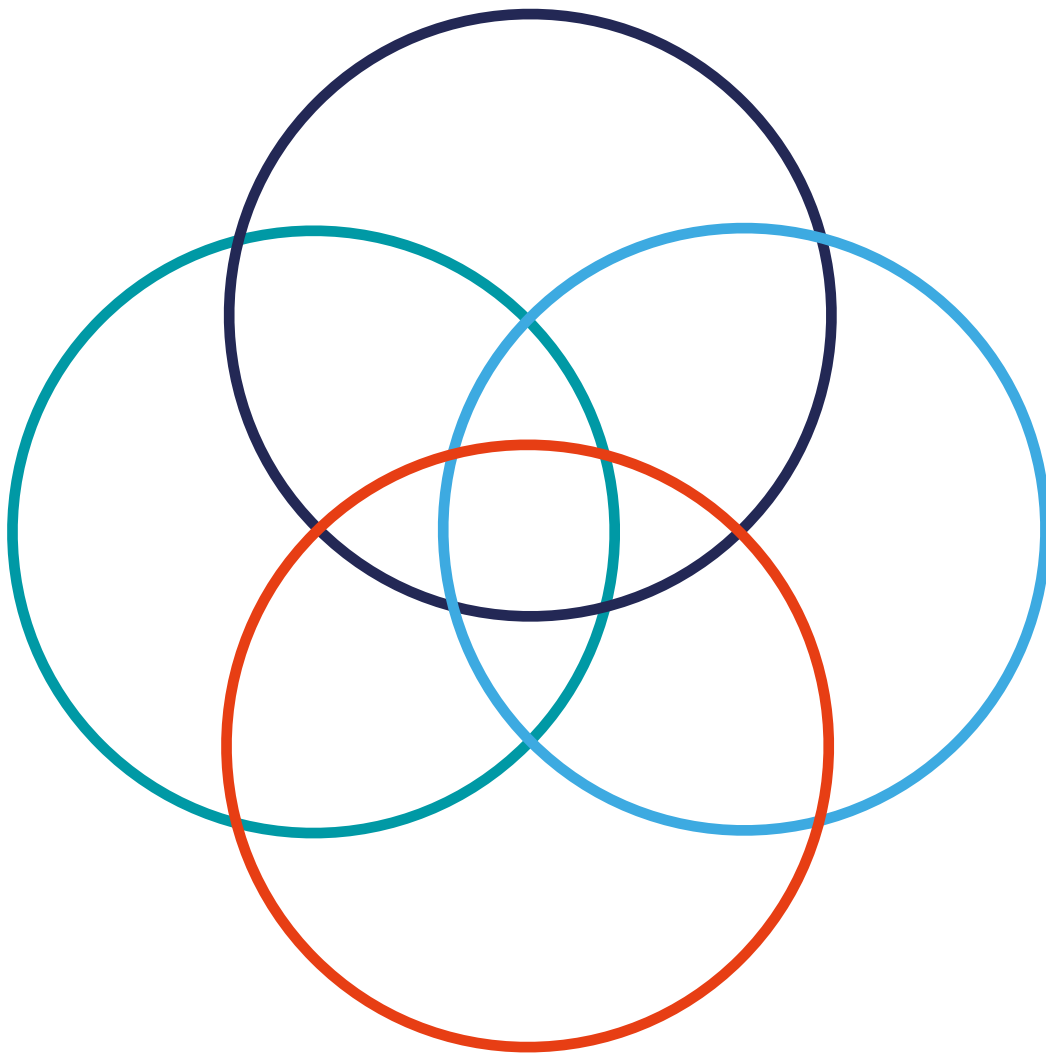


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# A One Health Priority Research Agenda for Antimicrobial Resistance



Food and Agriculture  
Organization of the  
United Nations



World Health  
Organization



World Organisation  
for Animal Health  
Founded as OIE



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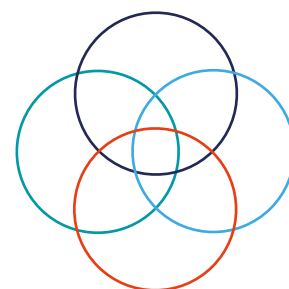
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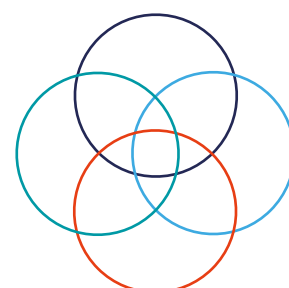
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# Foreword

The One Health Priority Research Agenda on Antimicrobial Resistance (AMR) sets out for the first time the priorities for which our organizations – as leaders in the multilateral system on human, animal, plant, and environmental health – will advocate to promote research and investment in the response to AMR.

The Research Agenda results from extensive stakeholder and expert engagement and was developed using a sound scientific methodology. The process identified major gaps in knowledge and evidence that require urgent scientific attention and resources. The document demonstrates how, by working together, we can effectively leverage our organizations' respective resources and strengths in the multilateral system.

Research undertaken under this Agenda will provide evidence to inform national action plans on AMR and support country and regional efforts to scale up national responses to AMR within the Sustainable Development Goals (SDGs).

We recognize that addressing the interlinked and multi-faceted challenges posed by AMR requires us to work together – across sectors, governments, academic disciplines, civil society, the private sector, and in the multilateral system – to advance a One Health approach. We strongly encourage all stakeholders, including countries, resource partners, researchers and regional and local authorities, to support the areas identified in the Research Agenda and to tailor them to their contexts and needs.

The Research Agenda emphasizes the need for increased inter- and multi-disciplinary research and strong global, regional and country research partnerships and platforms. Our organizations are committed to strengthening collaboration among us and with our partners as we advocate for funding and action on the research priorities in the coming years.

Above all, we hope that this Research Agenda will promote research on AMR with a One Health lens, improve human, animal, plant and environmental health, promote economic growth at national, regional, and global levels, and help to advance progress towards the SDGs.

**QU Dongyu**

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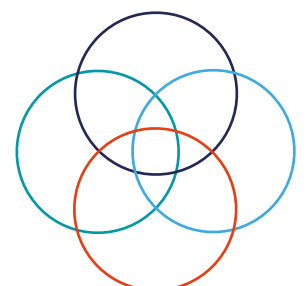
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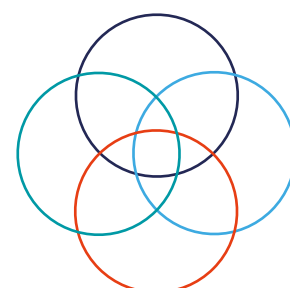
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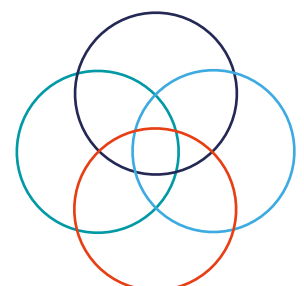
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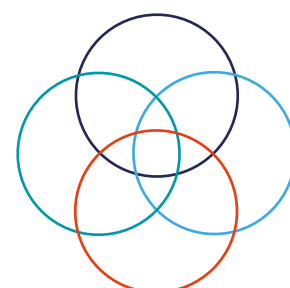
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# Acronyms and abbreviations

|                |  |
|----------------|--|
| <b>AMR</b>     | antimicrobial resistance   |
| <b>AMU</b>     | antimicrobial use  |
| <b>ANIMUSE</b> | ANimal antiMicrobial USE Global Database (WOAH)                  |
| <b>FAO</b>     | Food and Agriculture Organization of the United Nations          |
| <b>GAP</b>     | global action plan on antimicrobial resistance                   |
| <b>GLASS</b>   | Global Antimicrobial Resistance and Use Surveillance System      |
| <b>HIC</b>     | high-income country  |
| <b>IHR</b>     | International Health Regulations                                 |
| <b>InFARM</b>  | International FAO Antimicrobial Resistance Monitoring System     |
| <b>IPC</b>     | infection prevention and control                                 |
| <b>LMICs</b>   | low- and middle-income countries                                 |
| <b>NAPs</b>    | national action plans on antimicrobial resistance                |
| <b>SDGs</b>    | Sustainable Development Goals                                    |
| <b>TDR</b>     | Special Programme for Research and Training in Tropical Diseases |
| <b>UMIC</b>    | upper-middle-income country                                      |
| <b>UNEP</b>    | United Nations Environment Programme                             |
| <b>WASH</b>    | water, sanitation and hygiene                                    |
| <b>WHO</b>     | World Health Organization  |
| <b>WOAH</b>    | World Organisation for Animal Health (founded as OIE)            |



# Executive summary

Antimicrobial resistance (AMR) has been recognized as one of the greatest global threats to the health of humans and animals, plants and ecosystems as well as a threat to the achievement of the Sustainable Development Goals (SDGs). In our globally connected world, resistance to antimicrobials may spread and circulate among humans, animals, plants and the environment, necessitating a “One Health” approach.

One Health is an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals, and ecosystems (1). One Health recognizes that the health of humans, domestic and wild animals, plants and the wider environment (including ecosystems) are closely linked and interdependent. Consequently, addressing global health issues requires a multisectoral, multidisciplinary response to AMR at this One Health interface.

While the One Health approach is relevant to all efforts to prevent and control AMR, the priority research agenda presented here identifies research areas at the interface between sectors that are most relevant to low- and middle-income countries (LMICs), where the negative impacts of AMR are highest and are currently increasing.

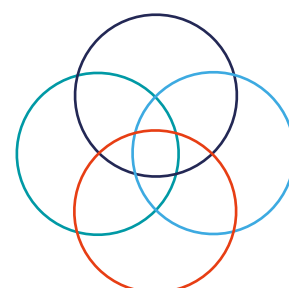
One Health AMR research strategies, interventions and policies are emerging, but further evidence is required to understand what works, in which contexts and for whom.

To structure the research priority-setting exercise, a preliminary agenda-scoping consultation process was conducted with key AMR One Health stakeholders. The process resulted in five pillars, namely: transmission, integrated surveillance, interventions, behavioural insights and change, and economics and policy. In addition, an equity lens with cross-cutting themes such as gender, vulnerable populations and sustainability was applied.

A structured, mixed-methods approach was undertaken to develop this research agenda within the SDG time frame to 2030. Reviews of academic and grey literature, together with an online open global survey, were conducted to ensure broad participation from a diverse range of global stakeholders. Analyses of these data were brought into a modified Delphi method, in which 89 global experts from different scientific disciplines with expertise in One Health and AMR prioritized research areas over three rounds of consensus against five assessment criteria: *important, strengthening research capacity in LMICs, actionable, inclusive and impactful*.

This research agenda is a guiding tool in One Health AMR research for investment, research activities and planning for countries and funding bodies. It also serves as a guide for One Health AMR research, helping policymakers, researchers and a multidisciplinary scientific community to work together on solutions that will prevent and mitigate AMR on a national, regional and global scale.

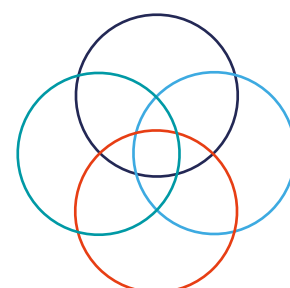
The priority research areas presented here require contextualization at the regional and country level and development of specific research questions relevant to the needs of different countries and One Health settings. Implementing this research agenda will support priority-setting and development of policy and practice-relevant evidence for countries to simultaneously address the threat of AMR and support national action plan (NAP) implementation and achievement of the SDGs for 2030.



The table that follows lists the 10 highest-priority research areas, considering the top two for each pillar.

| Pillar                                 | Highest-priority research areas  |   |
|--|--|---|
| <b>Transmission</b>                    | To what extent do <b>various IPC practices</b> in One Health settings impact the development and circulation of AMR in One Health sectors?   | What impacts the <b>transmission</b> of resistant microorganisms between humans, animals, plants and the environment, with a focus on conditions relevant to <b>LMICs</b> ?   |
| <b>Integrated surveillance</b>         | What are the optimum <b>strategies and minimum standards</b> (and resources) for adequate laboratory and human resource <b>capacity</b> to establish and maintain quality integrated AMR surveillance systems at scale?    | How can <b>existing AMR and AMU surveillance data</b> from humans, animals, plants and the environment be <b>meaningfully triangulated and/or integrated</b> to allow early identification of the development, escalation or circulation of resistance across One Health sectors?                         |
| <b>Interventions</b>                   | How can One Health interventions that have proven impactful for AMR control and mitigation most effectively be <b>translated and scaled up in different contexts or differently resourced settings</b> ?                   | What <b>challenges</b> exist to the <b>systematic collection and analysis</b> of data for risk assessment and intervention impact <b>assessment</b> (epidemiological, economic, social) in LMICs?   |
| <b>Behavioural insights and change</b> | How can structural <b>challenges and barriers</b> to behaviours related to AMR be <b>identified, characterized and assessed</b> in different <b>sociocultural contexts</b> ?   | What <b>strategies</b> can be used to <b>adapt effective behavioural interventions</b> (e.g. immunization) from one context to another (e.g. Africa to Asia / rural to urban / human prescribers to veterinarians)?   |
| <b>Economics and policy</b>            | What would a One Health AMR <b>socioeconomic impact assessment</b> based on accurate and cost-effectively collected data (e.g. harmonized methodology and indicators) in <b>low-resource settings</b> optimally look like? | How can governments identify, prioritize and institutionalize the most relevant <b>cross-cutting, sector-specific AMR policy options</b> and regulatory frameworks, and <b>financing strategies</b> to sustainably tackle AMR across One Health sectors, given their different implementation challenges? |

AMR: antimicrobial resistance; AMU: antimicrobial use; IPC: infection prevention and control; LMICs: low- and middle-income countries.



# 1. Introduction

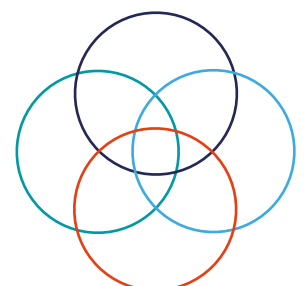
AMR has been recognized as one of the greatest global threats to the health of humans and animals, plants and ecosystems. In addition, AMR has been identified as a threat to the achievement of the SDGs (2, 3). In our globally connected world, resistance to antimicrobials may rapidly spread and circulate among humans, animals, plants and the environment. The increasing emergence and spread of AMR compromises our ability to treat infections and to manage AMR-associated economic impacts across all sectors. Consequently, a single-sector approach to preventing and controlling AMR is insufficient. Tackling the growing threat of AMR requires a One Health approach (1) (Box 1). One Health acknowledges the interconnection and interdependence of humans, animals, plants and the wider environment (including ecosystems) in the emergence and spread of AMR. Collaborative, multisectoral One Health approaches can leverage expertise and mandates across different organizations and sectors to prevent and control AMR, with the potential to facilitate health and economic benefits for all (4).

One Health research strategies, interventions and policies are being developed, but further evidence is required to understand what works, in which contexts and for whom (5). The need for more evidence to prevent and control AMR was recognized in the 2015 *Global action plan on antimicrobial resistance* (GAP), Objective 2, to “strengthen the knowledge and evidence base through surveillance and research [by] filling major gaps in knowledge on antimicrobial resistance” (6). The report of the UN Interagency Coordination Group on Antimicrobial Resistance asserted that “a more systematic and coordinated effort is ... needed to synthesize the evidence base and identify knowledge gaps across sectors and disciplines to guide One Health policy and implementation” (7). The Third Global High-Level Ministerial Conference on Antimicrobial Resistance in Oman in November 2022 emphasized the need for governments and philanthropic organizations to support research activities that focus on One Health AMR (8).

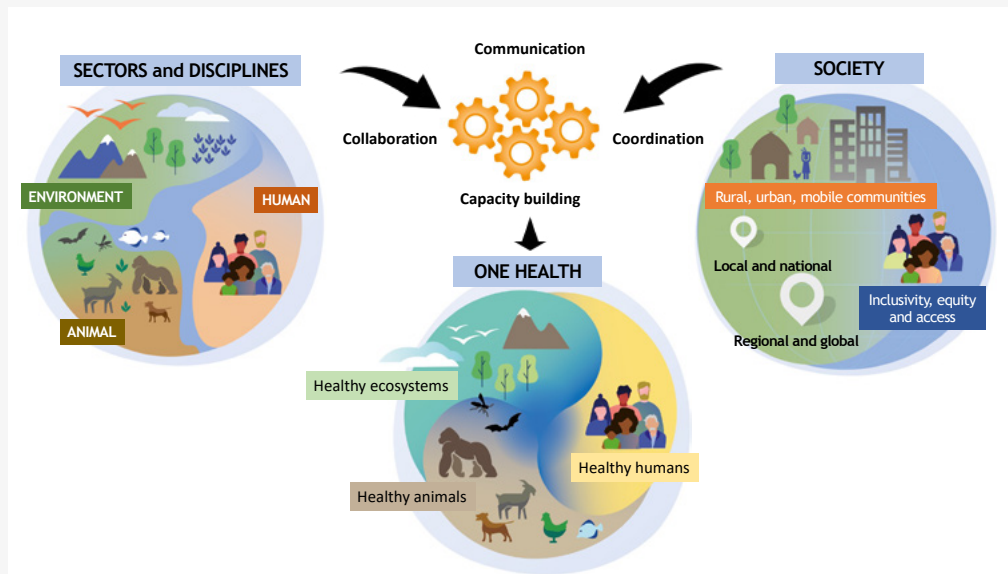
While several research agendas have emerged or are under development (9-12), the extent to which they tackle AMR at the One Health interface is limited. So far, only approximately 6% of research funding on AMR is allocated to projects that include more than one sector (13). To address these limitations, this global research agenda focuses specifically on AMR at the One Health interface.

While One Health approaches are relevant to all efforts to prevent and control AMR, this research agenda prioritizes research areas that are most relevant to and will catalyse action in LMICs. The World Bank estimates that while AMR could reduce global gross domestic product by 1.1–3.8% per annum by 2050, greater losses will be experienced in LMICs compared with upper-middle-income and high-income countries (UMICs/HICs) (14). The impact of AMR in LMICs has also demonstrated additional burden of disease (2, 15).

By focusing on LMICs, this One Health Priority Research Agenda for AMR can generate knowledge and evidence to support AMR prevention and control activities where they are most needed. The research agenda can also be relevant to, and benefit, HICs.



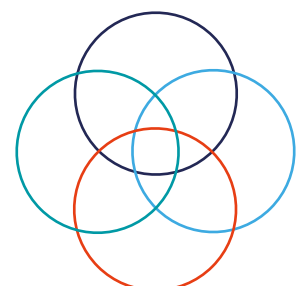
### Box 1. Quadripartite One Health High-Level Expert Panel definition of One Health



**One Health** is an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals, and ecosystems. It recognizes the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and interdependent. The approach mobilizes multiple sectors, disciplines, and communities at varying levels of society to work together to foster well-being and tackle threats to health and ecosystems, while addressing the collective need for healthy food, water, energy, and air, taking action on climate change, and contributing to sustainable development. This includes the following key principles:

1. **equity** between sectors and disciplines;
2. socio-political and multicultural **parity** (the doctrine that all people are equal and deserve equal rights and opportunities) and inclusion and engagement of communities and marginalized voices;
3. socioecological **equilibrium** that seeks a harmonious balance between human–animal–environment interaction and acknowledging the importance of biodiversity, access to sufficient natural space and resources, and the intrinsic value of all living things within the ecosystem;
4. **stewardship** and the responsibility of humans to change behaviour and adopt sustainable solutions that recognize the importance of animal welfare and the integrity of the whole ecosystem, thus securing the well-being of current and future generations; and
5. **trans-disciplinarity** and multisectoral collaboration, which includes all relevant disciplines, both modern and traditional forms of knowledge and a broad representative array of perspectives.

Source: One Health High-Level Expert Panel et al. (2022) (1).



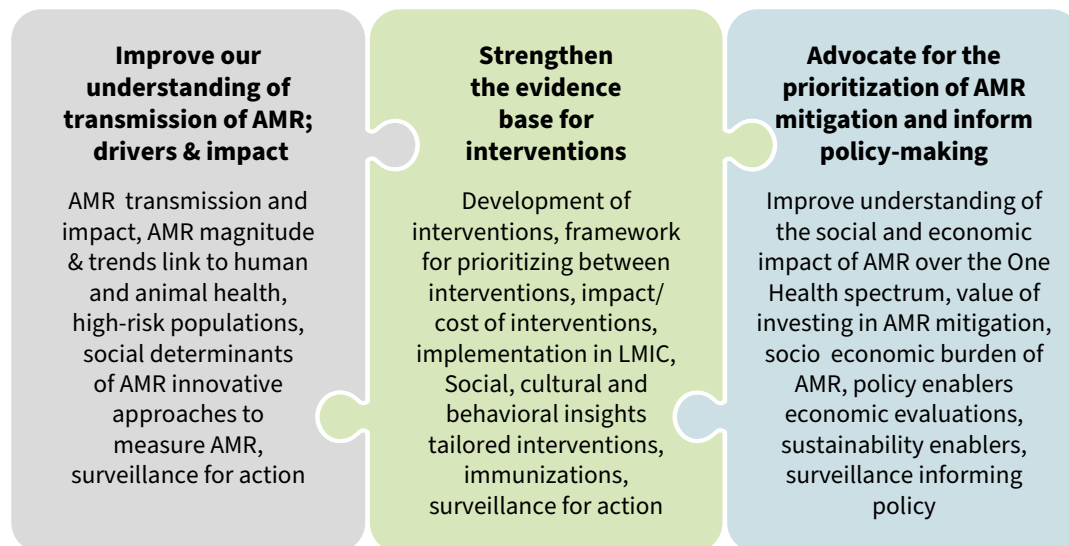
## 2. Purpose of the Research Agenda

This research agenda is a tool for prioritizing One Health AMR research to aid in directing and catalysing investment, research activities and planning for Member States and funding bodies. The research agenda also serves as a guide to One Health AMR that will help policymakers, researchers and a multidisciplinary scientific community work together on solutions to prevent and mitigate AMR within One Health on a national, regional and global scale.

In line with the SDGs, the time frame for this research agenda extends to 2030, recognizing that multisectoral One Health research may take more time to implement than single-sector One Health research.

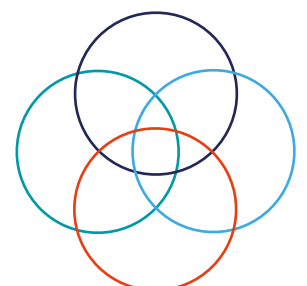
Figure 1 presents the key strategic objectives for this research agenda as outlined by the Quadripartite.

**Figure 1: Strategic objectives of the One Health Priority Research Agenda for Antimicrobial Resistance**



AMR: antimicrobial resistance; LMIC: low- and middle-income country settings.

As a final outcome this research agenda aims to develop evidence to inform the design of impactful One Health AMR national plans, policies, data and interventions across One Health sectors, chiefly in LMICs. At the country level, NAP on AMR research elements may be guided by these priorities.



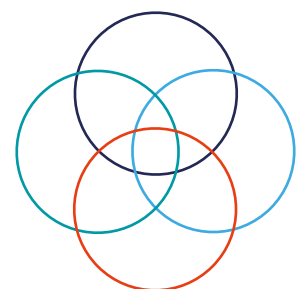
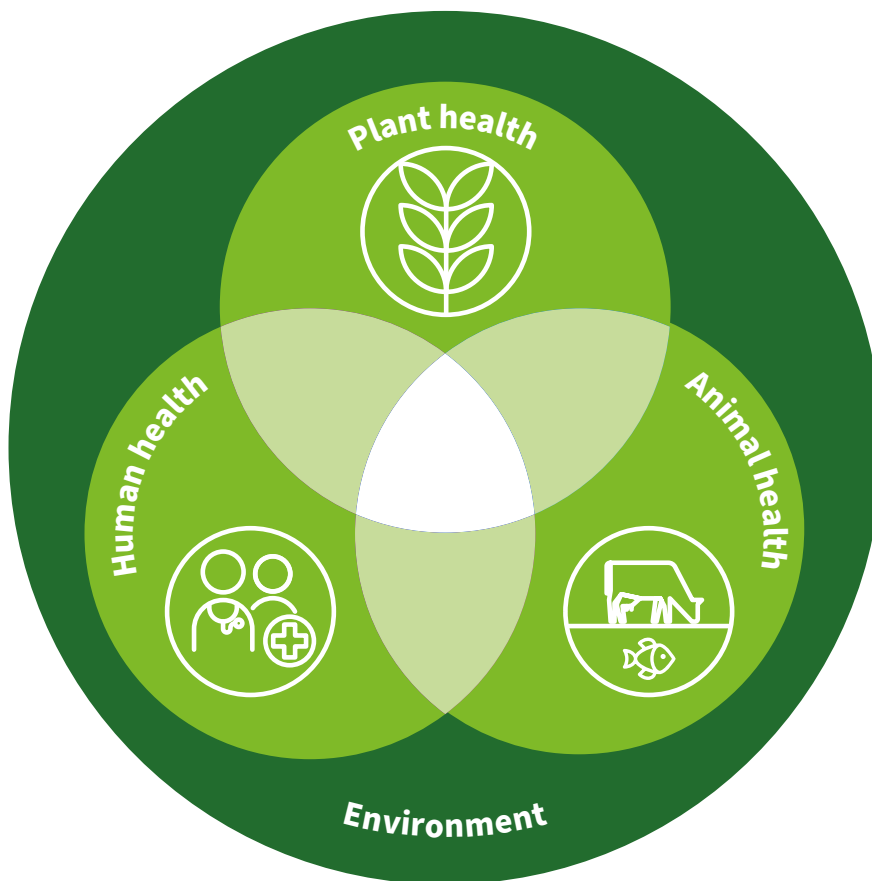
## 3. Scope

The One Health Priority Research Agenda for AMR focuses on the interface between One Health sectors (Figure 2). Product development, diagnostic development and research related to only one sector are thus out of scope.

The research agenda is built on five pillars: transmission, integrated surveillance, interventions, behavioural insights and change, and economics and policy. In addition, important cross-cutting themes such as gender, vulnerable populations and sustainability are also considered.

An equity lens was applied across the methodology. The research agenda addresses the differing contexts of LMICs. The potential research outcomes deriving from the research agenda are, however, relevant to all, including vulnerable groups.

**Figure 2: One Health interfaces**





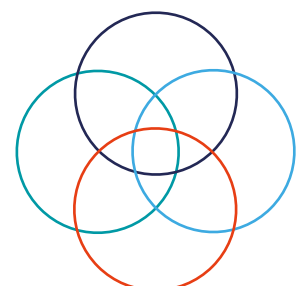
## 4. Target Audience

The target audience for the research agenda includes, but is not limited to, academia, research funders such as governments, international and national donors, and philanthropic organizations, as well as public-private partnerships that wish to develop and invest in One Health AMR research. The research agenda is designed to further support cross-disciplinary research and to strengthen One Health AMR research capacity and partnerships in low-resource settings.

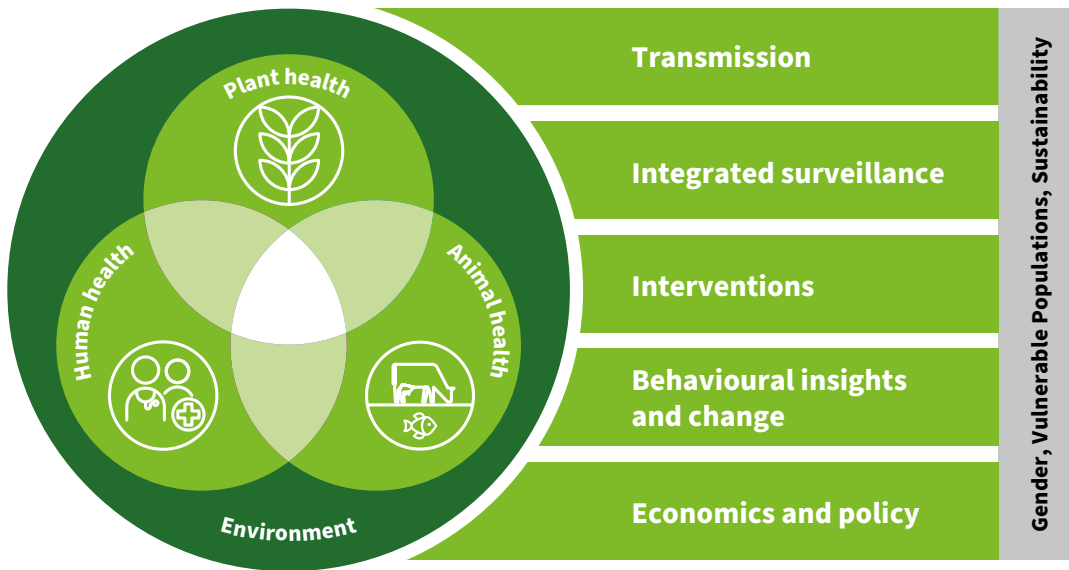
## 5. Developing the research agenda

To structure the research priority-setting exercise, a preliminary agenda-scoping consultation process was conducted with key AMR One Health stakeholders during April and May 2021 to identify areas where major research gaps exist (publicly available documents, expert opinion) in AMR prevention and control or where evidence is lacking. The total of 61 contributors included internal WHO headquarters and regional office professionals and external stakeholders in AMR and One Health. In addition, a Quadripartite organizations scoping session was held, and key donors active in the field of AMR research were consulted, including the Joint Programming Initiative on AMR, the Wellcome Trust, the UK aid programme through the Fleming Fund and the ESSENCE on Health Research network of research funders (16).

Five key areas (or pillars) emerged from the scoping process alongside three cross-cutting themes (Figure 3), namely: gender, vulnerable populations and sustainability. Gender is understood as a social construct (different from biological sex) that refers to socially constructed norms, roles, behaviours and attributes a given society considers appropriate. **Gender** plays a role in determining exposure to AMR, its potential impact and access to resources and interventions. **Vulnerability** is understood as relating to economically, socially or otherwise marginalized populations that harbour resistance microorganisms or are exposed to resistant infections, as well as populations that experience economic impacts indirectly related to AMR. Examples include poorer plant, livestock and aquaculture farmers threatened by the effects of AMR, as well as disadvantaged occupational groups in health care or livestock sectors. **Sustainability** is understood as the ability to meet the needs of the present generation without compromising the ability of future generations to also meet their needs. The concept comprises three aspects: economic/financial feasibility, environmental sustainability and social/cultural acceptance of AMR prevention and control initiatives. The five pillars and cross-cutting themes were used to structure data collection, analysis and a modified Delphi panel process, as well as reporting.



**Figure 3: The Five Pillars of the One Health Priority Research Agenda for Antimicrobial Resistance**



- **Transmission**

This pillar focuses on where transmission, circulation and spread of AMR occur among the environment, plants, animals and humans; what drives this transmission; where it happens; and its impact. This focus includes transmission dynamics, risk assessment and modelling, and how practices enacted by humans at the interface between humans, plants, animals and the wider environment (soil, water, air) enable the development and spread of resistance.

- **Integrated surveillance**

This pillar aims to identify priority research questions focusing on cross-sector surveillance that improves common technical understanding and exchange of information. Included are questions about harmonization, effectiveness, implementation of One Health integrated surveillance and applicability to LMICs; it may include considerations for innovative surveillance approaches to AMR.

- **Interventions**

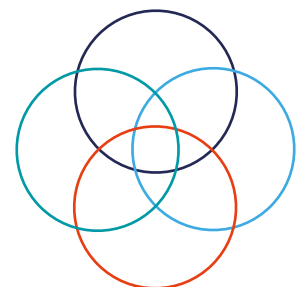
This pillar covers programmes, practices, tools and activities designed to prevent, contain or reduce the incidence, prevalence and dissemination of AMR, including optimal use of existing vaccines and other measures across the One Health spectrum.

- **Behavioural insights and change**

This pillar focuses on behavioural drivers of AMR by understanding influences on human behaviour in different contexts (social influences and support, livelihoods, financial resources, etc.). This pillar operates at multiple levels of complex systems, including organizational structures that enable or disable AMR mitigation, as well as individual and interpersonal sociocultural practices.

- **Economics and policy**

This pillar addresses investment and action in AMR mitigation from a One Health perspective. Included are policy, governance, legislative and regulatory instruments, cross-sector processes and strategies affecting AMR (e.g. regulation of antimicrobial manufacturing, use, disposal, monitoring), joint planning and policy goals among ministries. Cost-effectiveness considerations are also included to support development of the AMR investment case. Finally, this pillar includes financial sustainability and long-term financial impact.

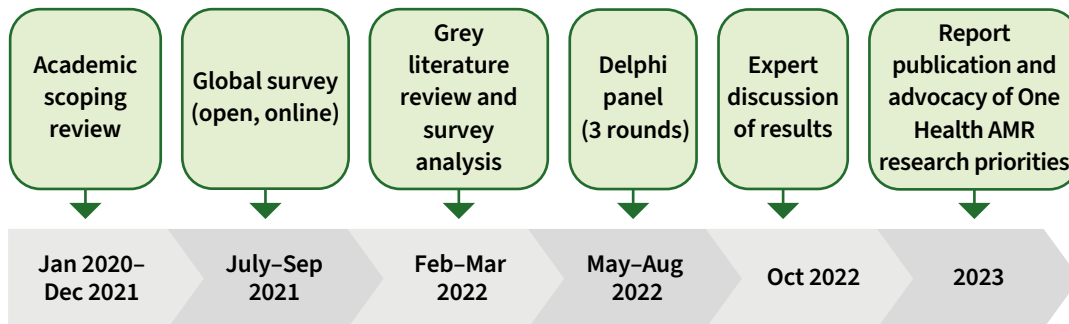


The pillars are not mutually exclusive. Further details on the methodology can be found in Annex 1 (“Detailed methodology”).

A mixed methods approach was implemented between January 2020 and October 2022 to identify and analyse One Health AMR research gaps and subsequently to prioritize a selection of them to establish the research agenda presented in this report.

Figure 4 illustrates the sequence of steps in the research agenda development process.

**Figure 4. Process and timeline for developing the One Health Priority Research Agenda for Antimicrobial Resistance**



## 5.1 Identifying research gaps

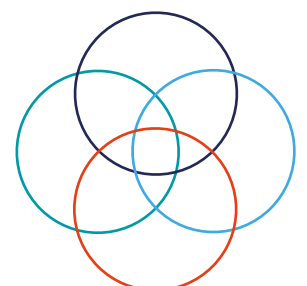
Four data sources were analysed to identify One Health AMR research gaps. These were:

- Results from a scoping review of academic literature published between January 2015 and December 2019 (17) conducted in January 2020, with an update at end of 2021.
- Results from a review of the grey literature conducted in February and March 2022. The same search approach was used as for the academic literature review and included literature published between January 2015 and January 2022.
- Results from a global open call online survey that targeted the One Health AMR stakeholder community conducted from July through September 2021.
- Opinion from global experts in the fields of AMR and One Health, obtained through the modified Delphi panel process (see section 5.2).

The following **exclusion criteria** were applied to all data sources:

- content on a single country, pathogen, disease, therapy, investigational agent, technology;
- not a research gap (e.g. capacity or training needs/gaps);
- product development or diagnostics;
- dated 2014 or earlier; and
- all languages except English.

The literature reviews identified 455 research gaps from 27 academic journal papers and 27 grey literature documents, respectively. The global open call online survey resulted in a total of 1620 anonymized responses to the call. From these responses, 290 participants filled out all demographic data. In total 2234 research suggestions were made. Gaps assigned to each pillar were analysed thematically to generate a set of consolidated research gaps per pillar. Evidence was not graded; rather, the focus was on harvesting and analysing a broad set of gaps for prioritization by global experts in the fields of One Health and AMR.



## 5.2 Prioritizing research gaps

To prioritize the consolidated research gaps, a modified Delphi panel process was conducted using an online platform. A Delphi panel process is a method for obtaining consensus “through controlled feedback from a panel – a group made up of experts or individuals knowledgeable on the subject” (18). A Delphi Panel process was used because it has wide validity across scientific communities, is suitable for online consultations and has been used by UN organizations in similar research prioritization exercises (19). The Delphi panel process used here is “modified”, because experts were given content to prioritize rather than being offered all content for their mutual consideration. Nevertheless, experts did have the opportunity to introduce additional research gaps not identified during earlier steps.

To ensure multidisciplinary and multisectoral contributions to the priority-setting exercise, the criteria for selection of experts considered their research expertise in One Health and/or AMR, and/or expertise in a scientific field relevant to the pillars.

Experts were selected to ensure global representation, including from low- and high-income settings, and balanced gender representation. Out of the 148 invited experts, 89 consented to take part in the modified Delphi panel process. During the consent process, experts were asked to state their primary areas of expertise and were consequently allocated to their respective pillars (65% both One Health and AMR; 24% AMR only; 3% One Health only; 8% declined to say).

Three rounds of the Delphi panel process were undertaken. In each round, experts were invited to assess the research gaps identified at the interface of One Health AMR against five criteria (Box 2). Round 1 used five criteria and Rounds 2 and 3 used four criteria. The “important” criterion was not used in Rounds 2 and 3, as it served as a screening question in Round 1

### Box 2. Definition of assessment criteria for the modified Delphi panel process

**Important:** This research question addresses a critical gap in current One Health AMR understanding and evidence generation.

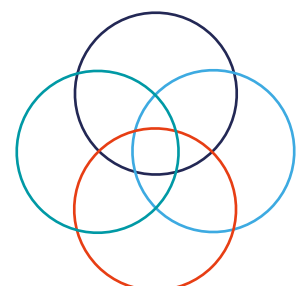
**Research capacity strengthening:** This research question is aimed at strengthening research capacity in LMICs.

**Actionable:** This research question will generate both understanding across One Health sectors and evidence that can realistically be implemented at scale in different settings, including those with low resources, over the short to medium term (4–8 years).

**Inclusive:** This research question will address the direct and indirect needs of the most vulnerable across One Health sectors over the short to medium term (4–8 years).

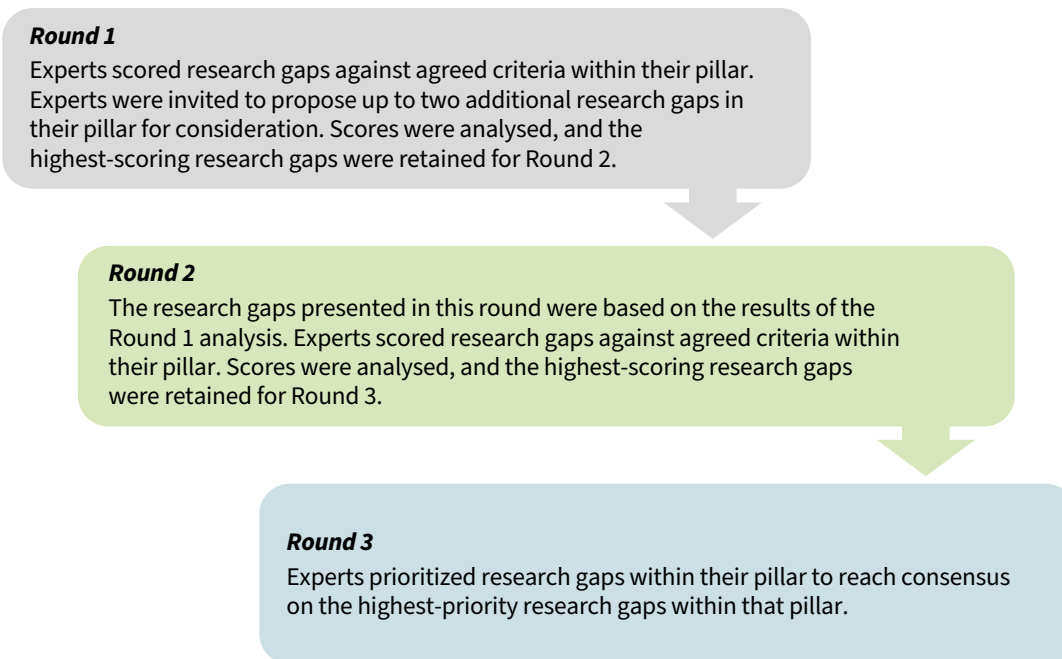
**Impactful:** This research question will generate and/or improve understanding and evidence across One Health sectors that can prevent, control and mitigate AMR over the short to medium term (4–8 years).

AMR: antimicrobial resistance; LMIC: low- and middle-income country.



The three rounds of the modified Delphi panel process were conducted between May and August 2022, as outlined in Figure 5.

### Figure 5. Modified Delphi panel process



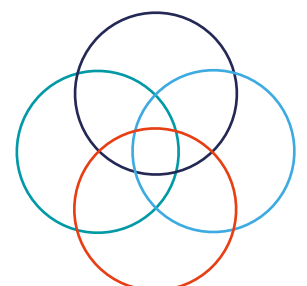
The total number of participants in the Delphi process was 78, 71 and 83 out of 89 experts for each round, respectively. Participation in each round varied between 13 and 18 experts by pillar. Not every invited expert participated in every round. Rounds remained open until a sufficient number of experts had participated per pillar. Annex 1 provides further details.

At the conclusion of the process, five interactive consultation workshops were convened, one per pillar, with the participating experts. The consultations were designed to share results from the modified Delphi panel process as well as to seek feedback and verification from the experts involved. The final wording of the priority research areas was sought and agreed to ensure consistency and clarity. Where experts agreed that two or more research areas overlapped, these areas were merged.

In addition, the consultation workshops agreed on five common reporting categories to provide priority research agenda users with further guidance on the sequence and potential impacts of the priority research areas:

- **methodology development** – research areas that focus on methodologies required to address research needs, particularly in LMICs;
- **operational research** – priority research areas that should be investigated under real-world conditions;
- **evaluation** – research areas that focus on understanding what works in different contexts;
- **framework conditions** – enabling structures and conditions that are a prerequisite to successful implementation, such as legislation and governance structures; and
- **dynamics and drivers of AMR** – research areas that focus on factors that accelerate the development and circulation of AMR.

After the priority research areas for each pillar were finalized, a set of top 10 research priority areas was extracted by taking the final two highest-priority research areas from each pillar. This step ensured representativeness of priorities across all five pillars.

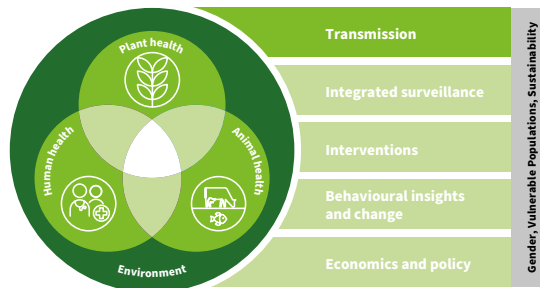


## 6. Results

In the results presented in this section, each pillar contains varying numbers of priority research areas. These results are built on consensus obtained by experts in the fields of One Health AMR in their respective pillar. The results section concludes with the final top 10 overall priority research areas.

### 6.1. Priority research areas for transmission

The research pillar for transmission focuses on development of AMR and where transmission, circulation and spread of AMR occur between the environment, plants, animals and humans; the drivers of transmission; and its impact in those sectors. This pillar includes transmission dynamics, risk assessment and modelling, and how practices at the One Health interface enable resistance to develop and spread.

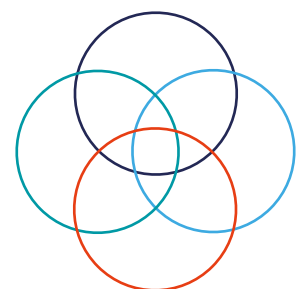


Current research on One Health AMR transmission has been characterized as anthropocentric (20), focusing on development and spread of AMR in sectors and activities that primarily impact human health. These include transmission in agrifood chains (21-29) and drug-resistant microorganisms in human health care facilities and clinical settings (30-34). Research on antimicrobials in crop/plant production (35-37) and the environment (37) is only just emerging. It is generally acknowledged that most AMR research has been undertaken predominantly in HIC and UMIC settings (23, 38-40) and that transmission dynamics outside HIC settings are less well understood (41). Globally, AMR might be more closely correlated to lack of sanitation than to reported use of antimicrobials (42, 43). However, the role of the environment as a reservoir of AMR is not fully understood (37, 44, 45).

Several areas require further exploration, including the drivers and dynamics of AMR (particularly at the interface of One Health); the transmission risks between humans, animals, plants and the environment; and the conditions that may drive development, including emergence of resistant profiles such as the presence and concentration of resistant genes and antimicrobial residues at the One Health interface.

To prioritize research areas in AMR transmission at the One Health interface, 21 global experts were invited to participate in the modified Delphi panel process. Twenty-five research gaps were introduced to Round 1. Twenty-five research gaps were taken forward to Round 2, which included nine research gaps suggested by experts in Round 1. Fifteen research gaps were taken forward to Round 3. Discussion during the post-Delphi webinar resulted in two research areas being merged (due to overlap) and one eliminated because fewer than half of the experts had voted for its inclusion.

The priority research areas identified for AMR transmission at the One Health interface focus on generating evidence of dynamics and drivers of AMR, especially to understand the impact of effluents and wastewater management across different sectors, under real-world conditions. Key differences in geographical settings, from urban to rural, and high to low income, change the configuration of major AMR risks at the One Health interface as well as how we understand and monitor transmission risks and drivers in resource-limited settings. These research areas also aim to elucidate knowledge on where interventions may be best targeted to curb the transmission of AMR and to reduce the spread of resistant microbes, particularly in the environment.

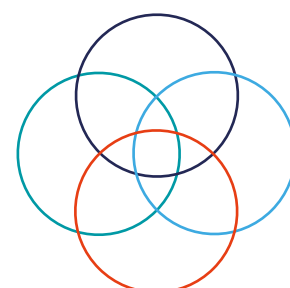


An important challenge for One Health AMR transmission research, as well as all other research pillars, is ownership of data and ethical conduct of research, including in low-income settings, that will ultimately benefit humans, animals, plants and the wider environment in that setting. Research may have different objectives which should be transparently defined in advance. Furthermore, agreed rules and sharing of data between different organizations, sectors and regions may be challenged by different levels of data protection requirements.

Table 1 presents the final set of priority research areas for transmission.

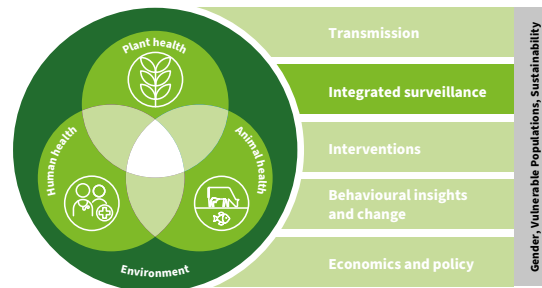
**Table 1. Final set of priority research areas for the transmission pillar**

|                                |   |
|--------------------------------|---|
| <b>Methodology development</b> | What are the low cost, high quality, high reliability methodologies that can be used to <b>identify and quantify sources and drivers, development, and circulation</b> of AMR between One Health sectors?   |
|                                | What are the highest quality, lowest cost, and most reliable <b>methods and (meta) data</b> for <b>describing and predicting</b> AMR transmission across One Health interfaces that could help inform policy?   |
| <b>Operational research</b>    | To what extent do <b>various infection prevention and control practices</b> in One Health settings <b>impact</b> the development and circulation of AMR in One Health Sectors?  |
|                                | How does AMR <b>transmission</b> (i.e., drivers, pathways, impact) across One Health sectors in HICs <b>differ</b> from LICs/LMICs?   |
|                                | What are the relative impacts of different <b>wastewater treatment</b> solutions on the development and circulation of AMR among One Health sectors?  |
|                                | How can the absence or poor management of critical water <b>sanitation</b> and hygiene <b>infrastructure</b> for human/animal/plant contribute to the circulation of AMR?   |
|                                | How does AMR circulation across One Health Sectors vary in the case of resistance to different <b>critically important antimicrobials</b> ?   |
| <b>Dynamics &amp; drivers</b>  | What impacts the <b>transmission</b> of resistant microorganisms between humans, animals, plants, and the environment, with a focus on conditions relevant to LIC/LMICs?  |
|                                | To what extent are human and animal <b>effluents and solid wastes</b> , and their <b>management and treatment</b> , from humans (including healthcare facilities and community settings) and from agri-food systems (including consumers) contributing to the development and circulation of AMR across One Health, <b>in different geographical settings</b> ? |
|                                | What are the most important AMR <b>transmission pathways</b> at the One Health interfaces in different settings including <b>LIC/LMIC settings</b> ?  |
|                                | What is the contribution of aquaculture to circulation of AMR in the One Health ecosystem by different types of <b>aquatic farming techniques/ systems</b> ?  |
|                                | In different <b>geographical settings</b> , what <b>economic factors</b> affect AMU and AMR transmission between One Health sectors?  |
|                                | To what extent are <b>effluents and solid waste</b> from <b>pharmaceutical and other industrial production</b> sites contributing to the <b>circulation</b> of AMR across One Health in different geographical settings?  |



## 6.2. Priority research areas for integrated surveillance

The research pillar for integrated surveillance focuses on cross-sector surveillance to improve common technical understanding and exchange of information about AMR/AMU between One Health sectors. This includes issues on harmonization, effectiveness and implementation of One Health integrated surveillance, and its applicability in LMICs. The surveillance pillar also considered innovations for AMR surveillance relevant to One Health.

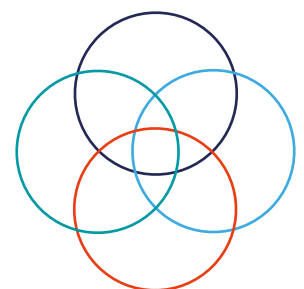


Several integrated surveillance systems have been implemented in countries, and others are in development. The International FAO Antimicrobial Resistance Monitoring (InFARM) data platform to track AMR in agrifood systems and AMU in crops and plants is currently in development by the FAO (46). WOAHA maintains the ANImal antiMicrobial USE Global Database (ANIMUSE) (47) that establishes baselines for countries to allow monitoring progress and implementation of regulatory frameworks. The WHO-led Global Antimicrobial Resistance and Use Surveillance System (GLASS) gathers AMR and AMU data in the human sector, collected from national coordinating bodies, with a growing number of participating countries (48). WHO has developed guidance on integrated surveillance of AMR in foodborne bacteria (49) and has also led integrated surveillance modelling of extended-spectrum beta-lactamase producing *Escherichia coli* across One Health sectors (50). The Codex Alimentarius guidelines support the design and implementation of integrated monitoring and surveillance of foodborne AMR/AMU along the agrifood chain and in food production settings (51). WOAHA has published standards on AMR and AMU surveillance and monitoring covering animals (52-54). The Quadripartite organizations are currently developing an integrated surveillance system platform across food, plant, environmental, animal and human sectors that will display the information collected by GLASS, InFARM and ANIMUSE.

Other than the monitoring systems noted, few other surveillance systems collect global data on AMR/AMU. Moreover, there is no global surveillance system for AMR in the environment nor are there any international guidelines or recommended methodologies to guide countries in setting up such a system. Surveillance infrastructure in LMICs is often hampered by a lack of sustainable financing, regulatory frameworks, laboratory capacity and human resources, necessary collection and analysis tools as well as poor data harmonization between existing systems across different One Health sectors (48). Harmonization should enhance the effectiveness and value of surveillance and determine what data to integrate (and how), as well as generate information that can be useful at the sector level (55). A clear gap is translating multisectoral surveillance data into policy and practice in local contexts.

Twenty-two experts were invited to participate in the integrated surveillance pillar. Seventeen research gaps were introduced in Round 1 of the modified Delphi panel process. Nineteen research gaps were taken forward to Round 2, which included five research gaps suggested by experts in Round 1. Fourteen research gaps were taken forward to Round 3. Analysis of the Round 3 results resulted in two research areas being eliminated because fewer than half of the experts voted for their inclusion. The integrated surveillance pillar had the highest level of consensus across all pillars and all rounds of the Delphi panel process.

Experts prioritized future research into methodological challenges for supporting integration of surveillance. Such research aims to ensure generation of meaningful data and analyses across all One Health sectors. Operational research and evaluation into how to develop and sustain surveillance in resource-constrained contexts were also considered important. Experts emphasized the need for globally agreed normative standards and criteria across One Health that can follow and measure the development and spread of AMR globally.





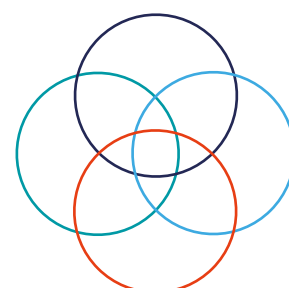
As noted previously, the difficulties in harmonizing integrated surveillance approaches have been well recognized. Determining comparability between different sectors remains challenging due to differences in geography and financial capacity within and between countries. Financial and infrastructural capacity to sustain integrated surveillance systems is a further barrier to effective surveillance. It is acknowledged that most data on current surveillance platforms are provided by HICs rather than by LMICs, suggesting that the availability of surveillance tools does not directly lead to surveillance at scale in all settings.

Table 2 lists the final set of priority research areas for integrated surveillance.

**Table 2. Final set of priority research areas for the integrated surveillance pillar**

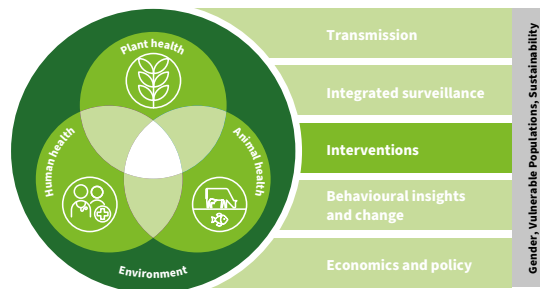
|                                |   |
|--------------------------------|---|
| <b>Methodology development</b> | What are the optimum <b>strategies and minimum standards</b> (and resources) for adequate laboratory and human resource <b>capacity</b> to establish and maintain quality integrated AMR surveillance systems at scale?   |
|                                | How can <b>existing AMR and AMU</b> surveillance data from humans, animals, plants and the environment be <b>meaningfully triangulated and/or integrated</b> to allow early identification of the development, escalation or circulation of resistance across One Health? |
|                                | What is the <b>minimum</b> feasible, representative and meaningful AMR/AMU monitoring/surveillance criteria and indicators package that can improve AMR/AMU monitoring across One Health in LMIC?   |
|                                | What are the highest-quality, lowest-cost and most reliable <b>approaches for sharing</b> integrated AMR/AMU surveillance data in a standardized <b>format</b> for different resource settings and the international community?   |
|                                | Which targets, methods and data-reporting formats most comprehensively characterize the <b>risks of evolution and circulation</b> of AMR across One Health sectors?   |
|                                | How can <b>priorities for implementation</b> of One Health integrated AMR/AMU surveillance components be identified and set and thereby address a current research gap?   |
|                                | How can <b>AMR hot spots</b> be proactively identified and mitigated using a One Health approach?   |
|                                | What are the <b>priority opportunities</b> for environmentally and financially sustainable <b>innovation</b> in integrated surveillance based on existing and emerging technology?  |
| <b>Operational research</b>    | How can the <b>limited availability of data</b> from integrated, multisectoral AMR surveillance programmes be addressed in <b>LMIC</b> ?  |
|                                | How can the <b>results</b> of integrated One Health AMR/AMU surveillance <b>be used</b> in practice by countries/regions?   |
| <b>Evaluation</b>              | What are the best approaches to <b>monitor and evaluate</b> integrated One Health surveillance <b>frameworks</b> for AMR/AMU in different <b>LMICs</b> ?  |

AMR: antimicrobial resistance; AMU: antimicrobial use; LMICs: low- and middle-income countries.



### 6.3. Priority research areas for interventions

The research pillar for interventions focused on programmes, practices, tools and activities designed to prevent, contain or reduce the incidence, prevalence and circulation of AMR. This pillar included optimal use of existing vaccines and measures at the One Health interface.



To date there is increasing, significant commitment to a One Health approach. Translation research was relatively well

funded before the COVID-19 pandemic (56). Interventions commonly implemented include clean and sustainable production and consumption of chemicals; water, sanitation and hygiene (WASH) measures; biosecurity and infection prevention and control (IPC) on farms and in health care facilities. However, significant gaps persist in understanding the availability of potential technical interventions and the reality of implementing these in LMIC contexts (57).

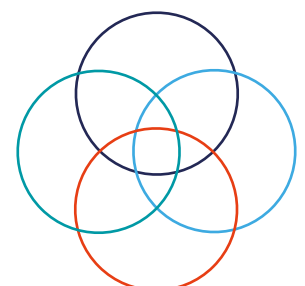
Few intervention models exist for measuring the impact of, for instance, optimal use of vaccination, despite increasing appreciation for the role they could play in reducing AMU (58). Recent studies of AMR dynamics in both LMICs and non-LMICs suggest that governance, sanitation, and human and animal health infrastructure may impact AMR more than AMU. But such interventions are difficult to evaluate for AMR impact (59). There is further a need to identify ways to better reflect equity and inclusion, including gender, in AMR interventions (60). Large-scale measures for mitigating risk along the antimicrobial life cycle (61), and measures of sustaining animal health that do not rely on veterinary antimicrobial drugs (57, 62) and thereby better integrate animal, human and plant health with biodiversity and ecosystem management (63), have been identified as possible areas of innovation.

Twenty-one experts were invited to participate in the interventions pillar. Twenty-eight research gaps were introduced in Round 1 of the Delphi panel process. Nineteen research gaps were taken forward to Round 2, which included five research gaps suggested by experts in Round 1. Fifteen research gaps were taken forward to Round 3. Discussion during the post-Delphi webinar resulted in two research areas being merged (due to overlap). In addition, one research area was eliminated as fewer than half of the experts voted for its inclusion.

Experts strongly prioritized evaluation of, and prioritization tools for, existing One Health interventions. The effectiveness of current and proposed interventions at the One Health interface, as well as how to evaluate them most efficiently, was also prioritized.

The long-term feasibility and localization of interventions, that is designing interventions that are not only fit for purpose but also adaptable to local conditions, remains a challenge. For interventions that have demonstrated success through robust evaluations, how to scale them in new settings and, accordingly, how to evaluate their effectiveness at scale remain a challenge. Criteria and measures for determining successful interventions at the One Health interface will likely differ by setting. Ensuring sustainable financing for interventions over the long term is essential. Efforts to obtain such financing should reiterate the critical need for robust evaluation and implementation research along the intervention design and implementation chain to ensure that interventions are cost-effective and achieve impact for AMR. Interdisciplinary and multisectoral collaboration to design, implement and evaluate interventions will be pivotal in addressing research priorities in different geographic and socioeconomic contexts.

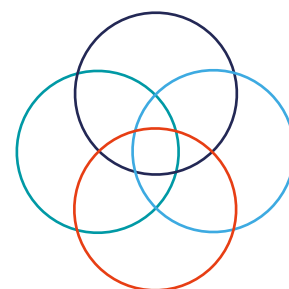
Table 3 lists the final set of priority research areas for interventions.



**Table 3. Final set of priority research areas for the interventions pillar**

|                                |   |
|--------------------------------|---|
| <b>Methodology development</b> | How can <b>research capacity in LMICs</b> be strengthened to catalyse <b>locally tailored collaboration and cooperation</b> between One Health-related sectors?   |
|                                | What <b>priority tools and frameworks</b> can assist tailoring of One Health interventions for national AMR action plans?   |
|                                | What <b>criteria</b> should be used to <b>assess</b> interventions that aim to prevent and control AMR at the One Health interface?   |
|                                | What <b>mix</b> of evidence and evaluation is needed to understand how to implement One Health AMR solutions most effectively in LMICs?   |
|                                | How could <b>implementation research</b> be <b>systematically incorporated</b> into the design of appropriate One Health interventions for AMR in <b>LMICs</b> ?  |
| <b>Operational research</b>    | How can One Health interventions that have proven impactful for AMR control and mitigation most effectively be <b>translated and scaled up in different contexts or differently resourced settings</b> ?            |
|                                | How can existing health and food production systems be <b>effectively integrated</b> and enhance One Health AMR interventions?  |
|                                | What are the <b>minimal resource</b> interventions required for supporting national integrated, multisectoral One Health AMR/AMU <b>surveillance</b> systems?   |
| <b>Evaluation</b>              | What <b>challenges</b> exist to the <b>systematic collection and analysis</b> of data for risk assessment and intervention impact <b>assessment</b> (epidemiological, economic, social, including equity) in LMICs? |
|                                | What has been the <b>relative impact</b> on AMR occurrence of: IPC, farm biosecurity, food safety, WASH and integrated pest management <b>measures</b> ?  |
|                                | What have been the most <b>impactful interventions</b> to prevent, control and mitigate AMR at the One Health interface?  |
|                                | What has been the <b>impact</b> on AMR across One Health sectors of <b>nationwide interventions</b> (e.g. vaccination, creation of/improvements to sewerage systems, legislation, education)?                       |
| <b>Framework conditions</b>    | How can we improve <b>early adaptation and innovation</b> for the prevention, control and mitigation of AMR across human health, animal health, plant health and the environment in <b>LMICs</b> ?                  |

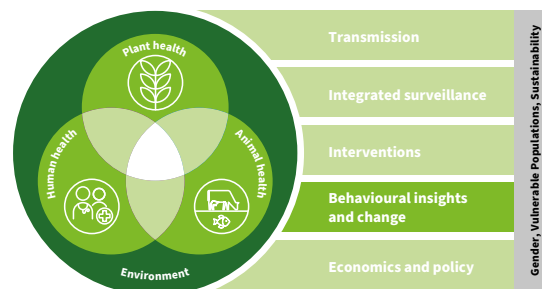
AMR: antimicrobial resistance; AMU: antimicrobial use; IPC: infection prevention and control; LMICs: low- and middle-income countries; WASH: water, sanitation and hygiene.



## 6.4. Priority research areas for behavioural insights and change

The research pillar for behavioural insights and change focuses on research addressing human behaviour that affects AMR, including ways to change behaviours that increase AMR risk. Research areas include understanding influences on human behaviour in varying contexts, such as social influences that support AMU in human, animal and plant sectors; livelihoods; and financial resources.

This pillar also considered behaviours at multiple levels of complex systems, including organizational structures that enable or disable AMR mitigation, as well as individual and interpersonal sociocultural practices.



A well-established literature on the rationale for treatment choice in the social sciences (64-67) provides many insights for understanding recourse to antimicrobials by different social groups across One Health sectors. Additionally, a substantial body of work has explored structural factors (68, 69) that constrain access to antimicrobials as well as enabling their production, sale and consumption (70). However, to date, comparatively few insights from the social and behavioural sciences have been applied (71) to AMR research at the One Health interface (72). This research agenda set out to explicitly recognize and remedy this lack.

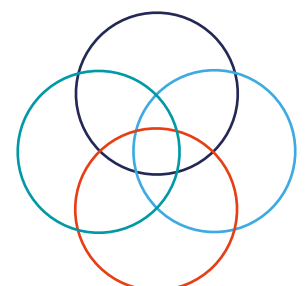
Research aimed at understanding the impact of humans on the dynamics of AMR transmission, risks and responses across One Health sectors is urgently needed. AMR approaches often do not consider how social, cultural and behavioural differences affect resistance development or transmission across One Health sectors (58). Several studies have identified a need for a fine-grained understanding of what influences and motivates human behaviour change for different stakeholders, such as antimicrobial manufacturers (72), policymakers (56), agrifood producers (36, 73) and other key actors along the antimicrobial production and consumption chain (57). Understanding how common interventions such as WASH and IPC measures are engaged with by different actors in different contexts has also been explored, although it has focused predominantly on human health considerations (74). Studies have also identified the need for research on human behaviour across terrestrial and aquatic farming systems, within their local regulatory and cultural contexts (75). Not least, the analysis of the link between AMR and gender is not often explored or understood, particularly how gender affects the responses to and effectiveness of interventions (76). Similarly, there is a clear lack of gender perspectives in One Health generally (77, 78).

Eighteen experts were invited to participate in the behavioural insights and change pillar. Thirty-one research gaps were introduced in Round 1 of the Delphi panel process. Twenty-four research gaps were taken forward to Round 2, which included four research gaps suggested by the experts in Round 1. Fifteen research gaps were taken forward to Round 3. Discussion during the post-Delphi webinar resulted in minor rewording only, for intelligibility. The behaviour insights and change pillar, together with the economics and policy pillar, had the lowest level of consensus across all pillars and in all rounds of the Delphi panel process, indicating its relative originality to the field.

The priority research areas focus on understanding behaviour across diverse groups and actors that are implicated in the development and circulation of AMR at the One Health interface. Experts prioritized operational research for understanding macrostructural and policy factors as well as microcommunity and individual behaviours. Methodology developments are clearly needed to support such novel research.

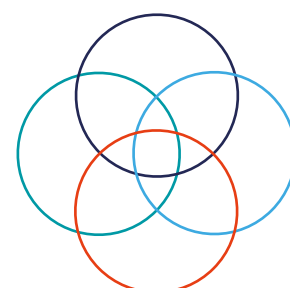
The challenges for the research priority areas are compounded by the complexity of understanding human behaviour across One Health sectors, regions and economic settings. The research priority areas in this pillar have explicitly taken account of context and variability in low-income settings. Multidisciplinary research teams with strong involvement in the social and behavioural sciences will be best placed to meet such challenges.

Table 4 details the final set of priority research areas for the behavioural insights and change pillar.



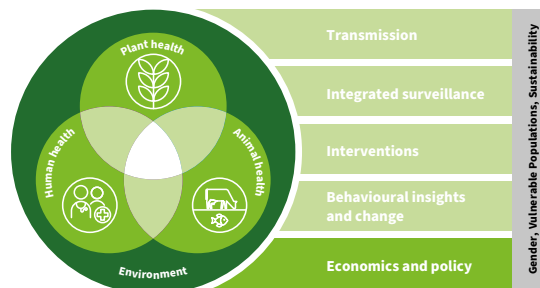
**Table 4. Final set of priority research areas for the behavioural insights and change pillar**

|                                |  |
|--------------------------------|--|
| <b>Methodology development</b> | How can <b>structural challenges and barriers</b> to behaviours related to AMR be <b>identified, characterized and assessed</b> in different <b>sociocultural contexts</b> ?   |
|                                | What is the role of <b>communication strategies</b> in promoting One Health AMR risk-reductive behaviours, and how can this role be leveraged?   |
|                                | What social/behavioural/economic strategies are most relevant for addressing One Health approaches to AMR?   |
| <b>Operational research</b>    | What strategies can be used to adapt effective behavioural interventions (e.g. immunization) from one context to another (e.g. Africa to Asia / rural to urban / human prescribers to vets)?   |
|                                | How can <b>information design sciences</b> (presenting information in an accessible and understandable way) be leveraged to improve effective understanding of the information across different stakeholders in the One Health AMR field?              |
|                                | Which strategies can improve community ownership and build consensus for AMR interventions directed at rationalizing the use of antimicrobials across sectors?   |
|                                | What are the barriers or drivers to translating behavioural insights and change findings into policy and implementation in different settings?   |
|                                | What behaviours and practices of antimicrobial product <b>manufacturers, wholesalers and retailers</b> create/drive development of AMR at the One Health interface, and how can these be changed to support prevention, control and mitigation of AMR? |
|                                | Which <b>actors and which of their behaviours</b> are believed to contribute most to AMR prevention, control and response across One Health sectors?   |
|                                | What <b>methods and tools</b> are needed to translate <b>gender and vulnerable group</b> considerations into inclusive behaviours related to AMR across One Health sectors.  |
|                                | How can <b>gender and vulnerable group-sensitive</b> behaviour change <b>methods</b> be integrated into One Health strategies for the prevention, control and mitigation of AMR?   |
| <b>Dynamics and drivers</b>    | What role do <b>people's attitudes and understanding of health and well-being</b> (for humans, animals, plants and the environment) play in influencing their attitudes and behaviour with respect to AMU and AMR?                                     |
|                                | What are the drivers of human exposure to AMR in diverse workplaces, communities and occupations across One Health sectors from a behavioural insights and change point of view?   |
| <b>Evaluation</b>              | What is the impact of incentives and disincentives (financial and nonfinancial) on AMR-relevant behaviour change across sectors and in different settings (e.g. diverse geographical contexts)?  |
|                                | What lessons can we learn from COVID-19 regarding behaviour change that can be adapted for the One Health approach to AMR?   |



## 6.5. Priority research areas for economics and policy

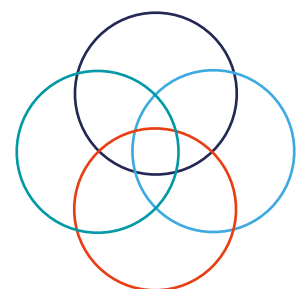
The research pillar for economics and policy addressed investment and action in AMR prevention and control from a One Health perspective. Included were policy, governance, legislative and regulatory instruments; cross-sector processes and strategies affecting AMR (e.g. regulations governing antimicrobial manufacturing, use, disposal, monitoring); and joint planning and policy goals among ministries. This pillar also considers cost-effectiveness in support of an AMR investment case, financial sustainability and long-term financial impact.



The GAP (Objective 4) encourages “effective and enforceable regulation and governance for licensing, distribution, use and quality assurance of antimicrobial medicines in human and animal health” (6). Since then, governance and oversight of antimicrobials along the supply chain have only grown in importance. The most recent call to action of the Global Leaders Group on AMR cited “strengthened governance and oversight” as the lead general principle to ensure an effective AMR response (79). One Health has provided “a converging way to conceptualise and address AMR”; moreover, such framing does not necessarily have to “reconcile conflicting values and interests but ... can ... clarify and help to explain the intrinsic tensions in the debate, and thereby facilitate discussion and negotiation” (34). The inclusion of economic analyses to understand efficient use of resources, cost-effectiveness and the marginal value of interventions (80) can further support the development of an investment case for AMR. Current AMR global governance relies on nonbinding governance mechanisms. These mechanisms make it possible to balance AMR response with other priorities, such as economic development and food security, but they do little to encourage sticking to voluntary commitments as set out in NAPs on AMR (81). However, it is clear that legally binding mechanisms are an important but insufficient condition in regulating AMU (82). Additionally, from the vantage of LMICs the global response to AMR appears to be largely driven by HICs, with little possibility for LMICs to share and drive the agenda. Better communication and increased LMIC participation on equal terms are required (56).

A dearth lack of risk assessment, cost-effectiveness and marginal costing studies has been recognized as an important research area to address (23, 56, 83, 84). Analysis of policy conflicts is notably lacking, particularly regarding potentially negative impacts of changes in AMU on the food supply and management of AMR in the food system (75). For instance, policy analyses in LIC/LMIC contexts on failure to enforce existing regulation would support reduced AMU (36). Successful AMR mitigation efforts may ultimately depend on national, subnational and local contexts (such as governance, sanitation and infrastructure), but relatively few data exist to assess cost-related outcomes (59). A persistent challenge is obtaining matching domestic funding from LMICs for donor funding and the recurring question of return on investment (e.g. advanced wastewater treatment plant systems deployed at financial cost but also significant health gains for all One Health sectors) (14, 56). Also notable is that human health tends to receive the greatest public investment in AMR mitigation, with significantly less going to animal, plant/crop and environmental sectors. There appears to be little clarity for policymakers on how countries could or should work towards an enabling environment for One Health AMR prevention and control within their own particular context (57).

Seventeen experts were invited to participate in the economics and policy pillar. Twenty-four research gaps were introduced in Round 1 of the Delphi panel process. Twenty-four research gaps were taken forward to Round 2, which included 11 topics suggested by experts in Round 1. Fourteen research gaps were taken forward to Round 3. Discussion during the post-Delphi webinar resulted in five research areas being merged to form two priority research areas (due to overlap) and three being eliminated as fewer than half of the experts voted for their inclusion.



Experts prioritized methodological developments that support policy implementation and governance decision-making, along with operational research and evaluation on how government structures and government behaviour can optimize AMR prevention and reduction. The priorities target practical research that can support governments to act on AMR within their specific context and constraints.

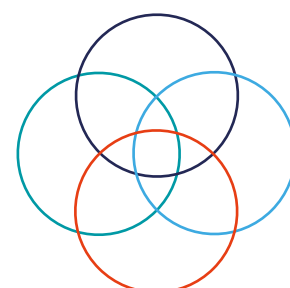
A clear challenge for pursuing these research priorities will be access to and management of financial information, as well as lack of data and poor reliability in contexts in which economic monitoring systems are weak.

Table 5 details the final set of priority research areas for the economics and policy pillar.

**Table 5. Final set of priority research areas for the economics and policy pillar**

|                                |   |
|--------------------------------|---|
| <b>Methodology development</b> | What would a One Health AMR <b>socioeconomic impact assessment</b> based on accurate and cost-effectively collected data (e.g. harmonized methodology and indicators) in <b>low-resource settings</b> optimally look like?  |
|                                | How can governments identify, prioritize and institutionalize the most relevant cross-cutting, sector-specific AMR <b>policy options</b> and regulatory frameworks, and <b>financing strategies</b> to sustainably tackle AMR across One Health sectors, given their different implementation challenges?   |
|                                | Which <b>innovative</b> (either new or adapted) <b>methods</b> that lead to actions are needed for the <b>evaluation of AMR prevention and control</b> across One Health sectors in LMICs, with a focus on low-cost, high-quality, high-reliability policy relevance?                                       |
|                                | What is the <b>optimal financial resource strategy</b> that will <b>sustain</b> support for <b>One Health AMR interventions</b> ?   |
|                                | What would a harmonized conceptual <b>framework, method and key indicators</b> that systematically include <b>equity</b> considerations in One Health AMR policies optimally look like?   |
| <b>Operational research</b>    | How can operational and/or implementation research systematically <b>capture learning from AMR NAP</b> implementation practice and serve as the basis for <b>improvement</b> at the country, regional and global level (for instance identification and development of impactful policies and legislation)? |
|                                | How can appropriate and acceptable <b>AMU or AMR reduction indicators or targets</b> for national governments or sectors be developed, reached and reported?  |
|                                | What <b>impacts</b> can <b>national and subnational policies</b> have on AMR prevention, control and response across One Health sectors, and how should they be measured?   |
| <b>Evaluation</b>              | What lessons and synergies for AMR reduction <b>can be learnt</b> and leveraged from other <b>policy initiatives</b> (e.g. climate change, fisheries management) to tackle <b>collective action problems</b> ?  |
|                                | How should governments <b>incentivize and drive material and immaterial innovation</b> into solutions to AMR in areas where the profit motive is currently insufficient?  |

AMR: antimicrobial resistance; AMU: antimicrobial use; LMIC: low- and middle-income country; NAP: national action plan.



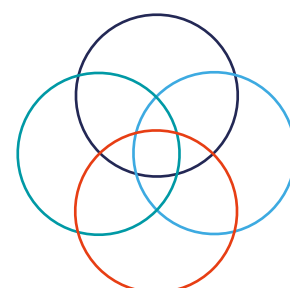
## 7. Consolidated top 10 priorities

The top 10 priority research areas are set out in Table 6. These 10 topics represent the highest-ranked research priorities across all three Delphi rounds per pillar and can be considered the most *important* research priority areas; having the greatest potential for *research capacity strengthening*; and being the most *actionable, inclusive and impactful* in the field of One Health AMR over the short to medium term (4–8 years).

**Table 6. Top 10 priority research areas**

| Pillar                                 | Highest-priority research areas  |   |
|--|--|---|
| <b>Transmission</b>                    | To what extent do <b>various IPC practices</b> in One Health settings <b>impact</b> the development and circulation of AMR in One Health sectors?  | What impacts the <b>transmission</b> of resistant microorganisms between humans, animals, plants and the environment, with a focus on conditions relevant to <b>LMICs</b> ?   |
| <b>Integrated surveillance</b>         | What are the optimum <b>strategies and minimum standards</b> (and resources) for adequate laboratory and human resource <b>capacity</b> to establish and maintain quality integrated AMR surveillance systems at scale?    | How can <b>existing AMR and AMU surveillance data</b> from humans, animals, plants and the environment be <b>meaningfully triangulated and/or integrated</b> to allow early identification of the development, escalation or circulation of resistance across One Health sectors?                         |
| <b>Interventions</b>                   | How can One Health interventions that have proven impactful for AMR control and mitigation most effectively be <b>translated and scaled up in different contexts or differently resourced settings</b> ?                   | What <b>challenges</b> exist to the <b>systematic collection and analysis</b> of data for risk assessment and intervention impact <b>assessment</b> (epidemiological, economic, social) in LMICs?   |
| <b>Behavioural insights and change</b> | How can structural <b>challenges and barriers</b> to behaviours related to AMR be <b>identified, characterized and assessed</b> in different <b>sociocultural contexts</b> ?   | What <b>strategies</b> can be used to <b>adapt effective behavioural interventions</b> (e.g. immunization) from one context to another (e.g. Africa to Asia / rural to urban / human prescribers to veterinarians)?   |
| <b>Economics and policy</b>            | What would a One Health AMR <b>socioeconomic impact assessment</b> based on accurate and cost-effectively collected data (e.g. harmonized methodology and indicators) in <b>low-resource settings</b> optimally look like? | How can governments identify, prioritize and institutionalize the most relevant <b>cross-cutting, sector-specific AMR policy options</b> and regulatory frameworks, and <b>financing strategies</b> to sustainably tackle AMR across One Health sectors, given their different implementation challenges? |

AMR: antimicrobial resistance; AMU: antimicrobial use; IPC: infection prevention and control; LMICs: low- and middle-income countries.





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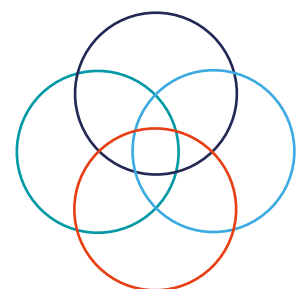
## 8. Considerations and limitations

The mixed methods approach taken to develop this One Health Priority Research Agenda for AMR ensured wide participation from experts and global stakeholders in the fields of One Health and AMR. Such an approach sought to capture the breadth of research gaps at the One Health interface, across disciplinary and geographic boundaries. The global open call online survey and the modified Delphi panel process were conducted online, enabling full and autonomous participation and ensuring confidence in the authenticity of views presented through these platforms. Rigorous review of both academic and grey literature ensured timeliness and comprehensiveness of research gaps presented to experts for their opinion during the modified Delphi process. The prioritization presented in this document reflects the outcome of the process and is ultimately based on the opinion of experts.

Several limitations within this approach are also acknowledged. The Delphi method is by nature subjective in that the prioritization process is influenced by experts' background, demographic characteristics, disciplinary qualifications and experience.

The research gaps presented in the Delphi panel process deliberately took a global perspective. Further work is needed to develop the final set of priority research areas into research questions that are relevant to local and regional settings.

Limitations are further discussed in Annex 1.



## 9. Research agenda for action

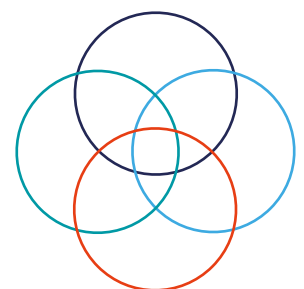
This report has presented a One Health Priority Research Agenda for AMR. It is focused on much needed research at the One Health interfaces and is complementary to other One Health sector-specific research agendas.

This research agenda aims to catalyse and direct future research in One Health AMR with a focus on low-resource settings, applying an equity lens. The research agenda reflects the urgent need to invest in One Health AMR research, develop new interdisciplinary local and global research partnerships, bring together diverse research skills and generate new methodologies and evidence to support the prevention and control of AMR across One Health sectors. Research capacity building in LMICs will be key for addressing the research gaps and development of evidence to inform One Health NAPs on AMR.

Global experts in the fields of One Health and AMR identified research priority areas across five pillars which they regarded as being the most important; having the greatest potential for *research capacity* strengthening; and being the most actionable, *inclusive and impactful* in the field of One Health AMR over the short to medium term (4–8 years).

For the transmission pillar, priorities focus on generating evidence of dynamics and drivers of AMR under real-world conditions. For the integrated surveillance pillar, experts prioritize research into methodological challenges for supporting integration of surveillance, ensuring that research can generate meaningful and actionable data and analyses across all One Health sectors. Within the interventions pillar, priorities focus on implementation research with substantive evaluation of existing interventions in One Health and tools to enable such evaluation. Experts in the behavioural insights and change pillar prioritize understanding human behaviour across diverse groups and actors that are implicated in the development and circulation of AMR at the One Health interface. In the economics and policy pillar, priorities focus on social science research that can support governments in acting on AMR within their specific contexts and constraints.

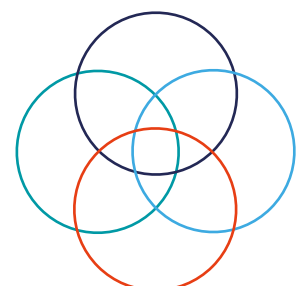
The research agenda described here requires contextualization at the regional and country level and development of specific research questions relevant to the needs of different countries and One Health settings. The implementation of the priority research agenda will require researcher engagement and funding. The findings will support development of policy and practice-relevant evidence for countries to simultaneously address the threat of AMR and facilitate their achievement of the SDGs for 2030.



# Glossary

The purpose of this glossary is solely to aid understanding and interpretation of the research agenda outlined in this document.

|                                    |  |
|------------------------------------|--|
| <b>Antimicrobials</b>              | Antimicrobials are agents used to prevent, control and treat infectious diseases in humans, animals and plants. They include antibiotics, fungicides, antiviral agents and parasiticides. Disinfectants, antiseptics, other pharmaceuticals and natural products may also have antimicrobial properties.   |
| <b>Antimicrobial resistance</b>    | Antimicrobial resistance (AMR) occurs when bacteria, viruses, fungi and parasites no longer respond to antimicrobial agents. As a result of drug resistance, antibiotics and other antimicrobial agents become ineffective and infections become difficult or impossible to treat, increasing the risk of disease spread, severe illness and death.  |
| <b>Development and circulation</b> | These terms cover the evolution and emergence, dissemination and spread of AMR.  |
| <b>Equity</b>                      | The absence of unfair, avoidable or remediable differences among groups of people, whether those groups are defined socially, economically, demographically or geographically or by other dimensions of inequality (e.g. sex, gender, ethnicity, disability or sexual orientation).  |
| <b>Gender</b>                      | A social construct (differing from biological sex) referring to socially constructed norms, roles, behaviours and attributes that a given society considers appropriate for a gender construct. Gender plays a role in determining exposure to AMR, potential impact and access to interventions.  |
| <b>Sustainability</b>              | Sustainability is understood here as being able to meet the needs of the present generation without compromising the ability of future generations to also meet their needs.   |
| <b>Vulnerability</b>               | In the context of AMR, vulnerability is understood as relating to economically, socially or otherwise marginalized populations that harbour or are exposed to resistant infections, as well as populations that experience economic impacts indirectly related to AMR. This includes poorer crop, livestock and aquaculture farmers threatened by the effects of AMR and disadvantaged occupational groups in health care or livestock sectors |



# Annex 1. Detailed methodology

Four sources were used to collect and analyse data to identify and prioritize One Health AMR research areas. These were:

- Results from a scoping review of academic peer-reviewed literature conducted in January 2020, searching literature published between January 2015 and December 2019, with an update at end of 2021.
- Results of a review of the grey literature conducted in February and March 2022. The same search approach was used as for the academic literature review and included literature published between January 2015 and January 2022.
- Results from a global open call online survey that targeted the One Health AMR stakeholder community and was conducted between July and September 2021.
- Opinion from global experts in the fields of AMR and One Health, obtained through the modified Delphi panel process (see section 5).

The data collection and analysis approach and steps taken are provided in detail in the following sections. To structure the research priority-setting exercise, a preliminary agenda-scoping consultation process was conducted with key AMR One Health stakeholders. The process resulted in five pillars, namely: transmission, integrated surveillance, interventions, behavioural insights and change, and economics and policy. In addition, an equity lens with cross-cutting areas such as gender, vulnerable populations and sustainability was applied. Full definitions of these pillars and the cross-cutting areas are found in the One Health Priority Research Agenda for AMR document.

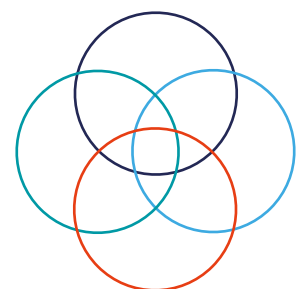
## 1. Academic literature review

WHO completed a scoping review focused on academic literature published between January 2015 and December 2019 (17). An update was conducted to capture any additional literature published up to end of 2021. English-language reviews or meta-analyses were sought in searches of four databases, using the following search terms:

- Web of Science: TI = ((antibiotic or antimicrobial or antifungal or antiparasitic) AND resistan\* AND (review or meta-analysis));
- PubMed: ((antibiotic[Title] OR antimicrobial[Title] OR antifungal[Title] OR antiparasitic[Title]) AND resistan\*[Title]) AND (review[Title] OR meta-analysis[Title]);
- Scopus: TITLE ((antibiotic OR antimicrobial OR antifungal OR antiparasitic) AND resistan\* AND (review OR meta-analysis)); and
- Ovid MEDLINE: ((antibiotic OR antimicrobial OR antifungal OR antiparasitic) and resist\* and (review or meta-analysis)).m\_titl.

Exclusions were made if the academic article focused on a single pathogen, country, disease, therapy, investigational agent or technology, or if it did not clearly identify a research gap or was in a language other than English.

The data from the initial and updated academic literature reviews were coded for research gaps for different One Health sectors and also across sectors using a code termed “interface”. Only research gaps that were coded as interface were extracted from the completed academic reviews for inclusion in this research prioritization exercise. From the original and updated scoping reviews of academic literature, and Quadripartite additions, 27 academic papers were identified for inclusion in the overall gaps analysed.



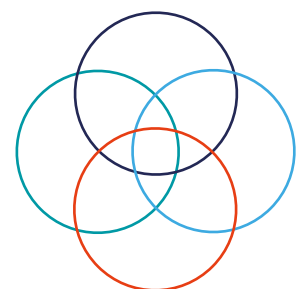
## 2. Grey literature review

A review of grey literature was undertaken in February and March 2022. The search parameters were the same as for the academic literature reviews completed earlier by WHO:

- Date range January 2015 to March 2022.
- English language.
- Publicly available.
- Reports and documents (see exclusion criteria in this section for types of grey literature that were excluded).
- Global, international, regional, multicountry.
- Specifically discusses “across sectors” using words or phrases such as: One Health (and spelling variations such as One health, Onehealth), multisectoral, integrated, intersectoral, interface, interconnected, interdependence, collaborative/collaboration and One Health coordination mechanisms, alongside the search terms outlined in section 1 in the academic review relating to antimicrobial resistance/AMR.
- Identifies research gaps using words or phrases such as: gaps; challenges; has/have not been studied/reported/elucidated; is required/needed; the key question is/remains; it is important to address; insufficient or inconsistent; lacking/lacks, poorly understood, poor quality (e.g. due to methodological shortcomings, sparse data or inconsistent results); or recommends further (specific) research (e.g. types of interventions, participants or outcome measures that should be assessed or included in that research).

Exclusion criteria were as follows: documents dated 2014 or earlier; all languages except English; news items, blogs, toolboxes; academic journal articles; reports on product development or diagnostics; and reports on a single: country, pathogen, disease, therapy, investigational agent, technology; a research gap not identified, gap was not One Health, gaps were not research gaps (e.g. capacity or training needs or gaps).

The initial search approach aimed to identify a list of important organizations in the field of One Health and AMR. Relevant organizational websites for key documents were searched that matched the criteria utilizing the keywords identified in sections 1 and 2 of this annex. Organizations targeted in the initial search included: FAO, UNEP, Wellcome Trust, WHO, WOH and the World Bank. However, the keyword search did not consistently turn up documents firmly focused on the interface or One Health AMR. In mid-February 2022, the approach was adapted to a narrative review of seminal documents starting with the most recent, relevant documents that used the core keywords (those in the search criteria outlined in sections 1 and 2). These documents were identified from Google searches. Suggestions from Quadripartite internal experts were included. The reference lists of the identified reports and documents were used to identify further relevant literature using a snowball approach. In addition, targeted searches were conducted using cross-cutting area keywords (equity, gender, sustainability) to capture further relevant resources.



### 3. Consolidating academic and grey literature review results

All documents identified through the academic and grey literature reviews were initially screened to determine whether they were relevant to or explicitly explored content at the One Health interface. Those that met inclusion criteria were saved to a bibliographic database. Documents were reviewed and relevant gaps harvested into a spreadsheet. While relevant to One Health and/or AMR, not all documents reviewed articulated specific research or implementation gaps within the criteria outlined in sections 1 and 2. Documents that did not meet all inclusion criteria were excluded. All harvested research gaps from the grey and academic literature were charted in a spreadsheet. A total of 455 research gaps were harvested from 54 (27 academic and 27 grey) documents and sorted into one or more of the five pillars. Some gaps were represented in more than one pillar owing to their relevance to multiple pillars.

Cross-cutting areas were identified when a harvested gap from a grey or academic literature review was sorted into a pillar. From all the gaps harvested, 23 gaps referring to a cross-cutting area were identified: eight explicitly referenced a need to include gender analyses in One Health AMR research; four referenced a need for equity and greater socioeconomic inclusiveness in research; 11 specifically noted a lack of research in LMICs.

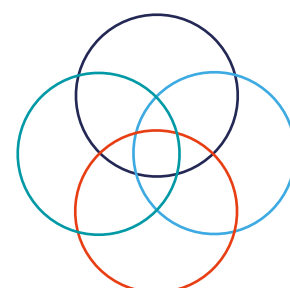
Gaps assigned to each pillar were analysed thematically over three rounds to generate a set of consolidated gaps per pillar. Reflection was conducted at each round of gap analysis to develop coherence across the data set. Neither the academic nor the grey literature reviews graded the available evidence. The focus was on harvesting all gaps identified within the documents available in the broad field of One Health AMR from 2015 to early 2022.

All gaps were consolidated and sorted into a pillar, resulting in a total of 455 gaps. Table A1.1 shows the breakdown per pillar.

**Table A.1. Research gaps identified from literature reviews by pillar**

| Pillar                          | No.        |
|---------------------------------|------------|
| Transmission                    | 131        |
| Integrated surveillance         | 74         |
| Interventions                   | 84         |
| Behavioural insights and change | 44         |
| Economics and policy            | 112        |
| <b>Relevant to all pillars</b>  | <b>10</b>  |
| <b>Total</b>                    | <b>455</b> |

The list of all academic and grey literature consulted is provided at the end of this document.



## 4. Global open call online survey

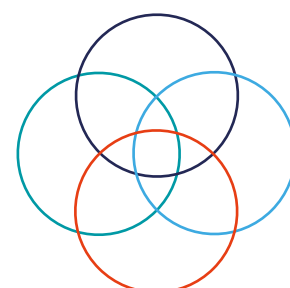
### 4.1. Data collection

A global open call online survey titled *Research questions for the development of a One Health priority research agenda for antimicrobial resistance* was conducted through an online WHO Dataform survey tool. The respondents were invited to nominate/select up to three research questions (rather than identify gaps per se) in each of the five pillars and one cross-cutting area. Survey respondents were also invited to nominate/suggest three additional research questions (not gaps per se) they considered to be important. The data were downloaded to a spreadsheet and analysed with the aim of collating suggested research questions from a global audience. A total of 1620 anonymized responses to the call were recorded. Two hundred ninety respondents filled out all demographic data. In total, 2234 research question suggestions were made. Of these, 2107 were nominated within pillars; 127 were proposed in the additional questions section and subsequently coded to one of the five pillars. Respondents were almost spread across geographies, with a slightly greater response rate from HICs.

Table A1.2 provides a breakdown of research suggestions by pillar.

**Table A.2. Research suggestions made by global open call online survey respondents**

| Pillar                          | Research questions proposed |
|---------------------------------|-----------------------------|
| Transmission                    | 468                         |
| Integrated surveillance         | 349                         |
| Interventions                   | 438                         |
| Behavioural insights and change | 308                         |
| Economics and policy            | 430                         |
| Cross-cutting areas             | 241                         |
| <b>Total</b>                    | <b>2234</b>                 |



**Table A.3. Survey respondents by pillar and country income level**

| Pillar                          | HICs       | LMICs     | Insufficient information | Missing demographic data | Total      |
|---------------------------------|------------|-----------|--------------------------|--------------------------|------------|
| Transmission                    | 76         | 41        | 38                       | 4                        | 159        |
| Integrated surveillance         | 70         | 38        | 39                       | 2                        | 149        |
| Interventions                   | 74         | 40        | 38                       | 3                        | 155        |
| Behavioural insights and change | 61         | 35        | 30                       | 3                        | 129        |
| Economics and policy            | 72         | 43        | 37                       | 3                        | 155        |
| Cross-cutting areas             | 39         | 28        | 19                       | 1                        | 87         |
| <b>Total</b>                    | <b>101</b> | <b>76</b> | <b>48</b>                | <b>65</b>                | <b>290</b> |

HICs: high-income countries; LMICs: low- and middle-income countries.

#### 4.2. Analysis

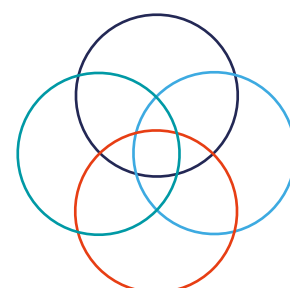
The Microsoft Excel data file was exported into NVivo for analysis. An iterative inductive and deductive thematic analysis of the data was conducted. The global open call online survey respondents were invited to suggest research questions under the pillars which were then used as an a priori structure for the analysis (hence deductive). Thereafter, within each pillar, the research questions proposed by respondents were analysed inductively and sorted into codes and within codes into subordinate themes. The coding structure was designed iteratively; codes and themes were cross-checked. Each research question was assigned to a single theme only within a code in each of the pillars. Consideration was given to whether the research question was relevant to LMICs and to One Health AMR. Each theme was subsequently defined, and exemplar questions indicative of the breadth of suggestions made and their relevance to the aims of the study were identified and/or developed before being collated. The researchers either proposed the most relevant research questions as exemplars for that theme, adapted the wording of the most relevant research questions for readability and clarity or adapted the wording to combine research questions as proposed elements of enquiry into a single research question.

#### 4.3. Integrating and finalizing research questions for the Delphi prioritization process

One hundred fifty-four research questions were generated across the pillars, integrating the literature review and global open call online survey analyses.

The themes identified through literature reviews and the exemplar questions identified through the online survey were collated and further analysed to develop a combined set of consolidated research questions to take into the Delphi process.

The data were reviewed several times to identify common themes within the data set. Each pillar was coded iteratively for recurrent themes arising within the identified themes across both data sources. There appeared to be more common themes within the transmission and integrated surveillance pillars generally than within the behavioural insights and change / economics and policy / interventions pillars. Common themes from both data sets were then refined to balance the challenge of being overly broad and not granular enough or, conversely, being so granular and detailed as to prevent expert engagement with the list in the modified Delphi process and consequently induce dropout.





During the literature review, some research gaps were identified across multiple data sources, whereas other research gaps emerged less often. Irrespective of how often research gaps arose during gap harvesting, all research gaps were considered of equal importance.

The final list of research questions emerging from the analysis of the combined survey and literature review data was reviewed for minor edits and intelligibility. Research questions were also edited to reduce overlap among the pillars. Nonetheless, the final set of research questions presented to experts participating in the modified Delphi process do contain some degree of overlap. In total, 126 research questions were presented to 89 global experts in the modified Delphi process for prioritization.

## 5. Modified Delphi process

To prioritize the consolidated research questions, a modified Delphi process was conducted through an online platform. The Delphi process aims at obtaining consensus “through controlled feedback from a panel – a group made up of experts or individuals knowledgeable on the subject” (18). The Delphi process offers wide validity across scientific communities, is suitable for online consultations and has been employed by UN organizations in similar research prioritization exercises (19). The Delphi process used here is “modified”, because experts were given content to prioritize rather than being offered all content for their mutual consideration. Nevertheless, experts did have the opportunity to introduce additional research questions not identified during earlier steps.

### 5.1. Expert selection

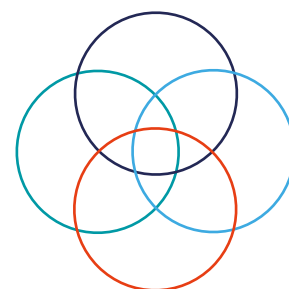
The Quadripartite identified experts to be invited to participate. Following their consent, they were allocated to their respective pillars in line with their areas of expertise. The experts were selected based on global representation, including participants from LMICs and HICs and also from a range of geographical regions. The following criterion was used to identify experts for invitation to the process:

- research background/frontline research in
  - One Health and/or
  - expertise in AMR and/or
  - expertise in a scientific field that may be relevant to AMR.

Ethical clearance to conduct the modified Delphi process was sought and obtained from the University of Melbourne Ethics Committee. One hundred forty-six experts from One Health and/or AMR and/or a scientific area relevant to AMR were invited to join. One hundred thirteen signed an informed consent form to join the process, and 89 joined the process with 18–21 experts per pillar.

Experts were chosen for their multidisciplinary and multisectoral expertise. Slightly more men than women participated (male 54%; female 46%). Most participants had primary expertise in One Health and AMR. Most participants (65%) self-nominated as having both One Health and AMR expertise. About one quarter (24%) self-identified as having AMR expertise only. Only 4% self-nominated One Health expertise only, and 7% nominated neither AMR nor One Health or left this question blank in their consent survey. Note that it was expected that some experts might have less One Health and/or AMR expertise, but they were selected based on their expertise in a pillar (such as economics and policy or behavioural insights and change) or a cross-cutting area (such as gender). These areas are generally less well developed for AMR and One Health.

All experts who consented to participate received a pre-Delphi pack outlining the overall process and were invited to a pre-Delphi briefing webinar. The webinar took place on 10 May 2022. The webinar covered: the background and aim of the One Health AMR research prioritization exercise; results from the research question formulation process; an overview of the modified Delphi process; questions regarding process; and summation/closing remarks.



## 5.2. Conducting the modified Delphi process

The modified Delphi process was conducted for each pillar in the same way and consisted of three rounds of consultation. It was undertaken between May and August 2022 using an online platform (Qualtrics) to deliver questionnaires and collect answers. Experts were invited to rate research questions in their pillar against a set of assessment criteria (see box).

*Important:* This research question addresses a critical gap in current One Health AMR understanding and evidence generation.

*Research capacity strengthening:* This research question is aimed at strengthening research capacity in LMICs.

*Actionable:* This research question will generate both understanding across One Health sectors and evidence that can realistically be implemented at scale in different settings, including those with low resources, over the short to medium term (4–8 years).

*Inclusive:* This research question will address the direct and indirect needs of the most vulnerable across One Health sectors over the short to medium term (4–8 years).

*Impactful:* This research question will generate and/or improve understanding and evidence across One Health sectors that can prevent, control and mitigate AMR over the short to medium term (4–8 years).

### Round 1

Experts were asked to rate each research question within their pillar against all five assessment criteria. The response options were:

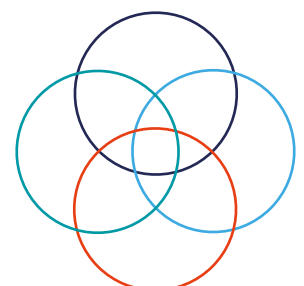
- *Yes:* agreed with the assessment criterion.
- *No:* disagreed or the question did not meet the assessment criterion.
- *Neutral:* the expert was uncertain or undecided about whether the question met the assessment criterion.
- *No response:* the expert decided not to respond to the research question under a specific criterion.

In the first round, experts were also invited to suggest up to two new research questions relevant to their pillar that they identified as missing from the current list and felt should be considered for the next round of the Delphi process.

Additional research questions proposed by experts were analysed in a stepped process:

1. The first screening step removed any research questions that were not relevant to a One Health interface, or suggestions not identified as questions. Questions were edited in this screening step for clarity and to align with current format.
2. Research questions were screened a second time to assess for repetition across other pillars or within the same pillar. Those that were similar or a replication were excluded.
3. The final screening assessed and changed wording for clarity of meaning, consistency and expression and to move any additions to other pillars where they did not replicate existing questions.

The list for relevance to the project criteria was reviewed, including relevance to LMICs before including the newly proposed research questions in Round 2 of the modified Delphi process.



## Round 2

The research questions retained at the end of Round 1 and any new research questions were used in Round 2. Experts were informed that new research questions had been introduced (described in Round 1). However, the new research questions were not specifically identified and were randomly dispersed throughout the Round 2 questionnaire.

The criterion “important” used as a screening question in the first Delphi round was dropped from Round 2. Research questions were therefore assessed against four assessment criteria. Otherwise, the same scoring and average and standard deviation calculations were used to rank research questions and identify a cut-off below which research questions dropped out.

## Round 3

Experts were asked to select up to 10 research questions as their choice for highest-priority research questions. Experts were asked simply to drag and drop 10 research questions into a selection space without ranking them 1–10.

Ten priorities were requested because it had been the original intention to retain only 10 top-ranked research questions per pillar. However, tied votes meant that this was ultimately not possible.

Experts were also invited to provide feedback on the Delphi process at the end of Round 3 through the same Qualtrics platform. These responses were analysed for inclusion in the discussion and analysis of the overall Delphi process results.

## 6. Analysing the results of the modified Delphi process

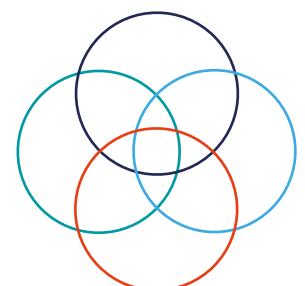
All rankings and selection of research questions occurred within a pillar, with no comparison or calculations between pillars. In line with standard methodology, the modified Delphi process was anonymous and the Quadripartite were not able to trace a response to a particular individual.

For Round 1, each *Yes*, *No* and *Neutral* response was assigned a score of 1, 0 or 0.5, respectively. An average score was calculated for each pillar per evaluation criterion. An average of the averages was calculated and used to rank research questions in each Delphi round. The degree of consensus among the experts in each pillar in each Delphi round for individual research questions was estimated by calculating the standard deviation of scores from all assessment criteria. Note that a score could rank a research question as having low importance within a pillar with strong consensus (i.e. a small standard deviation) among the experts.

The largest difference between two consecutively ranked research questions and a relatively large increase in standard deviation (i.e. a relative lack of consensus) were used together semi-quantitatively to identify the cut-off below which the research questions would drop out. By doing so, 50–80% of the original research questions were retained (approx. 13–21 questions per pillar before new proposed questions were added). This approach served both to retain sufficient research questions for the next Delphi round while reducing the number of research questions per round to minimize expert workload.

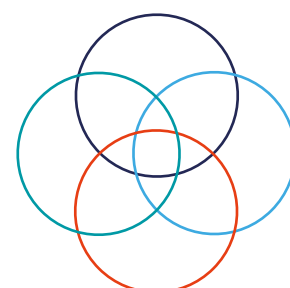
For Round 3, only research questions which at least 50% of the experts had placed in their top 10 were retained.

Table A1.4 provides a summary of participation, number of questions considered and consensus rates for each pillar in every Delphi round.



**Table A.4. Summary of Delphi participation and results per round**

| <b>Pillar</b>                           | <b>Transmission</b> | <b>Integrated surveillance</b> | <b>Interventions</b> | <b>Behavioural insights and change</b> | <b>Economics and policy</b> |
|---|---------------------|--------------------------------|----------------------|--|-----------------------------|
| <i>Round 1</i>                          |                     |                                |                      |  |                             |
| Number of participants                  | 16                  | 17                             | 18                   | 14                                     | 13                          |
| Number of research questions considered | 25                  | 17                             | 28                   | 31                                     | 24                          |
| Consensus rate applied                  | 0.75                | 0.75                           | 0.75                 | 0.70                                   | 0.70                        |
| <i>Round 2</i>                          |                     |                                |                      |  |                             |
| Number of participants                  | 13                  | 13                             | 15                   | 13                                     | 11                          |
| Number of research questions considered | 25                  | 19                             | 19                   | 24                                     | 24                          |
| Consensus rate applied                  | 0.82                | 0.82                           | 0.79                 | 0.76                                   | 0.66                        |
| <i>Round 3</i>                          |                     |                                |                      |  |                             |
| Number of participants                  | 17                  | 17                             | 19                   | 16                                     | 14                          |
| Number of research questions considered | 15                  | 14                             | 15                   | 15                                     | 15                          |
| Consensus rate applied                  | 0.50                | 0.50                           | 0.50                 | 0.50                                   | 0.50                        |



## 7. Post-Delphi expert discussion

All experts who participated in the Delphi process were invited to a post-Delphi online webinar per pillar. The meetings took place during the week of 4–7 October 2022, during which the results of the Delphi process were presented and discussed. Minor word changes to priority research questions were agreed for intelligibility; the final wording of the research priority questions was also agreed. In some cases, research questions were merged for consistency and intelligibility, where these were considered by experts to overlap. This discussion resulted in transforming the research questions into a set of finalized research priority areas for One Health AMR by pillar.

Webinar participants also discussed and agreed on following categories for the research priority areas. These were: methodology; operational research; evaluation; framework conditions; and dynamics and drivers of AMR. They are presented in the main *One Health priority research agenda for antimicrobial resistance* report.

## 8. Consolidated top 10

The two highest-scoring research areas were selected from each pillar to create an overall top 10 list of priority research areas.

The top 10 priority research areas represent the highest-ranked research areas across all three Delphi rounds per pillar and can be considered the most *important* research priority areas; having the greatest potential for *research capacity strengthening*; and being the most *actionable, inclusive and impactful* in the field of One Health AMR over the short to medium term (4–8 years).

## 9. Challenges

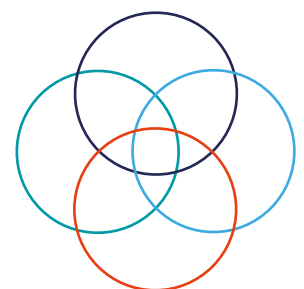
A Delphi process is subjective, as prioritization is influenced by a given expert's location, demographic characteristics, disciplinary qualifications and experience. While this research prioritization exercise was aimed at One Health interfaces between sectors, experts may have responded based on their own sector of expertise. However, the Delphi methodology proved to be relevant for consensus seeking for this online exercise, including interdisciplinary and multisectoral input.

The academic literature review employed targeted search terms and excluded information in any language other than English. This may have limited the breadth of the literature reviewed. A broader snowball approach was applied to the grey literature review to capture diverse research gaps and especially cross-cutting areas.

Additionally, the research gap identification process sought acknowledged gaps. This limits gaps to those previously identified and excludes gaps that have not yet been identified in the literature. For instance, for gender and vulnerability and AMR in particular, little research has been done. As a result, the absence of gender analyses has often neither been recognized nor acknowledged in the AMR/One Health literature.

During the gap-harvesting process from the literature review and the global open call online survey, nuance and specificity of research gaps may have been affected. Several reviews of thematic coding (grouping gaps with similar focus) were done during analysis to balance gap specificity with the need to cover the breadth of gaps that emerged.

The literature primarily documented research in HICs as opposed to LMICs; this is an acknowledged limitation. The One Health Priority Research Agenda for AMR aims to respond to this limitation. Further mitigation of this bias in literature was made by both focusing on grey literature publications that considered gaps relevant to LMICs and recruiting experts into the Delphi process from LMICs where possible. Further, experts participating in the Delphi process were given an opportunity to provide additional research questions for consideration during the first Delphi round to better reflect research questions that might not yet have been published or discussed in the literature.



The research questions presented during the modified Delphi process were of global relevance. Further work is needed to develop the identified research areas into research questions relevant to local/regional complexities.

The criteria used in the Delphi process were broad; whether a research question chosen for prioritization can actually build LMIC research capacity will depend on multiple factors. Expert opinion is based on the expert making the choice, not on external measures of capacity.

Some experts reported that they found it difficult to balance the Delphi process assessment criteria, as each criterion can operate along variable time frames.

Researchers' engagement and allocation of funding will be key for the implementation of this Priority Research Agenda.

## 10. List of all academic and grey literature used to develop initial research gaps

### 10.1. Academic article review

Ben Y, Fu C, Hu M, Liu L, Wong MH, Zheng C. Human health risk assessment of antibiotic resistance associated with antibiotic residues in the environment: a review. *Environ Res.* 2019;169:483–93.

Bueno I, Williams-Nguyen J, Hwang H, Sargeant JM, Nault AJ, Singer RS. Impact of point sources on antibiotic resistance genes in the natural environment: a systematic review of the evidence. *Anim Health Res Rev.* 2017;18:112–27

Bulteel AJB, Larson EL, Getahun H. Identifying global research gaps to mitigate antimicrobial resistance: a scoping review. *Am J Infect Control.* 2021;49(6):818–24.

Chatterjee A, Modarai M, Naylor NR, Boyd SE, Atun R, Barlow J et al. Quantifying drivers of antibiotic resistance in humans: a systematic review. *Lancet Infect Dis.* 2018;18:e368–78

Christou A, Aguera A, Bayona JM, Cytryn E, Fotopoulos V, Lambropoulou D et al. The potential implications of reclaimed wastewater reuse for irrigation on the agricultural environment: the knowns and unknowns of the fate of antibiotics and antibiotic resistant bacteria and resistance genes – a review. *Water Res.* 2017;123:448–67.

Davies R, Wales A. Antimicrobial resistance on farms: a review including biosecurity and the potential role of disinfectants in resistance selection. *Compr Rev Food Sci Food Saf.* 2019;18:753–74.

Escher N, Muhummed AM, Hattendorf J, Vonaesch P, Zinsstag J. Systematic review and meta-analysis of integrated studies on antimicrobial resistance genes in Africa – a One Health perspective. *Trop Med Int Health.* 2021;10:1153–63. doi: 10.1111/tmi.13642.

Founou LL, Amoako DG, Founou RC, Essack SY. Antibiotic resistance in food animals in Africa: a systematic review and meta-analysis. *Microb Drug Resist.* 2018;24:648–65.

Goulas A, Belhadi D, Descamps A, Andreumont A, Benoit P, Courtois S et al. How effective are strategies to control the dissemination of antibiotic resistance in the environment? A systematic review. *Environ Evid.* 2020;9:4. doi: 10.1186/s13750-020-0187-x.

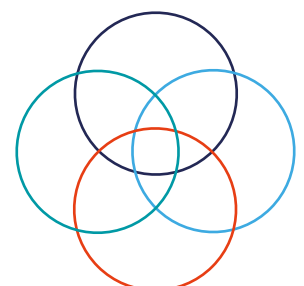
Hedman HD, Vasco KA, Zhang L. Review of antimicrobial resistance in poultry farming within low-resource settings. *Animals.* 2020;10:1264. doi: 10.3390/ani10081264.

Hiller C, Hubner U, Fajnorova S, Schwartz T, Drewes JE. Antibiotic microbial resistance (AMR) removal efficiencies by conventional and advanced wastewater treatment processes: a review. *Sci Total Environ.* 2019;685:596–608.

Hudson J, Frewer LJ, Jones G, Brereton PA, Whittingham MJ, Stewart G. The agrifood chain and antimicrobial resistance: a review. *Trends Food Sci Technol.* 2017;69:131–47.

Huijbers PMC, Blaak H, de Jong MCM, Graat EAM, Vandenbroucke-Grauls CMJE, de Roda Husman AM. Role of the environment in the transmission of antimicrobial resistance to humans: a review. *Environ Sci Technol.* 2015;49:11993–12004.

Jayabalasingham A, Seidman JC, Willem L, Grenfell B, Spiro D, Viboud C. Population-level mathematical modeling of antimicrobial resistance: a systematic review. *BMC Med.* 2019;17:1–28.



Larsson DGJ, Flach CF. Antibiotic resistance in the environment. *Nat Rev Microbiol.* 2022;20:257–69. doi: 10.1038/s41579-021-00649-x.

Medina-Pizzali ML, Hartinger SM, Salmon-Mulanovich G, Larson A, Riveros M, Mäusezahl D. Antimicrobial resistance in rural settings in Latin America: a scoping review with a One Health lens. *Int. J. Environ. Res. Public Health.* 2021;18:9837. doi: 10.3390/ijerph18189837.

Miller SA, Ferreira JP, LeJeune JT. Antimicrobial use and resistance in plant agriculture: a One Health perspective. *Agriculture.* 2022;12:289. doi: 10.3390/agriculture12020289.

Nhung NT, Cuong NV, Thwaites G, Carrique-Mas J. Antimicrobial usage and antimicrobial resistance in animal production in Southeast Asia: a review. *Antibiotics.* 2016;5:37.

Noyes NR, Slizovskiy IB, Singer RS. Beyond antimicrobial use: a framework for prioritizing antimicrobial resistance interventions. *Annu. Rev. Anim. Biosci.* 2021;9:313–32. doi: 10.1146/annurev-animal-072020-080638.

Nyberg O, Rico A, Guinée J, Henriksson P. Characterizing antibiotics in LCA – a review of current practices and proposed novel approaches for including resistance. *Int J Live Cycle Assess.* 2021;26:1816–31.

Sazykin IS, Khmelevtsova LE, Seliverstovaa EY, Sazykina MA. Effect of antibiotics used in animal husbandry on the distribution of bacterial drug resistance (review). *Appl Biochem Microbiol.* 2021;57(1):20–30.

Sekyere Jo, Mensah E. Molecular epidemiology and mechanisms of antibiotic resistance *Enterococcus* spp., *Staphylococcus* spp., and *Streptococcus* spp. in Africa: a systematic review from a One Health perspective. *Ann N Y Acad Sci.* 2020;1465(1):29–58.

Singh K, Anand S, Dholpuria S, Sharma JK, Blankenfeldt W, Shouche Y. Antimicrobial resistance dynamics and the one-health strategy: a review. *Env Chem Lett.* 2021;19:2995–3007.

Spruijta P, Petersen A. Multilevel governance of antimicrobial resistance risks: a literature review. *J Risk Res.* 2022;25(8):945–58. doi: 10.1080/13669877.2020.1779784.

Tang KL, Caffrey NP, Nóbrega DB, Cork SC, Ronsley PE, Barkema HW et al. Restricting the use of antibiotics in food-producing animals and its associations with antibiotic resistance in food-producing animals and human beings: a systematic review and meta-analysis. *Lancet Planet Health.* 2017;1:e316–27.

Wuijts S, van den Berg HH, Miller J, Abebe L, Sobsey M, Andremont A et al. Towards a research agenda for water, sanitation and antimicrobial resistance. *J Water Health.* 2017;15(2):175–84.

Zainab SM, Muhammad J, Xu N, Malik RN. Antibiotics and antibiotic resistant genes (ARGs) in groundwater: a global review on dissemination, sources, interactions, environmental and human health risks. *Water Res.* 2020;187:116455.

Zheng D, Yin G, Liu M, Chen C, Jiang Y, Hou L, Zheng Y. A systematic review of antibiotics and antibiotic resistance genes in estuarine and coastal environments. *Sci Total Environ.* 2021;777:146009. doi: 10.1016/j.scitotenv.2021.146009.

## 10.2. Grey literature review

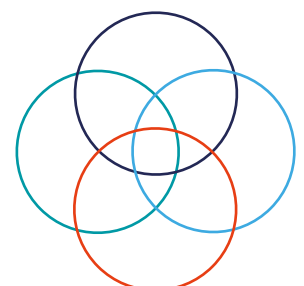
An analysis of the animal/human interface with a focus on low- and middle-income countries: Fleming Fund project to tackle global AMR. London: Royal Veterinary College; 2016.

Anderson M, Cecchini M, Mossialos E, editors. Challenges to tackling antimicrobial resistance: economic and policy responses. Geneva: World Health Organization; 2019.

Anderson M, Clift C, Schulze K, Sagan A, Nahrgang S, Ouakrim DA et al. Averting the AMR crisis: what are the avenues for policy action for countries in Europe? Copenhagen: World Health Organization Regional Office for Europe; 2019.

The animal health AMR R&D landscape in low- and middle-income countries: an analysis of funding patterns. In: Global AMR R&D Hub [website]. Braunschweig: German Center for Infection Research; 2021.

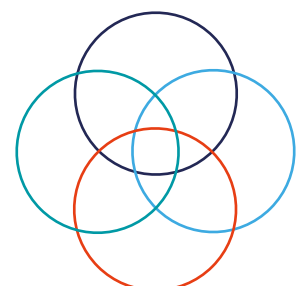
Antimicrobial resistance at the human-animal interface. In: One Health and the Sustainable Development Goals. Seventeenth Inter American Ministerial Meeting on Health and Agriculture, Asunción, Paraguay, 21–22 July 2016. Asunción: Pan American Health Organization; 2016.



- Comprehensive review of the WHO global action plan on antimicrobial resistance. Geneva: World Health Organization; 2021:1.
- Drug-resistant infections: a threat to our economic future. Washington (DC): World Bank; 2017.
- Environmental dimensions of antimicrobial resistance: summary for policymakers. Nairobi: United Nations Environment Programme; 2022.
- European One Health action plan against antimicrobial resistance (AMR). Brussels: European Commission; 2020.
- The global response to AMR: momentum, success, and critical gaps. London: Wellcome Trust; 2020.
- Health, environment and climate change: human health and biodiversity. Provisional agenda item 11.4. In: Seventy-first World Health Assembly, Geneva, 29 March 2018. Geneva: World Health Organization; 2018.
- Identifying One Health priorities in the Asia Pacific region. In: Regional Conference for Asia and the Pacific, 36th Session, 8–11 March 2022, Dhaka, Bangladesh. Rome: Food and Agriculture Organization of the United Nations; 2022.
- Impacts of pharmaceutical pollution on communities and environment in India. Fuengirola: Nordea Asset Management; 2016.
- Initiatives for addressing antimicrobial resistance in the environment: current situation and challenges. London: Wellcome Trust; 2018.
- A multi-stakeholder approach to pharmaceuticals in the environment: working together towards effective solutions. Brussels: Healthcare Without Harm; 2019.
- One Health in action: pharmaceuticals including antimicrobials and their environmental impact. Policy session, 2nd European One Health Conference. Summary report – 21 June 2019, Bucharest. Brussels: FEAM European Biomedical Policy Forum; 2019.
- One Health legislation: contributing to pandemic prevention through Law. Rome: Food and Agriculture Organization of the United Nations; 2020.
- Progress report. AMR Industry Alliance 2021 survey. Geneva: AMR Industry Alliance; 2022.
- Pulling together to beat superbugs: knowledge and implementation gaps in addressing antimicrobial resistance. Washington (DC): World Bank; 2019.
- Ruckert A, Das Neves CG, Amuasi J, Hindmarch S, Brux C, Winkler AS et al. One health as a pillar for a transformative pandemic treaty. Global Health Centre Policy Brief. Geneva: Graduate Institute of International and Development Studies; 2021.
- Scoping the significance of gender for antibiotic resistance. Uppsala: ReAct; 2020.
- Tackling antimicrobial resistance (AMR) together. Working paper 5.0: Enhancing the focus on gender and equity. Geneva: World Health Organization; 2018.
- Technical brief on water, sanitation, hygiene and wastewater management to prevent infections and reduce the spread of antimicrobial resistance. Geneva: World Health Organization (WHO), Food and Agriculture Organization of the United Nations (FAO) and World Organisation for Animal Health (OIE); 2020.
- Using the Dynamic Dashboard to identify gaps and opportunities for the development of veterinary vaccines in an effort to reduce antibiotic use. In: Global AMR R&D Hub [website]. Braunschweig: German Center for Infection Research; 2021.
- Veterinary medicine in European food production: perspectives on the environment, public health, and animal welfare. Brussels: Healthcare Without Harm; 2019.

## 11. Declaration of interests of experts

Declarations of interest (DOIs) were collected and thoroughly reviewed following WHO standard operating procedures. All experts submitted written disclosures of competing interests relevant for consideration to participate in the Delphi process. Of the 89 experts, 63 did not disclose any interests. Twenty-five experts disclosed interests that were reviewed by the WHO technical unit. In all cases, it was determined that the interests disclosed were not directly relevant to the scope of work of the OHPRA, and as a result the WHO technical unit granted their participation in the Delphi process.





## Annex 2. List of experts

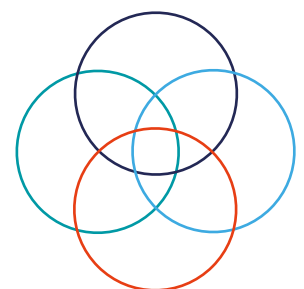
The Quadripartite acknowledges the following external experts for their contribution, listed by pillar and in alphabetical order.

### Transmission

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## Interventions

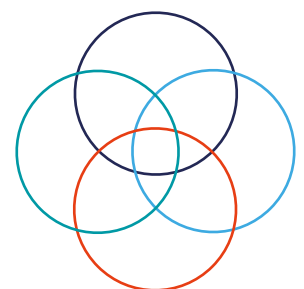
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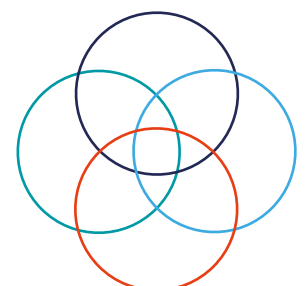
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Raheelah Ahmad (Imperial College London; City, University of London; SEDRIC (Surveillance and Epidemiology of Drug-resistant Infections Consortium) at Wellcome Trust, United Kingdom / Dow University of Health Sciences, Pakistan), Mónica Berger-González (Universidad del Valle de Guatemala, Guatemala), Esmita Charani (Imperial College London, United Kingdom), David Kelton (University of Guelph, Canada), Everly Macario (Harvard T.H. Chan School of Public Health Alumna, United States), Fadi Makki (Nudge Lebanon, Lebanon / Hamad Bin Khalifa University, Qatar), Shahinaz Mekheimer (Theodor Bilharz Research Institute, Egypt), Christine F. Najjuka (Makerere University, Uganda), Annegret Schneider (Robert Koch Institute, Germany), Anja Schreijer (Pandemic & Disaster Preparedness Center, Rotterdam, Netherlands), Andrea Caputo Svensson (ReAct Europe, Sweden), Philip Taylor (Centre for Agriculture and Bioscience International, United Kingdom), Beena Thomas (National Institute for Research in Tuberculosis, Chennai India), Cheryl Waldner (Western College of Veterinary Medicine, Canada), Luis Felipe Zago (Nursing School, Universidade Federal do Rio Grande do Sul, Brazil).

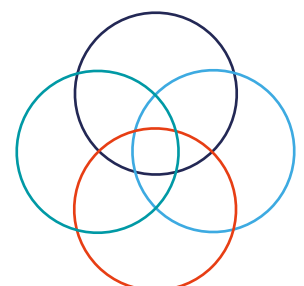


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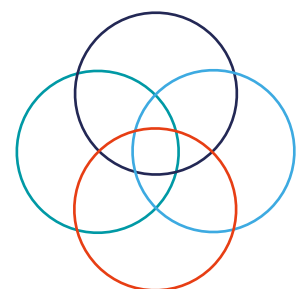
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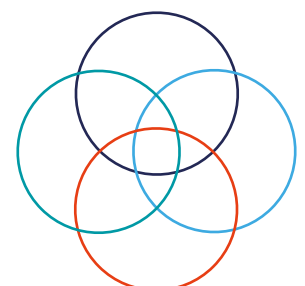
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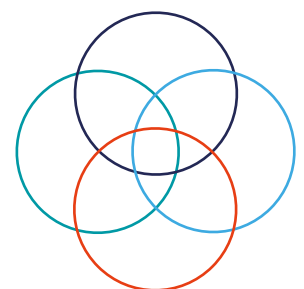
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UNEP: [www.unep.org](http://www.unep.org)

WHO: [www.who.int](http://www.who.int)

WOAH: [www.woah.org](http://www.woah.org)

