Preparing for Bacterial Pathogen X

Bacteria that have the possibility of causing pandemic (PHEIC) disease

Myron (Mike) M Levine, MD, DTPH

Center for Vaccine Development & Global Health
University of Maryland School of Medicine
Baltimore, MD, USA

Bacterial Pathogen X CORC Launch 24/2/2025

Two lessons re-learned by health authorities:

1) Must define what is meant by the term “pandemic”

2) Must clearly and concisely communicate critical health messages to the public

Factors defining a pandemic pathogen

- Something new, or different, or a re-appearance after a long (or moderate) absence
- **Affecting multiple countries & continents**
- Severe clinical illness
- Highly transmissible to/among humans

CVD

PHEIC
(public health emergency of international concern)

***PHEIC** – a much better way of declaring an infectious disease public health emergency that also assigns responsibilities to all nation states*

Public Health Emergency of International Concern (PHEIC)

- WHO formally declares:
  - An extraordinary, serious, sudden **global public health risk from international spread** of a disease
  - A **coordinated global response is required**
- Encoded by 2005 revision of the International Health Regulations (**IHR**) that followed 2002-2003 SARS calamity
- **IHR Emergency Committee** announces PHEICs
- **All nation states have a legal duty to respond to a PHEIC**
- **PHEICS:**
  - **1)** H1N1 swine flu; 2009;
  - **2)** Polio 2014;
  - **3) West Africa Ebola, 2014;**
  - **4)** Zika, 2016;
  - **5)** Kivu, DRC Ebola, 2019-20;
  - **6) COVID-19, 2020**
  - **7)** Clade 2 Monkeypox 2022-2023
  - **8)** Clade 1 Monkeypox 2024-

CVD

WHO Bacterial Pathogen X committee

Member	Institution	Nationality	Pathogen expertise	Scientific Expertise
Benjamin Howden, MD, PhD	U. of Melbourne, Australia	Australia	AMR bacteria: *Klebsiella*, *Pseudomonas*, *Staphylococcus aureus*, *Salmonella*	Clinical infectious diseases, Bacterial genomics, AMR
Khitam Muhsen, PhD, RN	Tel Aviv University	Israel	*Shigella, Giardia, E. coli, Cryptosporidium*	Epidemiology, vaccinology, vaccine field trials
Javier Pizarro, PhD	Institut Pasteur, Paris	Costa Rica	*Yersinia pestis*, other *Yersinia* species	Bacterial pathogenesis
Firdausi Qadri, PhD	ICDDR,B	Bangladesh	*Vibrio cholerae* O1, *S.* Paratyphi & *S.* Typhi	Immunology, bacteriology, vaccines
Nicholas Feasey, MBBS, PhD	Liverpool School of Tropical Medicine (now St Andrews)	United Kingdom	Epidemiology of AMR, Genomics, Clinical Infect Dis	Clinical ID, epidemiology, pathogenesis
Jerse Ann E, PhD	Uniformed Services University of the Health Sciences	U.S.A.	*Neisseria gonorrheae; Bacterial STDs*	*Neisseria gonorrheae* vaccines and pathogenesis;
Christoph Tang, MBBS, PhD	University of Oxford	United Kingdom	*Neisseria meningitidis* and *Shigella*	*Neisseria meningitidis* and *Shigella* vaccine development and pathogenesis
Gagandeep Kang, MBBS	Bill & Melinda Gates Foundation	India	Bacterial enterics, rotavirus,	Epidemiology, microbiology, diagnostics; product delivery
Sam Kariuki, PhD	Centre for Microbiology Research, KEMRI	Kenya	*AMR* and *Salmonella*	AMR, microbiology, environmental microbiology, reservoirs of infection

Bacteria group summary "at a glance"

10 independent experts from 8 countries (Australia, Bangladesh, France, India, Israel, Kenya, UK, USA)

30% from LMIC

40% women

76 bacteria proposed → **26** bacteria proposed → **5** Bacteria shortlisted

All 5 bacteria gave almost identical scores when run through the LSTMH computer program intended to down select

Members

First name	Last name	Title and Affiliation
Myron (Mike)	Levine (Chair)	University of Maryland School of Medicine
Benjamin	Howden	Doherty Institute
Khitam	Muhsen	School of Public Health, Tel Aviv U. Faculty of Medicine
Javier	Pizarro-Cerda	Microbiology Department of the Institut Pasteur (Plague and other Yersinioses)
Firdausi	Qadri	International Centre for Diarrheal Disease Research, Bangladesh (icddr,b)
Nicholas	Feasey	Liverpool School of Tropical Medicine
Ann E	Jerse	Uniformed Services University of the Health Sciences
Christoph	Tang	Sir William Dunn School of Pathology. University of Oxford
Gagandeep	Kang	Wellcome Trust Research Laboratory, Division of Gastrointestinal Sciences at the Christian Medical College (CMC) in Vellore
Sam	Kariuki	Centre for Microbiology Research, KEMRI

Expertise represented

Public Health Bacteriology, Bacterial Sexually Transmitted Infections, Antimicrobial Resistance, Plague Research, Enterobacterales Research, Enteric Pathogens, Biochemistry, Clinical Epidemiology, Host-Pathogen Interactions, Immunology, Molecular Biology, Pathogen Genomics, Vaccine Development.

Pre-Screening

- Each Bacteria Group member was asked to submit a proposed list of bacteria of epidemic and pandemic concern
- The compiled list included 76 proposed bacteria that were discussed in depth, and the list was reduced to 26 pathogens
- The 26 were organized into 4 categories and discussed during a series of calls
  - Can cause a pandemic in normal hosts
  - Can cause a pandemic in special hosts
  - Can cause a severe regional epidemic/pandemic
  - Can be of concern if weaponized
- 5 bacterial pathogens were prioritized for screening using the computerized questionnaire to reduce to 1 or 2. Computer program failed to eliminate any of the 5.

Can cause a true global pandemic in normal hosts

- *Shigella dysenteriae* 1
- *Shigella* (other serotypes)
- *Vibrio cholerae* (O1 or **other O serogroup**)
- *Yersinia pestis*

1) *Vibrio cholerae*
2) *Shigella dysenteriae* 1
3) *Yersinia pestis*

Can cause a pandemic in special hosts

- *Enterococcus faecium*
- *Staphylococcus aureus,*
- ***Klebsiella pneumoniae***
- *Acinetobacter baumannii*
- *Pseudomonas aeruginosa*
- Enterobacter species
- *Escherichia coli*

5) *Klebsiella pneumoniae*

Can cause a regional epidemic & PHEIC

- *Salmonella* Typhi-XDR
- *Salmonella* Paratyphi-XDR
- *Escherichia coli* - Shiga toxin producing
- Enterohemorrhagic *Escherichia coli*
- *Shigella* (certain serotypes)
- **Invasive non-typhoidal *Salmonella***
- *Bordetella pertussis*
- *Mycobacteria tuberculosis*-MDR/XDR
- *T. pallidum pertinue*
- *Streptococcus pneumoniae*
- *N. gonorrhoeae*-AMR

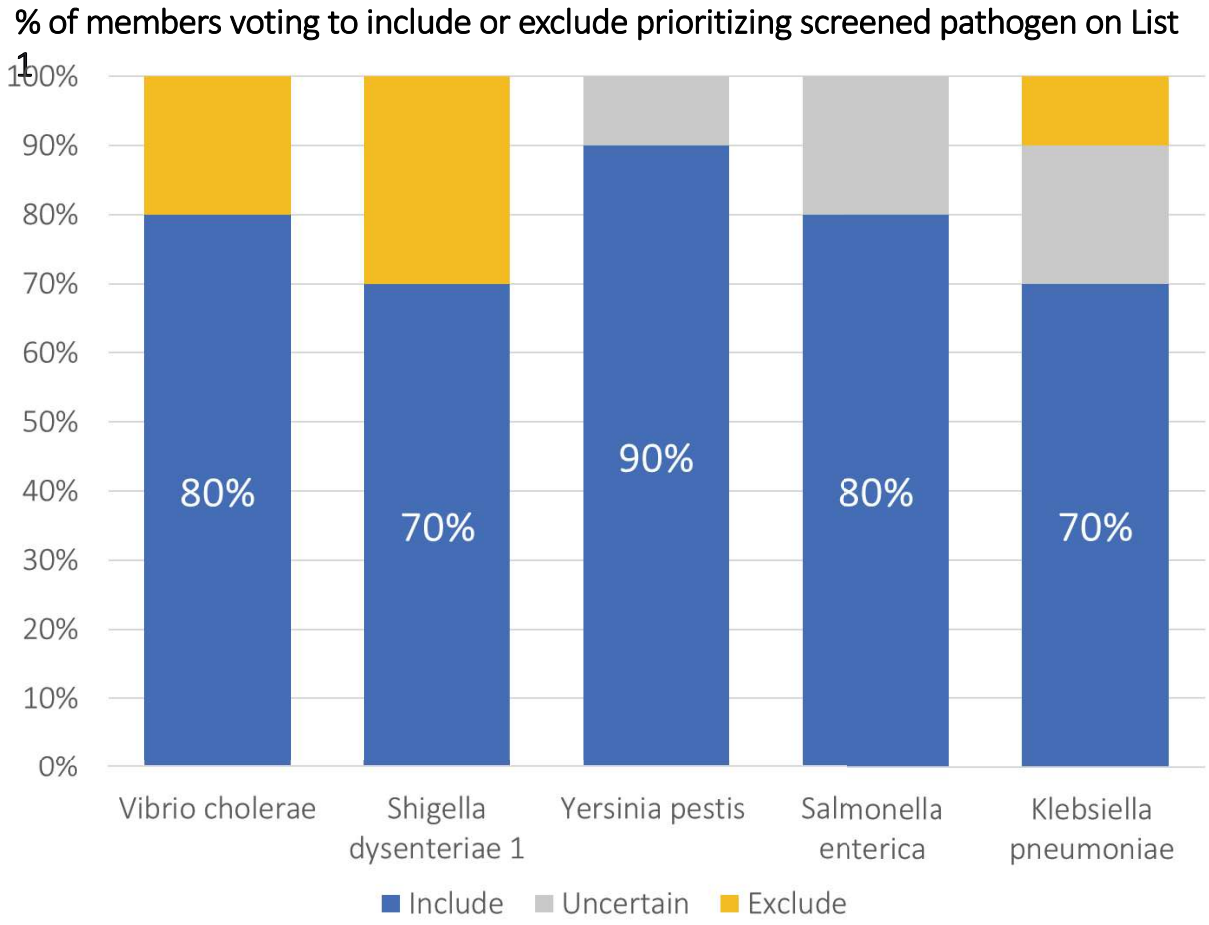
4) *Salmonella enterica invasive NTS*

Civilian bioterror concern if weaponized

- *Bacillus anthracis*
- *Borrelia burgdorferi*
- *Brucella melitensis*
- *Burkholderia pseudomallei*
- *Coxiella burnetti*
- *Francisella tularensis*
- *Non-typhoidal Salmonella*

Screening

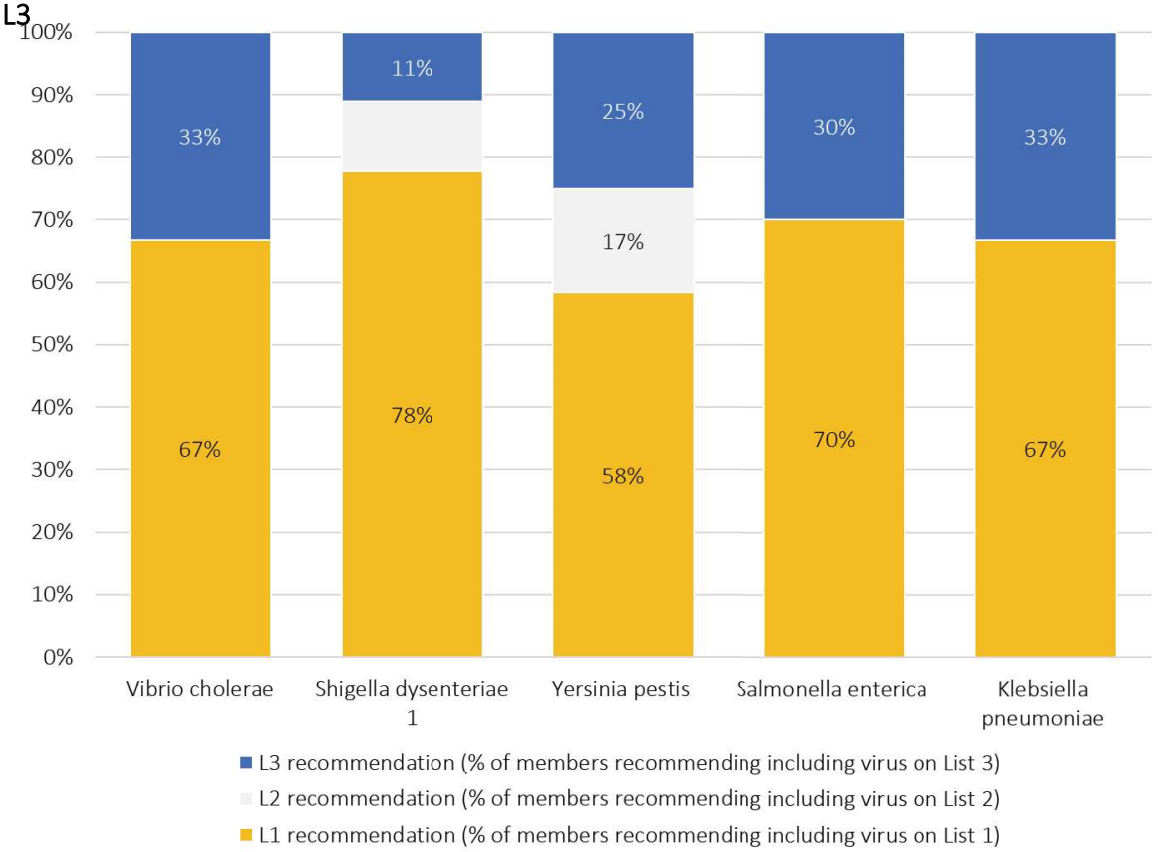
- **Screening results showed an impressively high degree of alignment among members**
- Results were reviewed and discussed by members during a group call
- Between 70% - 90% of members voted to prioritize bacteria on List 1
- The consensus from the group was for all 5 of these bacterial pathogens to move forward to post-Screening



Post-Screening

- Members reviewed and deliberated on the post-screening results on 5 September.
- All 5 bacteria are recommended as priorities for the R&D Blueprint prioritization.
- Majority of members recommended that the 5 bacteria be included in List 1 (highest priority)
  - ***Vibrio cholerae*** **is an increasing threat in LMICs due to climate change and if it were due to a serogroup other than O1 or O139 there would be no immediate vaccine availability.** There is already a global stockpile shortage of O1 vaccines (1 major supplier ceased supplying stockpile)
  - *Yersinia pestis* is still of concern (Madagascar case)
  - *Klebsiella pneumoniae* is the AMR "posterchild"

% of members voting to include or exclude prioritizing screened pathogens on L1, L2 and L3

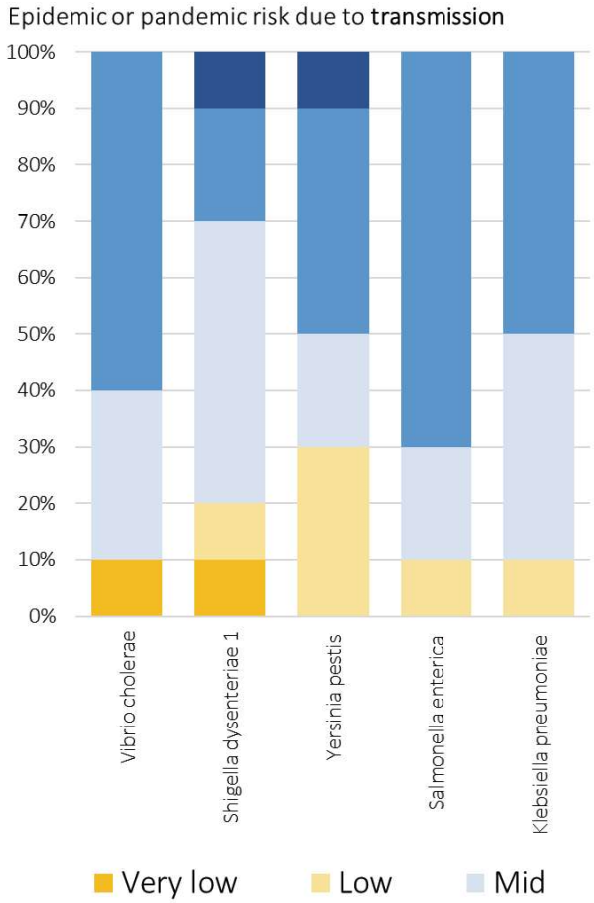


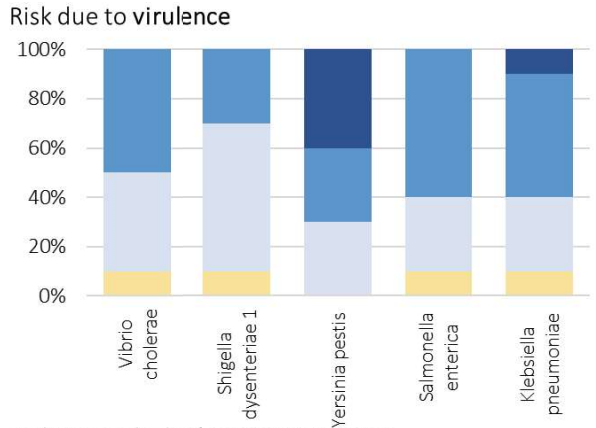
Results by Scientific Criteria

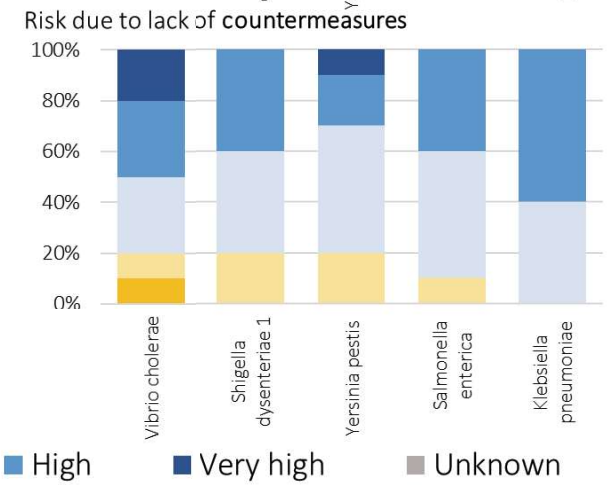
- Results by scientific criteria confirm the epidemic and pandemic risk of the 5 bacteria reviewed

- The 5 are
  - Highly transmissible
  - Highly virulent

- The epidemic and pandemic risk is high due to insufficient or ineffective medical countermeasures available (in particular, vaccines)







Recommendations

- Include these Pathogens “in” as a consensus was reached that the 5 bacteria need to be prioritized for R&D preparedness efforts.
- Address Equity in Countermeasure Access: concern about disparities in access to countermeasures implies a recommendation to address equity issues in distributing and making countermeasures available to all regions, not just high-income countries.
- Consider Diversity in Pathogen Characteristics: The group acknowledges the diversity in transmission mechanisms, host interactions, and characteristics of different pathogens. This suggests a recommendation to tailor preparedness efforts to the unique features of each pathogen

Epidemic/Pandemic Risk due to Modes of Transmission & Virulence			
		MODERATE	HIGH
Risk due to lack of availability of treatments and vaccines	MODERATE		***Vibrio cholerae*** **serogroup other than O1 or O139**
			Klebsiella pneumoniae (MDR & XDR clones)
	HIGH	***Shigella dysenteriae*** *1*	***Yersinia pestis*** **(pneumonic form)**
			Salmonella enterica **invasive non-typhoidal serovars (iNTS)**

Some past true pandemics caused by bacterial pathogens

- Cholera – 5th, 6th and 7th pandemics
  - Threat of *V. cholerae* serogroup O139 in the early 1990s
- *Shigella dysenteriae 1* (the Shiga bacillus)
  - Japan, 1890s; Central America 1967-71
  - SE Asia 1974
  - Central Africa 1990s
- Meningitis due to Group A *Neisseria meningitidis*
  - Meningococcal belt of sub-Saharan Africa

CVD

Acknowledgments

Bacterial Pathogen X Committee members	Who were the key to a successful exercise
Colin Sanderson	LSTMH (critical computer program)
Patrick Lydon	WHO
Regine Coste Bonnand	WHO
Ximena Laurie	WHO
Ana Maria Henao-Restrepo	WHO
Barney Graham	Morehouse School of Medicine
Neddy Mafunga	WHO
Cristina Cassetti	NIH

Bacterial Collaborative Open Research Consortium (CORC)

Megan E. Carey, PhD, MSPH
London School of Hygiene & Tropical Medicine & IAVI

Farah Naz Qamar, MBBS, FCPS, FRCP, MSc
Aga Khan University

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

THE AGA KHAN UNIVERSITY

iavi 25 years of innovation, partnerships, access

CORC activities

- Establish global open research consortium
- Develop an R&D roadmap
- Develop/refine TPPs for key medical countermeasures
- Harmonise research protocols and tools to facilitate evaluation of MCMs
- Promote coordinated pathogen surveillance
- Maintain open scientific dialogue

Bacterial pathogen family

- Distinct epidemiology, pathogen biology, genetic diversity, MCM availability
- We are not starting from zero with any of these pathogens
  - MCMs in development
  - Existing TPPs
  - Pathogen-specific research communities
- We propose to build on these efforts

PATHOGENS **PRIORITIZATION**

A SCIENTIFIC FRAMEWORK FOR EPIDEMIC AND PANDEMIC RESEARCH PREPAREDNESS

HEALTH EMERGENCIES programme

Annex 3: Summary of Epidemiological Information on Proposed Priority Pathogens

Family	Pathogen	Vector/ Reservoir	Mode of Transmission	Extent of person-to-person transmission	Spread	Areas with Documented Transmission
Bacteria	Vibrio Cholerae (sero 01)	Aquatic environment, human hosts	Fecal-oral transmission, contaminated water sources	Some	South Asia	Primarily in Developing countries, potential for global spread
Bacteria	Klebsiella Pneumonia	Humans, environmental reservoirs	Nosocomial transmission, person-to-person spread	Some	Global	Reported worldwide
Bacteria	Yersinia Pestis (Plague)	Rodents, fleas	Flea-borne transmission, person-to-person spread of pneumonic plague	Some	Asia, Africa, Americas	Endemic in parts of Asia, Africa, and the Americas, potential for global spread
Bacteria	Shigella Dysenteria 1	Humans	Fecal-oral transmission, contaminated food/water	Sufficient to cause outbreaks		Primarily in Developing countries, potential for global spread
Bacteria	Salmonella Enterica (invasive non-typhoidal)	Humans, animals, environmental reservoirs	Foodborne transmission, person-to-person spread	Sufficient to cause outbreaks	Global	Reported worldwide distribution

https://www.who.int/publications/m/item/pathogens-prioritization-a-scientific-framework-for-epidemic-and-pandemic-research-preparedness

How we will work together

Quarterly CORC meetings

- High level updates & discussion

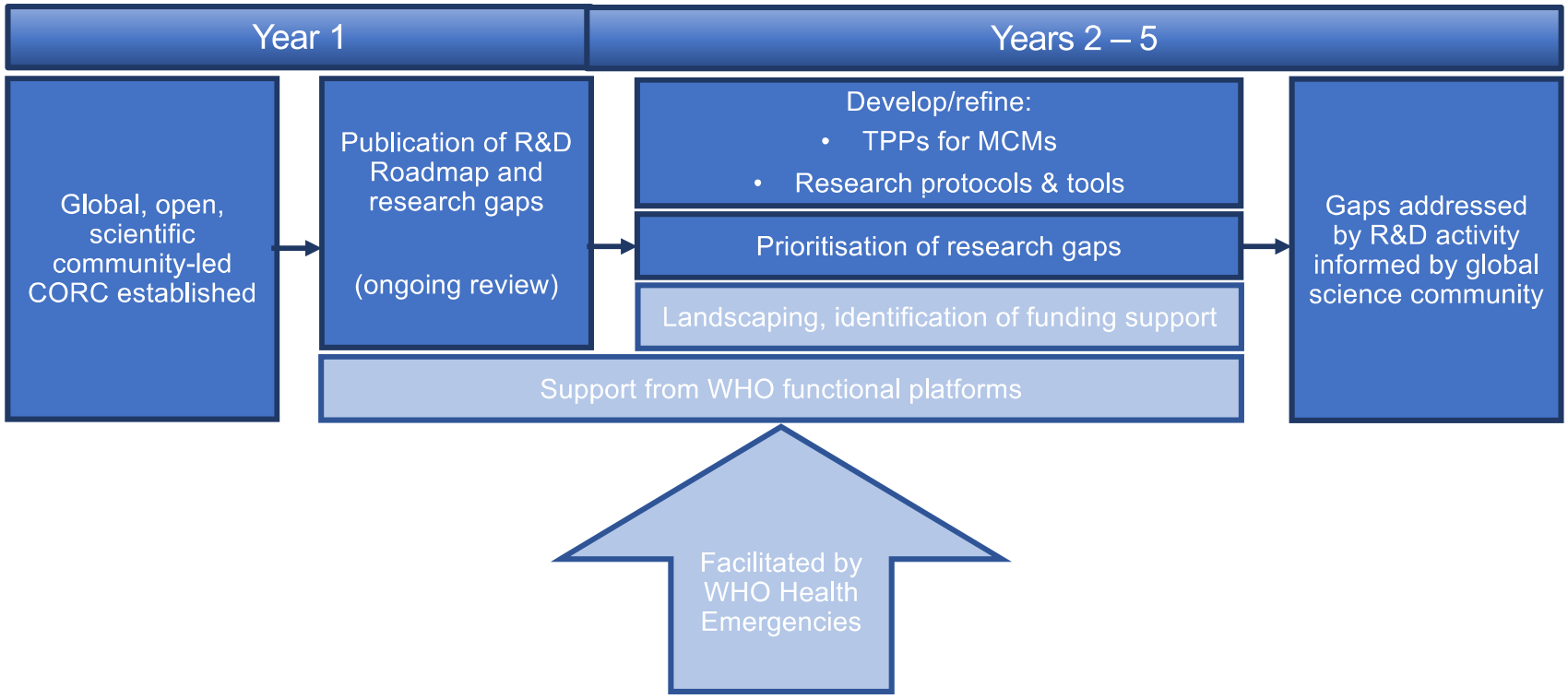
Pathogen-specific working groups

- Monthly meetings
- Two working group leads
- Draft R&D roadmap

Steering Committee

- Critically review work plan & deliverables

High-level timeline



Next steps

- Next CORC meeting will be scheduled in May
  - Meeting recordings will be circulated and saved here.
- Pathogen WGs to start meeting in March
- Using this form, please indicate your interest in:
  - Joining the consortium
  - Joining one (or more!) pathogen working groups
  - Co-leading a pathogen working group or serving on the steering committee
- Tell your friends!