

Partnering with regions and countries to identify priority pathogens for vaccines



Immunization, Vaccines and Biologicals

Vaccine Prioritization & Platforms Team

GVIRF 28 March 2023





What is our goal?

What and How are equally important

What

- **Identify R&D priorities**
 - To track progress in vaccine and immunization R&D under IA2030
 - To accelerate progress by aligning stakeholders and integrating initiatives

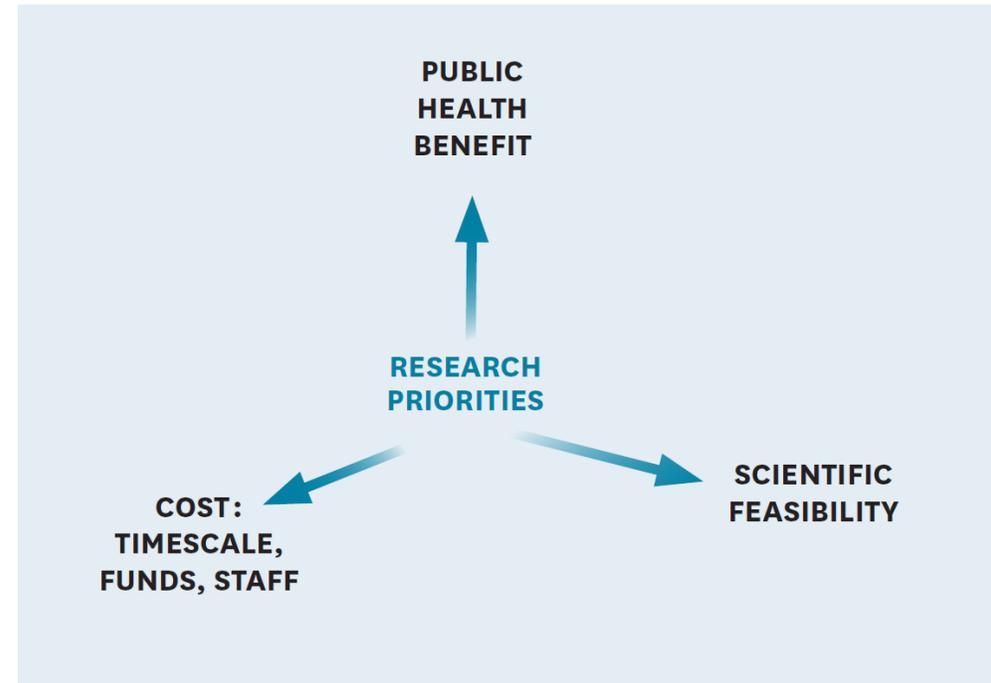
How

- **According to IA2030 Core Principles**
 - “People centered, data driven, partnership based, and country owned”
 - That is,
 - Systematic
 - Evidence-based
 - Transparent
 - **Focused on the perspectives of regional and country stakeholders**



Where do we start?

- **Focus on pathogens for new vaccine R&D**
 - No existing vaccines or important needs not met
 - Future prioritizations can consider 2nd generation or combo vaccines, technologies, etc.
- **Focus first on public health benefit**
 - Consider costs and feasibility in later stages





Two distinct stages

Multi-criteria decision analysis (MCDA)

- **Metrics-based prioritization**
 - Expert knowledge incorporated in pathogen scoring
 - Broad stakeholder perspectives captured through Preferences Surveys
 - Systematic, evidence-based and transparent

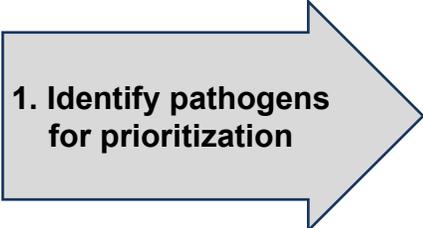
Regional consultations

- **Consensus-based synthesis**
 - Designed by regional stakeholders to serve regional needs
 - Considering costs and feasibility in the regional context
 - Building awareness, alignment, and buy-in within the region



MCDA Method - Overview

Consulted with regional advisors and technical experts at every stage



1. Identify pathogens for prioritization

- Landscaping identified over 150 potential R&D targets
- Filtered down to **26 pathogens** in scope
- Can add more pathogens as requested
- Emerging infectious diseases prioritized separately by R&D Blueprint



MCDA Method - Overview

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1. Identify pathogens for prioritization

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2. Formulate criteria to assess against

- Defined **8 criteria** based on precedents such as Gavi VIS
- Criteria are complete, non-overlapping, and independent of one another



MCDA Method - Overview

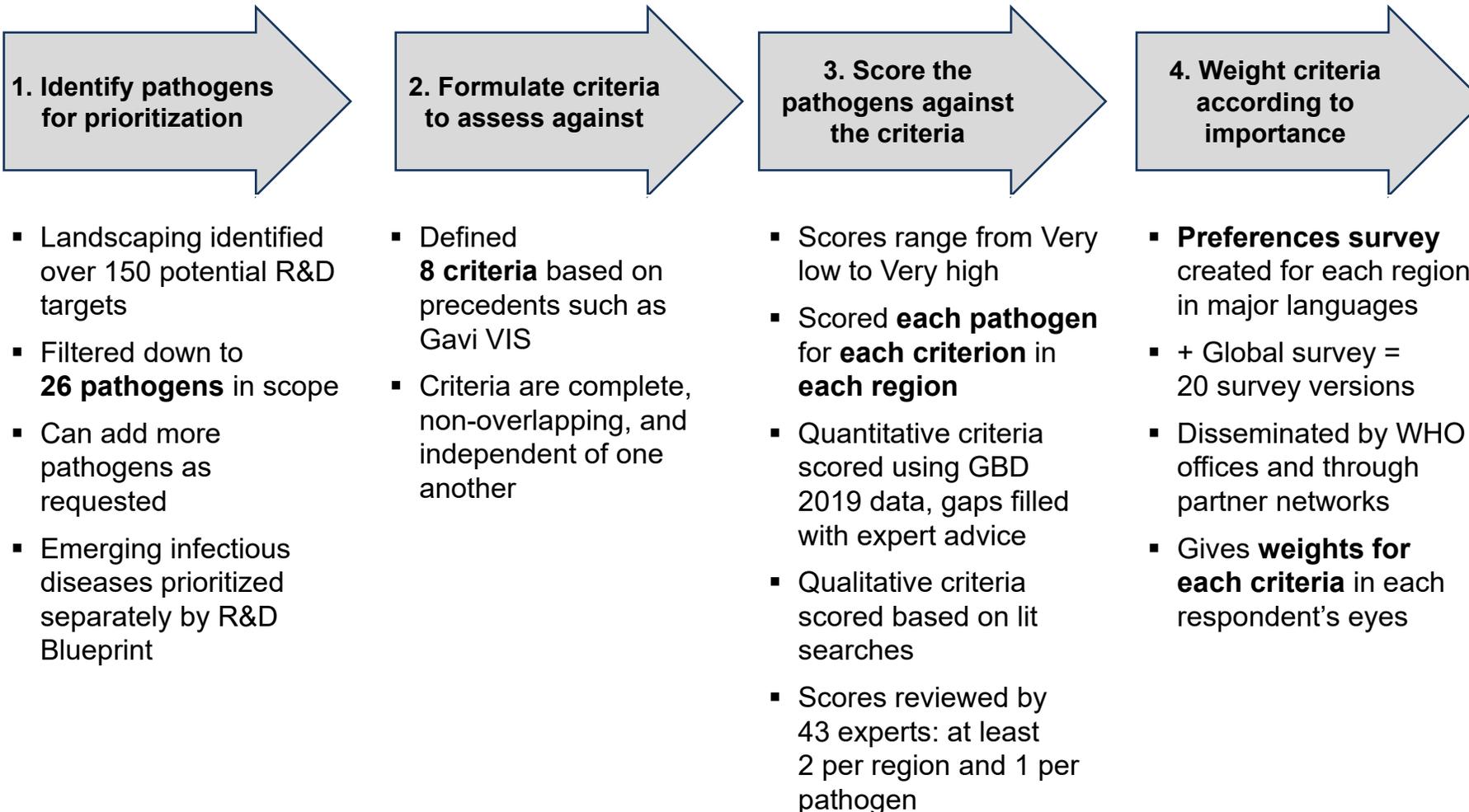
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- Landscaping identified over 150 potential R&D targets
 - Filtered down to **26 pathogens** in scope
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- Defined **8 criteria** based on precedents such as Gavi VIS
 - Criteria are complete, non-overlapping, and independent of one another
- Scores range from Very low to Very high
 - Scored **each pathogen** for **each criterion** in **each region**
 - Quantitative criteria scored using GBD 2019 data, gaps filled with expert advice
 - Qualitative criteria scored based on lit searches
 - Scores reviewed by 43 experts: at least 2 per region and 1 per pathogen

MCDA Method - Overview

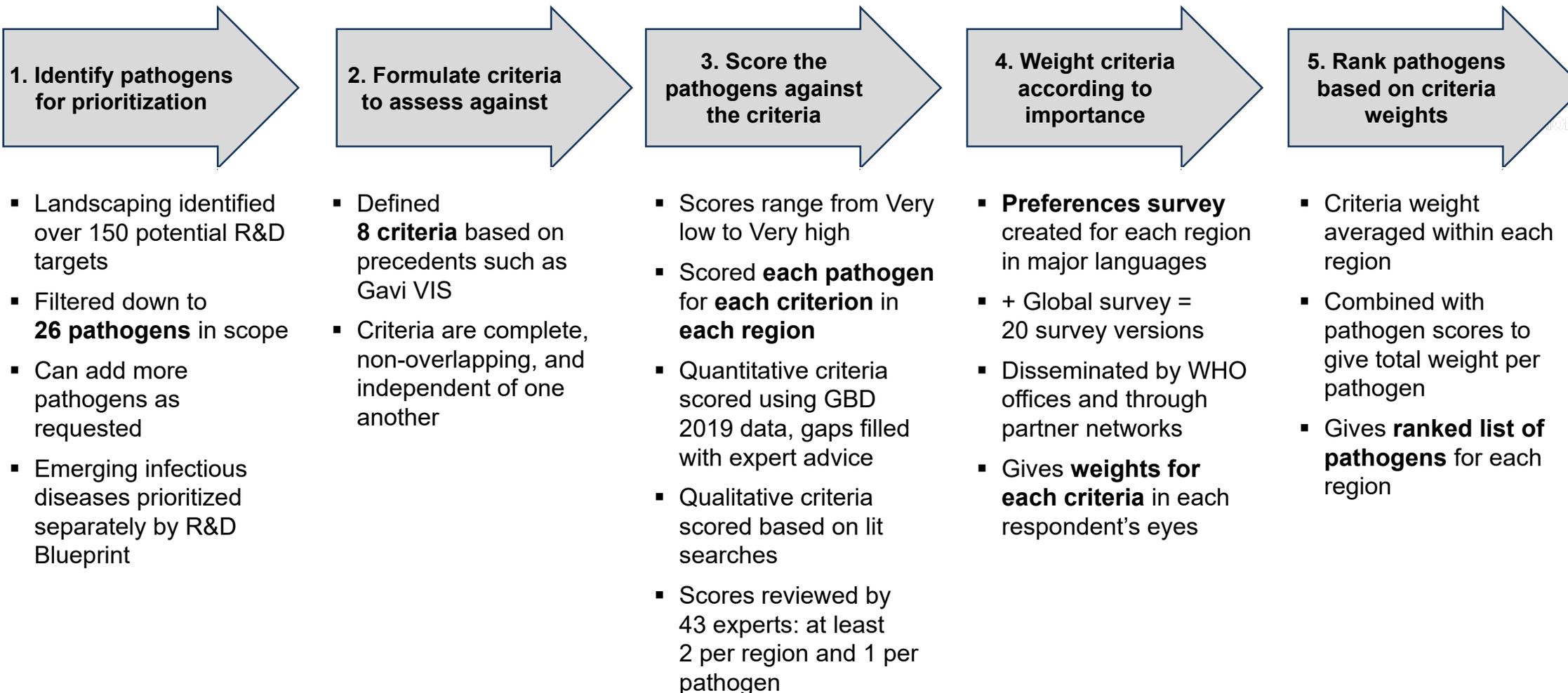
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MCDA Method - Overview

Consulted with regional advisors and technical experts at every stage



- Included pathogens that:
 - a. Affect humans
 - b. Not emerging infectious diseases (which require different criteria)
 - c. Lack licensed vaccines, or where existing vaccines do not meet needs of certain populations
 - d. With candidates in clinical development
 - e. Are prioritized for vaccine R&D by global stakeholders (for initial analysis)
- Pathogens can be added at any point in data analysis

PDVAC actively supporting ^a

Herpes simplex types 1 and 2

HIV-1

Influenza

Mycobacterium tuberculosis (TB)

Neisseria gonorrhoeae

Plasmodium falciparum

Respiratory syncytial virus (RSV)

Salmonella (non-typhoidal)

Shigella spp

Streptococcus agalactiae
(group B streptococcus)

Streptococcus pyogenes
(group A streptococcus)

PDVAC Vaccine Value Profiles

Chikungunya virus

Cytomegalovirus

Hookworm

Intestinal pathogenic *E. coli* (InPEC)

Leishmania spp

Norovirus

Salmonella Paratyphi

Schistosomes

Other pathogens in scope

Chlamydia trachomatis ^c

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

Hepatitis C virus ^c

Klebsiella pneumoniae

Mycobacterium leprae

Pseudomonas aeruginosa

Staphylococcus aureus

a. PDVAC: WHO Product Development Vaccines Advisory Committee

b. <https://www.who.int/teams/blueprint/who-r-and-d-blueprint-for-epidemics>

c. Added to scope after survey launch



Criteria for prioritization

Quantitative Scoring

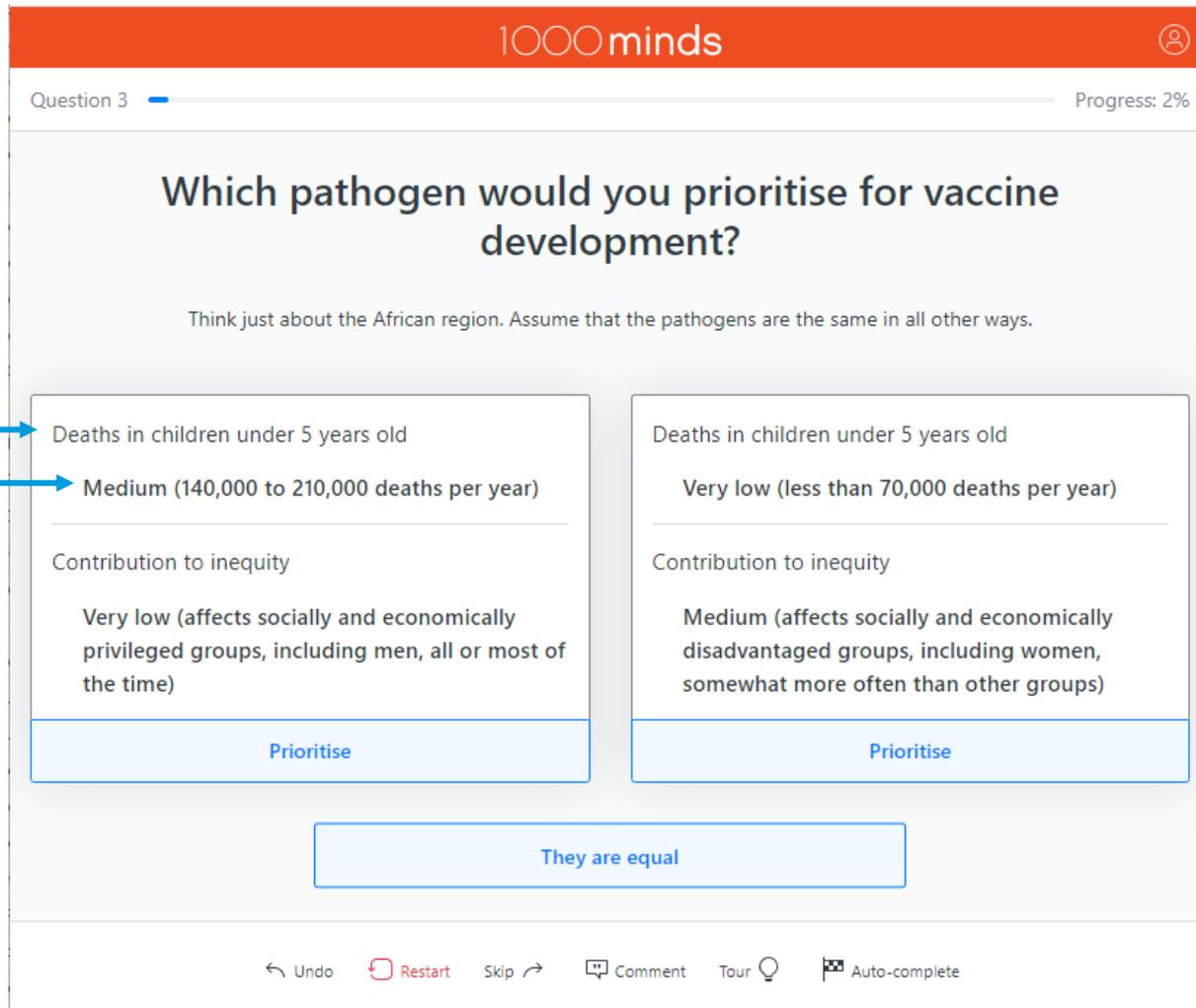
Annual deaths in children under 5	Deaths attributable to the pathogen in both sexes, < 5 years old
Annual deaths in people older than 5	Deaths attributable to the pathogen in both sexes, ≥ 5 years old
Years lost to disability (all ages)	Years of healthy life lost each year due to disability or ill-health caused by the pathogen

Qualitative Scoring

Social and economic burden per case	Reflects individual social and economic impact such as stigma and the costs of prevention, health care, and lost productivity.
Disruption due to outbreaks	Reflects societal impact due to outbreaks and epidemics, including social disruption; impact on healthcare systems, trade or tourism; and the cost of containment measures
Contribution to inequity	Reflects disproportionate impact on socially and economically disadvantaged groups, including women
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
Unmet needs for prevention and treatment	Reflects the effectiveness and suitability of alternative measures



Preferences Survey



1000 minds

Question 3 Progress: 2%

Which pathogen would you prioritise for vaccine development?

Think just about the African region. Assume that the pathogens are the same in all other ways.

<p>Criteria → Deaths in children under 5 years old</p> <p>Level → Medium (140,000 to 210,000 deaths per year)</p> <p>Contribution to inequity</p> <p>Very low (affects socially and economically privileged groups, including men, all or most of the time)</p> <p>Prioritise</p>	<p>Deaths in children under 5 years old</p> <p>Very low (less than 70,000 deaths per year)</p> <p>Contribution to inequity</p> <p>Medium (affects socially and economically disadvantaged groups, including women, somewhat more often than other groups)</p> <p>Prioritise</p>
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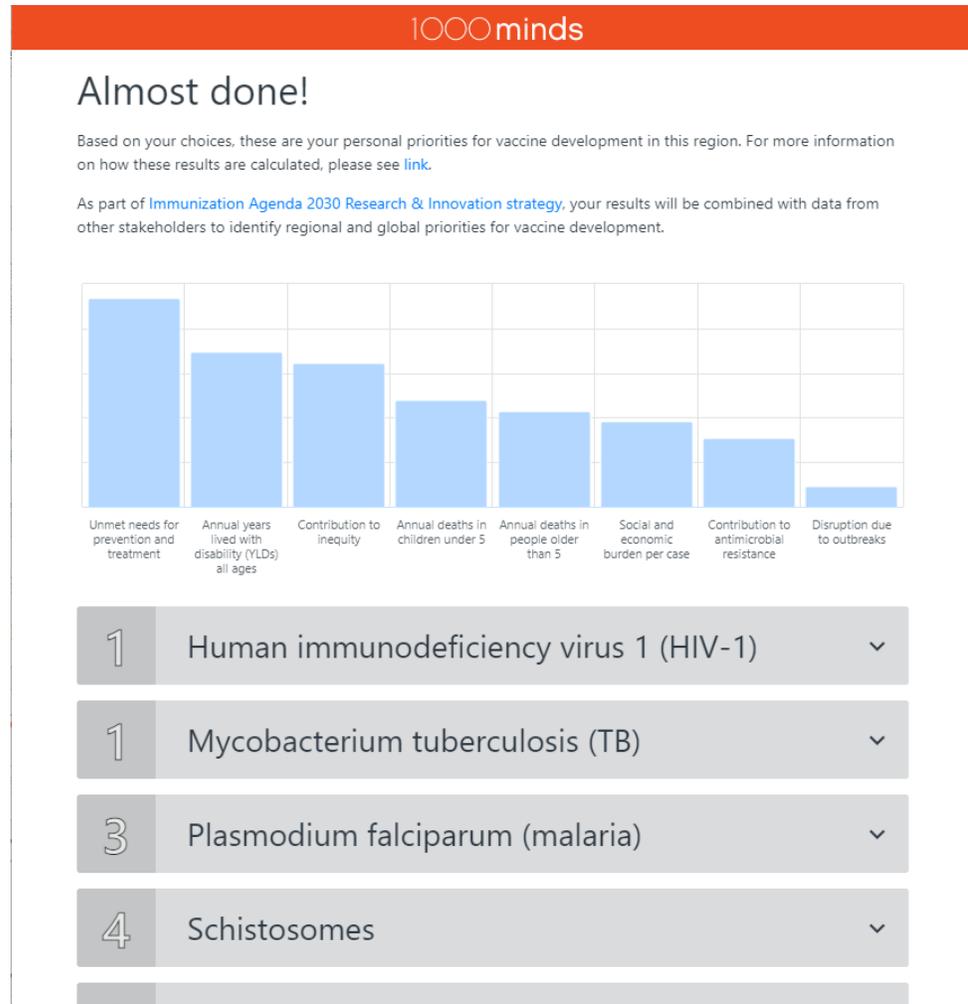
They are equal

Undo Restart Skip Comment Tour Auto-complete

- **Focus on criteria** reduces bias and means that people without pathogen-specific expertise can participate
- **Tailored to each region** and translated into key languages to enable broader participation
- **Targeted dissemination** to experts and policy makers starting in November 2022
- Survey links shared by WHO offices, partners, and directly by project team
- Surveys remain open. Data as of February 15, 2023 are shown here



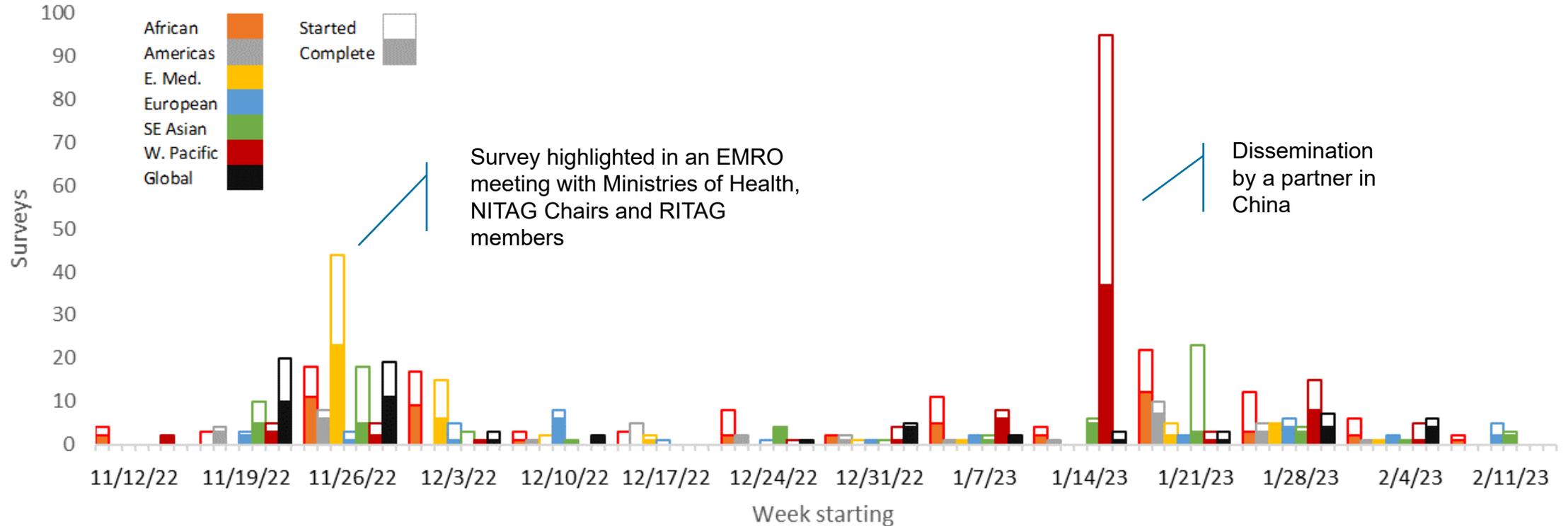
Rank pathogens based on weights x scores



- At the end of each survey, users will see:
 - What criteria they value most
 - Their personal priorities
- Data analysis will summarize priorities for each region
- Can include additional pathogens and updated scores



Survey responses over time



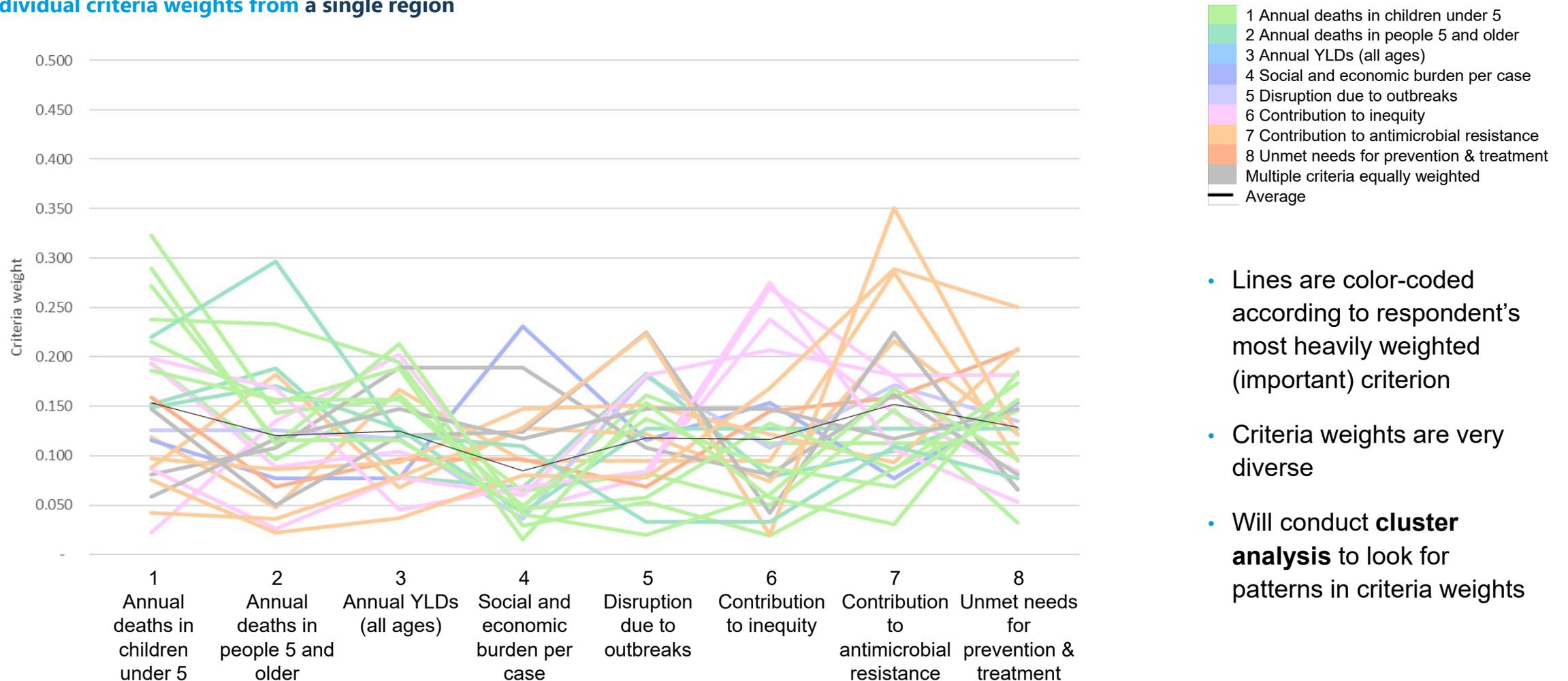
- 58% of people who start the survey complete it. This rate is common for complex surveys
- 225 complete regional responses as of 15 February 2023



Survey results show great diversity



Individual criteria weights from a single region



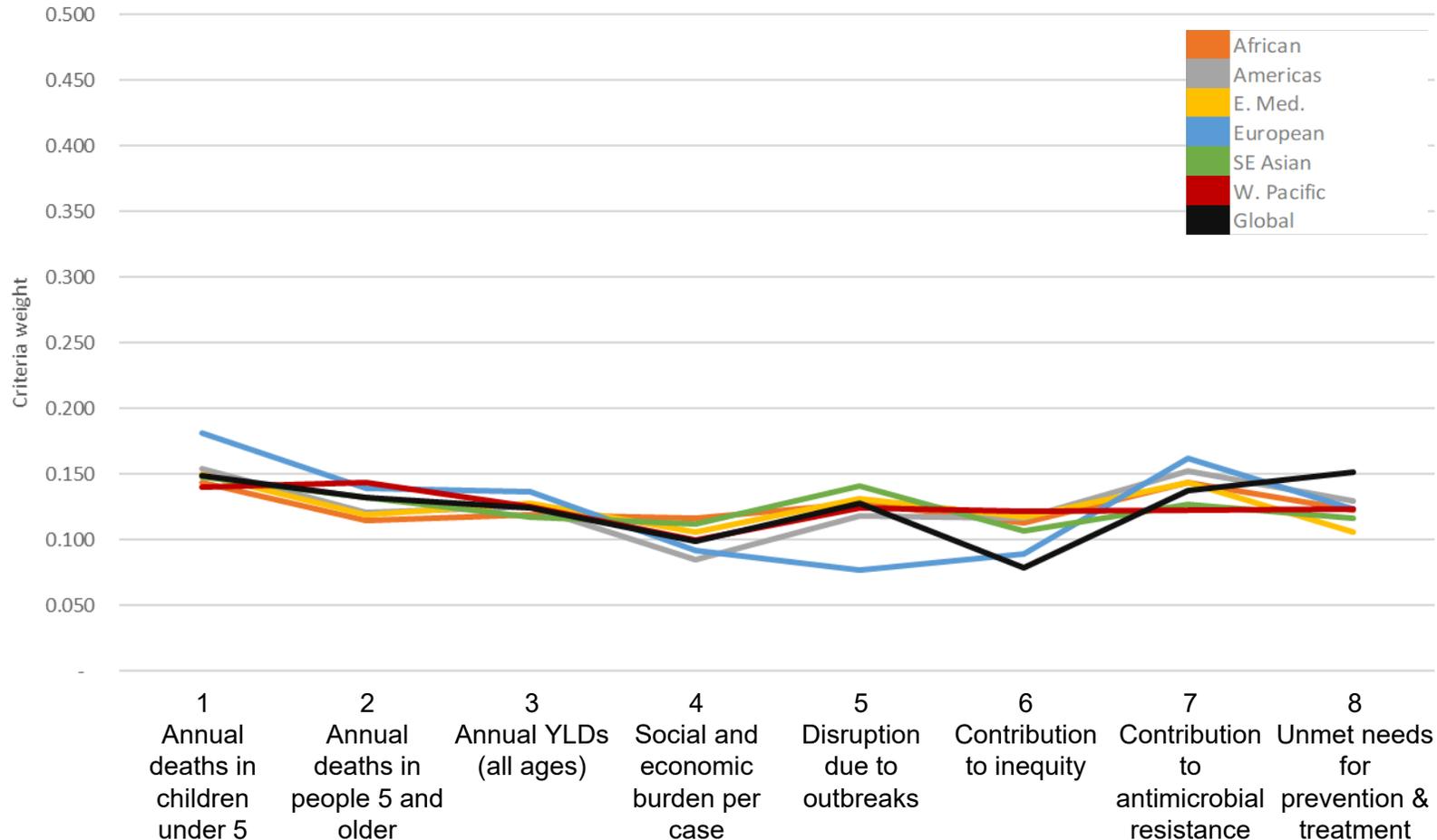
- Lines are color-coded according to respondent's most heavily weighted (important) criterion
- Criteria weights are very diverse
- Will conduct **cluster analysis** to look for patterns in criteria weights



When averaged, criteria are similarly weighted within and across regions



Average criteria weight within each region



- Lines are color-coded by region
- Within any region, all 8 criteria have similar importance (weight)
- Criteria weights are also similar across regions



Top 10 pathogens in each region



Rank	African (N=50)	Americas (N=25)	E. Med. (N=38)	European (N=22)	SE Asian (N=30)	W. Pacific (N=60)
1	<i>P. falciparum</i> (malaria)	HIV-1	TB	<i>Staph. aureus</i>	TB	TB
2	TB	<i>Staph. aureus</i>	<i>Staph. aureus</i>	TB	HIV-1	<i>Staph. Aureus</i>
3	HIV-1	<i>Klebsiella pneumoniae</i>	<i>Klebsiella pneumoniae</i>	HIV-1	<i>Klebsiella pneumoniae</i>	HIV-1
4	<i>Klebsiella pneumoniae</i>	TB	HIV-1	ExPEC	<i>Staph. aureus</i>	GAS
5	<i>Staph. aureus</i>	ExPEC	Leishmania	<i>Klebsiella pneumoniae</i>	GAS	<i>Klebsiella pneumoniae</i>
6	<i>Shigella</i>	<i>P. aeruginosa</i>	ExPEC	<i>P. aeruginosa</i>	ExPEC	RSV
7	Non-typhoidal Salmonella (NTS)	Group A streptococcus (GAS)	<i>Shigella</i>	GAS	RSV	<i>P. aeruginosa</i>
8	<i>P. aeruginosa</i>	RSV	Hepatitis C virus	RSV	<i>P. aeruginosa</i>	ExPEC
9	Extra-intestinal pathogenic <i>E. coli</i> (ExPEC)	<i>Shigella</i>	<i>P. aeruginosa</i>	Cytomegalo- virus	<i>Shigella</i>	Influenza
10	Respiratory syncytial virus (RSV)	Influenza	GAS	Hepatitis C virus	Hepatitis C virus	Hepatitis C virus

- 6 pathogens (in blue) are in Top 10 for all regions
- 9 more (in gray) are in Top 10 for some regions
- *What can we learn from these lists?*

Key

Top 10 in all regions

Top 10 in some regions



Why is HIV #4 in the Eastern Mediterranean?



HIV-1 Scores in the E. Med region

Criteria	Score
1 Annual deaths in children under 5	Very low
2 Annual deaths in people 5 and older	Low
3 Annual years lived with disability (all ages)	Very low
4 Social and economic burden per case	Very high
5 Disruption due to outbreaks	High
6 Contribution to inequity	Very high
7 Contribution to antimicrobial resistance	Very high
8 Unmet needs for prevention & treatment	High

- Burden of HIV-1 is relatively low in terms of deaths and YLDs in the region
 - But it was scored High and Very high for the other criteria
 - Since survey respondents thought that these criteria are also important, HIV-1 ranked #4 overall
- **These 8 criteria give a more complete picture of pathogen burden**



Why isn't RSV higher in the ranks?



RSV scores in all regions

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

- In most regions, RSV deaths are relatively high in children under 5
- But in older age groups, RSV deaths and morbidity are low compared to TB, HIV, and Group A strep
- RSV outbreaks primarily affect care facilities and healthcare settings, not society at large, so it was scored High for this criterion
- If feasibility is factored in, RSV would be ranked at or near the top

➤ **Next steps are crucial: must consider costs and feasibility in setting priorities**



Why does *Klebsiella* rank so high?



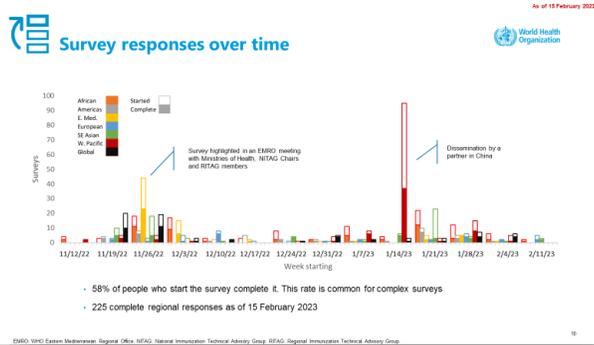
Klebsiella scores in all regions

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

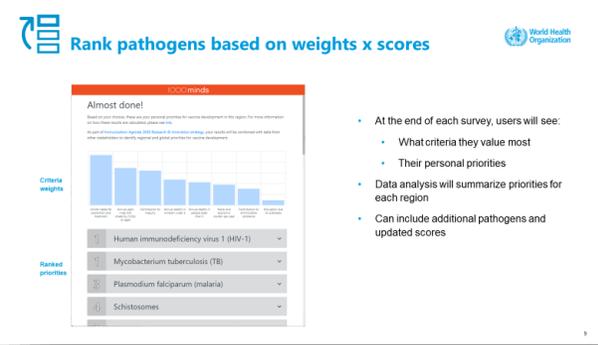
- *Klebsiella* deaths are relatively high in both children under 5 and older people
 - *In sensitivity testing, scaling back deaths and YLDs by 20% did not drop Klebs out of the top 10 lists*
- In addition, *Klebsiella* is a “critical” antimicrobial resistance concern
 - *In sensitivity testing, omitting the AMR criterion did not drop Klebs out of the top 10 lists*
- ***Klebsiella* may be an under-recognized issue**



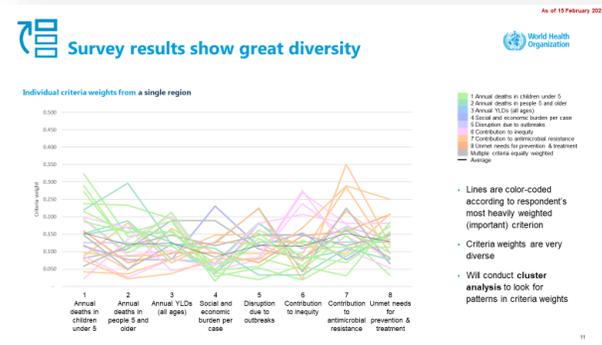
What have we learned?



Challenging to engage with regional and country stakeholders, but great interest and collaboration once contact is made



MCDA is much more flexible than group consensus methods. Focus on criteria reduces bias and reveals personal values



Important to be inclusive: individual perspectives are very diverse within a region, country, role, or area of expertise

Top 10 pathogens in each region

Rank	African (WES)	Americas (WE2)	E. Med. (NE3)	European (WE2)	SE Asian (WE3)	W. Pacific (NE5)
1	<i>P. falciparum</i> (malaria)	HIV-1	TB	<i>Staph. aureus</i>	TB	TB
2	TB	<i>Staph. aureus</i>	<i>Staph. aureus</i>	TB	HIV-1	<i>Staph. aureus</i>
3	HIV-1	<i>Klebsiella pneumoniae</i>	<i>Klebsiella pneumoniae</i>	HIV-1	<i>Klebsiella pneumoniae</i>	HIV-1
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9	State Haemolysing E. coli (EPEC)	Shigella	<i>P. aeruginosa</i>	Cytomegalovirus	Shigella	Influenza
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Key: Top 10 in all regions (blue), Top 10 in some regions (gray)

- 6 pathogens (in blue) are in Top 10 for all regions
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- What can we learn from these lists?

After weighing potential benefits, must also consider costs and feasibility in setting priorities



What's next?



- This work was presented to SAGE last week; considered a **systematic and robust approach** for evaluating regional pathogen priorities... but we need more data points in three regions to finalize the priority pathogens
- We're in the process of planning a consultation with AFR for Q4 to identify regional vaccine R&D priorities.
- Collaborating with Gavi on the vaccine investment strategy and other funders to align R&D in and investment in priorities
- Participating in the WHO mRNA hub and spoke partners meeting in April – focus on strategies for regional sustainability
- Continuing collaboration with SP7 to identify and support regional R&D priorities, leveraging WHO's Product Development for Vaccines Advisory Committee.



Contributors

Strategic discussions and guidance

PDVAC Members and meeting participants

SAGE Members and meeting participants

SP7 Working Group members and meeting participants

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