

8. Survey preparation and dissemination

Surveys were built using PAPRIKA, proprietary decision-making software from 1000minds (1000minds.com). Regional surveys were prepared in multiple languages to enable completion by a greater diversity of stakeholders, as shown in Figure 4. English versions of the surveys were pilot tested by team members and colleagues. Survey translations were reviewed by native speakers familiar with the subject matter.

Figure 4 Survey Versions

Survey	English	Portuguese	French	Spanish	Arabic	Russian
African	■	■	■			
Americas	■	■		■		
E. Mediterranean	■		■		■	
European	■	■	■	■		■
South-East Asian	■	■				
Western Pacific	■		■			
Global	■					

Pathogen lists and final scores for each region were also translated and uploaded into the surveys. All surveys were reviewed in detail before publication and launch. As of mid-November, invitation letters from WHO with links to the surveys are being disseminated as shown in Table 10. The surveys will remain open until December 16, 2022.

Table 10 Preferences Survey Dissemination Channels

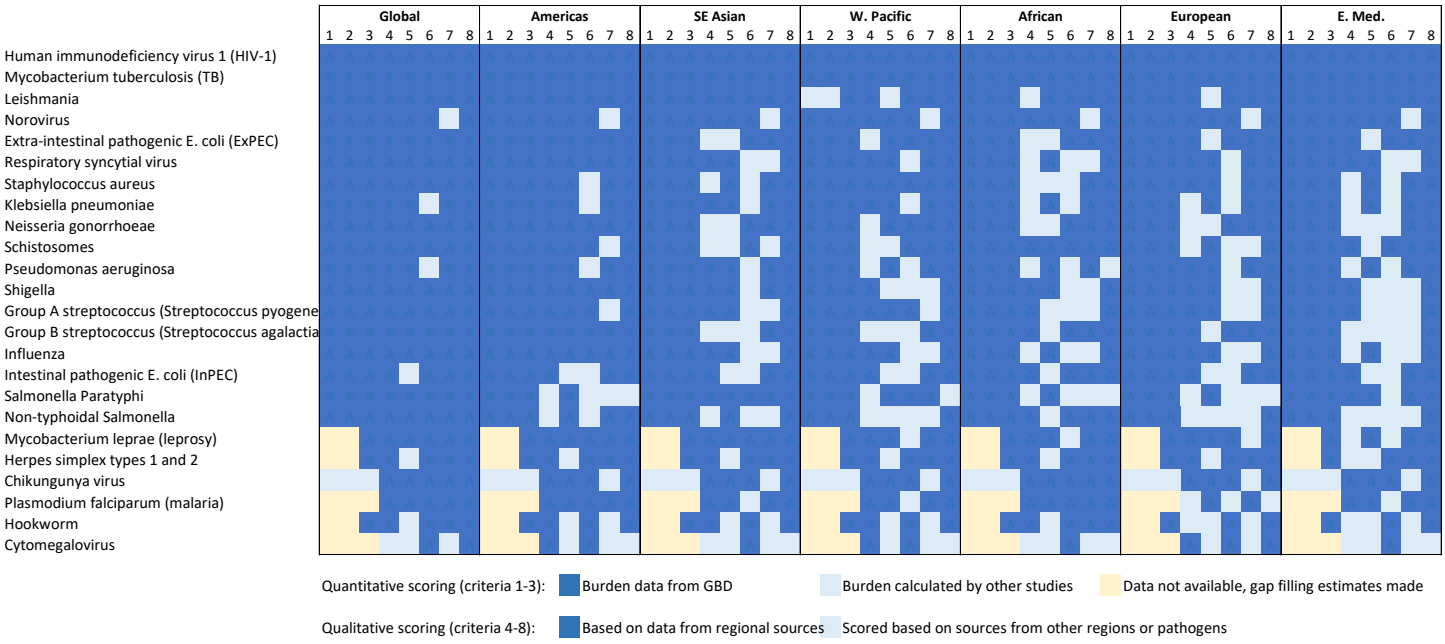
Surveys	Dissemination Channels (as of November 2022)
Regional	• WHO Regional Advisors for Immunization – invited to participate and send onward to country experts • RITAG Chairs – invited to participate and send onward to RITAG members • Global NITAG Network members – invited to participate • AFRO Science and Technology Cluster – invited to participate and send to colleagues • African CDC and Partnerships for African Vaccine Manufacturing – invited to participate and send to colleagues
Global	• Developing Country Vaccine Manufacturers Network (DCVMN) – sending onward to member companies • International Federation of Pharmaceutical Manufacturers Associations (IFPMA) – sending onward to member companies • PDVAC members, SP7 Working Group members, and WHO Immunization, Vaccines, and Biologicals staff invited to participate

B. Pathogen Scoring Results

1. Data availability

Figure 5 gives an overview of the data used to score each combination of pathogen, region, and criterion. Data were most readily found for the Americas, and most difficult to find for the Eastern Mediterranean region. Cytomegalovirus and hookworm had the most gaps in data for scoring. *Plasmodium falciparum* had many data gaps because much of the available literature does not distinguish between *P. falciparum* and other species of malaria parasites.

Figure 5 Data Availability for Pathogen Scoring

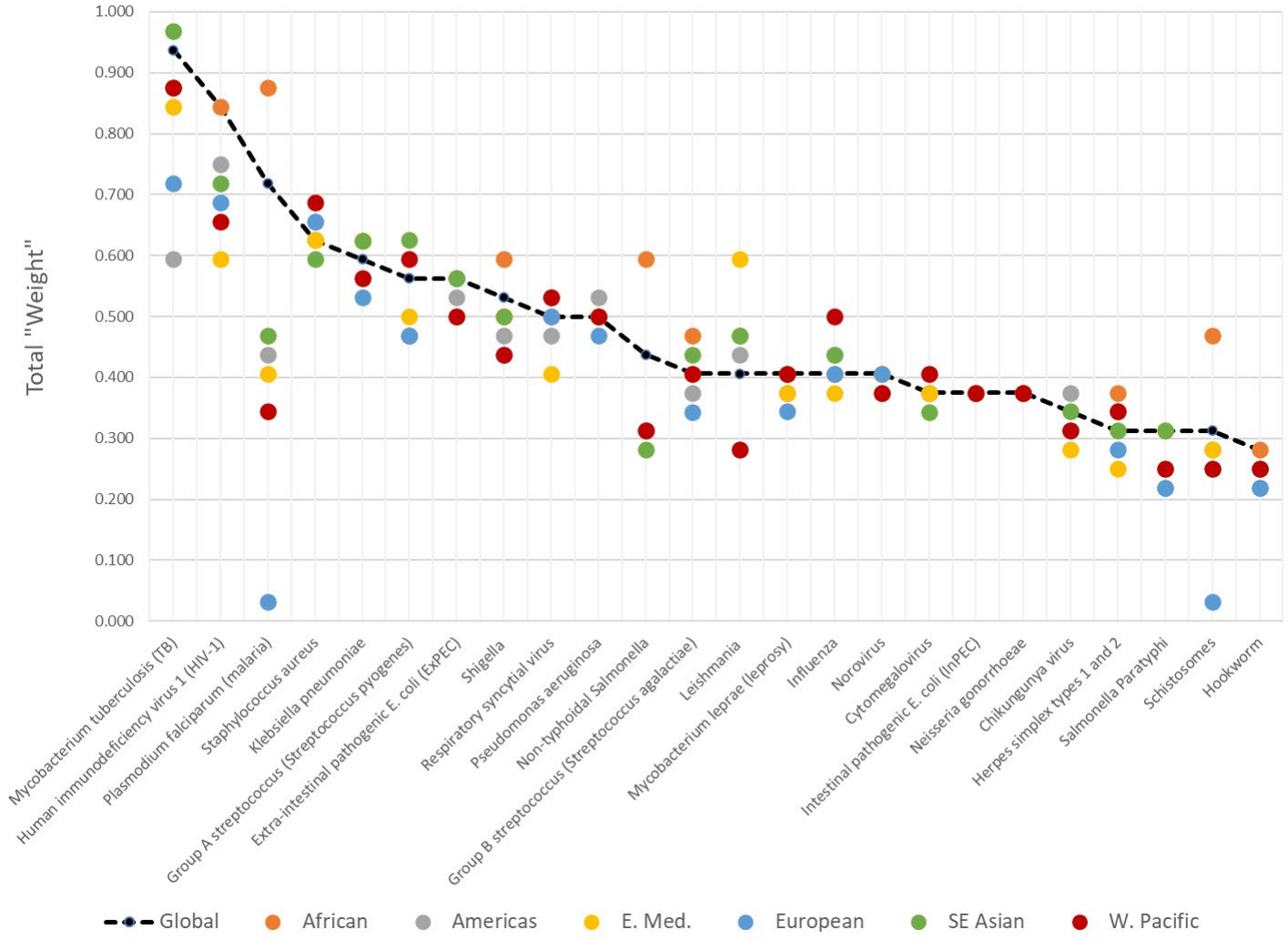


2. Pathogen scores

Final scores for each pathogen are given in Annex D: Pathogen Summaries and Annex E: Regional Summaries.

The Preferences Surveys are now collecting data on the relative importance of each of the 8 criteria in the eyes of regional and country stakeholders. In the meantime, by assuming that ***all criteria have equal weight***, it is possible to understand the starting point—or base case—for their prioritization. These results are shown in Figure 6.

Figure 6 "Base Case" pathogen weights



In this figure, total "weights" are calculated for each pathogen and each region using default weights assigned by PAPRIKA. (For each Very high: 0.125, for each High: 0.094, for each Medium: 0.063, for each Low: 0.031, and for each Very low: 0, across all 8 criteria.) Pathogens are listed from high to low weight based on their global scores and colored dots show their weights for each region.

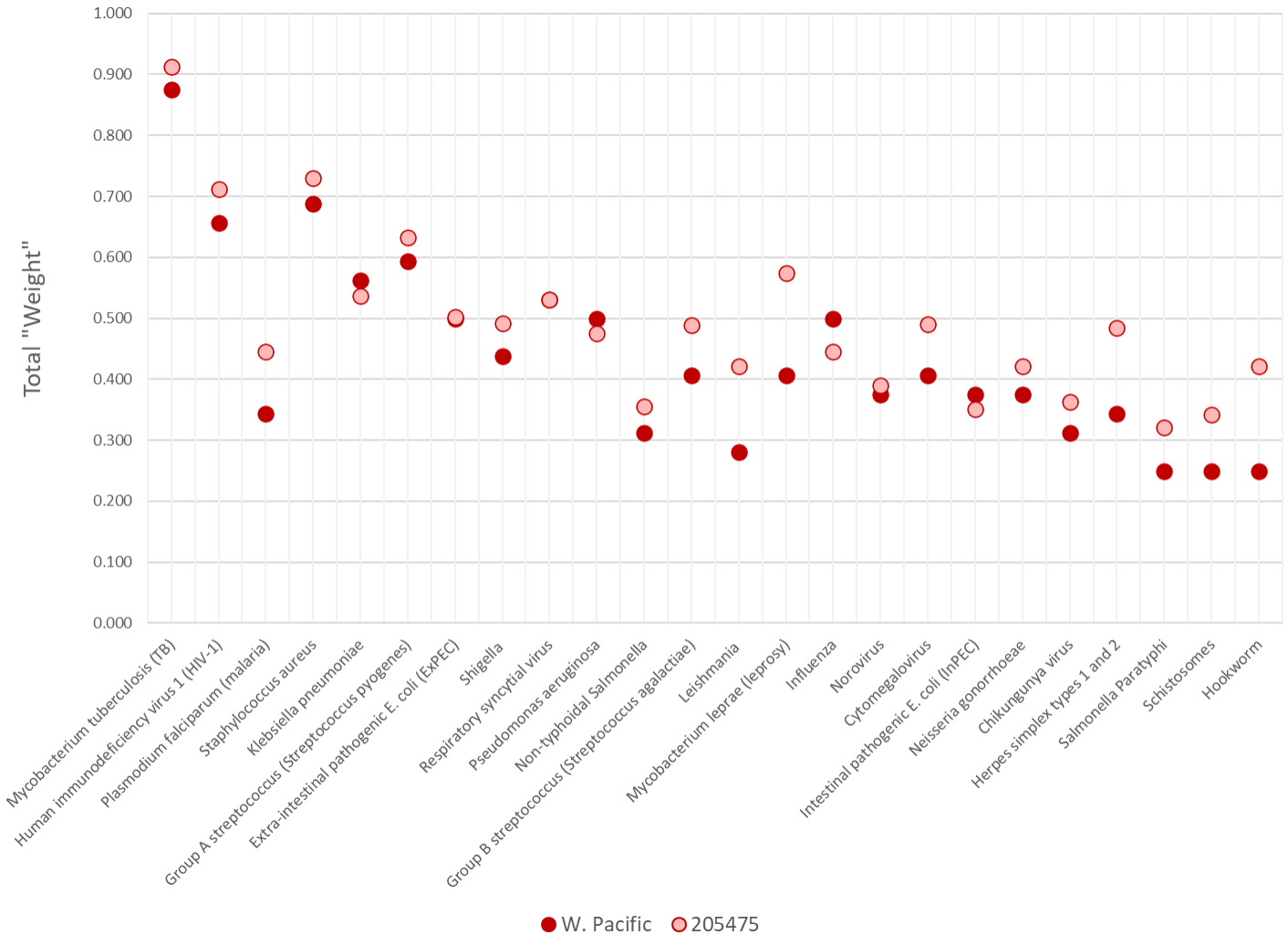
Globally and across regions, *Mycobacterium tuberculosis* was among the most heavily weighted, scoring Very high for most criteria in most regions. Conversely, hookworm generally had the lowest weight, scoring Very low or Low for most criteria in most regions. For a given pathogen, diversity in total weight reflects diversity in scores across regions. For example, both *P. falciparum* and schistosomes have very low prevalence in the European region, and therefore had lower scores and were less heavily weighted in that region.

PAPRIKA results from each region will replace the default weights with values that reflect the perspectives of survey respondents. This will shift these results so that they reflect regional and country perspectives, not just pathogen scores.

Figure 7 illustrates this effect. For each pathogen, it compares the base case weights in the Western Pacific region with results from a single survey respondent from that region. Because this person's most heavily weighted (i.e. most

important) criterion was *Contribution to inequity*, highly inequitable pathogens such as *Mycobacterium leprae* and hookworm have greater total weight (i.e. greater priority) for this person than in the base case.

Figure 7 Example: Individual response from the Western Pacific



See Annex F: Additional Data Analysis for more results from the pathogen scoring. Full analysis of criteria and pathogen weights by region will be conducted after the close of the Preferences Surveys on December 16, 2022.

3. Lessons learned from pathogen scoring

From the scoring and review process, several lessons have emerged:

- **Highlight the context**. For feasibility, this process is addressing the narrow question of priorities for new vaccine R&D and setting aside important issues such as ways to improve introduction and coverage of existing vaccines. Acknowledging such limitations and providing information on the other ways those concerns are being addressed can help stakeholders understand how this prioritization fits into the greater context of immunization research and innovation. Within this process, the Preferences Surveys are the first step, and will inform regional stakeholder consultations to finalize the pathogen prioritization. These consultations will also incorporate considerations such as the probability of success and market attractiveness for new vaccines, which were too complex to include in the surveys. Contextualizing the surveys helps prepare for the consultations and strengthens understanding of the overall approach.
- **"Right-size" the scoring effort**. n conducting literature searches and scoring the pathogens, it is important to strike the right balance between rigor and practicality. For example, some practices that are essential to evidence-informed policy making (such as assessing the quality of the evidence) were not as relevant to this project, which is intended to inform product development.
- **Improve understanding of GBD data**. GBD data were used to score 3 out of the 8 criteria and will therefore play an important role in the results of the Preferences Surveys. Awareness of GBD results and understanding of GBD methods varied across reviewers, and some expressed surprise about certain GBD estimates. Because of the importance of GBD data in priority setting, it is essential to continue improving the evidence base for GBD estimates, the quality of GBD data, the broader understanding of GBD methods, and understanding of the level of standardization in burden estimation methods from pathogen to pathogen.
- **Take a more structured approach to qualitative scoring**. The considerations in Table 7 were a useful guide but could be improved in future prioritizations. The list of considerations could be more complete and include numeric thresholds rather than descriptions such as "all or most of the time". Guidance could be provided on how to score pathogens such as non-Typhoidal *Salmonella* with multiple disease presentations that differ in incidence and severity. Guidance could also be provided on how to address data gaps and heterogeneity within WHO regions.
- **Increase engagement of regional experts**. Vaccine value profiles based on extensive literature reviews were developed by groups of subject matter experts for the majority of pathogens included in the prioritization exercise. These served as sources for the scoring exercise. However, greater consultation with regional experts would have enabled more rigorous and context-specific scoring.

C. Acknowledgments

This project has benefitted from timely and helpful contributions by many stakeholders, including:

- SP7 Working Group Chairs, KP Asante and David Kaslow, for sponsorship and advice.
- Regional Immunization Technical Advisory Group chairs who advised on the design of this prioritization approach and the regional engagement model.
- WHO Regional Advisors for Immunization, for advice and support on regional and country engagement.
- The regional and disease experts who reviewed pathogen scoring. These experts are listed in Table 9.
- MCDA experts who advised on the methodology. These experts are listed in Table 2.
- Mohsen Naghavi, Kelly Bienhoff, and Eve Wool of the Institute for Health Metrics and Evaluation (IHME) for data and advice on pathogen burden.
- Colleagues who reviewed translated versions of the Preferences Surveys:
    - Arabic: Bader Al Rawahi (Ministry of Health, Oman), Dina Youssef, and Ibrahim Khalil
    - French: Megan Williamson
    - Spanish: Enric Jané
    - Portuguese: Ana Paula Szylovec
    - Russian: Irina Morozova
- Technical support from Paul Hansen and colleagues at 1000minds, the creators of the PAPRIKA MCDA survey tool.

The project team consists of:

- WHO Immunization, Vaccines and Biologicals
    - Team lead: Birgitte Giersing
    - Contributors: Mateusz Hasso-Agopsowicz and Erin Sparrow
- Bridges to Development
    - Team lead: Angela Hwang
    - Contributors: Ísis Umbelino, Anastasia Pantelias, Maria Dreher
    - Managing partner: Alan Brooks

III. Annexes

A. Annex A: Advice from experts in priority setting

A series of interviews was conducted with experts in MCDA and prioritization methods (Table 2). Key points from these discussions are given in Figure 8. Points relating to the design and implementation of Preferences Surveys have been addressed as described in this report.

Figure 8 Advice from experts in priority setting

Prioritization process, including survey design	Seek advice on methodology from experts in priority-setting, not just MCDA experts. Consider the principles of fair processes, which include revisability, transparency, inclusion, and revisability. Most people find five levels per criterion intuitive and easy to use. Simplify labels and descriptions to reduce cognitive load on users. Test the survey before deployment to ensure clarity. The "think aloud" method can be helpful in user testing. After each survey, ask the user about the face validity of criteria weights. The more responses the better. Fewer than 30 responses could be seen as problematic, 100 responses could be reported on. The uncertainty ranges generated by the 1000minds tool could give useful information. The 1000minds tools are very easy to adapt and use and can even be used in a consensus-building exercise in the regional consultations.
Criteria	Need to ensure that the criteria make sense to the people completing the Preferences Survey. Instead of using disability-adjusted life years (DALYs) as a criterion, consider years of healthy life lost to disability (YLDs). YLD do not overlap with mortality, and statistics are available from the IHME GBD project. YLD do overlap with the morbidity criterion, which could be eliminated. The qualitative criteria include properties that could theoretically be measured, but for which we do not have data, consider another label. Criteria do not fully capture the social impacts of disease, such as effects on education and social welfare. This could be incorporated in the Economic burden criterion. Economic burden should also consider the societal perspective, such as impacts on tourism, trade, etc. As a guide to scoring, can call out factors that drive economic burden such as requiring hospitalization or causing loss of work. Regarding current alternatives for prevention and treatment, consider clarifying the question about access to existing interventions: does this refer to access today, or to the potential benefit of increased access?

	Criteria should have clear operating definitions. Depending on their background, experts may interpret vaccine R&D as including more (or less) basic research. While economic burden is more relevant to this prioritization, some decision-makers are more focused on financial burden, which has greater impact on national budgets. The Equity criterion should range from equal effects on all to negatively affecting disadvantaged groups all or most of the time. It should not have an "affects privileged groups" level. This should consider how the burden is distributed, while the Economic/social burden criterion considers the scale of the burden.
Quantitative thresholds	Setting quantitative thresholds on an exponential scale (such that each level is N-fold higher in burden than the previous) reflects common thinking but raises ethical questions because it values lives less as burden increases. Consider alternative approaches that value lives more equally. The best approach for setting quantitative thresholds (linear or exponential) bears more thinking. The difficulty in deciding which method to use illustrates the value of having multiple criteria—no single statistic can adequately distinguish between pathogens. For quantitative thresholds, "don't judge, be transparent and observe". For example, to decide whether to use linear or exponential thresholds, can design a consensus-finding process with 3 groups (linear, exponential, and no numbers) who complete the survey, then compare and discuss results. For quantitative criteria, linear thresholds are good because they • Are consistent with perspectives of vaccine developers and implementers, since vaccine markets and program costs rise linearly • Are neutral, and do not superimpose a set of expectations on the data For quantitative criteria, it is more important that the scoring be useful and relevant to policy makers than for the thresholds to be set objectively or systematically.
Pathogen scope	In defining the pathogen scope, the distinction between Group A and Group B pathogens is based on existing global priorities. Because of that, it will be important to give regional stakeholders an opportunity to add Group B pathogens into the scope of prioritization. (This will be possible in the regional consultations but is not feasible in the Preferences Survey.)
Scoring pathogens	For legitimacy, also document how pathogens are scored for each of the criteria, including who does the scoring, how they are scored, and how the scores are evaluated. In scoring, make the level of uncertainty more explicit. Define degrees, e.g. level inferred by data from another region / level based on minimal data from this region / level based on more data from this region. When data are lacking, it is ok to transparently infer levels. "That's just how it is, if you don't guess there is nothing." WHO regions include great diversity in geography, health infrastructure, and socioeconomic indicators. Consider alternative country groupings. Consider also taking a global perspective, for example by scoring pathogens globally rather than region-by-region. Consider giving examples in pathogen scoring worksheets to improve consistency. Regional experts who are scoring pathogens will benefit from brief descriptions of the pathogen. These descriptions will also be helpful for survey participants.

Survey participants	Validity of the survey results will depend on who is surveyed, focus on identifying the right stakeholders. Disseminate the survey through additional channels, beyond WHO offices and ministries of health. Consider NITAGs, VACFA, APEC. Broadcasting the survey, while easier administratively, creates the potential for bias. Asking regional and country focal points to identify people to invite to complete the survey would likely lead to more balanced results. Can consider taking both approaches in parallel. Don't "protect" countries from participating in this kind of exercise, thinking that they are too busy to engage. Invite them to participate and let them decide whether it is worth their time. If engagement is low, proceed transparently with the input we receive, and use initial results to build credibility and momentum for future efforts. It will be important to capture descriptive information on the respondents. This will allow us to expand data collection to fill gaps, weight based on respondent attributes, and explore differences in perspective.
Data analysis	Sensitivity testing that focuses on criteria with the greatest weights and pathogens with most limited supporting data is a reasonable approach. Cluster analysis can be used to identify similarities in how users weight criteria and interactions between criteria.
Regional consultations	Regional consultations will give feedback on both the survey method and the results. They will not be able to advise on criteria in advance of the survey, given practical limitations, but can give feedback on the criteria for future prioritization efforts. Can conduct regional consultations with partners outside the WHO system, such as the African Academy of Sciences. These could be in addition to or in place of the NITAG-led consultations. COVID-19 has led to new efforts to build regional capacity for vaccine R&D. This evolving ecosystem will have more interest in "priorities that are owned by the people they impact" than the previous, centralized system driven by high-income country markets. Connect with regional organizations such as AU, ECOWAS, and NEPAD who have an interest in advancing regional capacity. Regional consultations should adhere to best practices in revising priorities. For example, changes in pathogen scores should be evidence-based, and new criteria added should be non-overlapping with existing criteria. Document inclusion/exclusion criteria for who participates in regional consultations and assess representativeness based on those criteria. Be prepared to accept results that may not align with global perspectives and be prepared to explain to funders and developers why those results are important. If consultations are not possible before our deadlines, be explicit about this as a limitation.

R&D Blueprint priority-setting	The R&D Blueprint (RDB) prioritization effort is considering what viral families should be prioritised for R&D based on their potential to contribute to public health emergencies. They are conducting an evidence-based global consultative process with regional representation. Viral Family Review Groups are answering brief questionnaires to reduce the scope from over 20 families to a shorter list. They are not concerned with endemic diseases, so the shorter list will not include many of the pathogens in our scope. A Prioritization Review Group will then consider more detailed information on each family and additional information such as social and economic burden to identify R&D priorities. This consultation is being planned for late 2022, and results will be presented to SAGE in early 2023. In their reviews, they are considering many of the issues we have addressed through our filtering of pathogen scope and our prioritization criteria. This indicates that the two projects have the potential to learn from each other.

B. Annex B: Instructions to reviewers

Thank you very much for your help. This data package contains (a) these brief "Quick Start" instructions, (b) materials for your review, and (c) detailed methods, in case additional information is helpful for your review.

*Please send your feedback to Angela Hwang (angela@ahwang.net) by **31 October 2022**. If you have any questions or would like to discuss your feedback, please don't hesitate to reach out.*

Context

WHO is partnering with regions and countries to identify **priority pathogens for vaccine research and development** under Immunization Agenda 2030 (IA2030). This approach will apply multi-criteria decision analysis (MCDA) to identify context-specific priorities, followed by regional consultations to deliberate on the results and finalize priorities.

The pathogen scope includes **24 endemic pathogens** that are important to human health, with vaccine candidates in the pipeline, and where any existing vaccines do not address public health needs for all regions. (Section II.A.1 discusses pathogen scope in greater detail.) Additional pathogens can be included for the regional consultations.

In MCDA, regional and country stakeholders will complete online "Preferences Surveys" to weight **criteria for prioritization**. (Table 11 shows the criteria, and Section II.A.3 describes how they were developed.) Criteria weights from the Preferences Surveys will be mapped to pathogen information to reveal the **relative priorities** of the pathogens in the scope of this exercise. We are asking you to review the pathogen information, to enable this mapping.

Country and regional level stakeholders will complete the Preferences Survey in the coming weeks. WHO is planning face-to-face consultations with stakeholders at the regional and country level to deliberate on the Preferences Survey results and align on priorities in early 2023. These results will be presented to WHO's Strategic Advisory Group of Experts on Immunization (SAGE) in April 2023, and the priority pathogens will ultimately be used as indicators for the Research and Innovation strategic priority component of IA2030.

Table 11 MCDA Criteria

Criteria	Description	Scoring
1. Annual deaths in children under 5	Deaths attributable to the pathogen in both sexes, < 5 years old	Quantitative
2. Annual deaths in people 5 and older	Deaths attributable to the pathogen in both sexes, ≥ 5 years old	Quantitative
3. Years lived with disability (all ages)	Years of healthy life lost each year due to disability or ill-health caused by the pathogen	Quantitative
4. Social and economic burden per case	Reflects individual social and economic impact such as impact on education, stigma, and the costs of prevention, health care, and lost productivity. To avoid "double-counting" disease prevalence, this criterion is evaluated on a ***per case basis***	Qualitative

Criteria	Description	Scoring
5. Disruption due to outbreaks	Reflects societal impact due to outbreaks, including social disruption, impact on healthcare, trade and tourism, and the cost of containment measures	Qualitative
6. Contribution to inequity	Reflects disproportionate impact on socially and economically disadvantaged groups, including women	Qualitative
7. Contribution to antimicrobial resistance (AMR)	Reflects the threat of resistance, based on current levels of resistance, contribution to antibiotic use, and designation as an AMR priority	Qualitative
8. Unmet needs for prevention and treatment	Reflects the effectiveness and suitability of alternative measures. Considers whether current measures are "deliverable" to those who need them, but does not consider current levels of access	Qualitative

To prepare the Preferences Surveys, we have compiled **data on each of the pathogens** for each of the criteria and in each WHO region, as of October 2022. For quantitative Criteria 1-3, data were obtained from the Global Burden of Disease project and IHME. For the qualitative criteria, data were obtained from draft Vaccine Value Profiles developed by groups of subject matter experts and from literature searches.

These data have been used to give **preliminary scores** for each pathogen in each region, based on consensus between 3 analysts. (Sections II.A.4 and II.A.5 give more detail on the scoring.) Scores have been coded (A) or (B) to indicate the level of data found (see Table 8). Every effort has been made to score consistently across regions and across pathogens. This document includes the full set of scores, organized in two ways:

- Annex D: Pathogen Summaries shows all scores for that pathogen and give notes and selected citations for scoring.
- Annex E: Regional Summaries shows how the pathogens compare, relative to each other, within each region. Each region has eight tables, one for each criterion.

Your review is needed to ensure that the scoring appropriately reflects current evidence or, in cases where evidence is sparse, to advise on plausible scores to evaluate in sensitivity testing.

Instructions for Reviewers

You have been invited to review the scoring for a specific WHO Region or pathogen. If time permits, please feel free to browse and to comment on other sections, especially if there are important data we have missed.

As you review, please consider whether the scores reflect your understanding of each pathogen *in the context of each region.* Please keep in mind that the scores are relative to all the other pathogens per region, and that for quantitative data the scoring ranges have been customized according to the data in that region, as discussed in Section II.A.4.

Make your comments directly in this document, either as tracked changes or as comments, and give detailed reasons for your changes and citations if available. ***Please return to angela@ahwang.net by email by 31 October 2022****.*

C. Annex C: Declarations of Interest

Relevant declarations are shown in the tables below. Reviewers not listed had no relevant interests to declare.

Region	Reviewers	Declarations
African Region	**Kwaku Poku Asante**, Kintampo Health Research Centre	• I am the principal investigator of the RTSS malaria vaccine. My institution received funds for research from GSK, the sponsor of RTSS malaria vaccine.
	Helen Rees, Wits Reproductive Health and HIV Research Institute	•
Region of the Americas	**Peter Figueroa**, University of the West Indies	•
Eastern Mediterranean	**Ahmed Deemas Al Suwaidi**, Department of Pediatrics, College of Medicine and Health Sciences - United Arab Emirates University	• I advise the Ministry of Health in the United Arab Emirates on issues related to vaccines/immunization in my capacity as a chairperson of the National Immunization Technical Advisory Group (NITAG)
	Ghassan Dbaibo, American University of Beirut	• Research grant from Sanofi for influenza surveillance, completed 2018 • Research grant from ARK Biosciences for RSV therapeutic, completed 2019 • Honoraria from Sanofi for lectures on influenza vaccines, ongoing
European	**Helena Hervius Askling**, Karolinska Institutet	• Consulting expert. Medical reviewer of the information on a national website directed to Swedish health professionals and including all vaccines used in Sweden. • 2016- . Representing Swedish Infectious Diseases Medical doctors in the Reference Group on National Vaccination programmes at the Public Health Agency (NITAG equivalent). • 2020- . Head of Swedish Infectious Diseases Society Vaccination Group.
	Anh Wartel, International Vaccine Institute	•
South-East Asian	**Sonali Kochhar**, University of Washington	•
Western Pacific	**David Durrheim**, University of Newcastle, Australia	•
	Kim Mulholland, Murdoch Children's Research Institute	• Collaborate research on adult pneumonia in Mongolia.

Region	Reviewers	Declarations
Global	**Kathleen Neuzil**, University of Maryland School of Medicine Center for Vaccine Development and Global Health	• Serves as a member of the Board of Directors for the US National Foundation of Infectious Diseases. • Serves as PI for NIH-funded Collaborative Influenza Vaccine Innovation Center program. • Serves as co-investigator on an NIH contract for a Vaccine and Treatment Evaluation Unit. As part of this contract, she is principal investigator for 3 studies: A trial of Tdap among pregnant women in Mali, clinical studies of H7N9 influenza vaccines among U.S. adults, and clinical study of H5N8 vaccine among U.S. adults, and an influenza challenge study. • Served as the IDSA liaison representation to the U.S. Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices from 2010-December 31, 2018. • Her institution receives research support for the following study: Double-Blind, Randomized, Pacebo-Controlled Phase 2b Study to Evaluate the Safety, Tolerability, Efficacy, and Immunogenicity of a 2-Dose and 3-Dose Regimen of V160, Human Cytomegalovirus Vaccine in Healthy Seronegative Adolescent and Adult Women 16-35 Years of Age funded by Merck. • Serves as principal investigator for the NIH funded NIH T32 Fellowship Training Program in Vaccinology .

Pathogen	Reviewers	Declarations
Group A streptococcus	**Andrew Steer**, Murdoch Children's Research Institute	• Received funding for GAS vaccine development
Herpes simplex virus (Types 1 and 2	**Katharine Looker**, Population Health Sciences, Bristol Medical School, University of Bristol	• Research funding from GSK for Modelling impact of a gonorrhea vaccine among adolescents in England
HIV-1	**Pat Fast**, IAVI	• Employed by IAVI
Hookworm	**Julie Jacobson**, Bridges to Development	• Research support from Johnson & Johnson to look at new AI technology for improving the diagnosis of soil-transmitted helminths in Kato Katz, completed in 2022.

Pathogen	Reviewers	Declarations
Klebsiella pneumoniae	**Alan Cross**, Center for Vaccine Development and Global Health, U. of Maryland School of Medicine	• I have been collaborating with Affinivax LLC in the development of a *Klebsiella* and *Pseudomonas* vaccine using their novel technology. Under a Research Agreement with my university, they provide funds to my laboratory to conduct studies to test the functional activities of their antibody. Together we have submitted patent applications for this vaccine to multiple countries. • Independently of my collaboration with Affinivax I have been evaluating a *Klebsiella* and *Pseudomonas* glycoconjugate vaccine that we developed under an NIH grant.
Leishmania	**Paul Kaye**, University of York	• Received funding to conduct vaccine trials
Mycobacterium leprae	**Julie Jacobson**, Bridges to Development	• Support from the Globap Program for Zero Leprosy to provide ad hoc strategy advice on partnerships and funding opportunities for leprosy elimination
Norovirus	**Ben LOPMAN**, Department of Epidemiology, Rollins School of Public Health Emory University	• Consultant for Hillevax LLC • Consultant for Epidemiologic Research and Methods
Plasmodium falciparum	**Muhammed Afolabi**, London School of Hygiene and Tropical Medicine	• Since 2021, a member of the Independent Diagnostic Adjudication panel for a phase III randomised controlled multi-centre trial to evaluate the efficacy of the R21/Matrix-M vaccine in African children against clinical malaria (VAC078). The Sponsor of the trial is the Jenner Institute, University of Oxford. The main responsibilities of the panel are to review all blinded data on hospital admissions and deaths throughout the trial and meet with other members of the panel at specified time points to discuss the data and come to a consensus on diagnoses or causes of death. The roles are entirely voluntary and no payments are made to the members for the work they do.
Pseudomonas aeruginosa	**Alan Cross**, Center for Vaccine Development and Global Health, U. of Maryland School of Medicine	• I have been collaborating with Affinivax LLC in the development of a *Klebsiella* and *Pseudomonas* vaccine using their novel technology. Under a Research Agreement with my university, they provide funds to my laboratory to conduct studies to test the functional activities of their antibody. Together we have submitted patent applications for this vaccine to multiple countries. • Independently of my collaboration with Affinivax I have been evaluating a *Klebsiella* and *Pseudomonas* glycoconjugate vaccine that we developed under an NIH grant.

Pathogen	Reviewers	Declarations
Respiratory syncytial virus	**Harish Nair**, Centre for Global Health at The University of Edinburgh	• Advisory Board for Global Influenza and RSV initiative, funded by Sanofi • RSV advisory boards for Sanofi, GSK, Merck, and ReViral • Grants for RSV and Influenza research, from IMI, Foundation for Influenza Epi, NIHR, WHO, Pfizer, and Icosavax • 2b Honoraria for speakership from Sanofi
	Ruth Karron, Johns Hopkins Bloomberg School of Public Health	•
Staphylococcus aureus	**Jean C. Lee**, Harvard Medical School	• Member of the Scientific Advisory Board for a company that is working to develop a toxin-based vaccine for the prevention of *S. aureus* skin and soft-tissue infection • Grant support for a subcontract from the NIH for a small business grant awarded to Integrated Biotherapeutics. The goal was to construct Infection Site Targeted antitoxin Antibodies (ISTAbs) from human monoclonal antibodies that neutralize *S. aureus* pore-forming toxins and to evaluate the *in vivo* activity of the ISTAbs in *S. aureus* infection models.

D. Annex D: Pathogen Summaries

Below you will find one datasheet per pathogen, including scores, notes on rationale, and selected citations. A full list of references relating to each pathogen is available on request.

Because pathogens are scored in terms of the regional context compared to other pathogens, comparisons across regions for the same pathogen may not be valid. See Section III.E for region-by-region summaries of scores.

1. Chikungunya virus

Table 12 Chikungunya virus

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
1 Annual deaths in children under 5	0 Very low (B)	0 Very low (B)	0 Very low (B)	0 Very low (B)	0 Very low (B)	0 Very low (B)	0 Very low (B)
2 Annual deaths in people 5 and older	2 Very low (B)	206 Very low (B)	1 Very low (B)	0 Very low (B)	17 Very low (B)	4 Very low (B)	230 Very low (B)
3 Annual years lived with disability (all ages)	Acute: 10 Chronic: 814 Very low (B)	Acute: 1,089 Chronic: 87,314 Low (B)	Acute: 7 Chronic: 580 Very low (B)	Acute: 0 Chronic: 9 Very low (B)	Acute: 88 Chronic: 7,066 Very low (B)	Acute: 22 Chronic: 1,729 Very low (B)	Acute: 1,216 Chronic: 97,513 Very low (B)
4 Social and economic burden per case	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)
5 Disruption due to outbreaks	Medium (A)	High (A)	Low (A)	Medium (A)	High (A)	High (A)	High (A)
6 Contribution to inequity	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)
7 Contribution to antimicrobial resistance	Very Low (A)	Very low (B)	Very low (B)	Very low (B)	Very low (B)	Very low (B)	Very low (A)
8 Unmet needs for prevention & treatment	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	High (A)	Very high (A)

Notes and selected citations

1-3 Annual deaths in children under 5, Annual deaths in people 5 and older, Annual years lost to disability (all ages)

- Burden not estimated by the Global Burden of Disease project as of November 2022.
- Source: Puntasecca et al, 2021, S4 Table, which gives annual fatal cases for 2015. Assumed that these deaths are all among people over 5 because the median age at onset is 40 years and median age at death is 60 years. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7932082/
- Burden estimates between 2010 and 2019 show chikungunya (CHIK) “caused substantial burden throughout this time frame and place them among the most problematic mosquito-borne viral diseases worldwide.” Highest burden in the Americas https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7932082/
- Due to several challenges including in surveillance, the real burden of chikungunya is unknown. The disabilities caused by subacute and chronic chikungunya are believed to be higher than the reported.

4 Social and economic burden per case

- Burden to families includes the costs of hospitalization, productivity losses, and ongoing disability due to persistent arthralgia and other long-term sequelae. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7932082/

5 Disruption due to outbreaks

- Burden to societies includes the cost of vector control and social disruption as a result of outbreaks, which "can overwhelm health systems and devastate local communities through supply chain dysfunction, economic downturn, and political disruption." https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7932082/
- Vector species are found on every continent, so all regions are at some risk. In sensitivity testing, evaluate a "High" score for Europe. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4493616/
- Multiple reports and investigations in Europe. https://link.springer.com/article/10.1186/1471-2334-10-31
- Outbreaks can have a significant impact on the health services due to the high proportion of symptomatic cases. https://www.sciencedirect.com/science/article/pii/S0166354213001666?via%3Dihub

6 Contribution to inequity

- "The disabling sequelae of CHIKV and ZIKV disproportionately affect resource-poor communities, where they frequently cause chronic impairment that can greatly reduce patients' qualities of life" https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7932082/

7 Contribution to antimicrobial resistance

- While infections can contribute to inappropriate use of antibiotics, chikungunya has not been identified as an AMR threat. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7932082/

8 Unmet needs for prevention and treatment

- Currently, there is no vaccine or antiviral treatment for chikungunya. Prevention focuses on vector control and limiting exposure to vectors. At least one candidate vaccine is likely to be licensed by at least one regulator in 2023. https://www.sciencedirect.com/science/article/pii/S0166354213001666?via%3Dihub

Current context for prioritization

- The Partnership for African Vaccine Manufacturing lists chikungunya as one of its 22 priority diseases. https://africacdc.org/download/partnerships-for-african-vaccine-manufacturing-pavm-framework-for-action/?ind=1646295399995&filename=PAVM-Framework-for-Action.pdf
- AMRO has published a preparedness and response plan for CHIK outbreaks. https://www.paho.org/en/documents/preparedness-and-response-chikungunya-virus-introduction-americas
- In EMR, an under-recognized disease. https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0005707
- In EUR, a reportable disease. In SEAR, benefits from Dengue control programs which share many interventions. In WPR, there is limited surveillance for chikungunya, suggesting that it is not a high public health priority. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6455125/
- Globally, chikungunya is included in the Global Roadmap for Neglected Tropical Diseases, the Global Arbovirus Initiative, the WHO R&D Blueprint for action to prevent epidemics, and is a Coalition for Epidemic Preparedness Innovations (CEPI) priority pathogen. https://www.who.int/publications/i/item/9789240010352 , https://cdn.who.int/media/docs/default-source/blue-print/final-report-of-the-global-research-and-innovation-forum-2022.pdf?sfvrsn=4a59021f_5&download=true

2. Cytomegalovirus

Table 13 Cytomegalovirus (CMV)

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
1 Annual deaths in children under 5)	Very low (C)	Low (C)	Very low (C)	Medium (C)	Very low (C)	Medium (C)	Very low (C)
2 Annual deaths in people 5 and older	Low (C) (test V. low and Medium)	Low (C) (test V. low and Medium)	Low (C) (test V. low and Medium)	Low (C) (test V. low and Medium)	Low (C) (test V. low and Medium)	Low (C) (test V. low and Medium)	Low (C) (test V. low and Medium)
3 Annual years lived with disability (all ages)	Medium (C) (test Low to High)	Medium (C) (test Low to High)	Medium (C) (test Low to High)	Medium (C) (test Low to High)	Medium (C) (test Low to High)	Medium (C) (test Low to High)	Medium (C) (test Low to High)
4 Social and economic burden per case	High (B)	High (A)	High (B)	High (A)	High (B)	High (A)	High (B)
5 Disruption due to outbreaks	Very low (B)	Very low (B)	Very low (B)	Very low (B)	Very low (B)	Very low (B)	Very low (B)
6 Contribution to inequity	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)
7 Contribution to antimicrobial resistance	Very low (B)	Very low (B)	Very low (B)	Very low (B)	Very low (B)	Very low (B)	Very low (B)
8 Unmet needs for prevention & treatment	Very high (B)	Very high (B)	Very high (B)	Very high (A)	Very high (B)	Very high (B)	Very high (A)

Notes and selected citations

1 Annual deaths in children under 5

- Data not found. Approximated deaths as follows:
  - Obtain birth cohorts from the State of the Worlds' Children statistical tables
  - Use US mortality rate from congenital CMV for a low estimate of potential CMV deaths in children under 1. Because this rate is derived from census reporting, it is likely to be an under-estimate. (Bristow et al 2011)

- Use South African rates of congenital CMV (cCMV) and case fatality rates for a high estimate. Because this study considered outcomes at time of hospital discharge, it may also be an under-estimate. (Diar and Velaphi, 2014)
- Multiply by birth cohorts to get deaths per region in children under 1 (low and high estimates).
- Use the 68% figure for the proportion of CMV deaths that occurred in the first year of life from Australia to scale up to deaths in children under 5. (Smithers-Sheedy et al 2015) This would tend to over-estimate the number of under-5 deaths, since the age range covered by that study was < 15 years.
- Compare the resulting high and low estimates of under 5 deaths to the cutoffs for each region (Table 4) to score.
- Use the scores for the High estimates in the Preferences survey and consider using the Low estimates for sensitivity testing.

	Birth cohort (thousands)	Low estimate for infant deaths: birth cohort x 8.34 deaths /million infants	**Low estimate for deaths in children under 5: /0.68**	High estimate for infant deaths: Birth cohort x 0.26 cases/ thousand live births x 42% mortality	**High estimate for deaths in children under 5: /0.68**	Scores for Low and High estimates
AFRO	38,071	318	**467**	4,157	**6,114**	Very low – Very low
PAHO	14,688	122	**180**	1,604	**2,359**	Very low – Low
EMRO	18,017	150	**221**	1,967	**2,893**	Very low – Very low
EURO	10,887	91	**134**	1,189	**1,748**	Very low – Medium
SEARO	34,666	289	**425**	3,786	**5,567**	Very low – Very low
WPRO	23,116	193	**284**	2,524	**3,712**	Very low – Medium
Global	139,589	1,164	**1,712**	15,243	**22,416**	Very low – Very low

2 Annual deaths in people 5 and older

- Data not found. Scored **Low** and will conduct sensitivity testing evaluating Very low and Medium.

3 Annual years lost to disability (all ages)

- Data not found. Scored Medium and will conduct sensitivity testing evaluating Low to High.

4 Social and economic burden per case

- A US modeling study projected that children who have severe microcephaly and associated brain anomalies resulting from symptomatic cCMV could incur 3.8 million US dollars in costs of care in the first 40 years of life https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7131228/
- cCMV is associated with substantial increases in economic burden during early childhood. The increased utilization of inpatient and outpatient health care services among children with likely cCMV is highest during the first year of life, reflected by incremental direct medical costs reaching $1687 USD https://www.sciencedirect.com/science/article/abs/pii/S0149291821005002
- In Netherlands, The costs of children with long-term impairment were two times higher in children with cCMV (€17 205) compared with children without cCMV (€8332). https://pubmed.ncbi.nlm.nih.gov/29363491/ In the UK, a model estimated that the total cost of cCMV in 2016 was £732million. https://pubmed.ncbi.nlm.nih.gov/30472664/

- In Japan, a model estimated that the overall cost due to cCMV in 2019 was 27.6 billion JPY. https://pubmed.ncbi.nlm.nih.gov/32912713/
- Economic data from LMICs are lacking.
- CMV contributes to cognitive, hearing and vision impairment. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3553672/
- CMV in HIV+ populations which may incur in additional deaths in older than 5 and disability.

5 Disruption due to outbreaks

- Seroprevalence is high and CMV infection and ubiquitous in human populations already. Some portion of CMV infection is due to congenital transmission. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4164178/

6 Contribution to inequity

- Worldwide, seropositivity is higher among non-whites and lower socioeconomic status (OR1.33), slightly higher among women https://pubmed.ncbi.nlm.nih.gov/20564615/
- Congenital CMV infection disproportionately affects disadvantaged populations in high-income countries. The absolute majority of infants with cCMV around the world live in less developed countries. CMV seroprevalence is higher in LMICs and in individuals from lower socioeconomic groups/regions at any given age https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7131228/
- In US women, racial and/or ethnic differences were significant; between ages 10-14 years and 20-24 years, seroprevalence increased 38% for non-Hispanic black persons, 7% for non-Hispanic white persons, and <1% for Mexican Americans https://pubmed.ncbi.nlm.nih.gov/17029132/ Native Americans and African Americans are more likely to die from congenital CMV than White Americans, Asian Americans and Hispanic Americans are less likely to die from congenital CMV than Whites. https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0001140
- US birth prevalence highest among Black infants. https://pubmed.ncbi.nlm.nih.gov/20564615/

7 Contribution to antimicrobial resistance

- Resistance of CMV to ganciclovir and valganciclovir has been reported among congenitally infected infants, although data are limited https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7131228/

8 Unmet needs for prevention and treatment

- No treatment or prevention measures available during pregnancy to prevent congenital transmission. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4164178/ and https://www.nhs.uk/conditions/cytomegalovirus-cmv/

Current context for prioritization

- Awareness high in HICs. CMV vaccine cited as high priority by National Vaccine Advisory Committee https://pubmed.ncbi.nlm.nih.gov/15307033/ and the National Academy of Medicine https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5717185/ and many areas in US and Canada require education and/or newborn screening for congenital CMV infection.
- Reliable information on public health priority in LMICs is lacking. For example, Diagnosis and treatment of CMV-related disease is broadly neglected in Africa. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4967964/

3. Extra-intestinal pathogenic *E. coli* (ExPEC)

Note: Extra-intestinal pathogenic *E. coli* (ExPEC) includes uropathogenic *E. coli* (which causes urinary tract infections), neonatal meningitis *E. coli*, sepsis-associated *E. coli*, and avian pathogenic *E. coli*.

Table 14 Extra-intestinal pathogenic *E. coli* (ExPEC)

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
1 Annual deaths in children under 5	65,376 Medium (A)	4,632 High (A)	20,663 High (A)	1,983 Medium (A)	29,061 High (A)	4,786 High (A)	126,538 High (A)
2 Annual deaths in people 5 and older	74,075 High (A)	134,281 High (A)	44,831 Very high (A)	197,802 Very high (A)	166,938 Very high (A)	144,876 Medium (A)	768,011 Very high (A)
3 Annual years lived with disability (all ages)	42,045 Very low (A)	46,649 Very low (A)	25,075 Very low (A)	43,528 Low (A)	77,862 Very low (A)	31,396 Very low (A)	266,947 Very low (A)
4 Social and economic burden per case	Medium (B)	Medium (A)	Medium (A)	Medium (A)	Medium (B)	Medium (B)	Medium (B)
5 Disruption due to outbreaks	Low (B)	Low (A)	Low (B)	Low (B)	Low (B)	Low (A)	Low (A)
6 Contribution to inequity	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)
7 Contribution to antimicrobial resistance	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)
8 Unmet needs for prevention & treatment	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)

Notes and selected citations

1-3 Annual deaths in children under 5, Annual deaths in people 5 and older, Annual years lived with disability

- Source: Institute for Health Metrics and Evaluation (IHME), University of Oxford. Global Bacterial Antimicrobial Resistance Burden Estimates 2019. Seattle, United States of America: Institute for Health Metrics and Evaluation (IHME), 2022.

- Values are totals of antibiotic resistant and susceptible forms, presenting as bacterial skin infections, bone and joint infections, bloodstream infections, cardiac infections, central nervous system infections, intra-abdominal infections, lower-respiratory and thorax infections, and urinary tract infections. (These are all the non-diarrheal presentations in the dataset relevant to *E. coli*.)
- YLDs are calculated by subtracting Years of Life Lost (YLLs) from Disability Adjusted Life Years (DALYs).

4 Social and economic burden per case

- *E. coli* accounts for 25-35% of catheter-associated infections in the US, with an associated treatment cost of $676 per episode. Other *E. coli* infections, such as cystitis and pyelonephritis, are associated with similar costs of treatment. https://www.sciencedirect.com/science/article/abs/pii/S1286457903000492
- Urinary tract infections (UTIs), including those caused by *E. coli*, can negatively impact quality of life. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6502976/
- Antibiotic resistance complicates UTI treatment, leading to higher treatment costs and greater social and economic burden. https://bmjopen.bmj.com/content/8/4/e020251, https://www.sciencedirect.com/science/article/pii/S2212109920300352

5 Disruption due to outbreaks

- "The existence of ExPEC outbreaks was well supported." https://pubmed.ncbi.nlm.nih.gov/20642873/
- Although an extremely common infection, UTI outbreaks due to ExPEC have been reported. https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-015-0974-0, https://www.futuremedicine.com/doi/10.2217/fmb-2017-0304

6 Contribution to inequity

- Women are at higher risk for UTIs and for recurrent UTIs and have a greater incidence of *E. coli* bacteremia. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6502976/, https://pubmed.ncbi.nlm.nih.gov/32406495/
- In developing countries, pregnant women are at greater risk for UTIs than non-pregnant women. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7245001/

7 Contribution to antimicrobial resistance

- *Enterobacteriaceae*, including *E. coli*, are a "critical" priority for R&D of new antibiotics. https://www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed
- Reports of increasing antibiotic resistance, including multi-drug resistance from multiple regions. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7245001/

8 Unmet needs for prevention and treatment

- Recurrent and drug-resistant UTIs are an unmet need. https://www.frontiersin.org/articles/10.3389/fmicb.2020.01509/full
- Vaccine development presents challenges, but progress is being made. https://pubmed.ncbi.nlm.nih.gov/26333944/, https://pubmed.ncbi.nlm.nih.gov/30828388/

Current context for prioritization

- The UK has an initiative to reduce Gram-negative infections, including E. coli, by 50% from 2017 to 2021. https://www.gov.uk/government/collections/escherichia-coli-e-coli-guidance-data-and-analysis
- Surveillance for AMR in Europe is relatively stringent. https://doi.org/10.1016/S2468-2667(22)00225-0

4. Group A streptococcus (GAS, *Streptococcus pyogenes*)

Note: Scoring for Group A Streptococcus focuses on the burden of rheumatic heart disease. GAS also causes pharyngitis, skin, and other infections. These presentations are included in the quantitative scoring but are not included in the qualitative scoring.

Table 15 Group A streptococcus (GAS)

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
1 Annual deaths in children under 5 (source 1)	13,378 Very low (A)	2,108 Low (A)	4,880 Very low (A)	848 Low (A)	5,867 Very low (A)	1,732 Low (A)	28,843 Very low (A)
(source 2)	1,790 Very low (B)	535 Very low (B)	1,016 Very low (B)	367 Very low (B)	1,452 Very low (B)	911 Very low (B)	6,087 Very low (B)
2 Annual deaths in people 5 and older (source 1)	31,908 Low (A)	41,468 Low (A)	37,986 High (A)	57,289 Low (A)	184,075 Very high (A)	120,205 Medium (A)	474,512 Medium (A)
(source 2)	17,057 Very low (B)	23,742 Very low (B)	31,115 High (B)	37,549 Very low (B)	152,667 Very high (B)	100,023 Medium (B)	362,819 Low (B)
3 Annual years lived with disability (all ages) (source 1)	561,972 Medium (A)	292,741 Very high (A)	225,217 Very high (A)	125,480 Very high (A)	644,180 Very high (A)	416,724 Very high (A)	2,271,207 Very high (A)
(source 2)	516,585 Medium (B)	240,581 Very high (B)	200,113 High (B)	79,571 High (B)	570,779 Very high (B)	379,030 Very high (B)	1,990,209 Very high (B)
4 Social and economic burden per case	High (B)	Medium (A)	Medium (B)	Medium (B)	High (B)	High (A)	High (A)
5 Disruption due to outbreaks	Very low (B)	Very low (A)	Very low (B)	Very low (A)	Very low (A)	Very low (A)	Very low (A)
6 Contribution to inequity	High (B)	Medium (A)	Medium (B)	Medium (B)	High (B)	High (A)	High (A)
7 Contribution to antimicrobial resistance	High (B)	High (B)	High (B)	High (B)	High (B)	High (B)	High (A)

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
8 Unmet needs for prevention & treatment	High (A)	Medium (A)	Medium (A)	Medium (A)	High (A)	High (A)	High (A)

Notes and selected citations

1-3 Annual deaths in children under 5, Annual deaths in people 5 and older, Annual years lived with disability

- Source 1: Sum of these values
    - Source: Institute for Health Metrics and Evaluation (IHME), University of Oxford. Global Bacterial Antimicrobial Resistance Burden Estimates 2019. Seattle, United States of America: Institute for Health Metrics and Evaluation (IHME), 2022.
        - Values are totals of antibiotic resistant and susceptible forms of GAS. YLDs are calculated by subtracting Years of Life Lost (YLLs) from Disability Adjusted Life Years (DALYs).
        - Presentations include BSI, bacterial skin infections, bone and joint infections, and cardiac infections
    - Source: GBD Results [Internet]. Institute for Health Metrics and Evaluation. [cited 2022 Oct 5]. Available from: https://vizhub.healthdata.org/gbd-results
        - Values for the burden of rheumatic heart disease (RHD) from the Cause of Death dataset
- Source 2: Sum of these values
    - Source: SAVAC, Jeffrey Cannon, personal communication
        - Burden of invasive GAS (iGAS) estimated using incidence and case fatality rates from a systematic review conducted by SAVAC and population estimates from the GBD project.
    - Source: GBD Results [Internet]. Institute for Health Metrics and Evaluation. [cited 2022 Oct 5]. Available from: https://vizhub.healthdata.org/gbd-results
        - Values for the burden of rheumatic heart disease (RHD) from the Cause of Death dataset

4 Social and economic burden per case

- Most commonly causes sore throats with very low burden due to missed school or work (by caregivers) https://academic.oup.com/cid/article-abstract/74/6/983/6311854, https://publications.aap.org/pediatrics/article-abstract/121/2/229/68725/Burden-and-Economic-Cost-of-Group-A-Streptococcal
- Also causes auto-immune responses leading to rheumatic fever and rheumatic heart disease. https://www.who.int/health-topics/rheumatic-heart-disease#tab=tab_2, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8978297/pdf/trab156.pdf

5 Disruption due to outbreaks

- Case clusters occur among school children and in care facilities. Control measures include screening for GAS, antibiotic treatment, isolating cases until 2 days after start of antibiotics, and sanitizing environments. https://www.cdc.gov/groupastrep/outbreaks.html
- Rising cases have been reported in the UK and China. https://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099(17)30693-X.pdf, https://weekly.chinacdc.cn/en/article/doi/10.46234/ccdcw2019.019

6 Contribution to inequity

- Higher rates of GAS and sequelae observed in groups with lower socioeconomic status, including indigenous and migrant populations. Prevalence is decreasing in high-income countries. https://www.researchgate.net/publication/233931261_Group_A_Streptococcal_Diseases_and_Their_Global_Burden

7 Contribution to antimicrobial resistance

- Global sources note that concern about GAS drives presumptive treatment of sore throats resulting in high levels of inappropriate antibiotic use. Region-specific sources on this concern were not found. https://apps.who.int/iris/bitstream/handle/10665/279392/WHO-IVB-18.08-eng.pdf

8 Unmet needs for prevention and treatment

- GAS remains susceptible to penicillins, however treatment may not prevent progression to rheumatic heart disease or other long-term complications. https://apps.who.int/iris/bitstream/handle/10665/279392/WHO-IVB-18.08-eng.pdf
- No vaccines are available for GAS.

Current context for prioritization

- While a roadmap and target product profile for GAS vaccines have been established, the need for greater research on GAS is a recurrent theme. https://apps.who.int/iris/bitstream/handle/10665/279392/WHO-IVB-18.08-eng.pdf, https://apps.who.int/iris/rest/bitstreams/1171023/retrieve
- SAVAC has been established to quantify the value of GAS vaccine: https://savac.ivi.int/
- Resolutions in Africa and the World Health Assembly have noted the need for greater action on rheumatic heart disease and progress in EMRO has been highlighted. https://www.pascar.org/uploads/files/ADDIS_ABABA_COMMUNIQU%C3%89_ON_ERADICATION_OF_RHUEMATIC_HEART_DISEASE_IN_AFRICA_-_Submission1.pdf, https://apps.who.int/gb/ebwha/pdf_files/WHA74/A74_40-en.pdf
- Scarlet fever is a notifiable disease in China and Korea. https://weekly.chinacdc.cn/en/article/doi/10.46234/ccdcw2019.019, https://icjournal.org/DOIx.php?id=10.3947/ic.2018.50.1.65

5. Group B streptococcus (GBS, Streptococcus agalactiae)

Table 16 Group B streptococcus (GBS)

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
1 Annual deaths in children under 5	73,759 High (A)	3,886 Medium (A)	22,495 High (A)	1,289 Low (A)	31,001 High (A)	4,926 High (A)	137,384 High (A)
2 Annual deaths in people 5 and older	27,255 Low (A)	29,411 Very low (A)	11,104 Low (A)	26,270 Very low (A)	41,249 Low (A)	44,811 Very low (A)	181,168 Very low (A)
3 Annual years lived with disability (all ages)	40,824 Very low (A)	16,085 Very low (A)	15,408 Very low (A)	10,898 Very low (A)	46,704 Very low (A)	13,817 Very low (A)	144,026 Very low (A)
4 Social and economic burden per case	High (A)	High (A)		High (A)	High (B)	High (B)	High (A)
5 Disruption due to outbreaks	Low (B)	Low (A)	Low	Low (B)	Low (B)	Low (B)	Low (A)
6 Contribution to inequity	Medium (A)	Medium (A)	Medium	Medium (A)	Medium (B)	Medium (B)	Medium (A)
7 Contribution to antimicrobial resistance	Low (A)	Low (A)		Low (A)	Very low (A)	Low (A)	Low (A)
8 Unmet needs for prevention & treatment	Very high (A)	High (A)		High (A)	Very high (A)	High (A)	High (A)

Notes and selected citations

1-3 Annual deaths in children under 5, Annual deaths in people 5 and older, Annual years lived with disability

- Source: Institute for Health Metrics and Evaluation (IHME), University of Oxford. Global Bacterial Antimicrobial Resistance Burden Estimates 2019. Seattle, United States of America: Institute for Health Metrics and Evaluation (IHME), 2022.
- Values are total deaths from antibiotic resistant and susceptible forms of GBS. YLDs are calculated by subtracting Years of Life Lost (YLLs) from Disability Adjusted Life Years (DALYs).
- A 2022 analysis of pregnancy-related GBS burden estimated that 91,900 deaths occurred globally in 2020 due to invasive GBS in the first 3 months of life. https://pubmed.ncbi.nlm.nih.gov/35490693/

4 Social and economic burden per case

- Costs per case consistently high across different country income levels. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6858852/pdf/EMS84883.pdf, https://www.sciencedirect.com/science/article/pii/S0264410X14007920?via%3Dihub, https://pubmed.ncbi.nlm.nih.gov/19002511/

5 Disruption due to outbreaks

- GBS disease is generally considered a sporadic disease but outbreaks in healthcare facilities have been reported. https://www.journalofinfection.com/article/S0163-4453(19)30346-9/fulltext

6 Contribution to inequity

- Risk of GBS infection is greater among HIV-exposed, uninfected infants. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378461/pdf/14-1562.pdf, https://pubmed.ncbi.nlm.nih.gov/20732944/
- Studies on risk factors for colonization have given conflicting results on links with socio-economic status. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5848259/pdf/cix658.pdf, https://www.nejm.org/doi/full/10.1056/NEJM200001063420103

7 Contribution to antimicrobial resistance

- First-line antibiotics remain effective and consumption of antibiotics for prophylaxis is low, so contribution to AMR is likely slight. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8483371/
- Penicillin resistance has been observed in Canada, Ethiopia, Germany, Japan, Mozambique, and the United States. https://pubmed.ncbi.nlm.nih.gov/35401756/, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9241772/

8 Unmet needs for prevention and treatment

- Antibiotics administered to pregnant women who are colonized with GBS, or at risk of GBS colonization, have been used to prevent GBS disease in their infants. These strategies are not likely to prevent most GBS-associated stillbirths, preterm births, or late-onset sepsis. https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(22)00093-6/fulltext
- Evidence on antibiotic prophylaxis for GBS is mixed (https://pubmed.ncbi.nlm.nih.gov/24915629/) and there are concerns about their feasibility in low-resource settings (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378461/pdf/14-1562.pdf)
- There is no vaccine for GBS.

Current context for prioritization

- WHO has prioritised the development of a GBS vaccine suitable for use in pregnant women and use in LMICs and the Bill & Melinda Gates Foundation is funding GBS vaccine development. https://www.gatesfoundation.org/ideas/media-center/press-releases/2022/09/gates-foundation-announces-grants-to-reduce-infant-mortality
- That said, individual countries and stakeholders within these countries have differing awareness and preparedness of/for a GBS vaccine. https://apps.who.int/iris/rest/bitstreams/1087677/retrieve, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8776310/

6. Herpes simplex virus (Types 1 and 2)

Table 17 Herpes simplex virus (HSV, Types 1 and 2)

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
Estimated annual cases neonatal herpes	5270	3091	1000	999	1313	2583	14,257
X 60% case fatality rate (see notes below)	3162	1855	600	599	788	1550	8,554
1 Annual deaths in children under 5	Very low (C)	Low (C)	Very low (C)	Very low (C)	Very low (C)	Low (C)	Very low (C)
2 Annual deaths in people 5 and older	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)
3 Annual years lived with disability (all ages)	51,121 Very low (A)	52,503 Very low (A)	15,209 Very low (A)	26,633 Low (A)	45,915 Very low (A)	60,652 Very low (A)	252,863 Very low (A)
4 Social and economic burden per case	Very high (A)	High (A)	Medium (B)	Medium (A)	High (A)	High (A)	High (A)
5 Disruption due to outbreaks	Very low (B)	Very low (B)	Very low (B)	Very low (B)	Very low (B)	Very low (B)	Very low (B)
6 Contribution to inequity	Very high (A)	High (A)	Medium (A)	Medium (A)	High (A)	High (A)	High (A)
7 Contribution to antimicrobial resistance	Low (A)	Low (A)	Low (A)	Low (A)	Low (A)	Low (A)	Low (A)
8 Unmet needs for prevention & treatment	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)

Notes and selected citations

1 Annual deaths in children under 5

- Data not found. Scored based on estimates of neonatal herpes cases per region and approximate case fatality rate of 60% for neonatal herpes. https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(16)30362-X/fulltext#seccestitle10

2 Annual deaths in people 5 and older

- Data not found. Scored as Very low and will evaluate Low in sensitivity testing.

3 Annual years lived with disability (all ages)

- Source: GBD Results [Internet]. Institute for Health Metrics and Evaluation. [cited 2022 Oct 5]. Available from: https://vizhub.healthdata.org/gbd-results
- YLD values are reported by GBD for "genital herpes" for HSV-2 and do not capture the full spectrum of disabilities caused by HSV. These include ocular HSV, central nervous system disease, genital herpes due to HSV-1, and sequelae from neonatal herpes. Higher YLD scores will be evaluated in sensitivity testing. (https://www.who.int/publications/i/item/9789241515580, https://pubmed.ncbi.nlm.nih.gov/34622738/)

4 Social and economic burden per case

- Costs include antiviral treatment, neonatal herpes prevention among pregnant mothers, and management of neonatal herpes. https://bmjopen.bmj.com/content/bmjopen/12/1/e049618.full.pdf?with-ds=yes, https://pubmed.ncbi.nlm.nih.gov/33492102/
- Evidence suggests that HSV-2 infection increases risk of HIV acquisition and transmission, and most published models estimate that at least one-third of incident (i.e., new) HIV infections from sexual transmission globally are likely attributable to HSV-2. https://pubmed.ncbi.nlm.nih.gov/34117163/
- HSV can also lead to emotional and social distress. https://pubmed.ncbi.nlm.nih.gov/35199654/

5 Disruption due to outbreaks

- Outbreaks and epidemiologically linked case clusters not found on web search.

6 Contribution to inequity

- The burden of genital ulcer disease is approximately double in women compared to men. Compared to general populations, seroprevalence of HSV 2 is higher among men who have sex with men and transgender people, HIV-positive individuals, and female sex workers. https://gh.bmj.com/content/5/3/e001875, https://www.thelancet.com/journals/lanwpc/article/PIIS2666-6065(21)00085-7/fulltext, https://pubmed.ncbi.nlm.nih.gov/32514197/

7 Contribution to antimicrobial resistance

- Although resistance has been identified, especially in immunocompromised individuals, acyclovir remains the first-line treatment. https://pubmed.ncbi.nlm.nih.gov/15494896/, https://apps.who.int/iris/bitstream/handle/10665/250693/9789241549875-eng.pdf

8 Unmet needs for prevention and treatment

- No preventive intervention exceeds 50% efficacy. Antivirals are used as episodic treatment or suppressive therapy, and do not cure herpes infections. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6794147/pdf/nihms-1054669.pdf, https://apps.who.int/iris/rest/bitstreams/1217528/retrieve

Current context for prioritization

- SEA strategy for sexually transmitted infection (STI) calls for prevention of vertical transmission of HSV. https://www.who.int/southeastasia/activities/seeking-inputs-developing-an-integrated-regional-action-plan-for-viral-hepatitis-hiv-and-stis-in-the-south-east-asia-region-2022-2026
- STI strategies often focus on HIV and treatable infections such as gonorrhea, chlamydia, syphilis, and trichomoniasis, and other regional sources do not include HSV-specific actions. https://www.afro.who.int/sites/default/files/2019-03/STI.EN_.pdf, https://www.paho.org/en/documents/plan-action-prevention-and-control-hiv-and-sexually-transmitted-infections-2016-2021, https://applications.emro.who.int/aiecf/WHO_EM_STD_089_en.pdf?ua=1, https://www.euro.who.int/__data/assets/pdf_file/0007/524059/HIV-Hepatitis-STIs-actions-plans-consult-eng.pdf
- Global strategies highlight the need for HSV vaccine development. https://apps.who.int/iris/rest/bitstreams/1032114/retrieve, https://apps.who.int/iris/rest/bitstreams/1217528/retrieve
- A Vaccine Value Profile for HSV is in preparation.

7. HIV-1 (Human immunodeficiency virus 1)

Table 18 HIV-1 (Human immunodeficiency virus 1)

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
1 Annual deaths in children under 5	39,833 Low (A)	1,753 Low (A)	1,609 Very low (A)	483 Very low (A)	3,281 Very low (A)	1,921 Low (A)	48,928 Low (A)
2 Annual deaths in people 5 and older	595,790 Very high (A)	49,304 Low (A)	15,352 Low (A)	30,660 Very low (A)	73,468 Medium (A)	49,304 Very low (A)	814,909 Very high (A)
3 Annual years lived with disability (all ages)	2,804,864 Very high (A)	356,691 Very high (A)	48,727 Very low (A)	201,942 Very high (A)	401,051 High (A)	189,114 Medium (A)	4,006,533 Very high (A)
4 Social and economic burden per case	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)
5 Disruption due to outbreaks	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)
6 Contribution to inequity	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)
7 Contribution to antimicrobial resistance	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)
8 Unmet needs for prevention & treatment	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)

Notes and selected citations

1-3 Annual deaths in children under 5, Annual deaths in people 5 and older, Annual years lived with disability

- Source: GBD Results [Internet]. Institute for Health Metrics and Evaluation. [cited 2022 Oct 5]. Available from: https://vizhub.healthdata.org/gbd-results

4 Social and economic burden per case

- Stigma and discrimination against people living with HIV are widespread. Peak resource needs of the Global AIDS Strategy amounts to US$ 29 billion for the HIV response in 2025. While this is a global total, it reflects the high per-case cost of AIDS prevention and treatment. https://www.unaids.org/sites/default/files/media_asset/global-AIDS-strategy-2021-2026_en.pdf

5 Disruption due to outbreaks

- The AIDS epidemic remains a global crisis. Progress has slowed markedly in some countries and communities. In others, the numbers of new infections and deaths are rising. https://www.unaids.org/sites/default/files/media_asset/global-AIDS-strategy-2021-2026_en.pdf

6 Contribution to inequity

- HIV disproportionately affects the most marginalized communities. The majority of people who are newly infected with HIV and who are not accessing life-saving HIV services are from the key population groups and live in vulnerable contexts, where inadequate political will, funding and policies prevent their access to health care. https://www.unaids.org/sites/default/files/media_asset/global-AIDS-strategy-2021-2026_en.pdf

7 Contribution to antimicrobial resistance

- HIV drug resistance is a global priority, and HIV infection increases risks of AMR. https://www.who.int/news/item/17-11-2020-hiv-drug-resistance-world-antimicrobial-awareness-week-2020, https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00161-0/fulltext

8 Unmet needs for prevention and treatment

- There is no vaccine or cure for HIV. Antiretroviral drugs reduce viral load and prevents progression to AIDS, but must be taken daily throughout a person's life. https://www.unaids.org/sites/default/files/media_asset/global-AIDS-strategy-2021-2026_en.pdf

Current context for prioritization

- Globally, HIV/AIDS has been the subject of 4 World Health Assembly resolutions. UNAIDS is leading the global effort to end AIDS as a public health threat by 2030. The International AIDS Vaccine Initiative is developing HIV vaccines and antibodies.
- Regional scores are based on the regional profiles in the UNAIDS Global AIDS Strategy 2021 – 2026. https://www.unaids.org/sites/default/files/media_asset/global-AIDS-strategy-2021-2026_en.pdf

8. Hookworm

Table 19 Hookworm

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
1 Annual deaths in children under 5	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)
2 Annual deaths in people 5 and older	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)
3 Annual years lived with disability (all ages)	523,433 Medium (A)	46,595 Very low (A)	66,527 Low (A)	4,205 Very low (A)	245,232 Low (A)	96,260 Low (A)	983,860 Medium (A)
4 Social and economic burden per case	Low (A)	Low (A)	Low (B)	Low (B)	Low (A)	Low (A)	Low (B)
5 Disruption due to outbreaks	Very low (B)	Very low (B)	Very low (B)	Very low (B)	Very low (B)	Very low (B)	Very low (B)
6 Contribution to inequity	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)
7 Contribution to antimicrobial resistance	Low (A)	Low (B)	Low (B)	Low (B)	Low (B)	Low (B)	Low (A)
8 Unmet needs for prevention & treatment	Low (A)	Low (A)	Low (A)	Low (A)	Low (A)	Low (A)	Low (A)

Notes and selected citations

1-2 Annual deaths in children under 5, Annual deaths in people 5 and older

- Data not found. Scored as Very low and will evaluate Low in sensitivity testing.

3 Annual years lived with disability (all ages)

- Source: GBD Results [Internet]. Institute for Health Metrics and Evaluation. [cited 2022 Oct 5]. Available from: https://vizhub.healthdata.org/gbd-results

4 Social and economic burden per case

- Burden mainly due to loss of productivity due to cognitive, developmental, and physical effects of infection. Global productivity loss ranges from 5.7B to 138.9B USD. In India, health outcome cost estimated at between $258M-$471M. Brazil suggests a per infection cost of $353 USD (includes health cost and productivity loss). Nigeria suggests a per infection cost of $103. Scored EUR low because societal cost is low compared to countries with active de-worming programs. https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0004922

5 Disruption due to outbreaks

- Clusters may occur in very poor communities. https://www.npr.org/sections/goatsandsoda/2017/09/12/550387650/the-u-s-thought-it-was-rid-of-hookworm-wrong

6 Contribution to inequity

- Strongly associated with poverty and lack of sanitation. Contributes to the cycle of poverty. Large disparity in burden across HIC and LMICs with LMIC bearing the largest burden by far. https://www.who.int/publications/i/item/9789240010352

7 Contribution to antimicrobial resistance

- Billions of doses of albendazole are used annually for mass drug administration (MDA) which may contribute to the risk of development resistance. https://www.who.int/news-room/fact-sheets/detail/soil-transmitted-helminth-infections
- Resistance alleles detected but treatment failure has not been widely reported. https://www.ajtmh.org/view/journals/tpmd/100/2/article-p351.xml

8 Unmet needs for prevention and treatment

- MDA has been widely successful in decreasing burden but in areas of high prevalence, is not enough to reach elimination targets. https://www.who.int/publications/i/item/9789240010352

Current context for prioritization

- Hookworm and other soil-transmitted helminths are among the targets of “Ending the neglect to attain the Sustainable Development Goals: A road map for neglected tropical diseases 2021–2030”. https://www.who.int/publications/i/item/9789240010352
- Global elimination targets have also been adopted. https://www.who.int/news-room/fact-sheets/detail/soil-transmitted-helminth-infections
- A Vaccine Value Profile is in preparation for hookworm.

9. Influenza

Note: Quantitative scoring is based on the burden of seasonal influenza due to the difficulty of predicting the burden of influenza pandemics. Qualitative scoring considers both seasonal and pandemic influenza.

Table 20 Influenza

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
1 Annual deaths in children under 5	18,372 Very low (A)	2,466 Low (A)	5,585 Very low (A)	1,135 Low (A)	6,400 Very low (A)	3,069 Medium (A)	37,070 Very low (A)
2 Annual deaths in people 5 and older	23,779 Low (A)	37,065 Low (A)	8,905 Very low (A)	31,943 Very low (A)	37,021 Low (A)	65,571 Low (A)	206,601 Low (A)
3 Annual years lived with disability (all ages)	11,683 Very low (A)	15,391 Very low (A)	8,745 Very low (A)	11,996 Very low (A)	31,333 Very low (A)	22,755 Very low (A)	102,494 Very low (A)
4 Social and economic burden per case	Low (C)	Low (A)	Low (C)	Low (A)	Low (A)	Low (A)	Low (A)
5 Disruption due to outbreaks	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)
6 Contribution to inequity	Medium (B)	Medium (A)	Medium (B)	Medium (B)	Medium (B)	Medium (B)	Medium (A)
7 Contribution to antimicrobial resistance	Medium (B)	Medium (A)	Medium (B)	Medium (A)	High (B)	High (B)	Medium (A)
8 Unmet needs for prevention & treatment	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)

Notes and selected citations

1-3 Annual deaths in children under 5, Annual deaths in people 5 and older, Annual years lived with disability

- Source: GBD Results [Internet]. Institute for Health Metrics and Evaluation. [cited 2022 Oct 5]. Available from: https://vizhub.healthdata.org/gbd-results, https://www.thelancet.com/cms/10.1016/S0140-6736(20)30925-9/attachment/7709ecbd-5dbc-4da6-93b2-3fd0bedc16cc/mmc1.pdf

- Hospital-based studies may significantly under-estimate the burden of influenza. In sensitivity testing, evaluate higher scores for influenza deaths. https://pubmed.ncbi.nlm.nih.gov/29040527/
- A 2011 analysis estimated that there were 28,000-111,500 deaths in children under 5 attributable to influenza-associated ALRI in 2008. (https://pubmed.ncbi.nlm.nih.gov/22078723/) Based on these results, sensitivity testing will include 3-fold higher values for Annual deaths in children under 5.
- A 2018 analysis estimated that 291,243 – 645,832 seasonal influenza-associated respiratory deaths occur annually. Based on these results, sensitivity testing will include 3-fold higher values for Annual deaths in people 5 and older. (https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(17)33293-2/fulltext)

4 Social and economic burden per case

- While total economic burden is substantial, cost per episode is relatively low, ranging from $30 to $64 in studies from high- and middle-income countries. https://pubmed.ncbi.nlm.nih.gov/24055351/
- Compared to high-income economies, lower- and middle-income economies have higher productivity losses and lower direct costs due to influenza. https://pubmed.ncbi.nlm.nih.gov/26597032/

5 Disruption due to outbreaks

- Influenza A viruses cause worldwide pandemics, characterized by rapid spread of new influenza A subtypes that have the capacity for sustained human-to-human transmission. https://apps.who.int/iris/bitstream/handle/10665/354264/WER9719-eng-fre.pdf?sequence=1&isAllowed=y

6 Contribution to inequity

- In the US, minorities and those of lower socioeconomic status are more likely to be hospitalized for influenza and have lower rates of influenza vaccination. https://pubmed.ncbi.nlm.nih.gov/35429133/, https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2783448, https://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-021-11179-9

7 Contribution to antimicrobial resistance

- Influenza remains susceptible to first line drugs.
- Influenza contributes to inappropriate antibiotic use. https://pubmed.ncbi.nlm.nih.gov/32056049/, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7880080/pdf/IANN_52_1782460.pdf, https://academic.oup.com/eurpub/article/31/6/1137/6371856?login=true

8 Unmet needs for prevention and treatment

- “Safe and well-tolerated influenza vaccines that prevent severe influenza illness, provide protection beyond a single year, and are suitable for programmatic use, are needed for low- and middle-income countries.” https://apps.who.int/iris/rest/bitstreams/1087983/retrieve

Current context for prioritization

- 118 of 194 WHO Member States have national influenza vaccination policies and the WHA has endorsed the Pandemic Influenza Preparedness Framework. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8143996/pdf/main.pdf

10. Intestinal pathogenic *E. coli* (InPEC)

Note: Intestinal pathogenic *E. coli* (InPEC) includes enterotoxigenic *E. coli* (ETEC) and enteropathogenic *E. coli* (EPEC).

Table 21 Intestinal pathogenic *E. coli* (InPEC)

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
1 Annual deaths in children under 5 (Source 1)	12,932 Very low (A)	129 Very low (A)	3,486 Very low (A)	67 Very low (A)	5,212 Very low (A)	99 Very low (A)	21,925 Very low (A)
(Source 2)	26,500 Low (B)	600 Very low (B)	6,600 Very low (B)	200 Very low (B)	10,000 Low (B)	600 Very low (B)	44,400 Low (B)
2 Annual deaths in people 5 and older	3,965 Very low (A)	297 Very low (A)	2,233 Very low (A)	635 Very low (A)	24,710 Very low (A)	244 Very low (A)	32,084 Very low (A)
3 Annual years lived with disability (all ages)	45,000 Very low (A)	9,142 Very low (A)	34,410 Very low (A)	25,052 Very low (A)	85,000 Very low (A)	7,685 Very low (A)	206,536 Very low (A)
4 Social and economic burden per case	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)
5 Disruption due to outbreaks	Medium (B)	Medium (B)	Medium (B)	Medium (B)	Medium (B)	Medium (B)	Medium (B)
6 Contribution to inequity	Medium (A)	Medium (B)	Medium (B)	Medium (B)	Medium (B)	Medium (B)	Medium (B)
7 Contribution to antimicrobial resistance	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)
8 Unmet needs for prevention & treatment	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)

Notes and selected citations

1 Annual deaths in children under 5

- Source 1 (for use in Preferences Survey): Institute for Health Metrics and Evaluation (IHME), University of Oxford. Global Bacterial Antimicrobial Resistance Burden Estimates 2019. Seattle, United States of America:

Institute for Health Metrics and Evaluation (IHME), 2022. Values are totals of antibiotic resistant and susceptible forms of *E. coli* presenting as diarrhea.

- Source 2 (for use in Preferences Survey): Anderson JD, Bagamian KH, Muhib F, Amaya MP, Laytner LA, Wierzba T, et al. Burden of enterotoxigenic Escherichia coli and shigella non-fatal diarrhoeal infections in 79 low-income and lower middle-income countries: a modelling analysis. The Lancet Global Health [Internet]. 2019 Mar 1 [cited 2022 Nov 1];7(3):e321–30. Available from: https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(18)30483-2/fulltext. Quoted estimates are for deaths from ETEC diarrhea and ETEC-induced stunting.

2 Annual deaths in people 5 and older

- Source: Institute for Health Metrics and Evaluation (IHME), University of Oxford. Global Bacterial Antimicrobial Resistance Burden Estimates 2019. Seattle, United States of America: Institute for Health Metrics and Evaluation (IHME), 2022. Values are totals of antibiotic resistant and susceptible forms of *E. coli* presenting as diarrhea.
- Current IHME estimates for the African and South-East Asian regions are markedly lower than those previously reported for countries in those regions (https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0002705).
- Absent an alternative source for regional burden estimates, the IHME values will be used for the Preferences Survey and higher scores will be evaluated in sensitivity testing.

3 Annual years lost to disability (all ages)

- Source: Institute for Health Metrics and Evaluation (IHME), University of Oxford. Global Bacterial Antimicrobial Resistance Burden Estimates 2019. Seattle, United States of America: Institute for Health Metrics and Evaluation (IHME), 2022. Values are totals of antibiotic resistant and susceptible forms of *E. coli* presenting as diarrhea. YLDs are calculated by subtracting Years of Life Lost (YLLs) from Disability Adjusted Life Years (DALYs).
- Because the YLDs represent the burden of diarrhea alone, stunting and other consequences of InPEC infections may not be reflected in these estimates. Higher scores will be evaluated in sensitivity testing.

4 Social and economic burden per case

- Average direct medical costs per episode estimate $10.05 for outpatients and $82.25 for inpatients. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6668229/
- Repeated ETEC infections, as well as infections with other diarrheagenic *E. coli*, like EPEC and enteroaggregative *E. coli*, can induce or exacerbate stunting and other forms of malnutrition, reduce immune function, and increase the propensity for subsequent irritable bowel syndrome. This results in adverse consequences on growth and cognitive development and can lead to an increased risk of death due to other infectious disease causes. https://academic.oup.com/jid/article/224/Supplement_7/S848/6371002#324022360, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7024994/, https://pubmed.ncbi.nlm.nih.gov/30784633/, https://pubmed.ncbi.nlm.nih.gov/28381477/, https://pubmed.ncbi.nlm.nih.gov/31384741/

5 Disruption due to outbreaks

- ETEC is a common cause of foodborne illness outbreaks. https://pubmed.ncbi.nlm.nih.gov/28597303/
- Recent data from Africa, Haiti and South Asia indicates that ETEC can be a significant contributor to outbreaks of cholera-like illness that are occurring with increasing frequency in these areas. https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-020-05454-0, https://pubmed.ncbi.nlm.nih.gov/24445205/, https://pubmed.ncbi.nlm.nih.gov/16022790/
- Global climate change will likely lead to environmental conditions that will increase the likelihood of ETEC outbreaks as well as the overall global burden of ETEC and infections with other diarrheagenic E. coli and enteric bacterial pathogens https://pubmed.ncbi.nlm.nih.gov/35024531/

6 Contribution to inequity

- Economic status and household setting contribute to risk of ETEC. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7024994/

7 Contribution to antimicrobial resistance

- *Enterobacteriaceae*, including *E. coli*, are a "critical" priority for R&D of new antibiotics. https://www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed

8 Unmet needs for prevention and treatment

- ETEC infections can be prevented through improved sanitation and hygiene, however in many settings these are difficult to sustain. Antibiotics are used for travelers' diarrhea, but development of resistance is an ongoing, critical concern. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1195967/, https://pubmed.ncbi.nlm.nih.gov/33965254/

Current context for prioritization

- Global: prioritized by WHO due to risk of AMR and burden of diarrheal diseases. https://apps.who.int/iris/rest/bitstreams/1349138/retrieve
- Given the growing public health concerns regarding ETEC as an increasing AMR threat, the Wellcome Trust has recently recommended that vaccine development for enteric E. coli, like ETEC, be accelerated. https://vaccinesforamr.org/wp-content/uploads/2018/09/Vaccines_for_AMR.pdf
- ETEC is recognized as the leading bacterial cause of travelers' diarrhea among traveler and deploying military personnel from high-income countries visiting or deploying to endemic areas in Africa, South and Central America and South Asia, https://pubmed.ncbi.nlm.nih.gov/33965254/
- Regions: indications that endemic ETEC is a high priority at a regional level were not found. Scored based on the recognized importance of diarrheal diseases.

11. Klebsiella pneumoniae

Table 22 ***Klebsiella pneumoniae***

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
1 Annual deaths in children under 5	110,018 Very high (A)	7,575 Very high (A)	33,640 Very high (A)	2,592 High (A)	43,208 Very high (A)	7,529 Very high (A)	204,628 Very high (A)
2 Annual deaths in people 5 and older	85,529 Very high (A)	95,016 Medium (A)	41,852 Very high (A)	91,663 Medium (A)	153,644 Very high (A)	113,416 Medium (A)	584,299 High (A)
3 Annual years lived with disability (all ages)	30,414 Very low (A)	15,802 Very low (A)	13,913 Very low (A)	8,781 Very low (A)	49,470 Very low (A)	13,338 Very low (A)	131,997 Very low (A)
4 Social and economic burden per case	High (B)	High (A)	High (B)	High (B)	High (A)	High (A)	High (A)
5 Disruption due to outbreaks	Low (A)	Low (A)	Low (A)	Low (A)	Low (A)	Low (A)	Low (A)
6 Contribution to inequity	Low (B)	Low (B)	Low (B)	Low (B)	Low (B)	Low (B)	Low (B)
7 Contribution to antimicrobial resistance	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)
8 Unmet needs for prevention & treatment	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)

Notes and selected citations

1-3 Annual deaths in children under 5, Annual deaths in people 5 and older, Annual years lived with disability

- Source: Institute for Health Metrics and Evaluation (IHME), University of Oxford. Global Bacterial Antimicrobial Resistance Burden Estimates 2019. Seattle, United States of America: Institute for Health Metrics and Evaluation (IHME), 2022.
- Values are total deaths from antibiotic resistant and susceptible forms. YLDs are calculated by subtracting Years of Life Lost (YLLs) from Disability Adjusted Life Years (DALYs).

4 Social and economic burden per case

- Infection with resistant strains increases hospital stays and treatment costs. Examples include: https://academic.oup.com/cid/article/67/suppl_2/S225/5181281, https://www.ijidonline.com/article/S1201-9712(16)30263-6/fulltext#relatedArticles

5 Disruption due to outbreaks

- Often causes outbreaks in hospitals. https://www.ncbi.nlm.nih.gov/books/NBK519004/ Reports of outbreaks outside of healthcare settings were not found.

6 Contribution to inequity

- Risk factors for *K. pneumoniae* infections include prior antibiotic treatment, certain comorbidities, and medical interventions. https://pubmed.ncbi.nlm.nih.gov/34899618/, https://pubmed.ncbi.nlm.nih.gov/34470123/

7 Contribution to antimicrobial resistance

- *Enterobacteriaceae*, including *K. pneumoniae*, are a "critical" priority for R&D of new antibiotics. https://www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed
- Treatment failure rates exceed 50% in some settings. Examples: https://www.frontiersin.org/articles/10.3389/fmicb.2018.03198/full, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8479884/

8 Unmet needs for prevention and treatment

- High rates of resistance limit treatment options. http://vaccinesforamr.org/wp-content/uploads/2018/09/Vaccines_for_AMR.pdf

Current context for prioritization

- Prioritized as an antimicrobial resistance concern. Examples include https://www.who.int/southeastasia/health-topics/antimicrobial-resistance, https://www.who.int/news-room/feature-stories/detail/facing-the-threat-of-antibiotic-resistance-israel-s-success-to-prevent-and-control-the-spread-of-carbapenem-resistant-bacteria
- *K. pneumoniae* has become a high priority for the Gates Foundation as it is a leading cause of neonatal sepsis and potentially preventable by maternal immunization. https://champshealth.org/data/

12. Leishmania

Table 23 Leishmania

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
1 Annual deaths in children under 5	839 Very low (A)	198 Very low (A)	216 Very low (A)	12 Very low (A)	289 Very low (A)	0 Very low (A)	1,556 Very low (A)
2 Annual deaths in people 5 and older	1,720 Very low (A)	873 Very low (A)	490 Very low (A)	44 Very low (A)	1,028 Very low (A)	0 Very low (A)	4,157 Very low (A)
3 Annual years lived with disability (all ages)	9,425 Very low (A)	12,959 Very low (A)	269,827 Very high (A)	467 Very low (A)	823 Very low (A)	20 Very low (A)	293,813 Very low (A)
4 Social and economic burden per case	Very high (B)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (B)	Very high (A)
5 Disruption due to outbreaks	High (A)	Medium (A)	High (A)	Very low (B)	High (A)	Very low (B)	Medium (A)
6 Contribution to inequity	Very high (A)	High (A)	Very high (A)	High (A)	Very high (A)	High (A)	High (A)
7 Contribution to antimicrobial resistance	Medium (A)	Medium (A)	Medium (A)	Very low (A)	Medium (A)	Very low (A)	Medium (A)
8 Unmet needs for prevention & treatment	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)

Notes and selected citations

1-2 Annual deaths in children under 5, Annual deaths in people 5 and older

- Source: GBD Results [Internet]. Institute for Health Metrics and Evaluation. [cited 2022 Oct 5]. Available from: https://vizhub.healthdata.org/gbd-results
- While the GBD dataset reports zero deaths and very few YLDs for Leishmania in the Western Pacific region, higher figures have been reported for China. That said, the figures reported still score as “Very low”. https://weekly.chinacdc.cn/en/article/doi/10.46234/ccdcw2020.173

3 Annual years lived with disability (all ages)

- Including the disability burden of co-morbid major depressive disorder associated with cutaneous leishmaniasis gives much higher estimates of the disability burden of leishmaniasis than reported in the GBD 2016 or 2019 datasets. https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0007092, https://vizhub.healthdata.org/gbd-results/ Will test higher scores in sensitivity analysis.

4 Social and economic burden per case

- "Even with free treatment, households may suffer catastrophic health expenditure from direct and indirect medical costs, which compounds existing financial strain in low-income communities for households and healthcare systems." https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8236266/

5 Disruption due to outbreaks

- Transmitted by sandflies so there is a potential for outbreaks where vector and parasite mix. Conflict and displacement increase vulnerability. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8236266/, https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(21)00392-2/fulltext, https://academic.oup.com/trstmh/article-abstract/88/4/386/1899141?redirectedFrom=fulltext, https://pubmed.ncbi.nlm.nih.gov/10361752/

6 Contribution to inequity

- Poverty and occupation are the key risk factors. Malnutrition and HIV infection increase susceptibility and complicate diagnosis and treatment. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8236266/

7 Contribution to antimicrobial resistance

- Treatment regimens have been adapted due to drug resistance and there are concerns about the continued effectiveness of the current options. https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0006052

8 Unmet needs for prevention and treatment

- Vector control to prevent leishmaniasis can be costly and difficult to implement, and there are gaps in understanding its effectiveness and sustainability. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8118276/ , https://www.frontiersin.org/articles/10.3389/fcimb.2021.641632/full
- Treatments are difficult to administer and include painful injections. "In the absence of a topical, painless treatment, it is challenging to get patients with minor lesions to be diagnosed and treated." https://www.who.int/publications/i/item/9789240010352

Current context for prioritization

- Bangladesh, India, and Nepal launched a visceral leishmaniasis elimination initiative in 2005. Nepal and Bangladesh have achieved elimination and India is approaching elimination. https://www.bmj.com/content/bmj/364/bmj.k5224.full.pdf, https://www.who.int/news/item/29-07-2021-visceral-leishmaniasis-elimination-india-gears-up-to-overcome-last-mile-challenges.
- Kenya, Ethiopia, Sudan, and Uganda have established strategic plans for elimination, control, or detection and treatment of leishmaniasis. https://www.frontiersin.org/articles/10.3389/fitd.2022.965609/full
- Leishmaniasis is among the targets of "Ending the neglect to attain the Sustainable Development Goals: A road map for neglected tropical diseases 2021–2030". https://www.who.int/publications/i/item/9789240010352
- That said, the impact of cutaneous leishmaniasis is under-recognized. https://pubmed.ncbi.nlm.nih.gov/30802261/

13. Mycobacterium leprae (leprosy)

Table 24 *Mycobacterium leprae* (leprosy)

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
1 Annual deaths in children under 5	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)
2 Annual deaths in people 5 and older	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)	Very low (C) (test Low)
3 Annual years lived with disability (all ages)	6,049 Very low (A) (test Low)	2,944 Very low (A)	1,661 Very low (A)	20 Very low (A)	16,770 Very low (A)	1,371 Very low (A)	28,838 Very low (A)
4 Social and economic burden per case	Very high (A)	Very high (A)	Very high (B)	Very high (A)	Very high (A)	Very high (A)	Very high (A)
5 Disruption due to outbreaks	Very low (A)	Very low (A)	Very low (A)	Very low (A)	Very low (A)	Very low (A)	Very low (A)
6 Contribution to inequity	Very high (B)	Very high (A)	Very high (B)	Very high (A)	Very high (A)	Very high (B)	Very high (A)
7 Contribution to antimicrobial resistance	Low (A)	Medium (A)	Low (A)	Very low (B)	Medium (A)	Medium (A)	Medium (A)
8 Unmet needs for prevention & treatment	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)

Notes and selected citations

1-2 Annual deaths in children under 5, Annual deaths in people 5 and older

- GBD did not estimate deaths for leprosy. Will score as Very low for the Preferences Survey and evaluate Low in sensitivity testing.

3 Annual years lived with disability (all ages)

- Source: GBD Results [Internet]. Institute for Health Metrics and Evaluation. [cited 2022 Oct 5]. Available from: https://vizhub.healthdata.org/gbd-results
- GBD YLD results appear low in light of reported leprosy incidence, disability rates, and disability weights. https://apps.who.int/iris/bitstream/handle/10665/258841/WER9235.pdf, https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0009209.
- In sensitivity testing, will evaluate higher scores.

4 Social and economic burden per case

- Significant costs of treatment and lost productivity reported in Cameroon, China, and India. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5899508/,

https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-017-2869-8, https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0003431

- Stigma associated with leprosy impedes access to health care, high suicide rates have been reported. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7379324/, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4457619/, https://pubmed.ncbi.nlm.nih.gov/31517884/

5 Disruption due to outbreaks

- Because prolonged contact is required for transmission and the bacteria are slow-growing, leprosy outbreaks are unlikely to occur. https://www.cdc.gov/leprosy/transmission/index.html

6 Contribution to inequity

- Studies in Brazil, India, and Bangladesh report that poverty and lower socio-economic status is associated with higher risk of leprosy. https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0006622

7 Contribution to antimicrobial resistance

- Multi-drug regimens are recommended because monotherapies are associated with resistance and with relapsing disease. https://pubmed.ncbi.nlm.nih.gov/35643395/
- Rifampicin, an antibiotic used treat leprosy, is also used to treat other infections so leprosy treatment could drive up resistance in other pathogens. https://www.who.int/publications/i/item/SEA-GLP-7
- While this effect is likely to be small due to the low number of leprosy patients, increased use of rifampicin for chemoprophylaxis would increase antibiotic consumption and selective pressure. https://www.who.int/news/item/08-09-2020-leprosy-countries-should-step-up-prevention-initiatives-to-stimulate-sluggish-decline-in-new-cases

8 Unmet needs for prevention and treatment

- Prevention and treatments do not meet the needs of at-risk populations. Research priorities include diagnostics, digital technology and innovation, disability, epidemiological modelling and investment case, implementation research, stigma, post-exposure prophylaxis and transmission, and vaccines. https://idpjournal.biomedcentral.com/articles/10.1186/s40249-020-00774-4
- A course of treatment for susceptible infections lasts 6-12 months. Treatment for resistant infections requires 2 years. https://www.who.int/publications/i/item/9789290226383
- Prevention is preferable to treatment due to the stigma and potential for permanent disfigurement associated with leprosy. https://www.who.int/publications/i/item/9789240010352
- Chemoprophylaxis reduces transmission to contacts by 60% but is not widely used, in part due to stigma. https://www.who.int/publications/i/item/9789290226383
- Novartis donates multi-drug therapies for leprosy to WHO for use in treatment programs. https://www.novartis.com/news/media-releases/novartis-renews-who-medicine-donation-pledge-aim-ending-leprosy

Current context for prioritization

- Leprosy is targeted by the Global Leprosy Strategy 2016-2020 and by the Roadmap for Neglected Tropical Diseases. https://apps.who.int/iris/bitstream/handle/10665/208824/9789290225096_en.pdf, https://www.who.int/publications/i/item/9789240010352
- SEAR and WPR are actively addressing leprosy. https://www.who.int/news-room/articles-detail/call-for-experts-for-the-technical-advisory-group-for-leprosy, https://www.who.int/westernpacific/activities/reducing-leprosy-burden
- Vaccine trials have been sponsored by IDRI and BioManguinos/Fiocruz, and organizations such as the International Leprosy Congress and Association (https://www.ilc-india2022.com/) and the Global Partnership for Zero Leprosy are also targeting leprosy.

14. Mycobacterium tuberculosis (TB)

Table 25 *Mycobacterium tuberculosis*

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
1 Annual deaths in children under 5 (Source 1)	38,279 Low (B)	655 Very low (B)	12,055 Low (B)	1,306 Low (B)	77,220 Very high (B)	11,182 Very high (B)	140,696 High (B)
(Source 2)	32,799 Low (A)	469 Very low (A)	7,693 Low (A)	339 Very low (A)	7,378 Very low (A)	1,460 Very low (A)	50,163 Low (A)
2 Annual deaths in people 5 and older (source 1)	325,870 Very high (B)	22,863 Very low (B)	74,363 Very high (B)	19,611 Very low (B)	686,265 Very high (B)	109,160 Medium (B)	1,238,133 Very high (B)
(Source 2)	336,266 Very high (A)	19,841 Very low (A)	89,929 Very high (A)	24,663 Very low (A)	555,002 Very high (A)	103,124 Medium (A)	1,129,603 Very high (A)
3 Annual years lived with disability (all ages)	1,140,560 Very high (A)	84,655 Low (A)	384,456 Very high (A)	109,961 Very high (A)	1,934,071 Very high (A)	662,543 Very high (A)	4,319,540 Very high (A)
4 Social and economic burden per case	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)
5 Disruption due to outbreaks	Very high (A)	High (A)	High (A)	High (A)	Very high (A)	High (A)	Very high (A)
6 Contribution to inequity	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)
7 Contribution to antimicrobial resistance	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)
8 Unmet needs for prevention & treatment	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)

Notes and selected citations

1-2 Annual deaths in children under 5, Annual deaths in people 5 and older

- Source 1 (for use in Preferences Survey): WHO Global Tuberculosis Report 2022, Regional distribution of estimated TB mortality in HIV-negative people by age group. (https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022/tb-disease-burden/2-2-tb-mortality, deaths by age group and region obtained from the WHO TB team.)
- Source 2 (for use in sensitivity testing): GBD Results [Internet]. Institute for Health Metrics and Evaluation. [cited 2022 Oct 5]. Available from: https://vizhub.healthdata.org/gbd-results

3 Annual years lived with disability

- Source: GBD Results [Internet]. Institute for Health Metrics and Evaluation. [cited 2022 Oct 5]. Available from: https://vizhub.healthdata.org/gbd-results

4 Social and economic burden per case

- Source: Global tuberculosis report 2022. Geneva: World Health Organization; 2022. Licence: CC BY-NC-SA 3.0 IGO. https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022
- TB is a disease associated with poverty: a significant proportion of TB patients face substantial economic burden before, during and even after TB care. According to survey data, on average 50% of TB-affected households face catastrophic costs with a large proportion losing their jobs while on treatment. Furthermore, nearly 20% of global tuberculosis incidence is attributable to undernutrition.
- Stigma is an important barrier to TB care. https://www.stoptb.org/communities-rights-and-gender-crg/end-tb-stigma

5 Disruption due to outbreaks

- TB is a deadly air-borne bacterial lung infection, that can easily spread when a person with disease coughs, sneezes or spits. A person needs to inhale only a few bacilli to become infected, making it a lethal recipe for outbreaks particularly among people with health, environmental and socio-economic risk factors.
- Globally, close to a quarter of the world's population are infected with Mycobacterium tuberculosis, representing a substantial reservoir. https://erj.ersjournals.com/content/54/3/1900655

6 Contribution to inequity

- National TB prevalence surveys conducted in high-burden countries have consistently demonstrated higher disease burden among poorer individuals, with TB prevalence in the lowest income quintile on average 2.3 times greater than estimated for the highest income quintile. (National tuberculosis prevalence surveys 2007-2016 ; Global TB Report 2022)

7 Contribution to antimicrobial resistance

- Drug-resistant TB represents a global health threat. There were an estimated 450 000 incident cases in 2021. (Global TB Report 2022)

8 Unmet needs for prevention and treatment

- Treatment for drug-susceptible TB requires 4 to 6 months of therapy, and for drug-resistant forms of TB, the treatment duration is 6-20 months. The treatment success rate is 86% for drug-susceptible TB and 60% for drug-resistant TB. Treatment adherence is challenging given the complexity, side-effects and long duration of treatment. Non-adherence can result in emergence of drug-resistance. (Global TB Report 2022)

- The BCG vaccine is not effective in preventing adult pulmonary TB, which accounts for the majority of disease transmission worldwide. https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(22)00283-2/fulltext

Current context for prioritization

- TB is a global epidemic: As of 2021, it was the second of leading causes of death from an infectious agent (after Coronavirus-disease), the leading cause of death among people with HIV, and a significant cause of mortality from antimicrobial resistance (Global TB Report 2022)
- Heads of State and Government made a bold commitment to end the TB epidemic by 2030, through the adoption of the 2030 Agenda for Sustainable Development and its Sustainable Development Goals in 2015. https://documents-dds-ny.un.org/doc/UNDOC/GEN/N15/291/89/PDF/N1529189.pdf?OpenElement
- Member States have set TB goals in the WHO END TB Strategy endorsed by the sixty-seventh World Health Assembly in 2014, and in the Global Strategy for Tuberculosis Research and Innovation endorsed by the seventy-third World Health Assembly in 2020. https://apps.who.int/iris/bitstream/handle/10665/260211/A67_2014_REC1-en.pdf, https://apps.who.int/gb/ebwha/pdf_files/WHA73-REC1/A73_REC1-en.pdf#page=1
- Heads of States in the 2018 Political declaration of the UN General-Assembly High-Level Meeting on TB committed to deliver "as soon as possible, new, safe, effective, equitable, affordable, vaccines". https://documents-dds-ny.un.org/doc/UNDOC/GEN/N18/315/53/PDF/N1831553.pdf?OpenElement
- Several research institutes, universities and product-development partnerships are working to accelerate the development of more accurate diagnostics, more effective and safer drugs and regimens for the treatment of TB infection and disease; and new TB vaccines.

15. Neisseria gonorrhoeae (gonorrhea)

Table 26 *Neisseria gonorrhoeae* (gonorrhea)

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
1 Annual deaths in children under 5	0 Very low (A)	0 Very low (A)	0 Very low (A)	0 Very low (A)	0 Very low (A)	0 Very low (A)	0 Very low (A)
2 Annual deaths in people 5 and older	511 Very low (A)	340 Very low (A)	169 Very low (A)	274 Very low (A)	1,332 Very low (A)	332 Very low (A)	2,963 Very low (A)
3 Annual years lived with disability (all ages)	11,935 Very low (A)	4,885 Very low (A)	5,101 Very low (A)	3,815 Very low (A)	20,966 Very low (A)	12,169 Very low (A)	59,018 Very low (A)
4 Social and economic burden per case	Medium (B)	Medium (A)	Medium (B)	Medium (B)	Medium (B)	Medium (B)	Medium (B)
5 Disruption due to outbreaks	Low (B)	Low (A)	Low (B)	Low (B)	Low (B)	Low (A)	Low (A)
6 Contribution to inequity	High (A)	High (A)	High (B)	High (A)	High (A)	High (A)	High (A)
7 Contribution to antimicrobial resistance	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)
8 Unmet needs for prevention & treatment	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)

Notes and selected citations

1-3 Annual deaths in children under 5, Annual deaths in people 5 and older, Annual years lived with disability

- Source: GBD Results [Internet]. Institute for Health Metrics and Evaluation. [cited 2022 Oct 5]. Available from: https://vizhub.healthdata.org/gbd-results

4 Social and economic burden per case

- Data collected in the US show medical treatment costs for insured patients of $85 per case and productivity losses of $245 per case. https://pubmed.ncbi.nlm.nih.gov/33448729/, https://pubmed.ncbi.nlm.nih.gov/23987746/

- Estimates of the cost of gonorrhea in low-income settings were not found. Given the younger age composition and social factors contributing to delays in diagnosis and treatment, the cost per case of gonorrhea is likely to be significant. https://www.ncbi.nlm.nih.gov/books/NBK525195/

5 Disruption due to outbreaks

- Outbreaks can occur in vulnerable populations, especially with introduction of AMR strains. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7064409/

6 Contribution to inequity

- Prevalence is higher in low-income settings, and among indigenous populations and historically marginalized populations such as sex workers and men who have sex with men. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7064409/

7 Contribution to antimicrobial resistance

- *N. gonorrhoeae* has been highlighted by WHO as a "high" priority for R&D of new antibiotics. https://www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed
- The U.S. CDC listed *N. gonorrhoeae* as one of five pathogens in its AMR threat report. https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf
- Resistance to the last remaining mainstream treatment options has been reported, leading to concerns that gonorrhea may become an untreatable infection. https://pubmed.ncbi.nlm.nih.gov/29991383/
- Ceftriaxone is recommended for treatment in the U.S. and reports of declining susceptibility or treatment failure have been reported in the US, Europe, and Asia. https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2022.27.24.2200455, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5403062/

8 Unmet needs for prevention and treatment

- Gonorrhea can be prevented through safer sexual behavior and consistent, correct condom use.
- Antibiotic treatment can cure but reinfection is common. https://apps.who.int/iris/bitstream/handle/10665/246114/9789241549691-eng.pdf
- No vaccines are available for *N. gonorrhoeae*.

Current context for prioritization

- *N. gonorrhoeae* is targeted by the Global Health Sector Strategy on Sexually Transmitted Infections https://apps.who.int/iris/bitstream/handle/10665/246296/WHO-RHR-16.09-eng.pdf and as an antimicrobial resistance threat http://vaccinesforamr.org/wp-content/uploads/2018/09/Vaccines_for_AMR.pdf
- That said, *N. gonorrhoeae* prevalence monitoring is sub-optimal in many countries: https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-021-06381-4#Sec5
- A Vaccine Value Profile for *N. gonorrhoeae* is in preparation.

16. Non-typhoidal *Salmonella*

Table 27 Non-typhoidal *Salmonella*

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
1 Annual deaths in children under 5	81,059 High (A)	597 Very low (A)	2,956 Very low (A)	95 Very low (A)	3,875 Very low (A)	758 Very low (A)	89,362 Medium (A)
2 Annual deaths in people 5 and older	33,572 Low (A)	1,335 Very low (A)	2,775 Very low (A)	529 Very low (A)	11,676 Very low (A)	1,414 Very low (A)	51,330 Very low (A)
3 Annual years lived with disability (all ages)	50,321 Very low (A)	16,480 Very low (A)	14,092 Very low (A)	9,273 Very low (A)	16,866 Very low (A)	23,023 Very low (A)	130,415 Very low (A)
4 Social and economic burden per case	High (A)	Low (B)	Low (B)	Low (B)	Low (B)	Low (B)	Medium (A)
5 Disruption due to outbreaks	Medium (B)	Low (A)	Low (B)	Low (B)	Very low (A)	Low (B)	Medium (B)
6 Contribution to inequity	Very high (A)	High (B)	High (B)	High (B)	High (B)	High (B)	High (B)
7 Contribution to antimicrobial resistance	High (A)	High (A)	High (B)	High (B)	High (B)	High (B)	High (A)
8 Unmet needs for prevention & treatment	High (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)

Notes and selected citations

1-3 Annual deaths in children under 5, Annual deaths in people 5 and older, Annual years lived with disability

- Source: GBD Results [Internet]. Institute for Health Metrics and Evaluation. [cited 2022 Oct 5]. Available from: https://vizhub.healthdata.org/gbd-results
- As recommended by IHME, values are the sum of data from the GBD 2019 Cause of Death for Invasive Non-typhoidal *Salmonella* (iNTS) and data from the GBD 2019 Etiology dataset for non-typhoidal *Salmonella.*

4 Social and economic burden per case

- In developed countries, NTS infections most often result in self-limiting diarrhea or infrequently diarrhea requiring antibiotic treatment. (Invasive NTS Vaccine Value Profile, draft)
- In contrast, invasive NTS is concentrated in sub-Saharan Africa. https://pubmed.ncbi.nlm.nih.gov/34260964/

- Serious complications are common in cases of invasive NTS, and HIV, malaria, malnutrition, and anaemia all increase the risk of invasive disease https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00615-0

5 Disruption due to outbreaks

- In Africa, epidemic levels of invasive disease. https://journals.asm.org/doi/full/10.1128/ecosalplus.ESP-0007-2018
- Elsewhere, NTS outbreak response focuses on identifying the source of the pathogen and improving food safety. For example: https://pubmed.ncbi.nlm.nih.gov/35087664/

6 Contribution to inequity

- Illnesses are concentrated in socioeconomically disadvantaged groups, and it is likely that poor sanitation and unsafe water and food contribute to risk for infection. (Invasive NTS Vaccine Value Profile, draft)
- In Africa, risk factors for invasive NTS include HIV, malnutrition, malaria, and severe anemia. In high-income settings, risk factors include age ≥ 65 years, male sex, and certain chronic diseases and immunosuppressive drugs. https://journals.asm.org/doi/pdf/10.1128/ecosalplus.ESP-0007-2018

7 Contribution to antimicrobial resistance

- Globally, *Salmonellae*, including NTS, are a "high" priority for R&D of new antibiotics. https://www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed
- The Indian Priority Pathogen List to Guide Research, Discovery, and Development of New Antibiotics in India considers *Salmonella* species to be a "High" priority. https://dbtindia.gov.in/sites/default/files/IPPL_final.pdf
- High levels of multidrug resistance have been observed in Africa and the US. https://pubmed.ncbi.nlm.nih.gov/32677939/

8 Unmet needs for prevention and treatment

- Because invasive NTS is rapidly fatal and has a high case fatality ratio of 15%, a vaccine is urgently needed. (Invasive NTS Vaccine Value Profile, draft)

Current context for prioritization

- WHO regional offices and other regional bodies address NTS primarily as a food safety issue, focusing on interventions that reduce the risk of multiple pathogens. https://www.efsa.europa.eu/en/topics/topic/salmonella
- Global: prioritized by WHO due to risk of AMR and burden of diarrheal diseases

17. Norovirus

Table 28 Norovirus

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
1 Annual deaths in children under 5	30,121 Low (A)	1,367 Very low (A)	7,716 Low (A)	160 Very low (A)	3,432 Very low (A)	653 Very low (A)	43,481 Low (A)
2 Annual deaths in people 5 and older	29,785 Low (A)	5,881 Very low (A)	8,204 Very low (A)	2,433 Very low (A)	42,159 Low (A)	3,787 Very low (A)	92,317 Very low (A)
3 Annual years lived with disability (all ages)	177,538 Very low (A)	107,947 Low (A)	106,901 Low (A)	89,636 High (A)	125,426 Very low (A)	107,816 Low (A)	717,430 Low (A)
4 Social and economic burden per case	Medium (A)	Medium (A)	Medium (A)	Low (A)	Medium (A)	Medium (A)	Medium (A)
5 Disruption due to outbreaks	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)
6 Contribution to inequity	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)
7 Contribution to antimicrobial resistance	Low (B)	Low (B)	Low (B)	Low (B)	Low (B)	Low (B)	Low (B)
8 Unmet needs for prevention & treatment	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)

Notes and selected citations

1-3 Annual deaths in children under 5, Annual deaths in people 5 and older, Annual years lived with disability

- Source: GBD Results [Internet]. Institute for Health Metrics and Evaluation. [cited 2022 Oct 5]. Available from: https://vizhub.healthdata.org/gbd-results

4 Social and economic burden per case

- Modeling of the global economic burden of norovirus has assumed hospitalization rates of 0.2% to 1.7% depending on age, and 2-3 days hospitalization, and found an average cost $86 per case, primarily due to productivity losses. Individual costs may be modest but societal costs are high due to high incidence. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0151219

5 Disruption due to outbreaks

- Norovirus is the world's leading cause of epidemic gastroenteritis https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4284304/
- Outbreaks are common in healthcare facilities, long-term care facilities, schools, and childcare facilities, where vulnerable populations are affected. https://pubmed.ncbi.nlm.nih.gov/34225537/, https://pubmed.ncbi.nlm.nih.gov/35946340/

6 Contribution to inequity

- While incidence is similar in HICs and LICs, https://pubmed.ncbi.nlm.nih.gov/27115736/, individuals of lower socio-economic status are likely to suffer more from productivity losses associated with norovirus infection.

7 Contribution to antimicrobial resistance

- Norovirus poses a theoretical AMR threat through the inappropriate use of antibiotics but has not been highlighted as a driver of antibiotic resistance.
- Rotavirus vaccination has averted inappropriate antibiotic prescribing; norovirus vaccination may be expected to do the same. https://pubmed.ncbi.nlm.nih.gov/32376956/, https://pubmed.ncbi.nlm.nih.gov/35855006/

8 Unmet needs for prevention and treatment

- Care for norovirus focuses on treating symptoms, and there is no specific antiviral treatment. Preventive measures such as isolation of those infected, environmental cleaning, and food safety measures "are only modestly effective at best." https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3880795/

Current context for prioritization

- WHO regional offices address norovirus primarily as a food safety issue, focusing on interventions that reduce the risk of multiple pathogens. https://www.euro.who.int/__data/assets/pdf_file/0005/402989/50607-WHO-Food-Safety-publicationV4_Web.pdf
- However, the majority of norovirus gastroenteritis is directly-transmitted from person-to-person. National and regional public health bodies such as US CDC and ECDC and funders such as the Government of Canada (Link) and German DZIF have prioritized norovirus vaccines https://www.dzif.de/en/vaccine-development
- WHO is preparing a Vaccine Value Profile for norovirus vaccines.

18. Plasmodium falciparum (malaria)

Notes on quantitative scoring for *P. falciparum*:

- Global and region-specific data for deaths and YLDs attributable to *P. falciparum* could not be found.
- Given this gap, we propose to score *P. falciparum* with a maximum potential score, and then conduct sensitivity testing using the minimum potential scores.
- Maximum and minimum potential scores were assessed using the following data:
    - **% *P. vivax* cases by WHO region** from the World Malaria Report 2021 (WMR 2021) Tables 3.1-3.6. https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2021
    - **Total malaria deaths and YLDs by WHO region** from: GBD Results [Internet]. Institute for Health Metrics and Evaluation. [cited 2022 Oct 5]. Available from: https://vizhub.healthdata.org/gbd-results
- **Maximum potential score** assumes that all malaria deaths or YLDs are caused by *P. falciparum.* Since other malaria species, such as *Plasmodium vivax*, contribute to malaria burden, these scores would over-estimate the burden of malaria.
- **Minimum potential score** scales back the total burden of malaria by the percent of cases that are caused by *P. vivax* in each region (according to WMR 2021). In many cases, scaling back in this way does not change the score, as shown in Table 29.
    - Since *P. vivax* is generally considered to have a lower case fatality rate than *P. falciparum*, these scores are likely to under-estimate the deaths caused by *P. falciparum.*
    - YLDs are less clear-cut. If *P. vivax* causes similar or lower disability per case than *P. falciparum,* then this approach would also under-estimate the YLDs caused by *P. falciparum.* If *P. vivax* causes greater morbidity than *P. falciparum* (as considered in https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3553673/), scaling back total YLDs by the % *P. vivax* cases may not give a minimum potential value for *P. falciparum* YLDs per region. For that reason, expert advice is needed on the appropriate minimum score to evaluate in sensitivity testing.

Table 29 *Plasmodium falciparum* (malaria) – Quantitative scoring

	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
% *P. vivax* cases, 2019 (WMR 2021)	0.3%	77.4%	21.7%	--	51.6%	35.4%	2.8%
1 Annual deaths in children under 5							
Total malaria (GBD 2019)	342,099	144	4,085	0	9,809	150	356,363
Maximum	342,099 Very high (C)	144 Very low (C)	4,085 Very low (C)	0 Very low (C)	9,809 Low (C)	150 Very low (C)	356,363 Very high (C)
Minimum for sensitivity testing	341,072 Very high (C)	32 Very low (C)	3,199 Very low (C)	0 Very low (C)	4,748 Very low (C)	97 Very low (C)	346,384 Very high (C)

	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
2 Annual deaths in people 5 and older							
Total malaria (GBD 2019)	248,153	1,198	11,899	0	24,607	1,058	287,018
Maximum	248,153 Very high (C)	1,198 Very low (C)	11,899 Low (C)	0 Very low (C)	24,607 Very low (C)	1,058 Very low (C)	287,018 Low (C)
Minimum for sensitivity testing	247,409 Very high (C)	271 Very low (C)	9,317 Very low (C)	0 Very low (C)	11,910 Very low (C)	683 Very low (C)	278,982 Low (C)
3 Annual years lived with disability (all ages)							
Total malaria (GBD 2019)	2,363,663	11,869	77,760	120	147,421	11,323	2,613,114
Maximum	2,363,663 Very high (C)	11,869 Very low (C)	77,760 Low (C)	120 Very low (C)	147,421 Low (C)	11,323 Very low (C)	2,613,114 Very high (C)
Minimum for sensitivity testing	2,356,572 Very high (C)	2,682 Very low (C)	60,886 Low (C)	120 Very low (C)	71,352 Very low (C)	7,315 Very low (C)	2,539,947 Very high (C)

Qualitative scoring

Table 30 *Plasmodium falciparum* (malaria) – Qualitative scoring

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
4 Social and economic burden per case	High (A)	High (A)	High (A)	Low (B)	High (A)	High (A)	High (A)
5 Disruption due to outbreaks	High (A)	Low (A)	Low (A)	Very low (A)	Medium (A)	Low (A)	Medium (A)
6 Contribution to inequity	Very high (A)	High (B)	High (B)	Very Low (B)	High (B)	High (B)	High (B)
7 Contribution to antimicrobial resistance	High (A)	Low (A)	Medium (A)	Very low (A)	High (A)	Medium (A)	High (A)
8 Unmet needs for prevention & treatment	High (A)	Medium (A)	Medium (A)	Very low (B)	Medium (A)	Medium (A)	High (A)

Notes and selected citations

- **European region**. Malaria transmission is rare in Europe, and most cases are travel-related, so it was scored as "Very low" for many criteria in the region. https://www.ecdc.europa.eu/sites/default/files/documents/AER-malaria-2019.pdf

4 Social and economic burden per case

- A recent analysis of data from 180 countries between 2000 and 2017 showed a 10% reduction in malaria incidence was associated with an average rise of 0.3% in per capita gross domestic product (GDP) and faster GDP growth. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6896867/
- Among school-age children in Africa, malaria infections are associated with poor health, anemia, diminished cognitive function and lower educational achievement. https://pubmed.ncbi.nlm.nih.gov/33222799/

5 Disruption due to outbreaks

- Relaxation of malaria control measures can allow local resurgence. Epidemics escalate rapidly and on average last 3-4 months. https://apps.who.int/iris/bitstream/handle/10665/272284/9789241565578-eng.pdf, https://malariajournal.biomedcentral.com/articles/10.1186/1475-2875-11-122, https://www.nicd.ac.za/wp-content/uploads/2022/08/310822-NICD-Monthly-Communique-Aug-NW5.pdf

6 Contribution to inequity

- *P. falciparum* disproportionately affects the poor, due to greater incidence in areas with lower socioeconomic status and to greater cost of treatment and lost productivity relative to income. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(13)60851-X/fulltext

7 Contribution to antimicrobial resistance

- Resistance to current first-line drugs has emerged in Africa and South-east Asia and resistance or treatment failures has been reported from nearly all regions with malaria. Insecticide failure has also been reported. https://www.who.int/publications/i/item/who-wer9709-61%E2%80%9380, https://pubmed.ncbi.nlm.nih.gov/31366610/, https://apps.who.int/malaria/maps/threats/
- In the Eastern Mediterranean region, chloroquine-resistant *Plasmodium falciparum* is a major problem in a number of countries (e.g., Somalia (90%), Djibouti (60-70%) and Pakistan (20%)). Moreover, imported cases of malaria to the region from highly endemic countries in South Asia (with higher rates of chloroquine and artemisinin resistance) is a public health concern. https://www.cdc.gov/malaria/travelers/country_table/d.html

8 Unmet needs for prevention and treatment

- Approaches to prevention include insecticide-treated bednets, indoor residual spraying, seasonal malaria chemoprevention, and the RTS,S malaria vaccine (for regions with moderate to high malaria rates). https://www.who.int/publications/i/item/who-wer9709-61%E2%80%9380
- Malaria treatment and prevention programmes in many countries in SSA are still below optimal level of performance due to a combination of factors including widespread and increasing insecticide resistance of pyrethroid-based vector control with substantially higher costs of repurposed insecticides to address resistance, the emergence of artemisinin partial resistance, and insufficient funds for malaria control: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9421173/
- However, clinical trials have shown promising results in the appropriate deployment of imperfect interventions. CFor example, a combination of RTS,S vaccine with seasonal malaria chemoprevention (SMC) resulted in a substantially lower incidence of uncomplicated malaria, severe malaria, and death from malaria than either RTS,S or SMC alone: https://pubmed.ncbi.nlm.nih.gov/34432975/
- The current vaccine does not address all the use cases defined in the Preferred Product Characteristics for malaria vaccines. https://www.who.int/publications/i/item/WHO-IVB-14.09

Current context for prioritization

- WHO has defined Preferred Product Characteristics for malaria vaccines and a Vaccine Value Profile is in preparation. https://www.who.int/publications/i/item/WHO-IVB-14.09
- Malaria is prioritized by many global and regional strategies and partnerships. https://www.who.int/southeastasia/activities/eliminating-malaria-by-2030-south-east-asia-region-member-states-reaffirm-commitment, https://africacdc.org/download/partnerships-for-african-vaccine-manufacturing-pavm-framework-for-action, https://www.emro.who.int/health-topics/malaria/index.html, https://www.paho.org/en/campaigns/malaria-day-americas, https://www.who.int/publications/i/item/9789290618157
- European engagement in malaria is primarily as a funder or partner for efforts in other regions. http://www.edctp.org/web/app/uploads/2020/07/EDCTP_Strategic-Research-Agenda-version4_July2020.pdf

19. Pseudomonas aeruginosa

Table 31 ***Pseudomonas aeruginosa***

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
1 Annual deaths in children under 5	47,935 Medium (A)	4,605 High (A)	16,349 Medium (A)	1,713 Medium (A)	25,646 Medium (A)	4,821 High (A)	101,109 Medium (A)
2 Annual deaths in people 5 and older	46,733 Medium (A)	82,487 Medium (A)	28,480 Medium (A)	77,013 Low (A)	106,274 High (A)	113,120 Medium (A)	457,184 Medium (A)
3 Annual years lived with disability (all ages)	14,790 Very low (A)	11,260 Very low (A)	9,623 Very low (A)	6,158 Very low (A)	30,351 Very low (A)	9,306 Very low (A)	82,782 Very low (A)
4 Social and economic burden per case	High (B)	High (A)	High (B)	High (A)	High (A)	Medium (B)	High (A)
5 Disruption due to outbreaks	Low (A)	Low (A)	Low (A)	Low (A)	Very low (A)	Low (A)	Low (A)
6 Contribution to inequity	Low (B)	Low (B)	Low (B)	Low (B)	Low (B)	Low (B)	Low (B)
7 Contribution to antimicrobial resistance	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)
8 Unmet needs for prevention & treatment	High (B)	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)

Notes and selected citations

1-3 Annual deaths in children under 5, Annual deaths in people 5 and older, Annual years lived with disability

- Source: Institute for Health Metrics and Evaluation (IHME), University of Oxford. Global Bacterial Antimicrobial Resistance Burden Estimates 2019. Seattle, United States of America: Institute for Health Metrics and Evaluation (IHME), 2022.
- Values are totals of antibiotic resistant and susceptible forms. YLDs are calculated by subtracting Years of Life Lost (YLLs) from Disability Adjusted Life Years (DALYs).

4 Social and economic burden per case

- Multi-drug resistant infections lead to extended hospital stays and increased healthcare expenses and social costs. https://aricjournal.biomedcentral.com/articles/10.1186/2047-2994-3-32

5 Disruption due to outbreaks

- *P. aeruginosa* is mainly a nosocomial infection, with impact contained to medical facilities. https://erj.ersjournals.com/content/52/2/1701190#sec-2
- Outbreaks of community-acquired infection are typically small and localized, but a more widespread outbreak has been reported in South Africa. https://www.sciencedirect.com/science/article/pii/S1201971222000510

6 Contribution to inequity

- A review of evidence from Chile found that poverty and material deprivation may be important risk factors for transmission of antibiotic-resistant strains. https://iris.paho.org/bitstream/handle/10665.2/52265/v44e302020.pdf

7 Contribution to antimicrobial resistance

- *P. aeruginosa* has been highlighted by WHO as a "critical" priority for R&D of new antibiotics. https://www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed

8 Unmet needs for prevention and treatment

- High rates of resistance have been observed, limiting treatment options. http://vaccinesforamr.org/wp-content/uploads/2018/09/Vaccines_for_AMR.pdf
- Control of outbreaks in medical facilities requires deep cleaning, isolation in hospital wards, and rigorous hand hygiene. No vaccines are available for *P. aeruginosa*.

Current context for prioritization

- Prioritized as an antimicrobial resistance concern. Examples include https://ojs.wpro.who.int/ojs/index.php/wpsar/article/view/719, https://www.who.int/news-room/feature-stories/detail/facing-the-threat-of-antibiotic-resistance-israel-s-success-to-prevent-and-control-the-spread-of-carbapenem-resistant-bacteria, https://ojs.wpro.who.int/ojs/index.php/wpsar/article/view/719
- A Vaccine Value Profile for *P. aeruginosa* is in preparation.

20. Respiratory Syncytial Virus (RSV)

Table 32 Respiratory Syncytial Virus

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
1 Annual deaths in children under 5	72,040 High (A)	4,077 Medium (A)	10,052 Low (A)	3,404 Very high (A)	27,492 High (A)	6,588 Very high (A)	123,790 High (A)
2 Annual deaths in people 5 and older	30,023 Low (A)	39,269 Low (A)	6,401 Very low (A)	36,190 Very low (A)	63,633 Low (A)	38,477 Very low (A)	214,704 Low (A)
3 Annual years lived with disability (all ages)	8,926 Very low (A)	5,354 Very low (A)	3,034 Very low (A)	4,249 Very low (A)	23,838 Very low (A)	4,922 Very low (A)	50,426 Very low (A)
4 Social and economic burden per case	Medium (B)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)	Medium (A)
5 Disruption due to outbreaks	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)
6 Contribution to inequity	Medium (B)	Medium (A)	Medium (B)	Medium (B)	Medium (B)	Medium (B)	Medium (A)
7 Contribution to antimicrobial resistance	Medium (B)	Medium (A)	Medium (B)	Medium (A)	High (B)	High (A)	Medium (A)
8 Unmet needs for prevention & treatment	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)

Notes and selected citations

1-3 Annual deaths in children under 5, Annual deaths in people 5 and older, Annual years lived with disability

- Source: GBD Results [Internet]. Institute for Health Metrics and Evaluation. [cited 2022 Oct 5]. Available from: https://vizhub.healthdata.org/gbd-results

4 Social and economic burden per case

- RSV imposed a substantial economic burden on health systems, governments, and the society. https://academic.oup.com/jid/article/222/Supplement_7/S680/5813513?login=false#208099516

5 Disruption due to outbreaks

- Seasonal epidemics occur every year in the general population in most locations globally. RSV outbreaks reported in older adults in long-term care facilities. https://pubmed.ncbi.nlm.nih.gov/31382895/https://pubmed.ncbi.nlm.nih.gov/31303294/

6 Contribution to inequity

- While males are more likely to have RSV ALRI than females, the difference is slight. https://pubmed.ncbi.nlm.nih.gov/26682048/
- Higher RSV incidence observed in socioeconomically disadvantaged areas. https://pubmed.ncbi.nlm.nih.gov/33757443/

7 Contribution to antimicrobial resistance

- Antibiotics are administered quite frequently for RSV in children; however, the type of antibiotic used (penicillin derivative or other), would make a difference as penicillin-derived antibiotics are unlikely to contribute to AMR. Improved evidence regarding the type of antibiotic used is needed to have confidence in the assessment.
- Use of POC tests can significantly reduce antibiotic prescription for RSV bronchiolitis. https://pubmed.ncbi.nlm.nih.gov/33153518/
- Due to the high rate of RSV infections in young children and consistent picture across US, Finland, and China, scored as Medium. https://pubmed.ncbi.nlm.nih.gov/30657968/, https://pubmed.ncbi.nlm.nih.gov/27738052/, https://pubmed.ncbi.nlm.nih.gov/32093934/, https://pubmed.ncbi.nlm.nih.gov/34718202/

8 Unmet needs for prevention and treatment

- Palivizumab, a monoclonal antibody, has proven effectiveness for preventing laboratory-confirmed cases and hospitalization in high-risk children <2 y of age. https://pubmed.ncbi.nlm.nih.gov/28709160/, https://pubmed.ncbi.nlm.nih.gov/31378522/, https://pubmed.ncbi.nlm.nih.gov/33502928/
- Palivizumab is administered only to the highest risk infants in most high-income settings. Its high cost and dosing regimen makes it unsustainable and difficult to deliver in low-resource settings. https://pubmed.ncbi.nlm.nih.gov/35333332/
- There is no antiviral treatment for RSV. https://pubmed.ncbi.nlm.nih.gov/31541233/

Current context for prioritization

- WHO has defined Preferred Product Characteristics for RSV vaccines and monoclonal antibodies and a Vaccine Value Profile is in preparation. https://www.who.int/publications/i/item/WHO-IVB-17.11, https://www.who.int/publications/i/item/9789240021853
- Numerous professional societies have identified RSV prevention as a global unmet need, and are advocating for development of safe, effective, and affordable preventive interventions. In LICs, RSV disease remains largely unrecognized. https://media.path.org/documents/Advancing_RSV_Maternal_Immunization__A_Gap_Analysis_Report.pdf.
- Countries in every WHO region are participating in a RSV surveillance network. https://cdn.who.int/media/docs/default-source/influenza/who-rsv-surveillance-strategy-phase-26mar2021.pdf

21. Salmonella Paratyphi

Table 33 *Salmonella* Paratyphi

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
1 Annual deaths in children under 5	116 Very low (A)	1 Very low (A)	674 Very low (A)	0 Very low (A)	1,846 Very low (A)	89 Very low (A)	2,727 Very low (A)
2 Annual deaths in people 5 and older	249 Very low (A)	6 Very low (A)	4,772 Very low (A)	12 Very low (A)	15,051 Very low (A)	518 Very low (A)	20,610 Very low (A)
3 Annual years lived with disability (all ages)	126 Very low (A)	9 Very low (A)	1,902 Very low (A)	5 Very low (A)	8,157 Very low (A)	286 Very low (A)	10,486 Very low (A)
4 Social and economic burden per case	Low (B)	Low (B)	Low (A)	Low (B)	Very low (A)	Low (B)	Low (A)
5 Disruption due to outbreaks	Low (A)	Low (A)	Low (A)	Low (A)	Very low (A)	Low (A)	Low (A)
6 Contribution to inequity	High (B)	High (B)	High (B)	High (B)	High (A)	High (A)	High (A)
7 Contribution to antimicrobial resistance	Low (B)	Low (B)	High (A)	Low (B)	High (A)	Medium (A)	High (A)
8 Unmet needs for prevention & treatment	Medium (B)	Low (B)	Medium (A)	Low (B)	Medium (A)	Low (B)	Medium (A)

Notes and selected citations

1-3 Annual deaths in children under 5, Annual deaths in people 5 and older, Annual years lived with disability

- Source: GBD Results [Internet]. Institute for Health Metrics and Evaluation. [cited 2022 Oct 5]. Available from: https://vizhub.healthdata.org/gbd-results

4 Social and economic burden per case

- Hospitalization for enteric fever can result in a cost of illness up to 8.2% of annual income in Pakistan. Studies in Bangladesh and Nepal give similar results. https://pubmed.ncbi.nlm.nih.gov/33258941/, https://pubmed.ncbi.nlm.nih.gov/33258938/, https://pubmed.ncbi.nlm.nih.gov/33258941/

5 Disruption due to outbreaks

- Paratyphoid fever outbreaks occur more frequently in Asia, the Middle East, and Europe. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6821269/

6 Contribution to inequity

- Associated with poor water supply and sanitation, improvements in living conditions are associated with decreasing incidence. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0241217#sec006

7 Contribution to antimicrobial resistance

- Globally, *Salmonellae*, including *S.* Paratyphi, are a "high" priority for R&D of new antibiotics. https://www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed
- The Indian Priority Pathogen List to Guide Research, Discovery, and Development of New Antibiotics in India considers *Salmonella* species to be a "High" priority. https://dbtindia.gov.in/sites/default/files/IPPL_final.pdf
- High prevalence of fluoroquinolone non-susceptibility found in China, India, Nepal, and Bangladesh. https://bmcmedicine.biomedcentral.com/articles/10.1186/s12916-019-1443-1

8 Unmet needs for prevention and treatment

- *S.* Paratyphi infections can be prevented through improved sanitation and hygiene, however in many settings these are difficult to implement and sustain.
- Antimicrobial resistance is limiting treatment options. Treatment with ineffective microbials is associated with prolonged fecal shedding as well as poor treatment outcomes. https://bmcmedicine.biomedcentral.com/articles/10.1186/s12916-019-1443-1
- No vaccines are available for *S.* Paratyphi.

Current context for prioritization

- In most contexts, *S.* Paratyphi is overshadowed by *S.* Typhi, which also causes enteric fever.
- A Vaccine Value Profile for *S.* Paratyphi is in preparation, there has been discussion of combination vaccines that target both *S.* Typhi and *S.* Paratyphi. https://www.who.int/teams/immunization-vaccines-and-biologicals/diseases/paratyphoid-fever

22. Schistosomes

Table 34 Schistosomes

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
1 Annual deaths in children under 5	148 Very low (A)	0 Very low (A)	6 Very low (A)	0 Very low (A)	0 Very low (A)	0 Very low (A)	155 Very low (A)
2 Annual deaths in people 5 and older	8,977 Very low (A)	600 Very low (A)	1,052 Very low (A)	38 Very low (A)	10 Very low (A)	674 Very low (A)	11,360 Very low (A)
3 Annual years lived with disability (all ages)	971,899 Very high (A)	75,437 Low (A)	103,015 Low (A)	0 Very low (A)	154 Very low (A)	74,637 Very low (A)	1,228,103 Medium (A)
4 Social and economic burden per case	Medium (A)	Low (A)	Low (A)	Very low (B)	Low (B)	Low (B)	Low (A)
5 Disruption due to outbreaks	Low (A)	Low (A)	Low (B)	Low (A)	Low (B)	Low (B)	Low (B)
6 Contribution to inequity	Very high (A)	High (A)	High (A)	Very low (B)	High (A)	High (A)	High (A)
7 Contribution to antimicrobial resistance	Low (A)	Low (B)	Low (A)	Very low (B)	Low (B)	Low (A)	Low (A)
8 Unmet needs for prevention & treatment	High (A)	Medium (A)	Medium (A)	Very low (A)	Medium (A)	Medium (A)	Medium (A)

Notes and selected citations

1-3 Annual deaths in children under 5, Annual deaths in people 5 and older, Annual years lived with disability

- Source: GBD Results [Internet]. Institute for Health Metrics and Evaluation. [cited 2022 Oct 5]. Available from: https://vizhub.healthdata.org/gbd-results
- Extremely low burden in Europe was taken into consideration when scoring for the remaining criteria.

4 Social and economic burden per case

- Women and girls in sub-Saharan Africa are affected by female genital schistosomiasis (FGS), which impairs productivity and reproductive health, and is highly stigmatizing. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8293433/
- A 2020 systematic review found considerable variation in the per person treatment costs, from US$0.06-$4.46. Preventive chemotherapy interventions: $0.05-4.46. Preventive chemotherapy plus an individual diagnostic test to identify at-risk population: $1.19-4.45. Test and treat interventions: $0.35-2.51. https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0008098

5 Disruption due to outbreaks

- Localized outbreaks may occur around infested water sources. Examples: https://www.thelancet.com/journals/lanam/article/PIIS2667-193X(21)00140-X, https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0262524, https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(16)00175-4

6 Contribution to inequity

- **Schistosomiasis** is considered a poverty-related disease, and most individuals with active and late chronic disease are from poor rural areas, particularly agricultural and fishing populations. https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0004546, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8221481/

7 Contribution to antimicrobial resistance

- Praziquantal is the only drug for prevention or treatment of schistosomiasis. Resistance or treatment failures have been reported in Africa, Egypt, and China. https://journals.asm.org/doi/10.1128/AAC.02582-16

8 Unmet needs for prevention and treatment

- Achieving elimination is possible with current tools, but requires long-term, concerted efforts. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8341657/
- Preventive chemotherapy is provided free in most endemic areas, but programs typically target school-age children leaving a gap for accessing children who are outside school (most often girls) and women of reproductive age (to prevent and treat FGS).
- Globally, the large-scale donation program and implementation of mass drug administration requires significant resources (human and monetary) from drug donating companies and country health systems.
- Reducing exposure is difficult without improving access to clean water, which is difficult to implement and sustain in many settings.

Current context for prioritization

- Schistosomiasis is among the targets of “Ending the neglect to attain the Sustainable Development Goals: A road map for neglected tropical diseases 2021–2030”. https://www.who.int/publications/i/item/9789240010352
- Multi-stakeholder groups are working towards elimination as a public health problem or interruption of transmission of schistosomiasis.
- The Eastern Mediterranean region and China in particular have made progress by prioritizing elimination of schistosomiasis as a public health problem. https://www.emro.who.int/health-topics/schistosomiasis/, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8341657/

23. Shigella

Table 35 ***Shigella***

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
1 Annual deaths in children under 5 (Source 1)	77,589 High (A)	1,266 Very low (A)	7,812 Low (A)	151 Very low (A)	6,216 Very low (A)	760 Very low (A)	93,831 Medium (A)
(Source 2)			21,100 High (B)		11,200 Low (B)		
2 Annual deaths in people 5 and older	24,566 Low (A)	1,381 Very low (A)	3,883 Very low (A)	258 Very low (A)	23,720 Very low (A)	540 Very low (A)	54,371 Very low (A)
3 Annual years lived with disability (all ages)	260,743 Low (A)	69,264 Low (A)	122,346 Medium (A)	39,985 Low (A)	146,422 Low (A)	45,781 Very low (A)	685,980 Low (A)
4 Social and economic burden per case	High (A)	High (A)	Medium (A)	Medium (A)	High (A)	High (A)	High (A)
5 Disruption due to outbreaks	Medium (A)	Medium (A)	Medium (B)	Medium (A)	Medium (A)	Medium (B)	Medium (A)
6 Contribution to inequity	High (B)	High (A)	High (B)	High (B)	High (B)	High (B)	High (A)
7 Contribution to antimicrobial resistance	High (B)	High (A)	High (B)	High (B)	Very high (A)	High (B)	High (A)
8 Unmet needs for prevention & treatment	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)

Notes and selected citations

1-3 Annual deaths in children under 5, Annual deaths in people 5 and older, Annual years lived with disability

- Source 1 (for use in Preferences Survey): GBD Results [Internet]. Institute for Health Metrics and Evaluation. [cited 2022 Oct 5]. Available from: https://vizhub.healthdata.org/gbd-results
- Source 2 (for sensitivity testing): Anderson JD, Bagamian KH, Muhib F, Amaya MP, Laytner LA, Wierzba T, et al. Burden of enterotoxigenic Escherichia coli and shigella non-fatal diarrhoeal infections in 79 low-income and

lower middle-income countries: a modelling analysis. The Lancet Global Health [Internet]. 2019 Mar 1 [cited 2022 Nov 1];7(3):e321–30. Available from: https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(18)30483-2/fulltext. Although these estimates are only for low- and middle-income countries, for two regions the Anderson et al estimates are higher than the GBD results. For the these two regions, the higher estimates will be used for sensitivity testing.

2-3 Annual deaths in people 5 and older, Annual years lived with disability

- Source: GBD Results [Internet]. Institute for Health Metrics and Evaluation. [cited 2022 Oct 5]. Available from: https://vizhub.healthdata.org/gbd-results

4 Social and economic burden per case

- *Shigella* infections are associated with a number of long-term sequelae, including undernutrition, stunting, and impaired cognitive development. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(18)30475-4/fulltext
- An economic analysis concluded that the economic burden per case may be much greater than has been estimated, due to productivity losses associated with stunting. (Puett et al, submitted)

5 Disruption due to outbreaks

- Reports of *Shigella* outbreaks are common and include outbreaks in displaced populations. (for example: https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(95)90338-0.pdf)
- WHO gives specific outbreak preparedness and response guidelines. https://pubmed.ncbi.nlm.nih.gov/?term=shigella+outbreak, https://apps.who.int/iris/bitstream/handle/10665/43252/9241592330.pdf?sequence=1

6 Contribution to inequity

- Socio-economically disadvantaged groups are at greater risk of exposure due to inadequate sanitation and hygiene and at greater risk of adverse outcomes due to lower access to care and higher rates of comorbidities.
- Shigella deaths are strongly inversely correlated with sociodemographic index. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(18)30475-4/fulltext

7 Contribution to antimicrobial resistance

- Resistance rates among *Shigella* have been on the increase. https://pubmed.ncbi.nlm.nih.gov/29066021/
- In some low-income settings, *Shigella* is a leading driver of antibiotic treatment for diarrhea among children under 5. https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0008520#sec014
- *Shigella* has been highlighted by WHO as a “medium” priority for R&D of new antibiotics. https://www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed
- National bodies have also highlighted the threat of drug resistance in *Shigella*. https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf, https://cdn.who.int/media/docs/default-source/searo/india/antimicrobial-resistance/ippl_final_web.pdf

8 Unmet needs for prevention and treatment

- *Shigella* infections can be prevented through improved sanitation and hygiene, however in many settings these are difficult to implement and sustain. Antibiotics are used for travelers’ diarrhea, but development of resistance is an ongoing concern. https://apps.who.int/iris/bitstream/handle/10665/43252/9241592330.pdf?sequence=1

Current context for prioritization

- Perspectives on the importance of shigella among policy makers vary. https://www.sciencedirect.com/science/article/pii/S0264410X04008886

24. Staphylococcus aureus

Table 36 ***Staphylococcus aureus***

Criteria	African	Americas	E. Med.	European	SE Asian	W. Pacific	Global
1 Annual deaths in children under 5	78,401 High (A)	7,538 Very high (A)	24,632 High (A)	3,373 Very high (A)	32,268 High (A)	7,671 Very high (A)	153,959 High (A)
2 Annual deaths in people 5 and older	101,556 Very high (A)	184,839 Very high (A)	50,557 Very high (A)	189,025 Very high (A)	169,212 Very high (A)	246,670 Very high (A)	950,145 Very high (A)
3 Annual years lived with disability (all ages)	55,543 Very low (A)	33,483 Very low (A)	27,470 Very low (A)	23,506 Very low (A)	72,326 Very low (A)	28,911 Very low (A)	242,641 Very low (A)
4 Social and economic burden per case	High (B)	High (A)	High (B)	High (A)	High (B)	High (A)	High (A)
5 Disruption due to outbreaks	Low (B)	Low (A)	Low (A)	Low (A)	Very low (A)	Low (A)	Low (A)
6 Contribution to inequity	Medium (B)	Medium (B)	Medium (B)	Medium (B)	Medium (B)	High (A)	Medium (A)
7 Contribution to antimicrobial resistance	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)	Very high (A)
8 Unmet needs for prevention & treatment	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)	High (A)

Notes and selected citations

1-3 Annual deaths in children under 5, Annual deaths in people 5 and older, Annual years lived with disability

- Source: Institute for Health Metrics and Evaluation (IHME), University of Oxford. Global Bacterial Antimicrobial Resistance Burden Estimates 2019. Seattle, United States of America: Institute for Health Metrics and Evaluation (IHME), 2022.
- Values are totals of antibiotic resistant and susceptible forms. YLDs are calculated by subtracting Years of Life Lost (YLLs) from Disability Adjusted Life Years (DALYs).

4 Social and economic burden per case

- Data from China, Japan, the Netherlands, and the US show that resistant forms contribute to extended hospitalization and greater mortality. https://pubmed.ncbi.nlm.nih.gov/33512523/, https://pubmed.ncbi.nlm.nih.gov/18353496/, https://www.nature.com/articles/s41598-020-60825-6, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6710669/

5 Disruption due to outbreaks

- While there is some community transmission, outbreaks in healthcare settings represent the key concern. Although they require rigorous infection control, scored as Low because the impact would be contained the healthcare facilities.

6 Contribution to inequity

- Populations of lower socio-economic status have been observed to have higher rates of *S. aureus* bacteremia. https://bmcinfectdis.biomedcentral.com/articles/10.1186/1471-2334-12-249

7 Contribution to antimicrobial resistance

- *S. aureus* is a "high" priority for R&D of new antibiotics. https://www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed

8 Unmet needs for prevention and treatment

- High rates of resistance have been observed in nosocomial and community infections, limiting treatment options. http://vaccinesforamr.org/wp-content/uploads/2018/09/Vaccines_for_AMR.pdf
- No vaccines are available for *S. aureus*.

Current context for prioritization

- Prioritized as an antimicrobial resistance concern. Examples include https://cdn.who.int/media/docs/default-source/searo/amr/rd-flagship-5-amr.pdf?sfvrsn=3f583d07_2, https://www.who.int/cambodia/news/detail/23-12-2019-cambodia-launched-multi-sectoral-action-plan-for-guiding-national-control-of-antimicrobial-resistance, https://www.cdc.gov/mmwr/volumes/68/wr/mm6809e1.htm

E. Annex E: Regional Summaries

1. African Region

a) Quantitative scoring

Table 37 Annual deaths in children under 5 in the African region

Data Availability	Very low	Low	Medium	High	Very high
	<22,000	22,000-44,000	44,000-66,000	66,000-88,000	>88,000
A: Burden data from GBD 2019 or AMR dataset	Group A streptococcus Influenza Intestinal pathogenic *E. coli* (InPEC) Leishmania *Neisseria gonorrhoeae* *Salmonella* Paratyphi Schistosomes	HIV-1 Norovirus	Extra-intestinal pathogenic *E. coli* (ExPEC) *Pseudomonas aeruginosa*	Group B streptococcus Non-typhoidal *Salmonella* Respiratory syncytial virus *Shigella* *Staphylococcus aureus*	*Klebsiella pneumoniae*
B: Burden calculated by other studies	Chikungunya virus	*Mycobacterium tuberculosis* (TB)			
C: Data not available, will test a range of scores	Cytomegalovirus Herpes simplex types 1 and 2 Hookworm *Mycobacterium leprae* (leprosy)				*P. falciparum*

Table 38 Annual deaths in people 5 and older in the African region					
Data Availability	**Very low**	**Low**	**Medium**	**High**	**Very high**
	<20,000	20,000-41,000	41,000-61,000	61,000-81,000	>81,000
A: Burden data from GBD 2019 or AMR dataset	Intestinal pathogenic *E. coli* (InPEC) Leishmania *Neisseria gonorrhoeae* (gonorrhea) *Salmonella* Paratyphi Schistosomes	Group A streptococcus Group B streptococcus Influenza Non-typhoidal *Salmonella* Norovirus Respiratory syncytial virus *Shigella*	*Pseudomonas aeruginosa*	Extra-intestinal pathogenic *E. coli* (ExPEC)	HIV-1 *Klebsiella pneumoniae* *Staphylococcus aureus*
B: Burden calculated by other studies	Chikungunya virus				*Mycobacterium tuberculosis* (TB)
C: Data not available, will test a range of scores	Herpes simplex types 1 and 2 Hookworm *Mycobacterium leprae* (leprosy)	Cytomegalovirus			*P. falciparum*

Table 39 Years lived with disability (all ages) in the African region					
Data Availability	**Very low**	**Low**	**Medium**	**High**	**Very high**
	<190,000	190,000-390,000	390,000-580,000	580,000-780,000	>780,000
A: Burden data from GBD 2019 or AMR dataset	Extra-intestinal pathogenic *E. coli* (ExPEC) Group B streptococcus Herpes Simplex Virus (Types 1 and 2) Influenza Intestinal pathogenic *E. coli* (InPEC) *Klebsiella pneumoniae* Leishmania *Mycobacterium leprae* (leprosy) *Neisseria gonorrhoeae* (gonorrhea) Non-typhoidal *Salmonella* Norovirus *Pseudomonas aeruginosa* Respiratory syncytial virus *Salmonella Paratyphi* *Staphylococcus aureus*	*Shigella*	Group A streptococcus Hookworm		HIV-1 *Mycobacterium tuberculosis* (TB) Schistosomes
B: Burden calculated by other studies	Chikungunya virus				
C: Data not available, will test a range of scores			Cytomegalo-virus		*P. falciparum*

b) Qualitative scoring

Table 40 Social and economic burden per case in the African Region

Data Availability	Very low	Low	Medium	High	Very high
	Very low burden for each case	Low burden for each case	Moderate burden for each case	High burden for each case	Very high burden for each case
A: Based on data from regional sources		Hookworm	Chikungunya virus Intestinal pathogenic *E. coli* (InPEC) Norovirus Schistosomes	Group A streptococcus Group B streptococcus Non-typhoidal *Salmonella* *Plasmodium falciparum* (malaria) *Shigella*	Herpes simplex types 1 and 2 HIV-1 *Mycobacterium leprae* (leprosy) *Mycobacterium tuberculosis* (TB)
B: Score inferred based on sources from other regions		Influenza *Salmonella Paratyphi*	Extra-intestinal pathogenic *E. coli* (ExPEC) *Neisseria gonorrhoeae* Respiratory syncytial virus	Cytomegalovirus *Klebsiella pneumoniae* *Pseudomonas aeruginosa* *Staphylococcus aureus*	Leishmania

Table 41 Disruption due to outbreaks in the African Region					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	Little or no social disruption or impact on healthcare, trade or tourism	Slight social disruption or impact on healthcare, trade or tourism	Moderate social disruption or impact on healthcare, trade or tourism	High social disruption or impact on healthcare, trade or tourism, including due to preventive measures	Very high social disruption or impact on healthcare, trade and tourism, including due to preventive measures
A: Based on data from regional sources	*Mycobacterium leprae* (leprosy)	*Klebsiella pneumoniae* *Pseudomonas aeruginosa* *Salmonella Paratyphi* Schistosomes	Chikungunya virus *Shigella*	HIV-1 Leishmania Norovirus *Plasmodium falciparum* (malaria) Respiratory syncytial virus	Influenza *Mycobacterium tuberculosis* (TB)
B: Score inferred based on sources from other regions	Cytomegalovirus Group A streptococcus Herpes simplex types 1 and 2 Hookworm	Extra-intestinal pathogenic *E. coli* (ExPEC) Group B streptococcus *Neisseria gonorrhoeae* *Staphylococcus aureus*	Intestinal pathogenic *E. coli* (InPEC) Non-typhoidal *Salmonella*		

Table 42 Contribution to inequity in the African Region					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	Affects all communities equally	Burden falls on socially and economically disadvantaged groups, including women, **slightly** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, **moderately** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, **much** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, all or most of the time
A: Based on data from regional sources			Chikungunya virus Cytomegalovirus Extra-intestinal pathogenic *E. coli* (ExPEC) Group B streptococcus Intestinal pathogenic *E. coli* (InPEC) Norovirus	*Neisseria gonorrhoeae*	Herpes simplex types 1 and 2 HIV-1 Hookworm Leishmania *Mycobacterium tuberculosis* (TB) Non-typhoidal *Salmonella* *Plasmodium falciparum* (malaria) Schistosomes
B: Score inferred based on sources from other regions		*Klebsiella pneumoniae* *Pseudomonas aeruginosa*	Influenza Respiratory syncytial virus *Staphylococcus aureus*	Group A streptococcus *Salmonella Paratyphi* *Shigella*	*Mycobacterium leprae* (leprosy)

Table 43 Contribution to antimicrobial resistance in the African Region					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	Not resistant to first-line drugs and not associated with antibiotic use	Little resistance to first-line drugs and little association with antibiotic use	Some resistance to first-line drugs, associated with high antibiotic use	Significant resistance to first-line drugs, associated with high antibiotic use	A global resistance threat due to widespread resistance and association with high antibiotic use
A: Based on data from regional sources	Chikungunya virus	Group B streptococcus Herpes simplex types 1 and 2 Hookworm *Mycobacterium leprae* (leprosy) Schistosomes	Leishmania	Non-typhoidal *Salmonella* *Plasmodium falciparum* (malaria)	Extra-intestinal pathogenic *E. coli* (ExPEC) HIV-1 Intestinal pathogenic *E. coli* (InPEC) *Klebsiella pneumoniae* *Mycobacterium tuberculosis* (TB) *Neisseria gonorrhoeae* *Pseudomonas aeruginosa* *Staphylococcus aureus*
B: Score inferred based on sources from other regions	Cytomegalovirus	Norovirus *Salmonella Paratyphi*	Influenza Respiratory syncytial virus	Group A streptococcus *Shigella*	

Table 44 Unmet needs for prevention and treatment in the African Region					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	The alternatives for prevention or treatment meet the needs of most people	The alternatives for prevention or treatment meet the needs of many people	The alternatives for prevention or treatment meet the needs of some people	The alternatives for prevention or treatment meet the needs of few people	There are no effective alternatives for prevention or treatment
A: Based on data from regional sources		Hookworm	Extra-intestinal pathogenic *E. coli* (ExPEC) Intestinal pathogenic *E. coli* (InPEC) Leishmania *Neisseria gonorrhoeae*	Group A streptococcus Herpes simplex types 1 and 2 HIV-1 Influenza *Klebsiella pneumoniae* *Mycobacterium leprae* (leprosy) *Mycobacterium tuberculosis* (TB) Non-typhoidal *Salmonella* Norovirus *Plasmodium falciparum* (malaria) Respiratory syncytial virus Schistosomes *Shigella* *Staphylococcus aureus*	Chikungunya virus Group B streptococcus
B: Score inferred based on sources from other regions			*Salmonella Paratyphi*	*Pseudomonas aeruginosa*	Cytomegalovirus

2. Region of the Americas

a) Quantitative scoring

Table 45 Annual deaths in children under 5 in the Region of the Americas

Data Availability	Very low	Low	Medium	High	Very high
	<1,500	1,500-3,000	3,000-4,500	4,500-6,100	>6,100
A: Burden data from GBD 2019 or AMR dataset	Intestinal pathogenic *E. coli* (InPEC) Leishmania *Neisseria gonorrhoeae* Non-typhoidal *Salmonella* Norovirus *Salmonella* Paratyphi Schistosomes *Shigella*	Group A streptococcus HIV-1 Influenza	Group B streptococcus Respiratory syncytial virus	Extra-intestinal pathogenic *E. coli* (ExPEC) *Pseudomonas aeruginosa*	*Klebsiella pneumoniae* *Staphylococcus aureus*
B: Burden calculated by other studies	Chikungunya virus *Mycobacterium tuberculosis* (TB)				
C: Data not available, will test a range of scores	Hookworm *Mycobacterium leprae* (leprosy) *P. falciparum*	Cytomegalovirus Herpes simplex types 1 and 2			

Table 46 Annual deaths in people 5 and older in the Region of the Americas					
Data Availability	**Very low**	**Low**	**Medium**	**High**	**Very high**
	<37,000	37,000-74,000	74,000-110,000	110,000-150,000	>150,000
A: Burden data from GBD 2019 or AMR dataset	Group B streptococcus Intestinal pathogenic *E. coli* (InPEC) Leishmania *Neisseria gonorrhoeae* (gonorrhea) Non-typhoidal *Salmonella* Norovirus *Salmonella* Paratyphi Schistosomes *Shigella*	Group A streptococcus HIV-1 Influenza Respiratory syncytial virus	*Klebsiella pneumoniae* *Pseudomonas aeruginosa*	Extra-intestinal pathogenic *E. coli* (ExPEC)	*Staphylococcus aureus*
B: Burden calculated by other studies	Chikungunya virus *Mycobacterium tuberculosis* (TB)				
C: Data not available, will test a range of scores	Herpes simplex types 1 and 2 Hookworm *Mycobacterium leprae* (leprosy) *P. falciparum*	Cytomegalovirus			

Table 47 Years lived with disability (all ages) in the Region of the Americas					
Data Availability	**Very low**	**Low**	**Medium**	**High**	**Very high**
	<59,000	59,000-120,000	120,000-180,000	180,000-230,000	>230,000
A: Burden data from GBD 2019 or AMR dataset	Extra-intestinal pathogenic *E. coli* (ExPEC) Group B streptococcus Herpes Simplex Virus (Types 1 and 2) Hookworm Influenza Intestinal pathogenic *E. coli* (InPEC) *Klebsiella pneumoniae* Leishmania *Mycobacterium leprae* (leprosy) *Neisseria gonorrhoeae* (gonorrhea) Non-typhoidal *Salmonella* *Pseudomonas aeruginosa* Respiratory syncytial virus *Salmonella* Paratyphi *Staphylococcus aureus*	*Mycobacterium tuberculosis* (TB) Norovirus Schistosomes *Shigella*			Group A streptococcus HIV-1
B: Burden calculated by other studies		Chikungunya virus			
C: Data not available, will test a range of scores	*P. falciparum*	Cytomegalovirus			

b) Qualitative scoring

Table 48 Social and economic burden per case in the Region of the Americas					
Data Availability	**Very low**	**Low**	**Medium**	**High**	**Very high**
	Very low burden for each case	Low burden for each case	Moderate burden for each case	High burden for each case	Very high burden for each case
A: Based on data from regional sources		Hookworm Influenza Schistosomes	Chikungunya virus Extra-intestinal pathogenic *E. coli* (ExPEC) Group A streptococcus Intestinal pathogenic *E. coli* (InPEC) *Neisseria gonorrhoeae* Norovirus Respiratory syncytial virus	Cytomegalovirus Group B streptococcus Herpes simplex types 1 and 2 *Klebsiella pneumoniae* *Plasmodium falciparum* (malaria) *Pseudomonas aeruginosa* *Shigella* *Staphylococcus aureus*	HIV-1 Leishmania *Mycobacterium leprae* (leprosy) *Mycobacterium tuberculosis* (TB)
B: Score inferred based on sources from other regions		Non-typhoidal *Salmonella* *Salmonella Paratyphi*			

Table 49 Disruption due to outbreaks in the Region of the Americas					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	Little or no social disruption or impact on healthcare, trade or tourism	Slight social disruption or impact on healthcare, trade or tourism	Moderate social disruption or impact on healthcare, trade or tourism	High social disruption or impact on healthcare, trade or tourism, including due to preventive measures	Very high social disruption or impact on healthcare, trade and tourism, including due to preventive measures
A: Based on data from regional sources	Group A streptococcus *Mycobacterium leprae* (leprosy)	Extra-intestinal pathogenic *E. coli* (ExPEC) Group B streptococcus *Klebsiella pneumoniae* *Neisseria gonorrhoeae* Non-typhoidal *Salmonella* *Pseudomonas aeruginosa* *Salmonella Paratyphi* Schistosomes *Staphylococcus aureus*	Leishmania *Plasmodium falciparum* (malaria) *Shigella*	Chikungunya virus HIV-1 *Mycobacterium tuberculosis* (TB) Norovirus Respiratory syncytial virus	Influenza
B: Score inferred based on sources from other regions	Cytomegalovirus Herpes simplex types 1 and 2 Hookworm		Intestinal pathogenic *E. coli* (InPEC)		

Table 50 Contribution to inequity in the Region of the Americas					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	Affects all communities equally	Burden falls on socially and economically disadvantaged groups, including women, **slightly** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, **moderately** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, **much** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, all or most of the time
A: Based on data from regional sources			Chikungunya virus Cytomegalovirus Extra-intestinal pathogenic *E. coli* (ExPEC) Group A streptococcus Group B streptococcus Influenza Norovirus Respiratory syncytial virus	Herpes simplex types 1 and 2 *Neisseria gonorrhoeae* Schistosomes *Shigella*	HIV-1 Hookworm Leishmania *Mycobacterium leprae* (leprosy) *Mycobacterium tuberculosis* (TB) *Plasmodium falciparum* (malaria)
B: Score inferred based on sources from other regions		*Klebsiella pneumoniae* *Pseudomonas aeruginosa* *Staphylococcus aureus*	Intestinal pathogenic *E. coli* (InPEC)	Non-typhoidal *Salmonella* *Salmonella Paratyphi*	

Table 51 Contribution to antimicrobial resistance in the Region of the Americas					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	Not resistant to first-line drugs and not associated with antibiotic use	Little resistance to first-line drugs and little association with antibiotic use	Some resistance to first-line drugs, associated with high antibiotic use	Significant resistance to first-line drugs, associated with high antibiotic use	A global resistance threat due to widespread resistance and association with high antibiotic use
A: Based on data from regional sources		Group B streptococcus Herpes simplex types 1 and 2	Influenza Leishmania *Mycobacterium leprae* (leprosy) Respiratory syncytial virus	Non-typhoidal *Salmonella* *Plasmodium falciparum (malaria)* *Shigella*	Extra-intestinal pathogenic *E. coli* (ExPEC) HIV-1 Intestinal pathogenic *E. coli* (InPEC) *Klebsiella pneumoniae* *Mycobacterium tuberculosis* (TB) *Neisseria gonorrhoeae* *Pseudomonas aeruginosa* *Staphylococcus aureus*
B: Score inferred based on sources from other regions	Chikungunya virus Cytomegalovirus	Hookworm Norovirus *Salmonella Paratyphi* Schistosomes		Group A streptococcus	

Table 52 Unmet needs for prevention and treatment in the Region of the Americas					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	The alternatives for prevention or treatment meet the needs of most people	The alternatives for prevention or treatment meet the needs of many people	The alternatives for prevention or treatment meet the needs of some people	The alternatives for prevention or treatment meet the needs of few people	There are no effective alternatives for prevention or treatment
A: Based on data from regional sources		Hookworm	Extra-intestinal pathogenic *E. coli* (ExPEC) Group A streptococcus Intestinal pathogenic *E. coli* (InPEC) Leishmania *Neisseria gonorrhoeae* Non-typhoidal *Salmonella* *Plasmodium falciparum* (malaria) Schistosomes	Group B streptococcus Herpes simplex types 1 and 2 HIV-1 Influenza *Klebsiella pneumoniae* *Mycobacterium leprae* (leprosy) *Mycobacterium tuberculosis* (TB) Norovirus *Pseudomonas aeruginosa* Respiratory syncytial virus *Shigella* *Staphylococcus aureus*	Chikungunya virus
B: Score inferred based on sources from other regions		*Salmonella Paratyphi*			Cytomegalovirus

3. Eastern Mediterranean Region

a) Quantitative scoring

Table 53 Annual deaths in children under 5 in the Eastern Mediterranean region

Data Availability	Very low	Low	Medium	High	Very high
	<6,700	6,700-13,000	13,000-20,000	20,000-27,000	>27,000
A: Burden data from GBD 2019 or AMR dataset	Group A streptococcus HIV-1 Influenza Intestinal pathogenic *E. coli* (InPEC) Leishmania *Neisseria gonorrhoeae* Non-typhoidal *Salmonella* *Salmonella* Paratyphi Schistosomes	Norovirus Respiratory syncytial virus *Shigella*	*Pseudomonas aeruginosa*	Extra-intestinal pathogenic *E. coli* (ExPEC) Group B streptococcus *Staphylococcus aureus*	*Klebsiella pneumoniae*
B: Burden calculated by other studies	Chikungunya virus	*Mycobacterium tuberculosis* (TB)			
C: Data not available, will test a range of scores	Cytomegalovirus Herpes simplex types 1 and 2 Hookworm *Mycobacterium leprae* (leprosy) *P. falciparum*				

Because burden data were not available for *P. falciparum*, it was scored based on data for malaria and the % of *P. vivax* found in each WHO region. As discussed in D.18, this gave a maximum and a minimum potential score for *P. falciparum* in the region.

Table 54 Annual deaths in people 5 and older in the Eastern Mediterranean region

Data Availability	Very low	Low	Medium	High	Very high
	<10,000	10,000-20,000	20,000-30,000	30,000-40,000	>40,000
A: Burden data from GBD 2019 or AMR dataset	Influenza Intestinal pathogenic *E. coli* (InPEC) Leishmania *Neisseria gonorrhoeae* (gonorrhea) Non-typhoidal *Salmonella* Norovirus Respiratory syncytial virus *Salmonella* Paratyphi Schistosomes *Shigella*	Group B streptococcus HIV-1	*Pseudomonas aeruginosa*	Group A streptococcus	Extra-intestinal pathogenic *E. coli* (ExPEC) *Klebsiella pneumoniae* *Staphylococcus aureus*
B: Burden calculated by other studies	Chikungunya virus				*Mycobacterium tuberculosis* (TB)
C: Data not available, will test a range of scores	Herpes simplex types 1 and 2 Hookworm *Mycobacterium leprae* (leprosy) *P. falciparum* - minimum	Cytomegalovirus *P. falciparum* - maximum			

Table 55 Years lived with disability (all ages) in the Eastern Mediterranean region					
Data Availability	**Very low**	**Low**	**Medium**	**High**	**Very high**
	<54,000	54,000-110,000	110,000-160,000	160,000-220,000	>220,000
A: Burden data from GBD 2019 or AMR dataset	Extra-intestinal pathogenic *E. coli* (ExPEC) Group B streptococcus Herpes Simplex Virus (Types 1 and 2) HIV-1 Influenza Intestinal pathogenic *E. coli* (InPEC) *Klebsiella pneumoniae* *Mycobacterium leprae* (leprosy) *Neisseria gonorrhoeae* (gonorrhea) Non-typhoidal *Salmonella* *Pseudomonas aeruginosa* Respiratory syncytial virus *Salmonella* Paratyphi *Staphylococcus aureus*	Hookworm Norovirus Schistosomes	*Shigella*		Group A streptococcus Leishmania *Mycobacterium tuberculosis* (TB)
B: Burden calculated by other studies	Chikungunya virus				
C: Data not available, will test a range of scores		*P. falciparum*	Cytomegalo-virus		

b) Qualitative scoring

Table 56 Social and economic burden per case in the Eastern Mediterranean Region					
Data Availability	**Very low**	**Low**	**Medium**	**High**	**Very high**
	Very low burden for each case	Low burden for each case	Moderate burden for each case	High burden for each case	Very high burden for each case
A: Based on data from regional sources		*Salmonella Paratyphi* Schistosomes	Chikungunya virus Extra-intestinal pathogenic *E. coli* (ExPEC) Group A streptococcus Intestinal pathogenic *E. coli* (InPEC) Norovirus Respiratory syncytial virus *Shigella*	*Plasmodium falciparum* (malaria)	HIV-1 Leishmania *Mycobacterium tuberculosis* (TB)
B: Score inferred based on sources from other regions		Hookworm Influenza Non-typhoidal *Salmonella*	Herpes simplex types 1 and 2 *Neisseria gonorrhoeae*	Cytomegalovirus Group B streptococcus *Klebsiella pneumoniae* *Pseudomonas aeruginosa* *Staphylococcus aureus*	*Mycobacterium leprae* (leprosy)

Table 57 Disruption due to outbreaks in the Eastern Mediterranean Region					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	Little or no social disruption or impact on healthcare, trade or tourism	Slight social disruption or impact on healthcare, trade or tourism	Moderate social disruption or impact on healthcare, trade or tourism	High social disruption or impact on healthcare, trade or tourism, including due to preventive measures	Very high social disruption or impact on healthcare, trade and tourism, including due to preventive measures
A: Based on data from regional sources	*Mycobacterium leprae* (leprosy)	Chikungunya virus *Klebsiella pneumoniae* *Plasmodium falciparum* (malaria) *Pseudomonas aeruginosa* *Salmonella Paratyphi* *Staphylococcus aureus*		HIV-1 Leishmania *Mycobacterium tuberculosis* (TB) Norovirus Respiratory syncytial virus	Influenza
B: Score inferred based on sources from other regions	Cytomegalovirus Group A streptococcus Herpes simplex types 1 and 2 Hookworm	Extra-intestinal pathogenic *E. coli* (ExPEC) Group B streptococcus *Neisseria gonorrhoeae* Non-typhoidal *Salmonella* Schistosomes	Intestinal pathogenic *E. coli* (InPEC) *Shigella*		

Table 58 Contribution to inequity in the Eastern Mediterranean Region					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	Affects all communities equally	Burden falls on socially and economically disadvantaged groups, including women, **slightly** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, **moderately** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, **much** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, all or most of the time
A: Based on data from regional sources			Chikungunya virus Cytomegalovirus Extra-intestinal pathogenic *E. coli* (ExPEC) Herpes simplex types 1 and 2 Norovirus	Schistosomes	HIV-1 Hookworm Leishmania *Mycobacterium tuberculosis* (TB)
B: Score inferred based on sources from other regions		*Klebsiella pneumoniae* *Pseudomonas aeruginosa*	Group A streptococcus Group B streptococcus Influenza Intestinal pathogenic *E. coli* (InPEC) Respiratory syncytial virus *Staphylococcus aureus*	*Neisseria gonorrhoeae* Non-typhoidal *Salmonella* *Plasmodium falciparum* (malaria) *Salmonella Paratyphi* *Shigella*	*Mycobacterium leprae* (leprosy)

Table 59 Contribution to antimicrobial resistance in the Eastern Mediterranean Region					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	Not resistant to first-line drugs and not associated with antibiotic use	Little resistance to first-line drugs and little association with antibiotic use	Some resistance to first-line drugs, associated with high antibiotic use	Significant resistance to first-line drugs, associated with high antibiotic use	A global resistance threat due to widespread resistance and association with high antibiotic use
A: Based on data from regional sources		Herpes simplex types 1 and 2 *Mycobacterium leprae* (leprosy) Schistosomes	Leishmania *Plasmodium falciparum* (malaria)	*Salmonella Paratyphi*	Extra-intestinal pathogenic *E. coli* (ExPEC) HIV-1 Intestinal pathogenic *E. coli* (InPEC) *Klebsiella pneumoniae* *Mycobacterium tuberculosis* (TB) *Neisseria gonorrhoeae* *Pseudomonas aeruginosa* *Staphylococcus aureus*
B: Score inferred based on sources from other regions	Chikungunya virus Cytomegalovirus Group B streptococcus	Hookworm Norovirus	Influenza Respiratory syncytial virus	Group A streptococcus Non-typhoidal *Salmonella* *Shigella*	

Table 60 Unmet needs for prevention and treatment in the Eastern Mediterranean Region					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	The alternatives for prevention or treatment meet the needs of most people	The alternatives for prevention or treatment meet the needs of many people	The alternatives for prevention or treatment meet the needs of some people	The alternatives for prevention or treatment meet the needs of few people	There are no effective alternatives for prevention or treatment
A: Based on data from regional sources		Hookworm	Extra-intestinal pathogenic *E. coli* (ExPEC) Group A streptococcus Intestinal pathogenic *E. coli* (InPEC) Leishmania *Neisseria gonorrhoeae* Non-typhoidal *Salmonella* *Plasmodium falciparum* (malaria) *Salmonella Paratyphi* Schistosomes	Group B streptococcus Herpes simplex types 1 and 2 HIV-1 Influenza *Klebsiella pneumoniae* *Mycobacterium leprae* (leprosy) *Mycobacterium tuberculosis* (TB) Norovirus *Pseudomonas aeruginosa* Respiratory syncytial virus *Shigella* *Staphylococcus aureus*	Chikungunya virus
B: Score inferred based on sources from other regions					Cytomegalovirus

4. European Region

a) Quantitative scoring

Table 61 Annual deaths in children under 5 in the European region

Data Availability	Very low	Low	Medium	High	Very high
	<680	680-1,400	1,400-2,000	2,000-2,700	>2,700
A: Burden data from GBD 2019 or AMR dataset	HIV-1 Intestinal pathogenic *E. coli* (InPEC) Leishmania *Neisseria gonorrhoeae* Non-typhoidal *Salmonella* Norovirus *Salmonella* Paratyphi Schistosomes *Shigella*	Group A streptococcus Group B streptococcus Influenza	Extra-intestinal pathogenic *E. coli* (ExPEC) *Pseudomonas aeruginosa*	*Klebsiella pneumoniae*	Respiratory syncytial virus *Staphylococcus aureus*
B: Burden calculated by other studies	Chikungunya virus	*Mycobacterium tuberculosis* (TB)			
C: Data not available, will test a range of scores	Herpes simplex types 1 and 2 Hookworm *Mycobacterium leprae* (leprosy) *Plasmodium falciparum* (malaria)		Cytomegalovirus		

Table 62 Annual deaths in people 5 and older in the European region					
Data Availability	**Very low**	**Low**	**Medium**	**High**	**Very high**
	<40,000	40,000-79,000	79,000-120,000	120,000-160,000	>160,000
A: Burden data from GBD 2019 or AMR dataset	Group B streptococcus HIV-1 Influenza Intestinal pathogenic *E. coli* (InPEC) Leishmania *Neisseria gonorrhoeae* (gonorrhea) Non-typhoidal *Salmonella* Norovirus Respiratory syncytial virus *Salmonella* Paratyphi Schistosomes *Shigella*	Group A streptococcus *Pseudomonas aeruginosa*	*Klebsiella pneumoniae*		Extra-intestinal pathogenic *E. coli* (ExPEC) *Staphylococcus aureus*
B: Burden calculated by other studies	Chikungunya virus *Mycobacterium tuberculosis* (TB)				
C: Data not available, will test a range of scores	Herpes simplex types 1 and 2 Hookworm *Mycobacterium leprae* (leprosy) *Plasmodium falciparum* (malaria)	Cytomegalovirus			

Table 63 Years lived with disability (all ages) in the European region					
Data Availability	**Very low**	**Low**	**Medium**	**High**	**Very high**
	<25,000	25,000-50,000	50,000-75,000	75,000-100,000	>100,000
A: Burden data from GBD 2019 or AMR dataset	Group B streptococcus Hookworm Influenza Intestinal pathogenic *E. coli* (InPEC) *Klebsiella pneumoniae* Leishmania *Mycobacterium leprae* (leprosy) *Neisseria gonorrhoeae* (gonorrhea) Non-typhoidal *Salmonella* *Pseudomonas aeruginosa* Respiratory syncytial virus *Salmonella* Paratyphi Schistosomes *Staphylococcus aureus*	Extra-intestinal pathogenic *E. coli* (ExPEC) Herpes Simplex Virus (Types 1 and 2) *Shigella*		Norovirus	Group A streptococcus HIV-1 *Mycobacterium tuberculosis* (TB)
B: Burden calculated by other studies	Chikungunya virus				
C: Data not available, will test a range of scores	*P. falciparum*	Cytomegalovirus			

b) Qualitative scoring

Table 64 Social and economic burden per case in the European Region					
Data Availability	**Very low**	**Low**	**Medium**	**High**	**Very high**
	Very low burden for each case	Low burden for each case	Moderate burden for each case	High burden for each case	Very high burden for each case
A: Based on data from regional sources		Influenza Norovirus	Chikungunya virus Extra-intestinal pathogenic *E. coli* (ExPEC) Group A streptococcus Herpes simplex types 1 and 2 Intestinal pathogenic *E. coli* (InPEC) Respiratory syncytial virus *Shigella*	Cytomegalovirus Group B streptococcus *Pseudomonas aeruginosa* *Staphylococcus aureus*	HIV-1 Leishmania *Mycobacterium leprae* (leprosy) *Mycobacterium tuberculosis* (TB)
B: Score inferred based on sources from other regions	Schistosomes	Hookworm Non-typhoidal *Salmonella* *Plasmodium falciparum* (malaria) *Salmonella Paratyphi*	*Neisseria gonorrhoeae*	*Klebsiella pneumoniae*	

Table 65 Disruption due to outbreaks in the European Region					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	Little or no social disruption or impact on healthcare, trade or tourism	Slight social disruption or impact on healthcare, trade or tourism	Moderate social disruption or impact on healthcare, trade or tourism	High social disruption or impact on healthcare, trade or tourism, including due to preventive measures	Very high social disruption or impact on healthcare, trade and tourism, including due to preventive measures
A: Based on data from regional sources	Group A streptococcus *Mycobacterium leprae* (leprosy) *Plasmodium falciparum* (malaria)	*Klebsiella pneumoniae* *Pseudomonas aeruginosa* *Salmonella Paratyphi* Schistosomes *Staphylococcus aureus*	Chikungunya virus *Shigella*	HIV-1 *Mycobacterium tuberculosis* (TB) Norovirus Respiratory syncytial virus	Influenza
B: Score inferred based on sources from other regions	Cytomegalovirus Herpes simplex types 1 and 2 Hookworm Leishmania	Extra-intestinal pathogenic *E. coli* (ExPEC) Group B streptococcus *Neisseria gonorrhoeae* Non-typhoidal *Salmonella*	Intestinal pathogenic *E. coli* (InPEC)		

Table 66 Contribution to inequity in the European Region					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	Affects all communities equally	Burden falls on socially and economically disadvantaged groups, including women, **slightly** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, **moderately** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, **much** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, all or most of the time
A: Based on data from regional sources			Chikungunya virus Cytomegalovirus Extra-intestinal pathogenic *E. coli* (ExPEC) Group B streptococcus Herpes simplex types 1 and 2 Norovirus	Leishmania *Neisseria gonorrhoeae*	HIV-1 Hookworm *Mycobacterium leprae* (leprosy) *Mycobacterium tuberculosis* (TB)
B: Score inferred based on sources from other regions	*Plasmodium falciparum* (malaria) Schistosomes	*Klebsiella pneumoniae* *Pseudomonas aeruginosa*	Group A streptococcus Influenza Intestinal pathogenic *E. coli* (InPEC) Respiratory syncytial virus *Staphylococcus aureus*	Non-typhoidal *Salmonella* *Salmonella Paratyphi* *Shigella*	

Table 67 Contribution to antimicrobial resistance in the European Region					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	Not resistant to first-line drugs and not associated with antibiotic use	Little resistance to first-line drugs and little association with antibiotic use	Some resistance to first-line drugs, associated with high antibiotic use	Significant resistance to first-line drugs, associated with high antibiotic use	A global resistance threat due to widespread resistance and association with high antibiotic use
A: Based on data from regional sources	Leishmania *Plasmodium falciparum* (malaria)	Group B streptococcus Herpes simplex types 1 and 2	Respiratory syncytial virus		Extra-intestinal pathogenic *E. coli* (ExPEC) HIV-1 Intestinal pathogenic *E. coli* (InPEC) *Klebsiella pneumoniae* *Mycobacterium tuberculosis* (TB) *Neisseria gonorrhoeae* *Pseudomonas aeruginosa* *Staphylococcus aureus*
B: Score inferred based on sources from other regions	Chikungunya virus Cytomegalovirus *Mycobacterium leprae* (leprosy) Schistosomes	Hookworm Norovirus *Salmonella Paratyphi*	Influenza	Group A streptococcus Non-typhoidal *Salmonella* *Shigella*	

Table 68 Unmet needs for prevention and treatment in the European Region					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	The alternatives for prevention or treatment meet the needs of most people	The alternatives for prevention or treatment meet the needs of many people	The alternatives for prevention or treatment meet the needs of some people	The alternatives for prevention or treatment meet the needs of few people	There are no effective alternatives for prevention or treatment
A: Based on data from regional sources	Schistosomes	Hookworm	Extra-intestinal pathogenic *E. coli* (ExPEC) Group A streptococcus Intestinal pathogenic *E. coli* (InPEC) Leishmania *Neisseria gonorrhoeae* Non-typhoidal *Salmonella*	Group B streptococcus Herpes simplex types 1 and 2 HIV-1 Influenza *Klebsiella pneumoniae* *Mycobacterium leprae* (leprosy) *Mycobacterium tuberculosis* (TB) Norovirus *Pseudomonas aeruginosa* Respiratory syncytial virus *Shigella* *Staphylococcus aureus*	Chikungunya virus Cytomegalovirus
B: Score inferred based on sources from other regions	*Plasmodium falciparum* (malaria)	*Salmonella Paratyphi*			

5. South-East Asian Region

a) Quantitative scoring

Because burden data were not available for *P. falciparum*, it was scored based on data for malaria and the % of *P. vivax* found in each WHO region. As discussed in D.18, this gave a maximum and a minimum potential score for *P. falciparum* in the region.

Table 69 Annual deaths in children under 5 in the South-East Asian region

Data Availability	Very low	Low	Medium	High	Very high
	<8,600	8,600-17,000	17,000-26,000	26,000-35,000	>35,000
A: Burden data from GBD 2019 or AMR dataset	Group A streptococcus HIV-1 Influenza Intestinal pathogenic *E. coli* (InPEC) Leishmania *Neisseria gonorrhoeae* Non-typhoidal Salmonella Norovirus *Salmonella* Paratyphi Schistosomes *Shigella*		*Pseudomonas aeruginosa*	Extra-intestinal pathogenic *E. coli* (ExPEC) Group B streptococcus Respiratory syncytial virus *Staphylococcus aureus*	*Klebsiella pneumoniae*
B: Burden calculated by other studies	Chikungunya virus				*Mycobacterium tuberculosis* (TB)
C: Data not available, will test a range of scores	Cytomegalovirus Herpes simplex types 1 and 2 Hookworm *Mycobacterium leprae* (leprosy) *P. falciparum* - minimum	*P. falciparum* - maximum			

Table 70 Annual deaths in people 5 and older in the South-East Asian region					
Data Availability	**Very low**	**Low**	**Medium**	**High**	**Very high**
	<34,000	34,000-68,000	68,000-100,000	100,000-140,000	>140,000
A: Burden data from GBD 2019 or AMR dataset	Intestinal pathogenic *E. coli* (InPEC) Leishmania *Neisseria gonorrhoeae* (gonorrhea) Non-typhoidal *Salmonella* *Salmonella* Paratyphi Schistosomes *Shigella*	Group B streptococcus Influenza Norovirus Respiratory syncytial virus	HIV-1	*Pseudomonas aeruginosa*	Extra-intestinal pathogenic *E. coli* (ExPEC) Group A streptococcus *Klebsiella pneumoniae* *Staphylococcus aureus*
B: Burden calculated by other studies	Chikungunya virus				*Mycobacterium tuberculosis* (TB)
C: Data not available, will test a range of scores	Herpes simplex types 1 and 2 Hookworm *Mycobacterium leprae* (leprosy) *P. falciparum*	Cytomegalovirus			

Table 71 Years lived with disability (all ages) in the South-East Asian region					
Data Availability	**Very low**	**Low**	**Medium**	**High**	**Very high**
	<130,000	130,000-260,000	260,000-390,000	390,000-520,000	>520,000
A: Burden data from GBD 2019 or AMR dataset	Extra-intestinal pathogenic *E. coli* (ExPEC) Group B streptococcus Herpes Simplex Virus (Types 1 and 2) Influenza Intestinal pathogenic *E. coli* (InPEC) *Klebsiella pneumoniae* Leishmania *Mycobacterium leprae* (leprosy) *Neisseria gonorrhoeae* (gonorrhea) Non-typhoidal *Salmonella* Norovirus *Pseudomonas aeruginosa* Respiratory syncytial virus *Salmonella* Paratyphi Schistosomes *Staphylococcus aureus*	Hookworm Shigella		HIV-1	Group A streptococcus *Mycobacterium tuberculosis* (TB)
B: Burden calculated by other studies	Chikungunya virus				
C: Data not available, will test a range of scores	*P. falciparum* - minimum	Cytomegalovirus *P. falciparum* - maximum			

b) Qualitative scoring

Table 72 Social and economic burden per case in the South-East Asian Region					
Data Availability	**Very low**	**Low**	**Medium**	**High**	**Very high**
	Very low burden for each case	Low burden for each case	Moderate burden for each case	High burden for each case	Very high burden for each case
A: Based on data from regional sources		Hookworm Influenza *Salmonella Paratyphi*	Chikungunya virus Intestinal pathogenic *E. coli* (InPEC) Norovirus Respiratory syncytial virus	Group A streptococcus Herpes simplex types 1 and 2 *Klebsiella pneumoniae* *Plasmodium falciparum* (malaria) *Pseudomonas aeruginosa* *Shigella*	HIV-1 Leishmania *Mycobacterium leprae* (leprosy) *Mycobacterium tuberculosis* (TB)
B: Score inferred based on sources from other regions		Non-typhoidal *Salmonella* Schistosomes	Extra-intestinal pathogenic *E. coli* (ExPEC) *Neisseria gonorrhoeae*	Cytomegalovirus Group B streptococcus *Staphylococcus aureus*	

Table 73 Disruption due to outbreaks in the South-East Asian Region					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	Little or no social disruption or impact on healthcare, trade or tourism	Slight social disruption or impact on healthcare, trade or tourism	Moderate social disruption or impact on healthcare, trade or tourism	High social disruption or impact on healthcare, trade or tourism, including due to preventive measures	Very high social disruption or impact on healthcare, trade and tourism, including due to preventive measures
A: Based on data from regional sources	Group A streptococcus *Mycobacterium leprae* (leprosy) Non-typhoidal *Salmonella* *Pseudomonas aeruginosa* *Staphylococcus aureus*	*Klebsiella pneumoniae* *Salmonella Paratyphi*	*Plasmodium falciparum* (malaria) *Shigella*	Chikungunya virus HIV-1 Leishmania Norovirus Respiratory syncytial virus	Influenza *Mycobacterium tuberculosis* (TB)
B: Score inferred based on sources from other regions	Cytomegalovirus Herpes simplex types 1 and 2 Hookworm	Extra-intestinal pathogenic *E. coli* (ExPEC) Group B streptococcus *Neisseria gonorrhoeae* Schistosomes	Intestinal pathogenic *E. coli* (InPEC)		

Table 74 Contribution to inequity in the South-East Asian Region					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	Affects all communities equally	Burden falls on socially and economically disadvantaged groups, including women, **slightly** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, **moderately** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, **much** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, all or most of the time
A: Based on data from regional sources			Chikungunya virus Cytomegalovirus Extra-intestinal pathogenic *E. coli* (ExPEC) Norovirus	Herpes simplex types 1 and 2 *Neisseria gonorrhoeae* *Salmonella Paratyphi* Schistosomes	HIV-1 Hookworm Leishmania *Mycobacterium leprae* (leprosy) *Mycobacterium tuberculosis* (TB)
B: Score inferred based on sources from other regions		*Klebsiella pneumoniae* *Pseudomonas aeruginosa*	Group B streptococcus Influenza Intestinal pathogenic *E. coli* (InPEC) Respiratory syncytial virus *Staphylococcus aureus*	Group A streptococcus Non-typhoidal *Salmonella* *Plasmodium falciparum* (malaria) *Shigella*	

Table 75 Contribution to antimicrobial resistance in the South-East Asian Region					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	Not resistant to first-line drugs and not associated with antibiotic use	Little resistance to first-line drugs and little association with antibiotic use	Some resistance to first-line drugs, associated with high antibiotic use	Significant resistance to first-line drugs, associated with high antibiotic use	A global resistance threat due to widespread resistance and association with high antibiotic use
A: Based on data from regional sources	Group B streptococcus	Herpes simplex types 1 and 2	Leishmania *Mycobacterium leprae* (leprosy)	*Plasmodium falciparum* (malaria) *Salmonella Paratyphi*	Extra-intestinal pathogenic *E. coli* (ExPEC) HIV-1 Intestinal pathogenic *E. coli* (InPEC) *Klebsiella pneumoniae* *Mycobacterium tuberculosis* (TB) *Neisseria gonorrhoeae* *Pseudomonas aeruginosa* *Shigella* *Staphylococcus aureus*
B: Score inferred based on sources from other regions	Chikungunya virus Cytomegalovirus	Hookworm Norovirus Schistosomes		Group A streptococcus Influenza Non-typhoidal *Salmonella* Respiratory syncytial virus	

Table 76 Unmet needs for prevention and treatment in the South-East Asian Region					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	The alternatives for prevention or treatment meet the needs of most people	The alternatives for prevention or treatment meet the needs of many people	The alternatives for prevention or treatment meet the needs of some people	The alternatives for prevention or treatment meet the needs of few people	There are no effective alternatives for prevention or treatment
A: Based on data from regional sources		Hookworm	Extra-intestinal pathogenic *E. coli* (ExPEC) Intestinal pathogenic *E. coli* (InPEC) Leishmania *Neisseria gonorrhoeae* Non-typhoidal *Salmonella* *Plasmodium falciparum* (malaria) *Salmonella Paratyphi* Schistosomes	Group A streptococcus Herpes simplex types 1 and 2 HIV-1 Influenza *Klebsiella pneumoniae* *Mycobacterium leprae* (leprosy) *Mycobacterium tuberculosis* (TB) Norovirus *Pseudomonas aeruginosa* Respiratory syncytial virus *Shigella* *Staphylococcus aureus*	Chikungunya virus Group B streptococcus
B: Score inferred based on sources from other regions					Cytomegalovirus

6. Western Pacific Region

a) Quantitative scoring

Table 77 Annual deaths in children under 5 in the Western Pacific region

Data Availability	Very low	Low	Medium	High	Very high
	<1,500	1,500-3,100	3,100-4,600	4,600-6,100	>6,100
A: Burden data from GBD 2019 or AMR dataset	Intestinal pathogenic *E. coli* (InPEC) *Neisseria gonorrhoeae* Non-typhoidal *Salmonella* Norovirus *Salmonella* Paratyphi Schistosomes *Shigella*	Group A streptococcus HIV-1	Influenza	Extra-intestinal pathogenic *E. coli* (ExPEC) Group B streptococcus *Pseudomonas aeruginosa*	*Klebsiella pneumoniae* Respiratory syncytial virus *Staphylococcus aureus*
B: Burden calculated by other studies	Chikungunya virus Leishmania				*Mycobacterium tuberculosis* (TB)
C: Data not available, will test a range of scores	Hookworm *Mycobacterium leprae* (leprosy) *P. falciparum*	Herpes simplex types 1 and 2	Cytomegalovirus		

Table 78 Annual deaths in people 5 and older in the Western Pacific region					
Data Availability	**Very low**	**Low**	**Medium**	**High**	**Very high**
	<49,000	49,000-99,000	99,000-150,000	150,000-200,000	>200,000
A: Burden data from GBD 2019 or AMR dataset	Group B streptococcus HIV-1 Intestinal pathogenic *E. coli* (InPEC) *Neisseria gonorrhoeae* (gonorrhea) Non-typhoidal *Salmonella* Norovirus Respiratory syncytial virus *Salmonella* Paratyphi Schistosomes *Shigella*	Influenza	Extra-intestinal pathogenic *E. coli* (ExPEC) Group A streptococcus *Klebsiella pneumoniae* *Pseudomonas aeruginosa*		*Staphylococcus aureus*
B: Burden calculated by other studies	Chikungunya virus Leishmania		*Mycobacterium tuberculosis* (TB)		
C: Data not available, will test a range of scores	Herpes simplex types 1 and 2 Hookworm *Mycobacterium leprae* (leprosy) *P. falciparum*	Cytomegalovirus			

Table 79 Years lived with disability (all ages) in the Western Pacific region					
Data Availability	**Very low**	**Low**	**Medium**	**High**	**Very high**
	<83,000	83,000-170,000	170,000-250,000	250,000-330,000	>330,000
A: Burden data from GBD 2019 or AMR dataset	Extra-intestinal pathogenic *E. coli* (ExPEC) Group B streptococcus Herpes Simplex Virus (Types 1 and 2) Influenza Intestinal pathogenic *E. coli* (InPEC) *Klebsiella pneumoniae* Leishmania *Mycobacterium leprae* (leprosy) *Neisseria gonorrhoeae* (gonorrhea) Non-typhoidal *Salmonella* *Pseudomonas aeruginosa* Respiratory syncytial virus *Salmonella* Paratyphi Schistosomes *Shigella* *Staphylococcus aureus*	Hookworm Norovirus	HIV-1		Group A streptococcus *Mycobacterium tuberculosis* (TB)
B: Burden calculated by other studies	Chikungunya virus				
C: Data not available, will test a range of scores	*P. falciparum*	Cytomegalovirus			

b) Qualitative scoring

Table 80 Social and economic burden per case in the Western Pacific Region					
Data Availability	**Very low**	**Low**	**Medium**	**High**	**Very high**
	Very low burden for each case	Low burden for each case	Moderate burden for each case	High burden for each case	Very high burden for each case
A: Based on data from regional sources		Hookworm Influenza	Chikungunya virus Intestinal pathogenic *E. coli* (InPEC) Norovirus Respiratory syncytial virus	Cytomegalovirus Group A streptococcus Herpes simplex types 1 and 2 *Klebsiella pneumoniae* *Plasmodium falciparum* (malaria) *Shigella* *Staphylococcus aureus*	HIV-1 Leishmania *Mycobacterium leprae* (leprosy) *Mycobacterium tuberculosis* (TB)
B: Score inferred based on sources from other regions		Non-typhoidal *Salmonella* *Salmonella Paratyphi* Schistosomes	Extra-intestinal pathogenic *E. coli* (ExPEC) *Neisseria gonorrhoeae* *Pseudomonas aeruginosa*	Group B streptococcus	

Table 81 Disruptions due to outbreaks in the Western Pacific Region					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	Little or no social disruption or impact on healthcare, trade or tourism	Slight social disruption or impact on healthcare, trade or tourism	Moderate social disruption or impact on healthcare, trade or tourism	High social disruption or impact on healthcare, trade or tourism, including due to preventive measures	Very high social disruption or impact on healthcare, trade and tourism, including due to preventive measures
A: Based on data from regional sources	Group A streptococcus *Mycobacterium leprae* (leprosy)	Extra-intestinal pathogenic *E. coli* (ExPEC) *Klebsiella pneumoniae* *Neisseria gonorrhoeae* *Plasmodium falciparum* (malaria) *Pseudomonas aeruginosa* *Salmonella Paratyphi* *Staphylococcus aureus*		Chikungunya virus HIV-1 *Mycobacterium tuberculosis* (TB) Norovirus Respiratory syncytial virus	Influenza
B: Score inferred based on sources from other regions	Cytomegalovirus Herpes simplex types 1 and 2 Hookworm Leishmania	Group B streptococcus Non-typhoidal *Salmonella* Schistosomes	Intestinal pathogenic *E. coli* (InPEC) *Shigella*		

Table 82 Contribution to inequity in the Western Pacific Region					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	Affects all communities equally	Burden falls on socially and economically disadvantaged groups, including women, **slightly** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, **moderately** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, **much** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, all or most of the time
A: Based on data from regional sources			Chikungunya virus Cytomegalovirus Extra-intestinal pathogenic *E. coli* (ExPEC) Norovirus	Group A streptococcus Herpes simplex types 1 and 2 Leishmania *Neisseria gonorrhoeae* *Salmonella Paratyphi* Schistosomes *Staphylococcus aureus*	HIV-1 Hookworm *Mycobacterium tuberculosis* (TB)
B: Score inferred based on sources from other regions		*Klebsiella pneumoniae* *Pseudomonas aeruginosa*	Group B streptococcus Influenza Intestinal pathogenic *E. coli* (InPEC) Respiratory syncytial virus	Non-typhoidal *Salmonella* *Plasmodium falciparum* (malaria) *Shigella*	*Mycobacterium leprae* (leprosy)

Table 83 Contribution to antimicrobial resistance in the Western Pacific Region					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	Not resistant to first-line drugs and not associated with antibiotic use	Little resistance to first-line drugs and little association with antibiotic use	Some resistance to first-line drugs, associated with high antibiotic use	Significant resistance to first-line drugs, associated with high antibiotic use	A global resistance threat due to widespread resistance and association with high antibiotic use
A: Based on data from regional sources	Leishmania	Group B streptococcus Herpes simplex types 1 and 2 Schistosomes	*Mycobacterium leprae* (leprosy) *Plasmodium falciparum* (malaria) *Salmonella Paratyphi*	Respiratory syncytial virus	Extra-intestinal pathogenic *E. coli* (ExPEC) HIV-1 Intestinal pathogenic *E. coli* (InPEC) *Klebsiella pneumoniae* *Mycobacterium tuberculosis* (TB) *Neisseria gonorrhoeae* *Pseudomonas aeruginosa* *Staphylococcus aureus*
B: Score inferred based on sources from other regions	Chikungunya virus Cytomegalovirus	Hookworm Norovirus		Group A streptococcus Influenza Non-typhoidal *Salmonella* *Shigella*	

Table 84 Unmet needs for prevention and treatment in the Western Pacific Region					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	The alternatives for prevention or treatment meet the needs of most people	The alternatives for prevention or treatment meet the needs of many people	The alternatives for prevention or treatment meet the needs of some people	The alternatives for prevention or treatment meet the needs of few people	There are no effective alternatives for prevention or treatment
A: Based on data from regional sources		Hookworm	Extra-intestinal pathogenic *E. coli* (ExPEC) Intestinal pathogenic *E. coli* (InPEC) Leishmania *Neisseria gonorrhoeae* Non-typhoidal *Salmonella* *Plasmodium falciparum* (malaria) Schistosomes	Chikungunya virus Group A streptococcus Group B streptococcus Herpes simplex types 1 and 2 HIV-1 Influenza *Klebsiella pneumoniae* *Mycobacterium leprae* (leprosy) *Mycobacterium tuberculosis* (TB) Norovirus *Pseudomonas aeruginosa* Respiratory syncytial virus *Shigella* *Staphylococcus aureus*	
B: Score inferred based on sources from other regions		*Salmonella Paratyphi*			Cytomegalovirus

7. Global

a) Quantitative scoring

Table 85 Annual deaths in children under 5 – Global					
Data Availability	**Very low**	**Low**	**Medium**	**High**	**Very high**
	<41,000	41,000-82,000	82,000-120,000	120,000-160,000	>160,000
A: Burden data from GBD 2019 or AMR dataset	Group A streptococcus Influenza Intestinal pathogenic *E. coli* (InPEC) Leishmania *Neisseria gonorrhoeae* *Salmonella* Paratyphi Schistosomes	HIV-1 Norovirus	Non-typhoidal *Salmonella* *Pseudomonas aeruginosa* *Shigella*	Extra-intestinal pathogenic *E. coli* (ExPEC) Group B streptococcus Respiratory syncytial virus *Staphylococcus aureus*	*Klebsiella pneumoniae*
B: Burden calculated by other studies	Chikungunya virus			*Mycobacterium tuberculosis* (TB)	
C: Data not available, will test a range of scores	Cytomegalovirus Herpes simplex types 1 and 2 Hookworm *Mycobacterium leprae* (leprosy)				*P. falciparum*

Table 86 Annual deaths in people 5 and older – Global					
Data Availability	**Very low**	**Low**	**Medium**	**High**	**Very high**
	<190,000	190,000-380,000	380,000-570,000	570,000-760,000	>760,000
A: Burden data from GBD 2019 or AMR dataset	Group B streptococcus Intestinal pathogenic *E. coli* (InPEC) Leishmania *Neisseria gonorrhoeae* (gonorrhea) Non-typhoidal *Salmonella* Norovirus *Salmonella* Paratyphi Schistosomes *Shigella*	Influenza Respiratory syncytial virus	Group A streptococcus *Pseudomonas aeruginosa*	*Klebsiella pneumoniae*	Extra-intestinal pathogenic *E. coli* (ExPEC) HIV-1 *Staphylococcus aureus*
B: Burden calculated by other studies	Chikungunya virus				*Mycobacterium tuberculosis* (TB)
C: Data not available, will test a range of scores	Herpes simplex types 1 and 2 Hookworm *Mycobacterium leprae* (leprosy)	Cytomegalovirus *P. falciparum*			

Table 87 Years lived with disability (all ages) - Global					
Data Availability	**Very low**	**Low**	**Medium**	**High**	**Very high**
	<450,000	450,000-910,000	910,000-1,400,000	1,400,000-1,800,000	>1,800,000
A: Burden data from GBD 2019 or AMR dataset	Extra-intestinal pathogenic *E. coli* (ExPEC) Group B streptococcus Herpes Simplex Virus (Types 1 and 2) Influenza Intestinal pathogenic *E. coli* (InPEC) *Klebsiella pneumoniae* Leishmania *Mycobacterium leprae* (leprosy) *Neisseria gonorrhoeae* (gonorrhea) Non-typhoidal *Salmonella* *Pseudomonas aeruginosa* Respiratory syncytial virus *Salmonella* Paratyphi Staphylococcus aureus	Norovirus *Shigella*	Hookworm Schistosomes		Group A streptococcus HIV-1 *Mycobacterium tuberculosis* (TB)
B: Burden calculated by other studies	Chikungunya virus				
C: Data not available, will test a range of scores			Cytomegalovirus		*P. falciparum*

b) Qualitative scoring

Table 88 Social and economic burden per case - Global					
Data Availability	**Very low**	**Low**	**Medium**	**High**	**Very high**
	Very low burden for each case	Low burden for each case	Moderate burden for each case	High burden for each case	Very high burden for each case
A: Based on pathogen data		Hookworm Influenza *Salmonella Paratyphi* Schistosomes	Chikungunya virus Extra-intestinal pathogenic *E. coli* (ExPEC) Intestinal pathogenic *E. coli* (InPEC) *Neisseria gonorrhoeae* Non-typhoidal *Salmonella* Norovirus Respiratory syncytial virus	Group A streptococcus Group B streptococcus Herpes simplex types 1 and 2 *Klebsiella pneumoniae* *Plasmodium falciparum* (malaria) *Pseudomonas aeruginosa* *Shigella* *Staphylococcus aureus*	HIV-1 Leishmania *Mycobacterium leprae* (leprosy) *Mycobacterium tuberculosis* (TB)
B: Score inferred based on sources from other pathogens				Cytomegalovirus	

Table 89 Disruptions due to outbreaks - Global					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	Little or no social disruption or impact on healthcare, trade or tourism	Slight social disruption or impact on healthcare, trade or tourism	Moderate social disruption or impact on healthcare, trade or tourism	High social disruption or impact on healthcare, trade or tourism, including due to preventive measures	Very high social disruption or impact on healthcare, trade and tourism, including due to preventive measures
A: Based on pathogen data	Group A streptococcus *Mycobacterium leprae* (leprosy)	Extra-intestinal pathogenic *E. coli* (ExPEC) Group B streptococcus *Klebsiella pneumoniae* *Neisseria gonorrhoea* *Pseudomonas aeruginosa* *Salmonella Paratyphi* Schistosomes *Staphylococcus aureus*	Leishmania Non-typhoidal *Salmonella* *Plasmodium falciparum* (malaria) *Shigella*	Chikungunya virus HIV-1 Norovirus Respiratory syncytial virus	Influenza *Mycobacterium tuberculosis* (TB)
B: Score inferred based on sources from other pathogens	Cytomegalovirus Herpes simplex types 1 and 2 Hookworm		Intestinal pathogenic *E. coli* (InPEC)		

Table 90 Contribution to inequity - Global					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	Affects all communities equally	Burden falls on socially and economically disadvantaged groups, including women, **slightly** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, **moderately** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, **much** more than other groups	Burden falls on socially and economically disadvantaged groups, including women, all or most of the time
A: Based on data from regional sources			Chikungunya virus Cytomegalovirus Extra-intestinal pathogenic *E. coli* (ExPEC) Group B streptococcus Influenza Intestinal pathogenic *E. coli* (InPEC) Norovirus Respiratory syncytial virus *Staphylococcus aureus*	Group A streptococcus Herpes simplex types 1 and 2 Leishmania *Neisseria gonorrhoea* Non-typhoidal *Salmonella* *Plasmodium falciparum* (malaria) *Salmonella Paratyphi* Schistosomes *Shigella*	HIV-1 Hookworm *Mycobacterium leprae* (leprosy) *Mycobacterium tuberculosis* (TB)
B: Score inferred based on sources from other pathogens		*Klebsiella pneumoniae* *Pseudomonas aeruginosa*			

Table 91 Contribution to antimicrobial resistance - Global					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	Not resistant to first-line drugs and not associated with antibiotic use	Little resistance to first-line drugs and little association with antibiotic use	Some resistance to first-line drugs, associated with high antibiotic use	Significant resistance to first-line drugs, associated with high antibiotic use	A global resistance threat due to widespread resistance and association with high antibiotic use
A: Based on pathogen data	Chikungunya virus	Group B streptococcus Herpes simplex types 1 and 2 Hookworm Schistosomes	Influenza (seasonal and pandemic) Leishmania *Mycobacterium leprae* (leprosy) Respiratory syncytial virus	Group A streptococcus Non-typhoidal *Salmonella* *Plasmodium falciparum* (malaria) *Salmonella Paratyphi* *Shigella*	Extra-intestinal pathogenic *E. coli* (ExPEC) HIV-1 Intestinal pathogenic *E. coli* (InPEC) *Klebsiella pneumoniae* *Mycobacterium tuberculosis* (TB) *Neisseria gonorrhoea* *Pseudomonas aeruginosa* *Staphylococcus aureus*
B: Score inferred based on sources from other pathogens	Cytomegalovirus	Norovirus			

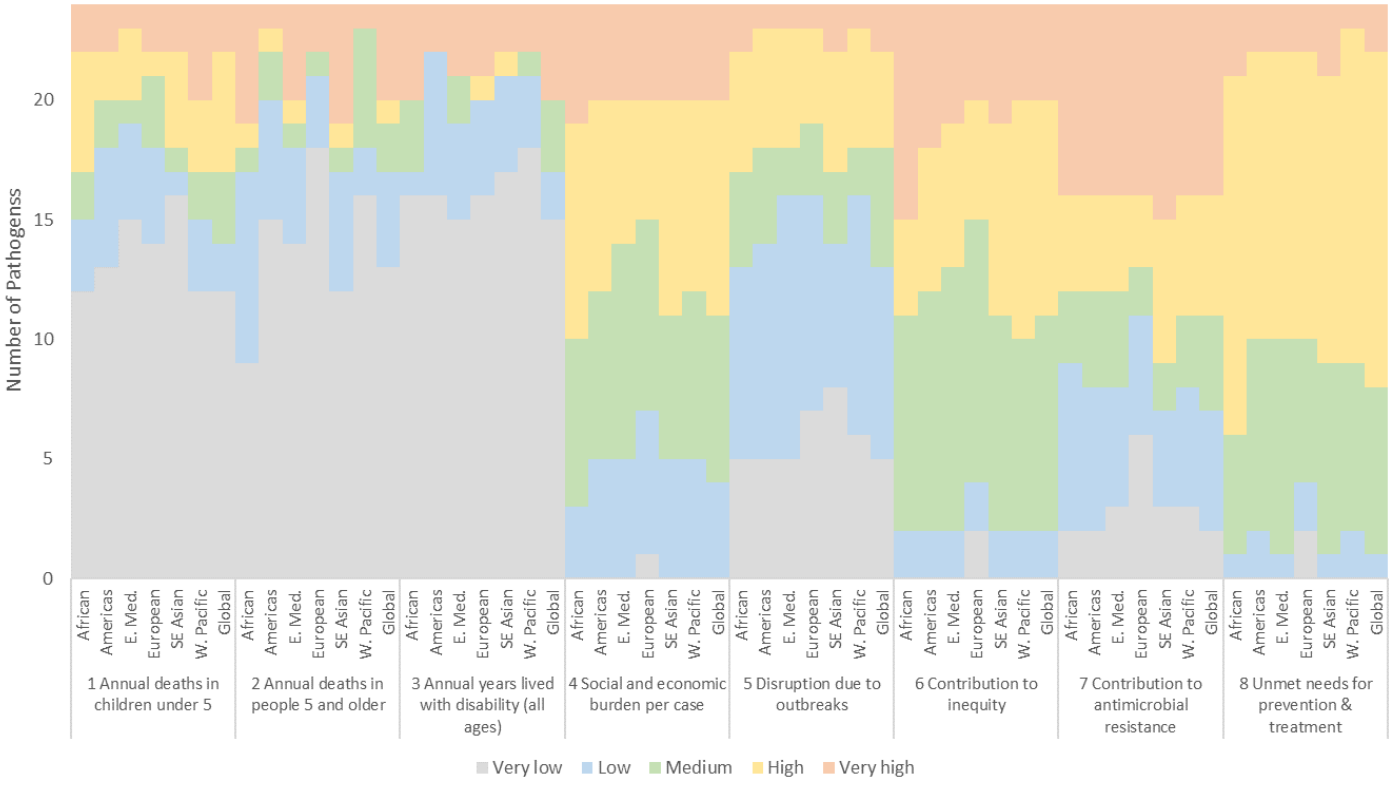
Table 92 Unmet needs for prevention and treatment - Global					
	Very low	**Low**	**Medium**	**High**	**Very high**
Data Availability	The alternatives for prevention or treatment meet the needs of most people	The alternatives for prevention or treatment meet the needs of many people	The alternatives for prevention or treatment meet the needs of some people	The alternatives for prevention or treatment meet the needs of few people	There are no effective alternatives for prevention or treatment
A: Based on pathogen data		Hookworm	Extra-intestinal pathogenic *E. coli* (ExPEC) Intestinal pathogenic *E. coli* (InPEC) Leishmania *Neisseria gonorrhoea* Non-typhoidal *Salmonella* *Salmonella Paratyphi*	Group A streptococcus Group B streptococcus Herpes simplex types 1 and 2 HIV-1 Influenza *Klebsiella pneumoniae* *Mycobacterium leprae* (leprosy) *Mycobacterium tuberculosis* (TB) Norovirus *Plasmodium falciparum* (malaria) *Pseudomonas aeruginosa* Respiratory syncytial virus Schistosomes *Shigella* *Staphylococcus aureus*	Chikungunya virus Cytomegalovirus
B: Score inferred based on sources from other pathogens					

F. Annex F: Additional Data Analysis

1. Scores by Criterion

Examining the scores not by pathogen, but by criterion, reveals differences between the criteria (Figure 9**Error! Reference source not found.**).

Figure 9 Scores by Criterion and Region



For criteria that were scored quantitatively (Criteria 1 - 3), most pathogens scored “Very low” or “Low”. This reflects the approach to setting quantitative thresholds (see II.A.4) and the underlying datasets, in which a few pathogens had extremely high burden.

Among the criteria that were scored qualitatively (Criteria 4 - 8), there were few scores of “Very low” for 4 Social and economic burden per case, 6 Contribution to inequity, and 7 Unmet needs for prevention and treatment. This reflects the pathogen scope, which focuses on pathogens for which there are no licensed vaccines (or for which the licensed vaccines do not fulfill critical target product attributes) and have been prioritized by a global mechanism or disease control strategy. This scope therefore favors pathogens with high burden per case, high contribution to inequity, and high unmet needs.

2. Base Case Pathogen Ranks by Region

Ranks are based on pathogen scoring for each region and assume that all criteria are weighted equally.

Rank	Global	African	Americas	E. Med.	European	SE Asian	W. Pacific
1	*Mycobacterium tuberculosis* (TB)	*Plasmodium falciparum* (malaria)	Human immunodeficiency virus 1 (HIV-1)	*Mycobacterium tuberculosis* (TB)	*Mycobacterium tuberculosis* (TB)	*Mycobacterium tuberculosis* (TB)	*Mycobacterium tuberculosis* (TB)
2	Human immunodeficiency virus 1 (HIV-1)	*Mycobacterium tuberculosis* (TB)	*Staphylococcus aureus*	*Staphylococcus aureus*	Human immunodeficiency virus 1 (HIV-1)	Human immunodeficiency virus 1 (HIV-1)	*Staphylococcus aureus*
3	*Plasmodium falciparum* (malaria)	Human immunodeficiency virus 1 (HIV-1)	*Mycobacterium tuberculosis* (TB)	*Klebsiella pneumoniae*	*Staphylococcus aureus*	Group A streptococcus (*Streptococcus pyogenes*)	Human immunodeficiency virus 1 (HIV-1)
4	*Staphylococcus aureus*	*Staphylococcus aureus*	*Klebsiella pneumoniae*	Human immunodeficiency virus 1 (HIV-1), Leishmania	Extra-intestinal pathogenic *E. coli* (ExPEC)	*Klebsiella pneumoniae*	Group A streptococcus (*Streptococcus pyogenes*)
5	*Klebsiella pneumoniae*	*Klebsiella pneumoniae*	*Pseudomonas aeruginosa*		*Klebsiella pneumoniae*	*Staphylococcus aureus*	*Klebsiella pneumoniae*
6	Group A streptococcus (*Streptococcus pyogenes*)	*Shigella*	Extra-intestinal pathogenic *E. coli* (ExPEC)	Extra-intestinal pathogenic *E. coli* (ExPEC)	Respiratory syncytial virus	Extra-intestinal pathogenic *E. coli* (ExPEC)	Respiratory syncytial virus
7	Extra-intestinal pathogenic *E. coli* (ExPEC)	Non-typhoidal *Salmonella*	*Shigella*	Group A streptococcus (*Streptococcus pyogenes*), *Shigella*	Group A streptococcus (*Streptococcus pyogenes*), *Pseudomonas aeruginosa*	Respiratory syncytial virus	Extra-intestinal pathogenic *E. coli* (ExPEC), *Pseudomonas aeruginosa*, Influenza
8	Shigella	Respiratory syncytial virus	Respiratory syncytial virus			*Shigella*, *Pseudomonas aeruginosa*	
9	Respiratory syncytial virus	Extra-intestinal pathogenic *E. coli* (ExPEC), *Pseudomonas aeruginosa*	Group A streptococcus (*Streptococcus pyogenes*)	*Pseudomonas aeruginosa*	*Shigella*		
10	*Pseudomonas aeruginosa*		*Plasmodium falciparum* (malaria)	Group B streptococcus (*Streptococcus agalactiae*)	Norovirus	*Plasmodium falciparum* (malaria)	*Shigella*
11	Non-typhoidal *Salmonella*	Group A streptococcus (*Streptococcus pyogenes*)	Leishmania	Respiratory syncytial virus	Influenza, Cytomegalovirus	Leishmania	Group B streptococcus (*Streptococcus agalactiae*)
12	Group B streptococcus (*Streptococcus agalactiae*)	Leishmania	Influenza	*Plasmodium falciparum* (malaria), Norovirus		Group B streptococcus (*Streptococcus agalactiae*), Influenza	*Mycobacterium leprae* (leprosy)
13	Leishmania, *Mycobacterium leprae* (leprosy)	Group B streptococcus (*Streptococcus agalactiae*), Schistosomes	*Mycobacterium leprae* (leprosy)		Intestinal pathogenic *E. coli* (InPEC), *Neisseria gonorrhoeae*		Cytomegalovirus
14			Group B streptococcus (*Streptococcus agalactiae*), Norovirus, Intestinal pathogenic *E. coli* (InPEC), Neisseria gonorrhoeae, Chikungunya virus	*Mycobacterium leprae* (leprosy), Influenza, Cytomegalovirus, Intestinal pathogenic *E. coli* (InPEC), *Neisseria gonorrhoeae*		Mycobacterium leprae (leprosy)	Norovirus, Intestinal pathogenic *E. coli* (InPEC), *Neisseria gonorrhoeae*
15	Influenza, Norovirus	Influenza, Norovirus			*Mycobacterium leprae* (leprosy)	Norovirus, Intestinal pathogenic *E. coli* (InPEC), *Neisseria gonorrhoeae*	
16					Group B streptococcus (*Streptococcus agalactiae*)		
17	Cytomegalovirus, Intestinal pathogenic *E. coli* (InPEC), *Neisseria gonorrhoeae*	*Mycobacterium leprae* (leprosy), Cytomegalovirus, Intestinal pathogenic *E. coli* (InPEC), *Neisseria gonorrhoeae*, Herpes simplex types 1 and 2			Non-typhoidal *Salmonella*, Chikungunya virus		Herpes simplex types 1 and 2
18						Chikungunya virus	*Plasmodium falciparum* (malaria)
19			Cytomegalovirus	Non-typhoidal *Salmonella*, *Salmonella* Paratyphi	Leishmania	Cytomegalovirus	Chikungunya virus
20	Chikungunya virus		Herpes simplex types 1 and 2		Herpes simplex types 1 and 2	Herpes simplex types 1 and 2	Non-typhoidal *Salmonella*
21	Herpes simplex types 1 and 2		Non-typhoidal *Salmonella*	Chikungunya virus	*Salmonella* Paratyphi, Hookworm	*Salmonella* Paratyphi	Leishmania
22	*Salmonella* Paratyphi	Chikungunya virus	Schistosomes	Schistosomes		Non-typhoidal *Salmonella*	*Salmonella* Paratyphi, Schistosomes
23	Schistosomes	Hookworm	*Salmonella* Paratyphi, Hookworm	Herpes simplex types 1 and 2	*Plasmodium falciparum* (malaria), Schistosomes	Schistosomes	
24	Hookworm	*Salmonella* Paratyphi		Hookworm		Hookworm	Hookworm