Microbial Reservoirs and Transmission Dynamics of Escalating Infectious Diseases

Wellcome Trust
The Global Health Network

THE GLOBAL HEALTH NETWORK
Enabling research by sharing knowledge

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Executive Summary

Wellcome and The Global Health Network conducted a research prioritisation study by engaging a broad research community (academic and non-academic public and animal health researchers, laboratory workers and policy/decision makers) to understand funding priorities for research on microbial reservoirs and transmission dynamics of escalating infectious diseases and outline important areas where Wellcome and other stakeholders are best placed to act.

The study was developed as a listening exercise focused on hearing from new voices from the communities, targeting Low- and Middle-Income Countries (LMICs) in the Global South. It consisted of a priority-setting survey, which assessed the perceived escalating diseases posing the greatest infection threats, the types of research needed, as well as barriers and enablers to conducting research. Over 3,500 infectious disease research stakeholders, most of them from LMICs, responded to the survey. This was followed by three hybrid regional workshops (in Asia-Pacific, Latin America and the Caribbean [LAC], and Africa) that built on the survey findings.

Survey respondents perceived Tuberculosis (TB), Malaria and Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS) to be the infection threats that presented the greatest risk of escalation or were currently escalating. Furthermore, the analysis from the regional workshops identified Vector-borne Diseases (VBDs) as a leading disease group of concern. Considering only responses by the Global North participants, antimicrobial resistance (AMR) was perceived as the primary “disease” of threat of escalation.

Participants recognised the drivers associated with the risk of infectious disease escalation to be climate change, socioeconomic factors, and AMR. Climate change was identified as a driver primarily of VBDs and Cholera across multiple regions, due to temperature increases and extreme weather events having an impact on pathogen and vector distribution. Socioeconomic drivers of disease escalation were multiple and diverse and perceived as having an impact on disease escalation due to poor disease awareness, population distribution, and urbanisation. AMR as a driver of disease escalation was a concern across all study regions, with poor antimicrobial stewardship as an oft-cited theme.

Participants in all study regions identified a need to improve the detection and investigation of disease threats, inclusion of transmission studies and understanding of socio-economic and cultural drivers in research. Participants perceived that research skills training, institutional support and access to funding are key factors that would enable infectious disease research in their setting.

The methodological approach taken in this study has generated important new insights into perspectives on infectious disease research priorities from the Global South. The outcomes of this report will contribute to informing Wellcome’s Infectious Disease Strategic Programme on the causes and risks of escalating infectious diseases, and the promotion of inclusive research and practice. The findings, data and methods will be made openly available for others to use and undertake further analysis.

Introduction

Wellcome, in collaboration with The Global Health Network (TGHN), conducted a research prioritisation study that sought to i) engage a broad research community to assemble a global perspective and understanding of funding priorities for research concerning microbial reservoirs and transmission dynamics of escalating infectious diseases, and ii) to support the implementation of Wellcome's diversity and inclusion strategy to make sure that in everything Wellcome does, the broadest possible range of people contribute to, and benefit from, science's potential to change the world. The overarching project objectives were:

- Identify key research gaps, priorities and barriers to inform the development of accessible interventions to prevent or control disease escalation.
- Outline priority areas where Wellcome and/or other key stakeholders are best placed to act.
- Ensure diverse, equitable and broad engagement with the global research community.

To help achieve these objectives and gain insight into the key research priorities relating to reservoirs, emergence and transmission of escalating infectious diseases, a study was developed within this perspective as a listening exercise focused on hearing from new voices from the communities, with whom Wellcome has not engaged before, and who face the greatest burden, particularly in Low- and Middle-Income Countries (LMICs) in the Global South. This mixed methods study applied a validated adapted Delphi approach that involved a cross-sectional global priority-setting survey launched in March 2023, followed by three regional workshops held in June 2023 that built on the survey findings.

The regional workshops were hosted in three geographies: Asia-Pacific, Latin America and the Caribbean (LAC) and Africa, with multidisciplinary participation that was representative of academic and non-academic public and animal health researchers, laboratory workers and policy/decision makers. Participants were from a range of career stages, bringing a diverse set of skills and experience. The intention was to facilitate a purposeful discussion that would lead to key recommendations for priority setting by working within this formal study framework. The survey and regional workshops were centred on three key themes outlined below in **Figure 1**.

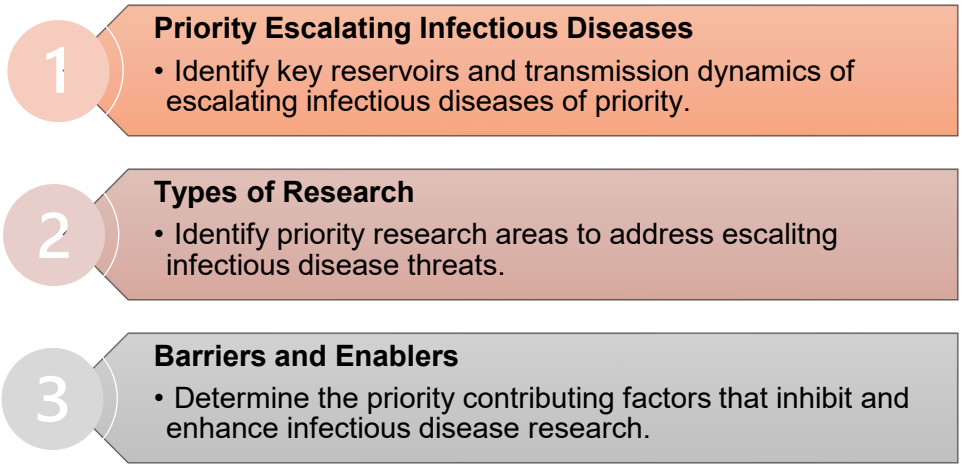

Figure 1 Priority-Setting Survey and Regional Workshop Themes

The project was a first step in trialling different approaches for Wellcome to encourage broader participation, facilitate discussion with the global healthcare community and to gain insight into the realities and variations across different regions and settings. The outcomes described in this report will contribute to informing Wellcome's Infectious Disease Strategic Programme on the causes and risks of escalating infectious diseases and how to inform future control and preventative strategies that are grounded in evidence-based research that promote inclusive research and practice. The findings, data and methods will be made openly available for others to use and undertake further analysis.

Methods

This study followed a validated, mixed-methods, crowd-based approach to consensus building, previously adapted from the Delphi technique (1-3). First, an open, cross-sectional priority-setting survey was conducted to identify broad global research priorities concerning microbial reservoirs and the transmission dynamics of escalating infectious diseases and to provide insight into the rationale and contextual factors driving these prioritisations. Second, three hybrid, Global South (Asia-Pacific, LAC and Africa) workshops were held to invite infectious disease research stakeholders to take the survey findings through this iterative Delphi approach to build a deeper understanding of the outcomes through explanation and contextualisation of the findings according to the infectious disease research contexts in each geographic region (**Figure 2**).

Figure 2 Workshop development steps

The Survey

An online survey was designed using the Jisc Online Surveys tool (v3). The survey was designed to assess three core research questions, i) which escalating diseases pose the greatest infection threat ii) what types of research are most urgently needed to combat these threats iii) what are the barriers and enablers to conducting this research? The target population was defined as follows:

Anybody whose work directly impacts human health (including those working at the human-animal interface), who have research experience on understanding the sources of infectious disease and drivers of disease escalation and those involved in research uptake and public health decision-making.

The survey questionnaire comprised 11 questions (including both open- and closed-ended questions) and was distributed in English, Spanish, Portuguese and French. The access link was live for a three-week period in March 2023, and was disseminated via Wellcome and The Global Health Network communications channels (mail lists, newsletters, and social media platforms). Survey participation was self-selective, and open to all individuals able to access the questionnaire hyperlink.

The Regional Workshops

Following analysis of the survey findings, three hybrid, Global South workshops were undertaken to address the following aims:

- Gain a deeper understanding of the survey findings relative to the participants' contexts.
- Expand on the challenges and gaps identified to reach a more detailed understanding of research priorities in the field of microbial reservoirs and transmission dynamics of escalating infectious diseases.
- Understand the barriers to this research and identify enabling mechanisms that can overcome these barriers.

- Discuss how Wellcome can best support the most pressing research needs, identify more broadly what support is needed in this space, and outline how key stakeholders can be best placed to act.
- Understand how research that will inform policy decisions and the development and use of accessible interventions can be best supported to ensure research uptake, impact, and lasting change.

The workshops were hosted in the three Global South regions aimed at the communities facing the greatest burden or risk of escalating infectious diseases, and to ensure that LMIC-targeted funding strategies developed following this study will be guided by context-relevant research priorities. The workshops were closed events, with participation via invitation only, to ensure equitable and diverse participant recruitment. Analyses were conducted for each of the following stratifications:

- Global (total of all responses)
- LMICs and High-Income Countries (HICs)[1] (survey data only).
- Regional (Asia-Pacific-Pacific, Africa, LAC and The Global North. Note that a Global North analysis was only conducted for the survey data. See **Region Definitions** for further information)

For the regional analyses, responses were divided according to region and analysed by researchers working in each respective region.

Exclusion Criteria and Data Cleaning

All qualitative survey responses were scanned by the research team prior to analysis, and any responses meeting the following exclusion criteria were removed from the final analysis in their entirety:

- Explicit misunderstanding of the survey aims or terminology.
- Inclusion of offensive, aggressive or derogatory language.
- Overt assertion of political agendas or ideologies.
- Clear indication that Artificial Intelligence software was used to provide responses.

Any responses deemed to meet the exclusion criteria were discussed amongst three members of the research team before a final decision on their exclusion was made. In addition, the dataset was checked for incidences of multiple responses (multiple submissions by the same participant) and by searching the data for repeated examples of unique identifier information (participant email addresses). Where multiple responses were identified, only a participant's first response was included in full in the final analysis; quantitative data from repeated responses was excluded. However, qualitative data from repeated responses (that differed in content from the first response) were merged with the qualitative data from the first response and included in the final analysis. Workshop transcripts were quality-checked prior to analysis.

Translation

Non-English free-text data (open-ended survey question responses and workshop transcripts) were translated into English prior to analysis. Spanish, Portuguese and French translation was conducted by native speakers of each language, who also possessed familiarity with the research topic. Any responses received in languages additional to those listed above were translated using online translation software (Google Translate).

Quantitative Analysis

Quantitative data (closed-ended question survey responses and workshop participant demographic data) underwent descriptive statistical analysis using Microsoft Excel.

Qualitative Analysis

Qualitative data (open-ended question survey responses and workshop transcripts) underwent inductive thematic analysis using the qualitative data analysis software NVivo (v1.5.2/13). Analysis involved an initial line-by-line review searching for concepts, themes, and ideas to develop a preliminary coding scheme. These initial coding schemes

[1] As defined by the Organisation for Economic Co-operation Development Assistance Committee List of Official Development Assistance Recipients (https://www.oecd.org/dac/financing-sustainable-development/development-finance-standards/daclist.htm).

were revised through discussion between all research team members, to create a study-wide coding scheme and allow accurate compilation and comparison of the qualitative data across each of the study target regions. In line with the priority-setting focus of the study, comments and discussion concerning the 5 highest-ranked survey responses for each workshop session were prioritised.

Results

Demographics

3,700 infectious disease research stakeholders (including academics, healthcare professionals, laboratory professionals, policy/decision makers, and industry representatives) responded to the survey, 86.9% of which were from LMICs, **Table 1**.

Table 1 Economic and Geographic Overview of Survey Participants

Stratification		Responses
Economic Classification	**LMIC**	86.9%
	HIC	13.1%
Study Region	**Africa**	48.3 %
	LAC	27.2 %
	Global North	12.6%
	Asia- Pacific	12.0 %

Percentages may not total 100 due to rounding.

The participants came from a diverse range of roles with strong representation from clinical researchers however, this extended wider to include representation from governments, animal sciences, and laboratory disciplines such as genomics and One Health.

Response to the question *'What infectious diseases do you consider pose the greatest threat of escalation?'*

Quantitative analysis from this priority-setting exercise identified that when considered collectively, respondents perceived Tuberculosis (TB), Malaria and Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS) to be the infection threats that presented the greatest risk of escalation, or currently escalating, across the globe (**Figure 3**).

Rank	Africa	LAC	Asia-Pacific	Global North
1	Malaria	Dengue	Tuberculosis	AMR
2	HIV/AIDS	Tuberculosis	Dengue	Influenza
3	Tuberculosis	HIV/AIDS	AMR	Tuberculosis
4	Cholera	Malaria	Malaria	Coronaviruses
5	COVID-19	COVID-19	Respiratory Infections	Avian Influenza
6	Viral Hepatitis	Arbovirus	HIV/AIDS	Malaria
7	Ebola	Respiratory Infections	Avian Influenza	Viral Infections
8	AMR	Vector-borne Diseases	Viral Hepatitis	Dengue
9	Lassa Fever	AMR	COVID-19	Emerging Diseases
10	Schistosomiasis	Chikungunya	Influenza	Respiratory Viruses

Figure 3 Initial survey prioritisation of diseases found to present the greatest risk of escalation. Data was generated through a free-text box addressing "Please tell us which disease(s), either at risk of escalation, or currently escalating, you feel poses the greatest infection threat, and why".

Antimicrobial resistance (AMR) was considered by the Global North participants to be the primary "disease" or threat of escalation (see **Antimicrobial Resistance (AMR)**). AMR was ranked 8th in Africa, 9th in LAC and was considered the 3rd highest escalating threat in Asia-Pacific. It is important to note that although AMR is not a disease and might appear incorrect to report next to the specific diseases in this way, this is how the respondents answered the question in the survey.

TB was found to be the greatest perceived threat in Asia-Pacific followed by ranking 2nd in LAC and joint 3rd in Africa and the Global North in the first round of analysis of the survey data. Malaria ranked highly as the perceived primary threat of escalation in Africa, and joint both 4th in LAC and Asia-Pacific and 6th in the Global North. HIV/AIDS did not rank in the Global North participants view as an emergent threat; however, HIV/AIDS ranked 2nd highest in Africa, 3rd in LAC and 6th in Asia-Pacific.

The three regional workshops provided the next step in the Delphi approach as the participants informed how the findings from step 1 (above) were to be refined, further understood and focused. This stage enabled further investigation into the prioritisation of the following groupings: Vector-borne Diseases (VBDs), Viral Haemorrhagic Fevers (VHFs), Neglected Tropical Diseases (NTDs) and responses relating to 'resistance' by grouping the relevant individual responses. This analysis identified VBDs as a leading disease group of concern (**Figure 4**).

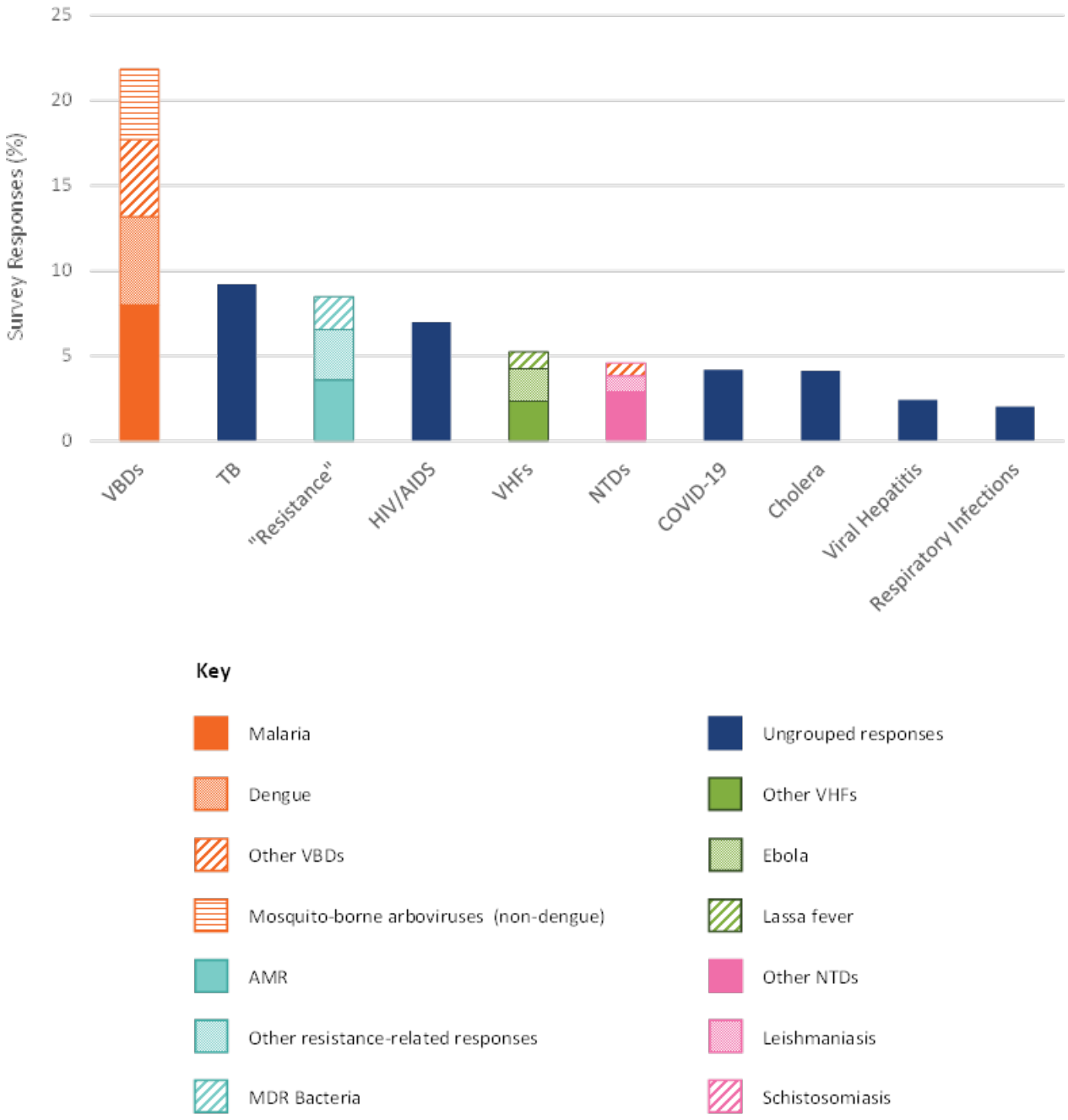

Figure 4 Comparison of disease groupings proposed by workshop participants, with highest-prioritised infection threats from the survey. For the categories 'Resistance', VHFs, and NTDs, the two highest-prioritised individual infection threats (e.g. Ebola and Lassa fever within VHFs) have been highlighted. 'Ungrouped responses' refers to infection threats featured above that have not been subjected to additional grouping (e.g. TB, HIV/AIDS, COVID-19 etc.), and represent only the total number of survey responses received for that individual infection threat.

Note: Due to the broad and diverse nature of these classifications, there is some overlap between groupings (e.g. Leishmaniasis responses, highlighted within NTDs, are also included in the 'Other VBDs' grouping). Dengue, highlighted in the VBD grouping, is not included in the VHF or NTD grouping. Whilst it is acknowledged that 'Severe Dengue' is considered to fall into both latter categories, as no distinction was made by any participants between Dengue and Severe Dengue, it has not been included in the VHF/NTD categories above.

Unranked priority diseases

During the workshops, delegates were asked to discuss the diseases that did not feature and what they were surprised to see not listed. Here neglected tropical diseases, sexually transmitted diseases and fungal infections were discussed. All three workshops agreed that these were diseases where there is low ongoing surveillance due to weak diagnostics and detection mechanisms resulting in minimal understanding of disease epidemiology, lack of evidence of disease burden and therefore low levels of research activities and funding opportunities.

Response to the question *'What factors do you consider are driving these escalating threats?'*

Drivers that are perceived to be associated with the risk of escalation of these infectious diseases included climate change due to its impact on vector and human population distribution, socioeconomic factors including poverty, overcrowding and poor public education and AMR.

Climate change

The qualitative evidence confirms that VBDs pose the highest risk of escalation due to climate change shifting the geographical range of mosquito (and other vector) populations.

Climate change was recognised by participants to be a key factor in the escalation of highly prioritised infectious diseases such as Malaria and Cholera. Notably, climate change was identified as a driver of VBDs and arbovirus escalation across all study regions, with Malaria and dengue cited as examples in every setting. Other specific diseases of which climate change was identified as a key driver of escalation across multiple regions included Chikungunya (Africa, LAC and the Global North), Zika (LAC and the Global North) and Cholera (Africa and LAC).

In addition to VBDs/arboviruses, several disease groupings, of which climate change was identified as a key driver of escalation across multiple regions, were identified, including zoonotic diseases (e.g. Lassa Fever, Leptospirosis, Japanese Encephalitis, West Nile Virus), VHFs (e.g. Marburg Virus, Hantavirus and Crimean-Congo Haemorrhagic Fever; Africa, LAC and Asia-Pacific-Pacific), and 'Respiratory Diseases' (Africa and LAC). There was consensus across all study regions that climate change (specifically temperature increases and changing precipitation patterns) contributes to the escalation of VBDs via its impact on vector distribution, including the expansion and shifting of vector ranges, increase in vector population densities and distribution of vector breeding sites:

> "Malaria [is the greatest escalating threat as] the vectors map to temperature. Climate change is increasing the areas that vectors can survive, hence the spread of disease to areas previously not at risk"
>
> Scientist (R&D), NGO, Kenya

The impact of climate change on food/waterborne infections (notably Cholera, globally and Typhoid in Asia) was also discussed, primarily regarding disease escalation in Africa and the Caribbean. Driving factors centred around the impact on water distribution, including water scarcity, negative impacts on water storage, and an increase in extreme weather events, specifically flooding, drought and tropical storms.

Socioeconomic factors

Socioeconomic factors emerged as a diverse, but significant, classification of disease escalation drivers. In general, socioeconomic drivers (primarily poverty, and its associated impact on habitation of informal settlements, living standards, local infrastructure capacity and unemployment) were found to overlap across diseases and regions. In particular, lower socioeconomic status was connected by Global South participants to disease awareness in the community:

"Tuberculosis and pneumonia [are the greatest infection threat] due to the poor economic conditions of the population and the low knowledge of the risk factors associated with transmission"

Epidemiologist, Government Ministry, Honduras

Parallels between the impact of socioeconomic drivers of disease escalation and climate change were also recognised. Their effect on human population distribution and displacement specifically, spurring international migration, and encroachment upon vector-borne disease endemic settings via deforestation and urbanisation:

"Zoonotic diseases currently represent the greatest public health risk in this region, since the advance of agricultural frontiers and urbanization, together with climate change and the tropicalization of the region, increase the probability of contact with new pathogens typical or related to wildlife, generating possible spill over routes to humans."

Academic, Public Health Institute, Argentina

Antimicrobial Resistance

AMR was identified as a priority escalating infection threat, and concern regarding the impact of AMR on disease escalation was common to all study regions. AMR was cited as a driver of TB escalation across all study regions, and a driver of Malaria and HIV/AIDS escalation by participants in the Africa and LAC regions (**Table 2**). In addition to TB, the escalating impact of AMR on gonorrhoea and nosocomial infections was identified across all three Global South study regions.

Table 2 Drivers of AMR escalation identified by participants in each study region.

Emergent Themes	Study Region			
	Africa	Asia-Pacific-Pacific	LAC	Global North
Inadequate antimicrobial stewardship (Irrational use, weak regulation, self-medication, etc)	✓	✓	✓	✓
Emergence of resistance in clinical settings	✓	✓	✓	✓
Lack of AMR surveillance systems	✓			✓
Lack of AMR-focused research		✓		✓
Limited diagnostic capacity	✓		✓	
Lack of knowledge in the community	✓		✓	
Limited access to antimicrobials	✓		✓	
Spillover of zoonotic resistant organisms	✓			
Low investment in IPC	✓			

Whilst multiple drivers of AMR escalation were identified, inadequate antimicrobial stewardship emerged as a recurrent theme across disease areas and study regions. Poor stewardship practices included the irrational use of antimicrobials in both human and animal populations, including overprescribing, empirical prescribing, Over the Counter dispensing, self-medication, and weak regulation.

Overlapping these concerns, the identification of nosocomial/hospital acquired infections in every study region identified clinical settings as key breeding grounds of AMR. Upon further inspection, wider health systems inadequacies, including limited diagnostic capacity and a lack of AMR surveillance systems were noted as contributing factors to AMR escalation. Limited diagnostic capabilities, including a lack of diagnostic tools, limited diagnostic facilities, and subsequent delay in accurate diagnosis was highlighted as a driver of empirical prescribing and subsequent escalation of AMR.

"I think that with AMR, the issue is the overuse of antibiotics, and use before diagnosis or use of culture... So the issue is the under use of diagnostics, overuse of the antibiotics. If you have under use of diagnostics, what healthcare professionals see is swept under the carpet, and no one can pick it up"

Academic, Academic Institution, Thailand

Response to the question *'What Research Should be Undertaken to Address These Threats?'*

When asked what type of research is needed to address these escalating threats, participants in all study regions identified a need to improve the detection and investigation of disease threats. A need for improved diagnostic facilities and tools to enable timely disease detection emerged as a key theme. Additionally, participants in all regions perceived further research into understanding disease transmission and measuring the impact of socioeconomic and cultural factors on disease escalation, to be high priorities.

Key Finding

More research on disease detection, transmission and the socioeconomic and cultural drivers of disease escalation is needed to combat the greatest infection threats.

Participants were asked to identify research areas concerning the sources or reservoirs of disease and factors influencing their escalation which they felt represented research priorities in their setting. Specifically, participants were asked to identify '*knowledge or research gaps which, if addressed, would contribute to the development and use of interventions for disease control*'.

This was a closed-ended question, and participants were required to prioritise up to three response options from a list of 12 predetermined research themes. 10,678 responses were received in total. Comparisons of the research theme rankings at the LMIC/HIC and regional levels are presented in **Table 3**. In addition, participants had the opportunity to share why they believed these research areas represented the greatest research priorities during both the survey (as an open-ended question) and during the Global South workshops.

Table 3 Ranked infectious diseases research priorities

Key: ■ = highest ranked priority ■ = second highest ranked priority ■ = third highest ranked

Research Theme (ranked according to global prioritisation)	Responses (%)					
			Region			
	LMIC	HIC	Africa	Asia-Pacific	LAC	Global North
Improving the **detection and investigation** of disease threats (e.g. diagnostics, sampling and surveillance, genomics studies, etc)	**20.3**	**20.1**	**20.0**	**20.5**	**19.9**	**20.1**
Understanding **disease transmission** (e.g. spillover, amplification), and the effectiveness and best use of transmission-blocking interventions (from non-pharmaceutical interventions such as practices, to medical countermeasures such as vaccines or medicines which interrupt transmission)	14.0	16.1	14.6	14.0	12.6	15.8
Measuring the impact of **socioeconomic and cultural factors** (population growth, land use, urbanisation, behaviours etc) on the emergence and spread of infectious diseases	12.9	10.2	12.3	12.7	13.5	10.3
Increasing **community engagement** in research into the sources of disease and drivers of escalation	9.3	6.2	10.8	8.7	7.5	6.4
Increasing **research uptake** and use of evidence by policymakers	7.8	9.8	8.1	9.7	8.4	9.7
Implementing **One Health** approaches to disease preparedness and prevention of escalation	8.5	8.6	9.3	8.1	7.1	8.9
Characterising disease reservoirs and the role of reservoirs in disease emergence and drivers of escalation (e.g. acquisition of virulence factors, resistance genes, etc)	6.3	6.5	5.3	5.2	8.4	6.2
Improving **data** access, analytics and sharing	5.3	7.7	4.2	5.3	7.2	7.7
Investigating the role of **climate and the environment** on the emergence and spread of infectious diseases	4.9	5.8	4.9	6.4	4.7	6.0
Predicting and identifying disease reservoirs	4.9	4.0	4.9	4.5	4.9	4.0
Understanding the role of **vectors** as sources of disease and drivers of escalation	3.9	2.6	3.9	2.9	4.0	2.7
Exploring **ethical considerations** regarding research into the sources of disease and drivers of escalation	1.8	2.3	1.6	2.0	1.9	2.3

Disease detection and investigation

These findings show a strong consensus that improving the detection and investigation of disease threats is perceived to be key to tackling escalating infectious disease threats. This is evidenced by the research theme 'detection and investigation's prioritisation across every study region/stratification (see **Table 3**).

The need for improved diagnostic facilities and tools to enable disease detection was a common theme across all study regions. This encompassed numerous considerations, including a need to improve existing diagnostics, to improve access to diagnostics, to develop rapid, affordable diagnostic tests, and to strengthen diagnostic infrastructures. Many participants highlighted the value of improved diagnostic capabilities in addressing the high-priority and escalating infectious disease groupings identified including AMR and VHFs.

> "Better microbiology diagnostic capacity can help reduce antibiotic use, antimicrobial resistance and surveillance and detection of outbreaks of viral haemorrhagic fevers, including Lassa Fever, which often present with non-specific symptoms, cannot be detected in a timely manner without better access to diagnostics"
>
> Academic, Academic Institution, Sierra Leone

An overall need to improve timely disease detection (for example, by increasing equitable access to rapid diagnostic tools, resources and laboratory facilities) was identified as a key focus for future disease detection and investigation research. In addition, harnessing community engagement (4th highest prioritized research theme among participants, see **Table 3**), primarily through education and recruitment of local champions, was also noted as a valuable approach to supporting disease surveillance activities.

Disease transmission

In addition to the detection and investigation of disease threats, our findings also recognise a universal consensus that further research into understanding disease transmission (ranked as the 2nd greatest research priority across all study regions except LAC, where it ranked as the 3rd highest priority) as necessary to tackle escalating infection threats.

Qualitative findings suggested that disease transmission represented a knowledge-deficient, a poorly understood and neglected component of infectious disease research across all study regions:

> "Although understanding disease transmission for outbreak/epidemic notification is part of International Health Regulations, this area is a clearly under-funded and perhaps one of the key weaknesses of public health systems in LMICs"
>
> Scientist R&D, Academic Institution, Vietnam

Reflecting the high prioritisation of detection and investigation research, developing real-time surveillance systems to track disease transmission was proposed as a key target for transmission-focused research in the Asia-Pacific-Pacific region. Notably, increasing intersectoral and international collaboration was identified as a key strategy to enable success in this field. Participants in the African region raised a need to focus on community transmission, including understanding community transmission modes and educating the general public. Complementing the identification of socioeconomic factors as key drivers of infectious disease escalation (see above), there was also consensus that the impact of socioeconomic and cultural factors on the emergence and spread of infection (ranked as the 3rd greatest research priority across all study regions except LAC, where it ranked as the 2nd highest priority) represented a pressing knowledge/research gap.

Social science

Social science was identified as a poorly funded, under studied component of infectious disease research across all study regions. In addition to economic drivers discussed above diverse cultural and behavioural factors were identified as key drivers of disease escalation (see **Table 4**) and consideration of socioeconomic and cultural factors was considered essential in the design of culturally sensitive, context-appropriate interventions. Several participants cited a need to conduct social science research to further understand specific diseases prioritised in the study:

> "It is extremely important to measure the impact of socioeconomic and cultural factors on infectious diseases such as TB, considering that it is a problem of social determinants rather than a biomedical one. For the same reason it is important to characterize it socio-demographically to understand its evolution and behaviour"
>
> Civil/Public Servant, Government Ministry, Paraguay

Moreover, due to the cross-cutting nature of social science research, incorporation of this research theme into all future infectious disease research was considered fundamental to effectively addressing infectious disease research priorities. In addition to ensuring the design of context-relevant interventions, such an approach was deemed crucial in ensuring the effective translation of evidence into practice. As noted across the other highly prioritised research themes discussed above, close collaboration between researchers and communities was identified as a key enabler of effective social science research.

Ethics research was deemed low priority in response to the survey question on what type of research should be undertaken. This low prioritisation was discussed heavily in the workshops. Some participants felt it was likely to be due to ethics review being considered part of the research process, rather than a standalone research topic itself. Others commented that ethics research is broader than just ethics approvals and that research questions on ethics are important and directly relevant to understanding the transmission dynamics of escalating infectious diseases. These workshop discussions also suggested that the focus on community engagement and a better understanding of social and economic factors that ranked higher would have included research into ethical considerations, hence the high rank for community engagement and social science and why ethics research was lower.

Table 4 Cultural and behavioural drivers of disease escalation in need of greater understanding identified by participants in each Global South study region.

Emergent Themes	Study Region		
	Africa	Asia-Pacific-Pacific	LAC
Local stigmas	✓	✓	
Traditional belief systems	✓		✓
Social diversity (ethnic, religious, cultural, language etc)	✓		✓
Health-seeking behaviours	✓		✓
Traditional family structures	✓		
Traditional diets		✓	
Myths about health interventions			✓

Note that no data from Global North participants is included above, as despite 'Measuring the impact of socioeconomic and cultural factors' ranking as the 3rd most highly prioritised type of research by Global North survey participants, no specific examples of sociocultural or behavioural factors raised as drivers of disease escalation by Global North participants were noted.

Response to the question *'What are the barriers and enablers to this research being undertaken?'*

Globally, participants consistently perceived research skills training, institutional support and access to funding as key factors that enable (or will enable, if implemented) infectious disease research in their setting. A frequently occurring view was that funding is siloed to larger institutes and it is difficult for smaller, emerging, and less experienced groups to break through. Another clear perspective from the participants is that grant writing as a skill is deficient across the Global South. This prevents researchers from being able to apply for and secure funding, especially early-career researchers:

"Most PhD trainings do not incorporate how to write grants or how to manage grants... in our university now, graduate students are asking for this training… maybe we should be looking at [pre-existing] training, and maybe by having more examples of such training, we will eventually be able to create a cohort of people that are able to win grants and do the research"

Scientist (R&D), Academic Institution, Ghana

Key Finding

Research skills training, institutional support and access to funding for research are the key factors that impede and enable (if resolved) vital research.

The quantitative findings in response to the question, 'What are the barriers and enablers to undertaking this research?' were highly consistent: 1) the reported barriers correspond closely with the enablers; and 2) all the elements reported as barriers, or indeed enablers, showed minimal variation among survey respondents (**Figure 5**).

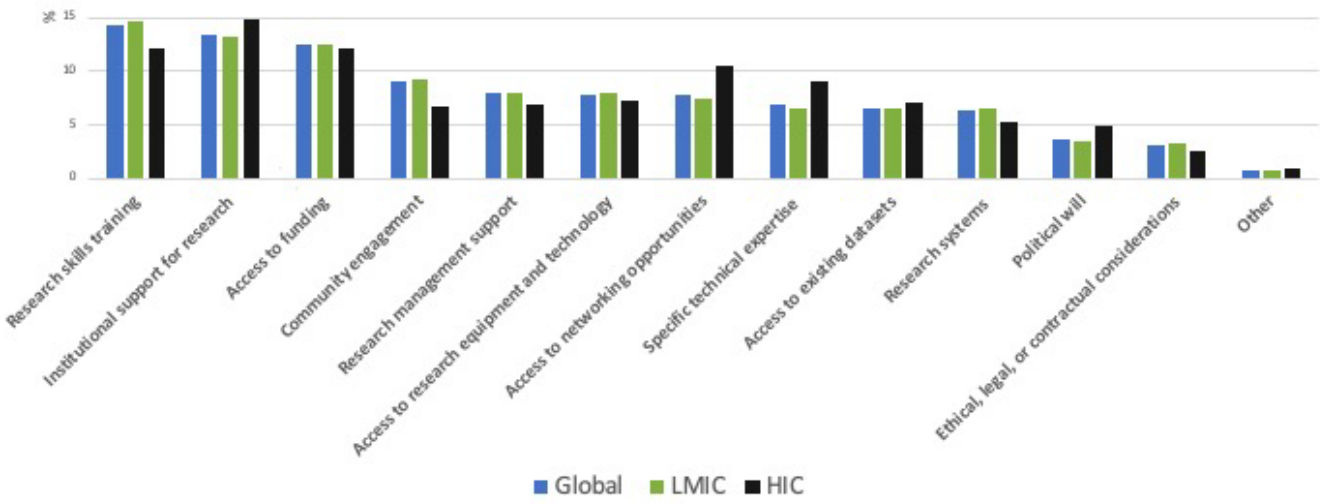

Figure 5 Factors identified as research enablers within the field of infectious diseases by survey participants. A breakdown of responses according to economic classification is included above.

Funding design and management

Many participants considered that funding comes with debilitating restrictions that are very difficult for teams in low-resource settings. It was particularly noted in Africa that funding for research is skewed towards diseases of public interest, is short-term and lacks consideration for basic sciences. There was a common perception that there was a lack of equity for females and not enough support for or focus on young researchers. Several respondents from the workshop discussions also highlighted the need for longer period funding and inclusion of representatives from the Global South who are more in touch with local problems within the funding agencies. Language barriers which hamper publications and grant applications stand out as a significant hurdle for researchers from LAC and the Caribbean.

Additionally, the lack of equity and flexibility, along with the transient nature of the existing funding opportunities, further compound the challenges in accessing funding. Researchers in Asia-Pacific-Pacific emphasized the dearth of soft skills and research management skills necessary to lead teams, communicate with collaborators and funders and manage grants as a barrier to research in the region.

Lack of institutional support for research was a clear, visible, and consistent finding common across participants. The discussion and comments indicated that the employers of health workers and other would-be researchers do not support time for or recognize the value of research. These employers could be hospitals, health clinics, government laboratories or NGOs, for example. It was also clear from these responses that there is a lack of research management support and availability of skills for key enabling systems such as finance, human resources, contracts and grant writing and administration.

Scalable global programmes could solve these barriers to research by funders adopting new approaches specific to these target areas, by providing access to cross-cutting research skills training and research system strengthening and by working with governments to build support for research within healthcare settings.

Interpretation of the findings

We consider this an important and unique dataset due to the very specific questions asked, the global scale and the detail within the responses. As a listening exercise, we asked the participants to report which infectious diseases they consider pose the greatest risk of escalation in their setting, not what they are working on now, or the greatest burden of disease. The reasons and explanations then given in the survey and workshops qualitative responses are striking. The respondents emphasised that they were reporting what they are experiencing, what was concerning to them, and explained why, stating also that they found this important to report and were pleased to be asked.

1. The methodological approach followed enabled perspectives to be shared by a large community of diverse stakeholders from across the world, particularly those from the Global South, and those not previously funded by Wellcome. Connecting these quantitative data to the qualitative findings explained why the participants were concerned about these diseases and gave a local contextual understanding of why they perceive these diseases as a significant threat for escalation.

2. This study has revealed clear perspectives among survey and workshop participants on priorities for infectious disease research among study participants, with the community perspectives being consistent with expected regional variations. Conducting regional workshops following the survey enabled more context-specific perspectives to be included in the analysis, which adjusted the initial findings from the survey. The qualitative evidence purposefully and thematically sought to explain why the participants held this concern when asked specifically ‘what diseases are at risk of escalation and why’.

3. Findings suggest that the community perspective for infection threats of primary concern for escalation are not emerging, or low-burden diseases at risk of sudden acceleration, but well-established, high-burden diseases (e.g. TB, HIV/AIDS, VBDs especially malaria and dengue). Escalation of these established threats is perceived to be catalysed primarily by climate change, the impact of low socioeconomic status, and AMR. To address these threats, the community suggests greater funding of research concerning disease detection, transmission and the socioeconomic drivers of disease escalation is urgently needed.

4. In designing future funding strategies, participants identified that attention should be placed on improving funding accessibility through equitable opportunity, by expanding opportunities for early career researchers, non-English speakers, and female researchers. In addition, supporting researchers to develop the necessary research skills, and building adequate institutional support for research and opportunities to network and collaborate were considered key catalysts for conducting successful research.

Conclusion

The methodological approach followed has generated important new insights into perspectives on infectious disease research priorities from the Global South, has enabled Wellcome to increase the diversity of stakeholders it engages with on strategically important areas, and overall, has contributed towards Wellcome's Diversity and Inclusion ambition. Whilst there are known limitations to the data set generated (e.g. gaps in geographical coverage, subjectivity in interpreting free-text options from the survey), perspectives and the contextual understanding of key research gaps, priorities and barriers were well communicated to inform Wellcome's approach for the development of accessible interventions to prevent or control disease escalation.

Strengths and limitations

The number of individuals responding to the survey was large, with 3700 participants, with many providing written responses. The workshops also achieved strong participation, in terms of detailed comments and views, both from the in-person and online delegates. These responses where all recorded, transcribed and coded into themes. The value and robustness of this study comes from the ability to consider the very large quantitative data in context with the corresponding qualitative data. However, the sheer amount made this a considerable undertaking.

This report is limited to gaining an understanding from the responses to the three key questions and then interpreting these using the qualitative findings. This was driven by the research's purpose. Therefore, the workshops were guided closely to keep the delegates focused, looking deeper into just those three questions and explaining the context in their perspective.

This vast dataset holds very many further questions that can and should now be asked by others looking from a different perspective. The fact that the dataset is so large gives an opportunity for meaningful new evidence to be generated by looking in far deeper detail in the different disease areas, grouping these differently, exploring the data on what types of research is needed, or looking more closely and the barriers and enablers to research.

In terms of potential for data bias we should firstly consider the participants. As expected, the demographics map closely the community demographics of The Global Health Network, although there was good uptake from wider roles, such as vets and One Health researchers. There was greater representation from the Global South compared to the Global North and this should be considered when evaluating the key findings. We were pleased with the range and diversity achieved but acknowledge that representation from the regions can only reflect a snapshot in terms of the view from the participants that took part.

A significant constraint in this study stems from the uneven distribution of survey data, with Africa contributing to approximately half of the responses and only 12% originating from the Asia-Pacific-Pacific region. Despite the broad geographical distribution of responses, the disproportionate representation could potentially influence the outcome. However, step 2 where the survey findings were discussed in each region addressed this somewhat because the overall findings and regional findings were explored in depth in each region and this allowed for these differences to be considered in the step 2 of the analysis

A key area where further analysis is needed on these data is the unexpected findings that deviate from the norm. These outliers were discussed during the workshops and strong consistent themes came through. However, the qualitative data set is so large it was beyond the scope of this round of analysis to undertake this.

Opportunities for further research, access to the data and methods

This is a vast and unique data set and there are many further studies that could be undertaken that we encourage others to undertake new studies of this data to explore new questions. The Global Health Network welcome requests for access to these findings and for groups to explore these further looking perhaps as specific disease areas, types of research or using the highly comprehensive data on barriers and enablers to research to support research system strengthening and capacity development programmes and activities? Here the evidence on the precise barriers and gaps should be highly informative for groups working to address this inequity.

The Global Health Network will be hosting the data. This report will be updated with the precise link. Alongside the data will be all the methodology such as the coding used in the qualitative analysis and the social science methodological approach used to run the workshops.

Appendix

Region Definitions

The regional classification used in this study ('Asia-Pacific', 'LAC', 'Africa', 'Global North') is based on the UN geoscheme regions used by the UN Statistics Division. It is based solely on continental regions. The UN states:

> '*The assignment of countries or areas to specific groupings is for statistical convenience and does not imply any assumption regarding political or other affiliation of countries or territories by the United Nations.*'

Only countries from which survey responses were received are included in the below list:

	Africa	LAC	Asia-Pacific	Global North*
Geoscheme regions	Eastern Africa, Western Africa, Northern Africa, Middle Africa, Southern Africa	South America, Central America, Caribbean	Southern Asia, South-eastern Asia, Western Asia, Eastern Asia, Central Asia, Melanesia	Northern Europe, Western Europe, Southern Europe, Eastern Europe, Northern America, Australia and New Zealand
	Kenya Uganda Nigeria Malawi Ethiopia Tanzania (United Republic of) Cameroon Ghana South Africa Rwanda Zambia Congo (Democratic Republic of the) Sierra Leone Zimbabwe Botswana Burkina Faso Côte d'Ivoire Gambia Somalia Mozambique Madagascar Sudan Benin Senegal Liberia Gabon Mali Egypt South Sudan Guinea Congo Eswatini Tunisia Burundi	Brazil Honduras Argentina Colombia Dominican Republic Mexico Peru Ecuador Panama Guatemala El Salvador Chile Bolivia (Plurinational State of) Paraguay Jamaica Venezuela (Bolivarian Republic of) Nicaragua Costa Rica Barbados Belize French Guyana† Grenada Guyana Saint Lucia Sint Maarten (Dutch part)† Suriname Trinidad and Tobago Virgin Islands (U.S.)† Uruguay Bahamas Haiti	India Nepal Bangladesh Pakistan Philippines Viet Nam Indonesia Thailand Sri Lanka Papua New Guinea Türkiye* Malaysia Cambodia United Arab Emirates Iran (Islamic Republic of) Bhutan Yemen Israel* Myanmar Palestine (State of) Afghanistan China Fiji Georgia Saudi Arabia Singapore* Armenia Azerbaijan Iraq Japan* Jordan Kazakhstan Korea (Republic of)* Kyrgyzstan Oman	United Kingdom Spain United States of America Australia Italy France Germany Greece Ireland Canada Switzerland Poland Belgium Netherlands Sweden Serbia Portugal Bosnia and Herzegovina Russian Federation Czechia Romania Ukraine Albania Austria Finland New Zealand Norway Slovakia Belarus Bulgaria Croatia Denmark Latvia Lithuania

	Morocco Chad Libya Namibia Cabo Verde Togo Niger Angola Djibouti Mauritius Seychelles Equatorial Guinea Lesotho Réunion†		Solomon Islands Syrian Arab Republic Uzbekistan	

*There is no universally agreed definition of 'The Global North'. Several countries commonly considered to be within the Global North are excluded for the above grouping (e.g., Japan, Korea [Republic of], Singapore, Turkey, Israel etc). The 'Global North' presented above correlates roughly to a combination of the UN Regional Groupings 'Western Europe and Other' and 'Eastern Europe' (but not precisely, Israel and Turkey are notable variations).

†The above is a purely geographic classification and does not make any political considerations or assumptions. For this reason, overseas sub-national administrative divisions (unincorporated and organized territories, overseas departments and regions, constituent countries etc) are grouped geographically according to their location, and not the location of their overarching, or administrative state (eg French Guyana is grouped by geography in LAC, as opposed to being grouped politically in Western Europe [as a department of France]).

Survey Questionnaire

What Research on Sources and Drivers of Escalating Infectious Disease Threats should be Prioritised for Funding?

Thank you for your interest in this Wellcome and The Global Health Network survey. Wellcome's mission is to reduce the risk and impact of escalating infectious diseases. To do this, Wellcome aims to support research that will help us better understand sources and drivers of disease, with a view to intervening earlier to limit escalation and informing the development and implementation of accessible and affordable interventions for disease control.

To inform our infectious disease funding strategy in this area, Wellcome are collaborating with The Global Health Network to gain an understanding of priority research needs on sources of disease and drivers of escalation. We are specifically keen to hear your views and perspectives on areas such as emerging infectious diseases, epidemics, drug-resistant infections and climate-sensitive infectious disease.

Who are we seeking to engage with this survey?

Anybody whose work directly impacts human health (including those working at the human-animal interface), who have research experience on understanding the sources of infectious disease and drivers of disease escalation and those involved in research uptake and public health decision-making.

About the survey

This survey consists of 11 questions and will take around 5-10 minutes to complete. Findings from the survey will be used to inform the design and content of three Global South, hybrid, regional workshops in Africa, Asia and Latin America and the Caribbean (LAC), on sources of disease and drivers of escalation, in June 2023.

We aim to invite a diverse and globally representative group of people to these workshops. If you are interested in attending, you are invited to express your interest and provide your contact details towards the end of this survey. Workshop invitations will be guided by survey responses.

The findings from this survey may be published in a report, a scientific journal, presented at a conference and made openly available. Your identity will remain anonymous in all publications, release of the data and presentations of the findings.

Your identity will only be requested if you give permission for us to keep in contact about this study and if you specify that you wish to be considered for invitation to one of the three regional workshops. Your identity and contact details will not be shared beyond Wellcome and The Global Health Network research team working on this study.
The information that you supply will be treated in accordance with the University of Oxford's Data Protection Policy. This project has been reviewed and approved by the Oxford Tropical Research and Ethics Committee (OxTREC). Reference number OxTREC 541-18.
For any other queries please email research@theglobalhealthnetwork.org.

About You

1) **Which of the following best describes your primary occupation?**

- Academic (Researcher and/or Teacher in Higher Education Institution)
- Civil/Public Servant
- Clinical Officer
- Community Health Worker
- Data Analyst
- Doctor
- Epidemiologist
- Ethicist
- Laboratory Professional (Manager, Technician etc)
- Microbiologist/Virologist
- Nurse
- Pharmacist
- Policymaker
- Politician
- Regulatory Affairs Professional
- Research Funding/Grants Professional

- Scientist (Research and Development)
- Statistician
- Student
- Veterinarian/Veterinary Nurse
- Other*
*If you selected Other, please specify

2) **Which of the following best describes the establishment where you work/study primarily?**

- Academic Institution (University, College, etc)
- Contract Research Organisation (CRO)
- Community Health Centre/Facility
- Consultancy
- Funder - Research Funding Organisation/Donor
- Government Ministry
- Hospital
- Industry - Biotechnology Company
- Industry - Pharmaceutical Company
- Non-Governmental Organisation (NGO)
- Public Health Institute
- Regulatory Authority
- Veterinary Clinic/Hospital
- Other*
*If you selected Other, please specify

3) **If your work focuses on infectious diseases, please identify your area of interest:**

- Bacteria
- Viruses
- Fungi
- Parasites/Protozoa
- Multiple Infectious Diseases/Non-specific
- Other*
*If you selected Other, please specify

3.a) Please specify your disease(s)/organism(s) of interest below

4) **Do you work in any of the following areas relating to infection threats? Please select all that apply:**

- Zoonotic diseases and/or spillover
- Reservoirs & reservoir ecology/biology
- Vectors & vector biology
- Resistance and/or escape mechanisms (e.g. resistance to treatments or escape from vaccines or diagnostics)
- Analytics and/or modelling
- One Health
- Climate science
- Design and use of interventions
- Knowledge translation and/or research uptake
- Public health policy and/or decision making
- Social sciences, community engagement and/or ethics
- Other*
*If you selected Other, please specify

5) **Which country do you work in? If you work in more than one country, please select the country in which you work primarily.**

[Drop down List, UNSD M49 countries list]

Understanding the Sources and Drivers of Infectious Disease

We want to hear your opinion on the key research priorities in this space, particularly on the sources or reservoirs of disease and factors influencing their escalation. We are keen to understand knowledge gaps or research priorities which, if addressed, would contribute to the development and use of interventions for disease control.
From the list below, please select **up to three** topics that are key research priorities in your region.

There is space below for you to give us any further information that you wish to share. **We are particularly keen to understand why you selected these topics, and hear about any research priorities that you think are not on the list.**

6) **Please select up to three topics that are key research priorities in your region:**

- Predicting and identifying disease reservoirs
- Characterising disease reservoirs and the role of reservoirs in disease emergence and drivers of escalation (e.g. acquisition of virulence factors, resistance genes, etc)
- Improving the detection and investigation of disease threats (e.g. diagnostics, sampling and surveillance, genomics studies, etc)
- Understanding disease transmission (e.g. spillover, amplification), and the effectiveness and use cases for transmission-blocking interventions (from non-pharmaceutical interventions such as practices, to medical countermeasures such as vaccines or medicines which interrupt transmission)
- Understanding the role of vectors as sources of disease and drivers of escalation
- Measuring the impact of socioeconomic and cultural factors (population growth, land use, urbanisation, behaviours etc) on the emergence and spread of infectious diseases
- Investigating the role of climate and the environment on the emergence and spread of infectious diseases
- Increasing community engagement in research into the sources of disease and drivers of escalation
- Implementing One Health approaches to disease preparedness and prevention of escalation
- Increasing research uptake and use of evidence by policymakers
- Improving data access, analytics and sharing
- Exploring ethical considerations regarding research into the sources of disease and drivers of escalation

6.a) Are there other research areas or topics relating to sources of disease and drivers of escalation that we have not covered above? Or would you like to add any further information around why you made your selections?

7) **Please tell us which disease(s), either at risk of escalation, or currently escalating, you feel poses the greatest infection threat, and why:**

Research Barriers and Enablers

8) **What are your main barriers to undertaking research into sources of infectious disease, and the factors that drive disease escalation?**

Please select **up to three** options from the list below:
- Access to funding
- Research skills training
- Institutional support for research
- Research management support (finance, grant writing, contracts etc.)
- Research systems (ethics committees/review boards)
- Access to research equipment and technology
- Access to existing datasets
- Access to networking opportunities
- Specific technical expertise (modelling/analytical expertise, laboratory training etc.)
- Community engagement
- Ethical, legal, or contractual considerations
- Political will
- Other*

*If you selected Other, please specify:

9) **What are your main enablers to undertaking research into sources of infectious disease, and the factors that drive disease escalation?**

Please select **up to three** options from the list below:
- Access to funding
- Research skills training
- Institutional support for research
- Research management support (finance, grant writing, contracts etc.)
- Research systems (ethics committees/review boards)
- Access to research equipment and technology
- Access to existing datasets
- Access to networking opportunities

- Specific technical expertise (modelling/analytical expertise, laboratory training etc.)
- Community engagement
- Ethical, legal, or contractual considerations
- Political will
- Other*

*If you selected Other, please specify:

10) Please use the space below to share anything else that you feel is relevant to research concerning the sources of disease and drivers of escalation, or any personal views on research in this space that you would like Wellcome and The Global Health Network to be aware of:

Workshop Invitation

11) Thank you for participating in this survey. The information you have provided will be used to inform future funding strategies regarding sources of disease and drivers of escalation. We plan to discuss the findings of this survey, and seek to build greater consensus on the priorities for research in this area, at three Global South, hybrid, regional workshops in June 2023. These workshops will be held in Addis Ababa (Ethiopia), New Delhi (India), and São Paulo (Brazil). If you wish to be kept up-to-date on the survey findings and upcoming workshop plans, please let us know:

- Yes
- No

11.a) Name:
11.b) Email:

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2. Walker R. Can building a community of practice improve pharmacovigilance in low-resource settings? : University of Oxford; 2022.
3. World Health O, de la Horra A, de Colombi NF, Baker B, Dahal P, Launois P, et al. Developing an evidence-led essential research skills training curriculum. Geneva: World Health Organisation; 2022 2022.

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