Pathogen prioritization at the global level: WHO Global Priority Endemic Pathogens for Vaccine R&D

World Health Organization

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17 priority endemic pathogens for vaccines research and development

Identifying WHO global priority endemic pathogens for vaccine research and development (R&D) using multi-criteria decision analysis (MCDA): an objective of the Immunization Agenda 2030

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Summary

Background To date, global priorities for new vaccine R&D have not been systematically identified for endemic pathogens. As part of Immunisation Agenda 2030 (IA2030), we have systematically identified priority endemic pathogens for new vaccine R&D based on country and regional stakeholder values to address this need.

Methods MCDA surveys targeting policy makers and immunisation stakeholders in each World Health Organization (WHO) region were used to weight eight criteria for prioritisation. Applying those weights to regional pathogen data yielded regional top ten pathogen lists, which are intended to inform regional deliberations on R&D priorities. The regional top ten lists were combined into an IA2030 global priority list. To inform R&D, use cases for new vaccines and monoclonal antibodies were identified, then categorized in terms of the activities needed to accelerate progress.

Findings In five out of six WHO regions, *Annual deaths in children under five* and *Contribution to antimicrobial resistance* were the most heavily weighted criteria. How participants weighted the criteria was not associated with their region, biographical characteristics, or areas of expertise. Five pathogens were common priorities across all regions: *M tuberculosis*, HIV-1, *K pneumoniae*, *S aureus*, and Extra-intestinal pathogenic *E coli*. Six pathogens were priorities in single regions. Combining regional top ten lists provided a global list of 17 priority pathogens for new vaccine R&D. Thirty-four distinct use cases were identified for new products targeting these pathogens. While most are in the "Advance product development" category, ten are in the "Research" category and seven are in the "Prepare to implement" category.

Interpretation These priorities for new vaccine R&D will help stakeholders better respond to regional and country needs. The use cases will inform R&D and enable monitoring of R&D under IA2030.

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Keywords: Vaccines; Priorities; Research; Development; IA2030

Introduction

Immunization has had an unparalleled impact on global morbidity and mortality, but because vaccine development is technically and commercially challenging, we lack vaccines against many pathogens that continue to impose a substantial public health burden.[1] Prioritization of pathogen targets for vaccine R&D is therefore crucial for the efficient use of limited resources, to

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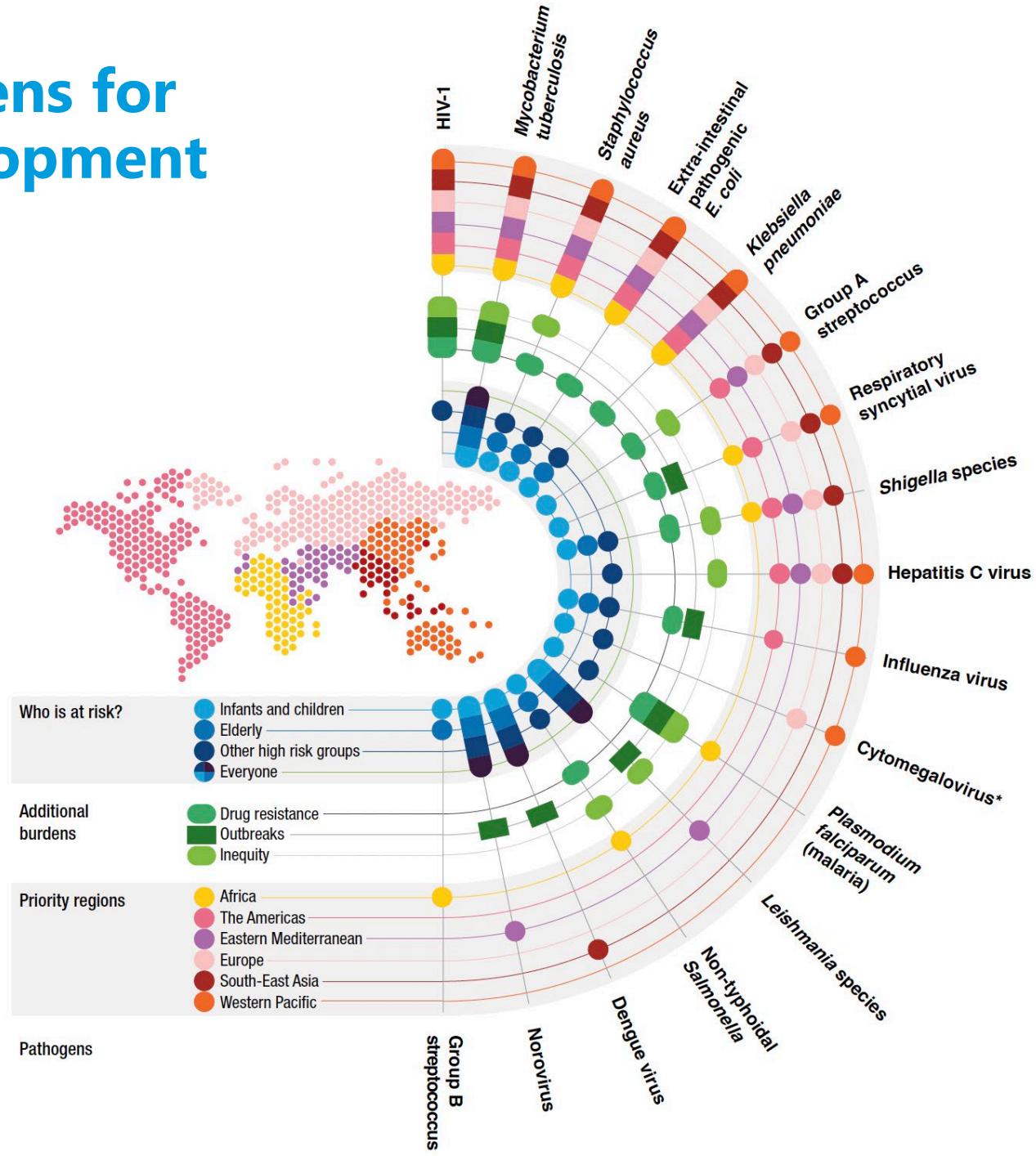

What is our goal?

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What?

- **Identify R&D priorities:** list of global endemic pathogen targets for new vaccines

Why?

- As a global health community, we must focus our efforts on developing vaccines for the pathogens that most impact communities across the world
- Because we want to accelerate vaccine development by aligning immunization stakeholders
- Because we want to track progress in vaccine and immunization R&D under IA2030

How?

- **According to IA2030 Core Principles**
  - *People centered*: vaccines are developed to meet people's needs
  - *Data driven*: systematic and evidence-based approach to identify priorities
  - *Partnership based*: in partnership with regions and immunization stakeholders;
  - *Country owned*: countries and regions can translate vaccine priorities into local R&D strategies

Process to identify endemic pathogens for new vaccine R&D

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We used robust research process engaging countries and regions to create the Global pathogen priority list for vaccine R&D.

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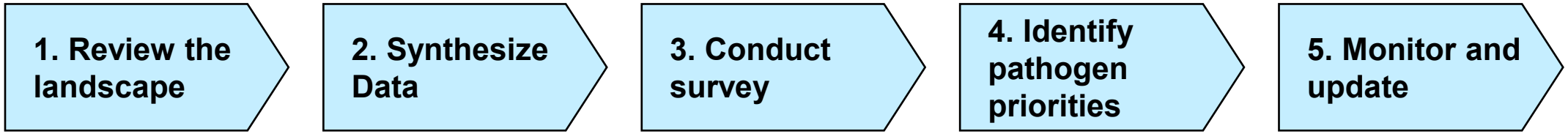

Process: identifying pathogens in scope

1. Review the landscape

- Understand existing priorities
- Learn from previous prioritization exercises
- **Identify pathogens in scope**
- Define criteria for prioritization

- Initial scope set by identifying pathogens through landscape review and applying screening questions

Screening questions	Rationale
Not emerging infectious diseases	WHO R&D Blueprint is identifying priorities
Human pathogens	Focus on human health
Without licensed vaccines, or where existing vaccines do not meet the needs of certain populations	Focus on the most acute needs
Have candidates in clinical development	Focus on targets with higher probability of success
Prioritized by existing roadmaps, TPPs, or VVPs, or recommended by regional advisors	Focus on pathogens of broad interest

26 PATHOGENS

13 BACTERIA

9 VIRUSES

4 PARASITES

MCDA: Multi-criteria decision analysis, PDVAC: Product Development for Vaccines Advisory Committee, IVB: WHO Headquarters Immunization, Vaccines, and Biologicals

Process: Define criteria for prioritisation

1. Review the landscape

- Understand existing priorities
- Learn from previous prioritization exercises
- Identify pathogens in scope
- **Define criteria for prioritisation**

- **8 criteria for prioritization** defined based on best practices and expert input

Criteria	Definition
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
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

MCDA: Multi-criteria decision analysis, PDVAC: Product Development for Vaccines Advisory Committee, IVB: WHO Headquarters Immunization, Vaccines, and Biologicals

Process: data synthesis

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2. Synthesize Data

- Burden for each pathogen scored **region-by-region** across all eight criteria
- Quantitative criteria scored using Global Burden of Diseases 2019 data
- Qualitative criteria scored based on literature searches, Vaccine Value Profiles
- Pathogens were categorised from Very low to Very high for each of the eight criteria
- Scores reviewed by at least 2 regional experts and 1 disease expert
- Significant effort to ensure that scores were harmonised, systematic, and informed by the most recent and relevant data.

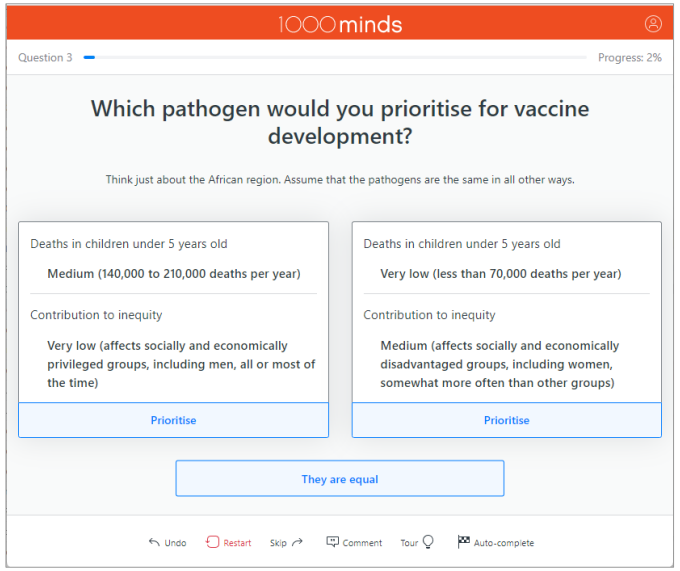
Pathogen	1 Annual deaths in children under 5	2 Annual deaths in people 5 and older	3 Annual years lived with disability (all ages)	4 Social and economic burden per case	5 Disruption due to outbreaks	6 Contribution to inequity	7 Contribution to antimicrobial resistance	8 Unmet needs for prevention & treatment
Mycobacterium tuberculosis (TB)	Very high	Very high	Very high	Very high	Very high	Very high	Very high	High
Human immunodeficiency virus 1 (HIV-1)	Very low	Low	High	Very high	High	Very high	Very high	High
Klebsiella pneumoniae	Very high	Very high	Very low	High	Low	Low	Very high	High
Staphylococcus aureus	High	Very high	Very low	High	Very low	Medium	Very high	High
Group A streptococcus (Streptococcus pyogenes)	Very low	Very high	Very high	High	Very low	High	High	High
Extra-intestinal pathogenic E. coli (ExPEC)	High	Very high	Very low	Medium	Low	Medium	Very high	Medium
Respiratory syncytial virus	High	Low	Very low	Medium	High	Medium	High	High
Shigella	Very low	Very low	Low	High	Medium	High	Very high	High
Hepatitis C virus	Very low	High	Very low	Very high	Low	Very high	Low	High
Dengue virus	Very low	Very low	Medium	Medium	Very high	Medium	Medium	High
Group B streptococcus (Streptococcus agalactiae)	High	Low	Very low	High	Low	Medium	Very low	Very high
Leishmania	Very low	Very low	Very low	Very high	High	Very high	Medium	Medium
Influenza	Very low	Low	Very low	Low	Very high	Medium	High	High
Plasmodium falciparum (malaria)	Low	Very low	Low	High	Medium	High	High	Medium
Mycobacterium leprae (leprosy)	Very low	Very low	Very low	Very high	Very low	Very high	Medium	High
Norovirus	Very low	Low	Very low	Medium	High	Medium	Low	High
Intestinal pathogenic E. coli (InPEC)	Very low	Very low	Very low	Medium	Medium	Medium	Very high	Medium
Neisseria gonorrhoeae	Very low	Very low	Very low	Medium	Low	High	Very high	Medium
Cytomegalovirus	Very low	Low	Medium	High	Very low	Medium	Very low	Very high
Chikungunya virus	Very low	Very low	Very low	Medium	High	Medium	Very low	Very high
Chlamydia trachomatis	Very low	Very low	Very low	Very high	Very low	High	Low	High
Salmonella Paratyphi	Very low	Very low	Very low	Low	Low	High	High	Medium
Herpes simplex types 1 and 2	Very low	Very low	Very low	High	Very low	High	Low	High
Non-typhoidal Salmonella	Very low	Very low	Very low	Low	Very low	High	High	Medium
Schistosomes	Very low	Very low	Very low	Low	Low	High	Low	Medium
Hookworm	Very low	Very low	Low	Low	Very low	Very high	Low	Low

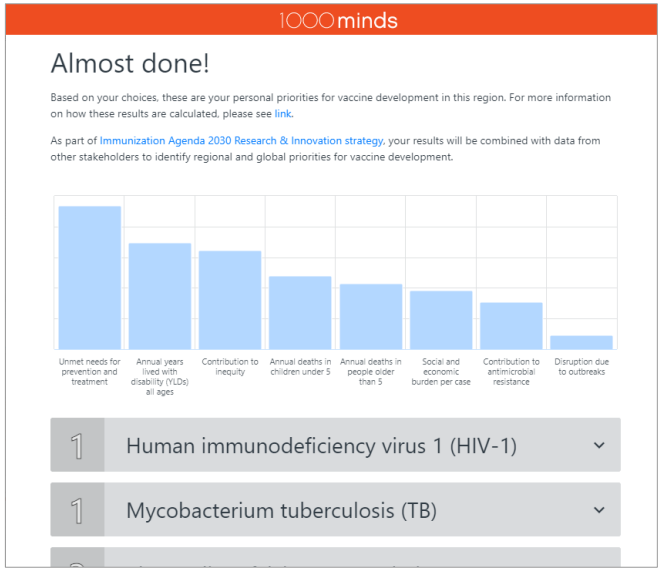
Process: conduct surveys

3. Conduct survey

- We used **multi-criteria decision analysis** (MCDA)– a robust methodology to assess health interventions
- Surveys populated with **pathogens scores for each of the WHO regions**, and translated into the major languages for each region
- Targeted dissemination by email to policy makers, health practitioners, and others from November 2022 to April 2023
- Participants carried out the survey without any pathogen names being present, they were asked to choose between hypothetical pathogens and values for their region.
- The tool calculated weights for criteria, multiplied by pathogen scores, to calculate the list of top 10 pathogens for each region.

Discrete choices





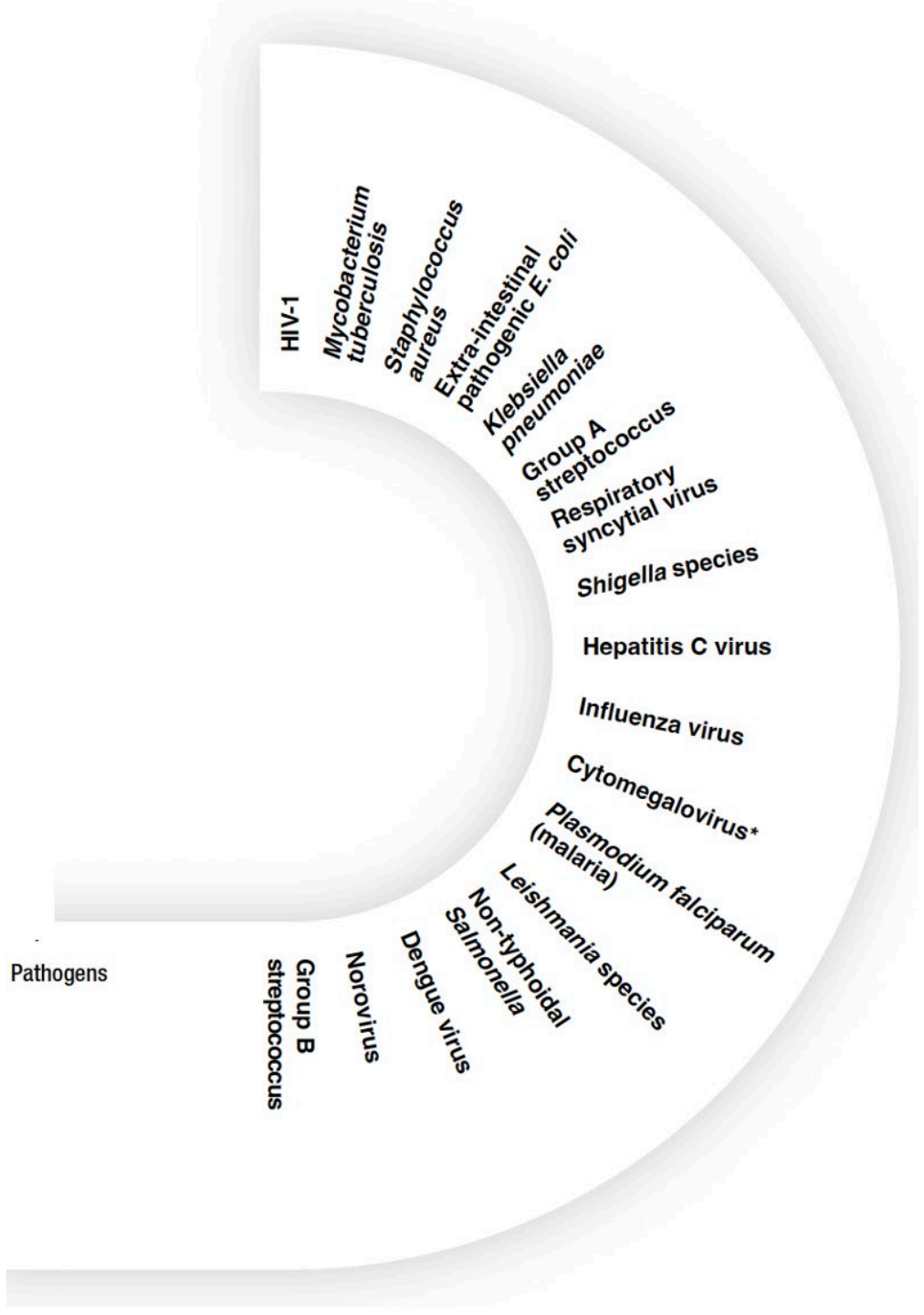
Criteria weights

Pathogen ranks

Results: compile global priority list

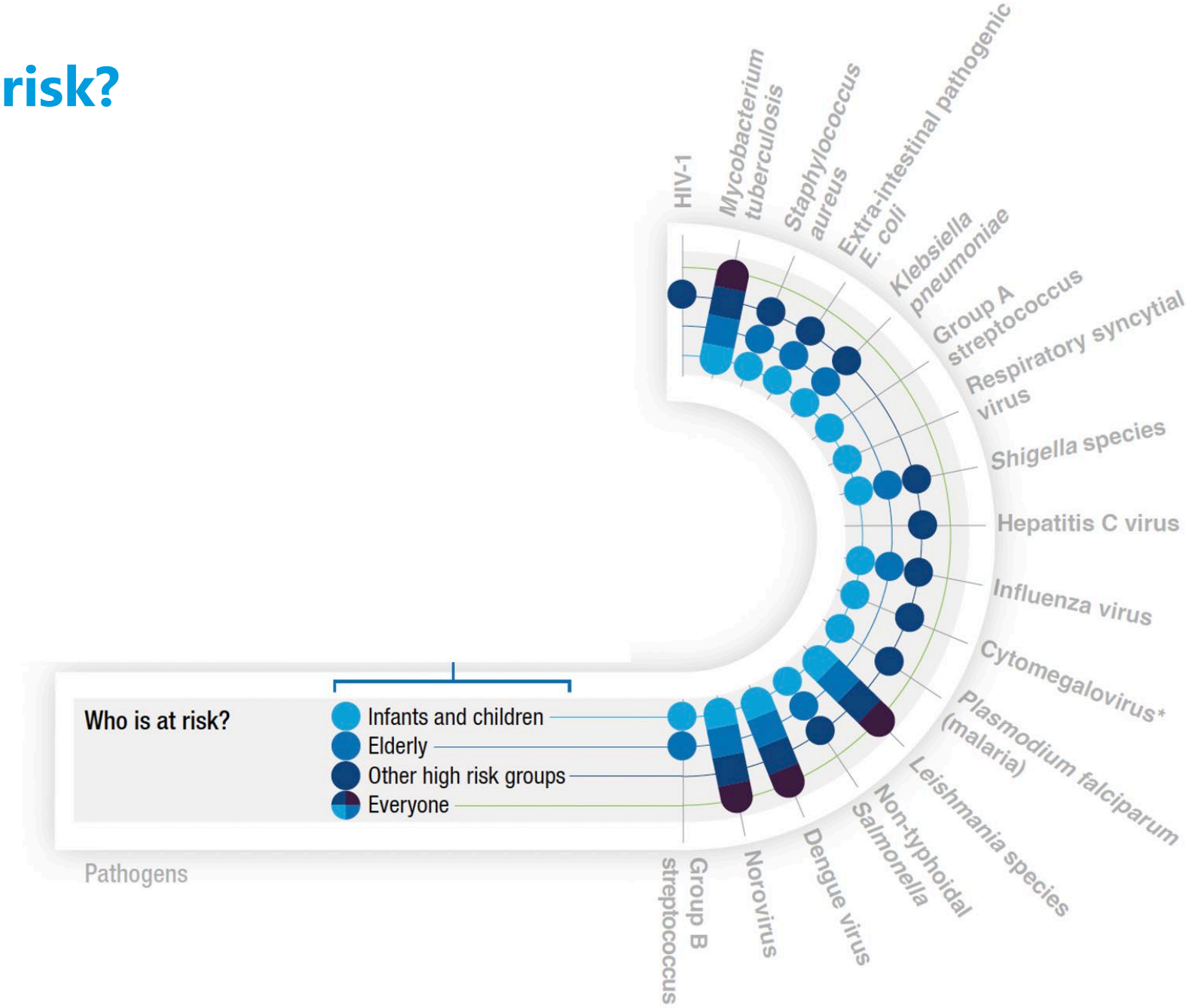
4. Identify pathogen priorities

- The Global priority pathogen list was created by bringing together all the pathogens that were identified by regions (**17 pathogens**).
- The Global List is robust: increasing the number of responses, dividing responses into clusters, and omitting selected criteria had no effect on its composition.
- Like IA2030, **these pathogens are diverse**
  - Reflect priorities of *all* regions
  - Affect people of all ages and all income levels



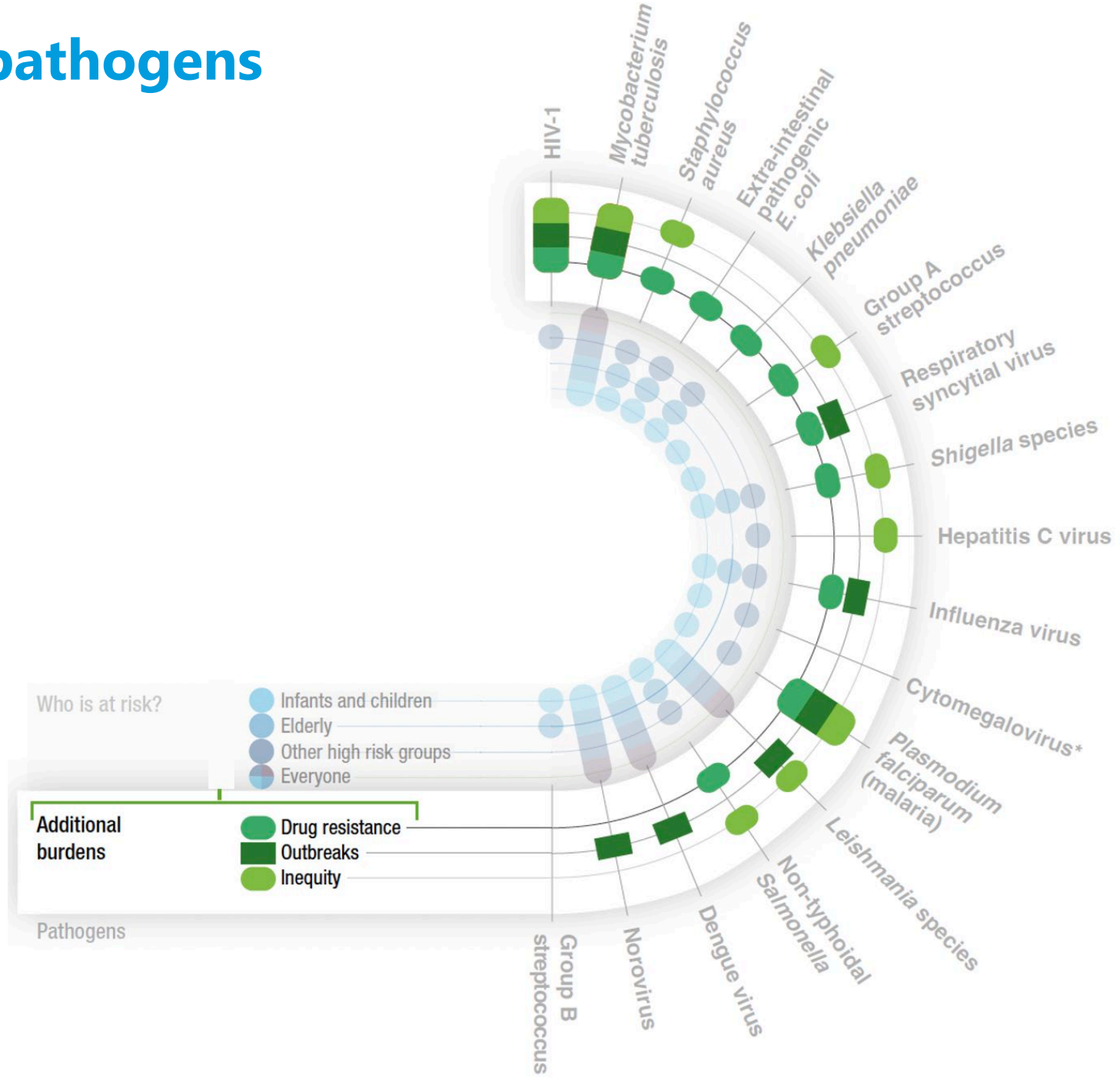
Results: who is at risk?

- The prioritized pathogens do not affect all people equally
- Almost all pathogens affect infants and children
- Some pathogens also affect the elderly and high risk groups.



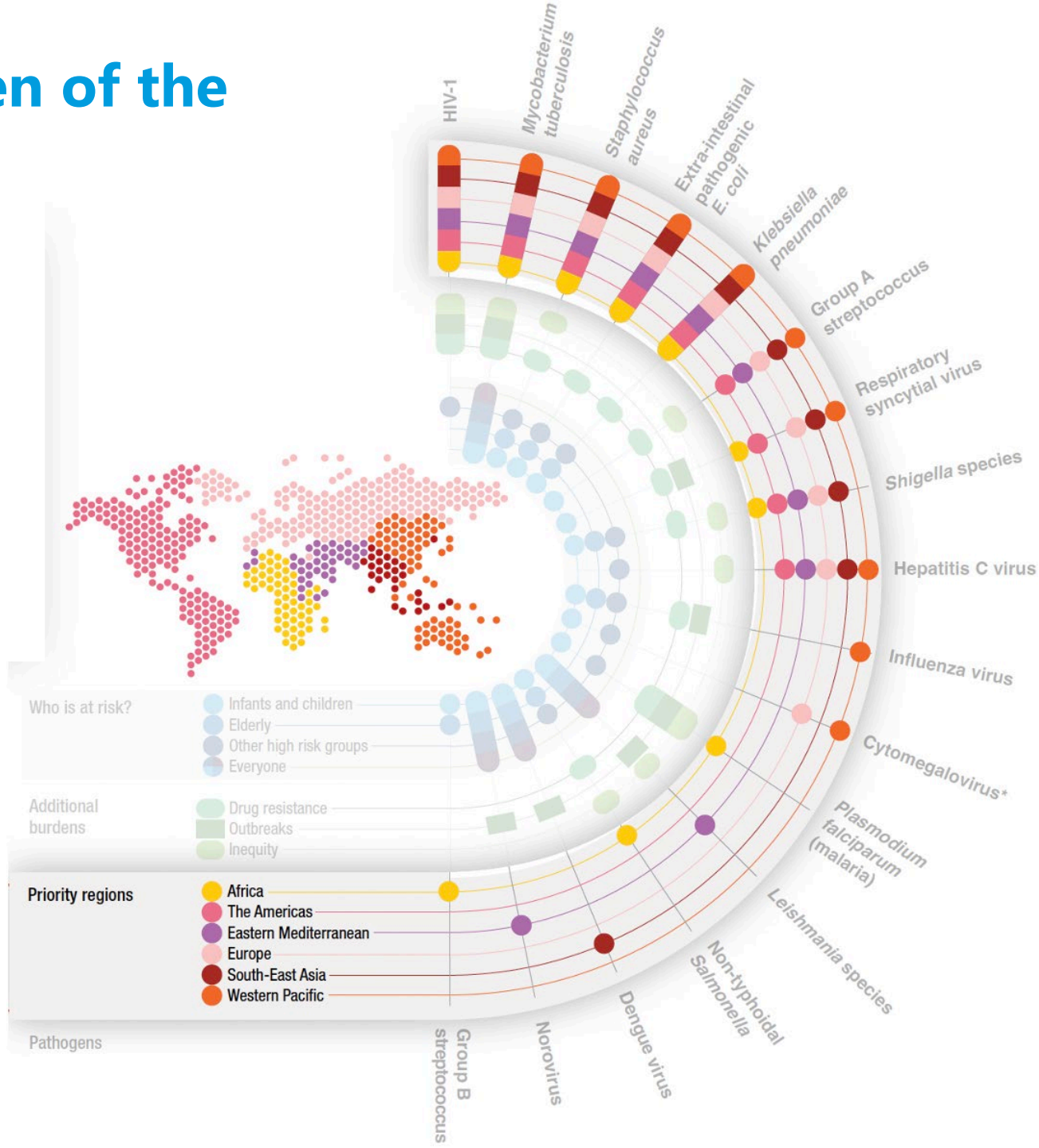
Results: why have the pathogens been prioritised?

- The prioritized pathogens cause a lot of disease and deaths
- They also are often highly resistant to antimicrobials, or are associated with high use of antimicrobials
- They cause outbreaks that disrupt daily life
- And, they increase social inequity



Results: where is the burden of the priority pathogens?

- Different regions struggle with different pathogens
- HIV-1, TB, *S. aureus*, ExPEC and *K. pneumoniae* have been highlighted as priorities in all WHO regions
- Four pathogens have been identified as priorities in all but one WHO region
- Some pathogens reflect regional burden– *P. falciparum* causing malaria has been identified as a priority in Africa only, and dengue in South-East Asia



What should be done to accelerate vaccine R&D for the priority pathogens?

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Action categories:	Research	Advance Product Development	Prepare to Implement
Pathogens:	• Group A streptococcus • Hepatitis C virus • HIV-1 • *Klebsiella pneumoniae*	• Cytomegalovirus • Influenza virus (broadly protective vaccine) • *Leishmania* species • Non-typhoidal *Salmonella* • Norovirus • *Plasmodium falciparum* (malaria) • Shigella species • *Staphylococcus aureus*	• Dengue virus • Group B streptococcus • Extra-intestinal pathogenic *E. coli* • *Mycobacterium tuberculosis* • Respiratory syncytial virus
Characteristics:	Few candidates in early clinical development or substantial technical challenges	Diverse candidates in development, including those in phase 2 studies	Candidates with high potential for approval by a WHO-listed authority before 2030
Recommended actions:	• Identify research gaps • Improve surveillance and burden estimates • Develop target product profiles • Assess potential vaccine value • Develop tools to improve technical feasibility	• Stimulate investment by raising awareness of opportunities for impact • Develop tools to inform decision-making (such as correlates of protection and economic models) • Create consensus on regulatory and policy pathways	• Build awareness of emerging products • Assemble evidence needed for policy decisions • Establish mechanisms for long-term, equitable access to approved products

Monitor:

- Pathogens with vaccines in Phase 3 trials
- Pathogens with vaccines that received a policy decision

How will the Global priority list be used?

Priorities will **inform** stakeholder strategies
Priorities should be **considered** in the context of existing global, regional and country R&D strategies

Regional stakeholders

- **Industry**: inform investments in vaccine R&D
- **Funders**: inform funding for vaccine R&D
- **Researchers**: inform evidence generation
- **Policy makers**: build awareness of R&D pipelines, and prepare for introduction

Global stakeholders

- **WHO:** inform activities to accelerate evidence generation, R&D, and policy making to serve low-resource settings
- **IA2030:** to monitor progress in global R&D for new vaccines
- **Gavi**: inform Vaccine Investment Strategy (next slide)

Gavi's Vaccine Investment Strategy informs 6.0 (2026–2030)

Evidence-based approach to identify immunisation investments for future strategic cycle(s), while sending valuable advance signals to vaccine developers and suppliers

- Every 5 years
- Transparent methodology
- Analytic review of evidence & modelling
- Consultations and independent expert advice

Informs Gavi strategy and resource mobilisation

Provides predictability for long-term planning by industry, governments and donors

Types of Investment:
- Vaccine programmes
- Global stockpiles
- Learning agendas

JUNE 2024 BOARD DECISION

Vaccine Investment Strategy 2024
Approved in principle

- Tuberculosis
- Group B streptococcus
- Dengue
- Hepatitis E
- Mpox

In response to public health threat or a research and development (R&D) milestone for a priority pathogen, diseases of epidemic/pandemic potential can be evaluated in real time, outside five-year cycle, through VIS epidemics framework.

How can we deliver so many vaccines?

Vaccine combinations could be a solution

Increase the number of vccines delivered during a single health visit.

Increase vaccine acceptability and coverage.

Vaccinate against less prevalent but still important pathogens.

Simplify vaccine storage, delivery and administration.

…. and many more

WHO and PATH, with support from Gates, have initiated a **project to identify, analyse and prioritise combination vaccines**, through:

1) Identifying combnation vaccines that are **programmatically feasible**;

2) Analyse the **technical feasibility** of combination vaccines;

3) Understand the **commercial feasibility** of combination vaccines;

4) Identify and apply **novel metrics** to assess the value of combination vaccines

In order to **inform vaccines R&D, decision processes about the development, use and introduction of combination vaccines, influence regulatory and policy decisions**.

Conclusions

- As a global health community we must focus our **efforts on developing vaccines** for the pathogens that most impact communities across the world.
- It is the right thing to do. And to do this right we need to **work together with regions and countries**. Too often decisions on the vaccines to prioritise have been taken only at a global level.
- The overall priority pathogen list was created by bringing together **all the pathogens that were identified by regions**.
- The Priority Pathogen list for vaccines R&D has reaffirmed long-standing priorities like HIV, malaria and TB, and identified new priorities like GAS or *K. pneumoniae*
- The Priority Pathogen list is an example of how we can work to be **country led** which is a core principle of the Immunization Agenda 2030.
- Working with regions and countries has provided other valuable insights and opportunities that can support the vaccine development community: **need for combination vaccines, improving existing vaccines, or enhancing regional research capacity**.
- The list is not intended to be restrictive, it is the result of a robust survey process with regions but **should be read alongside** other evidence and considerations e.g. feasibility of vaccine development, existing R&D strategies.

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Thank You