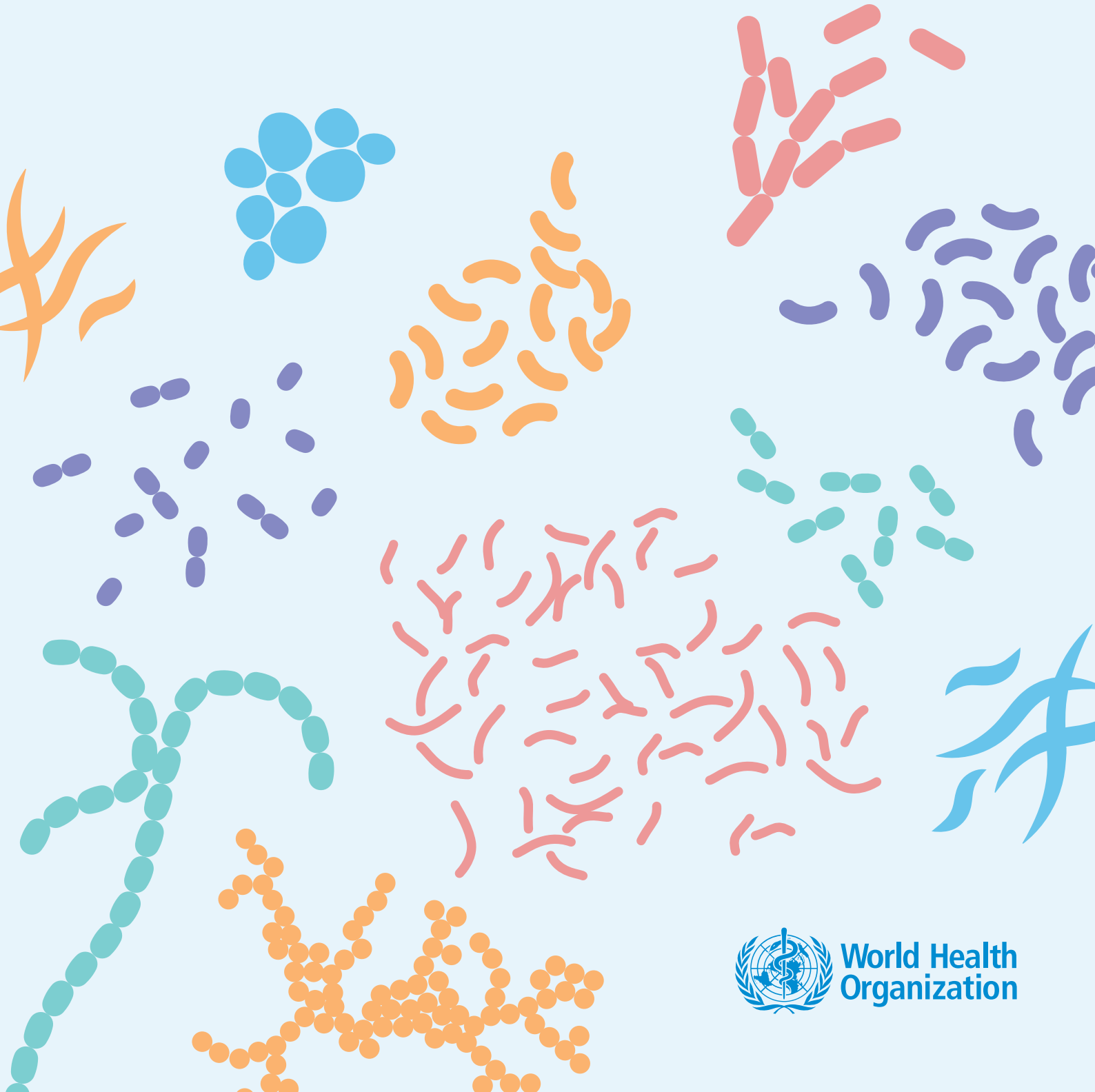
# Global research agenda for antimicrobial resistance in human health



World Health Organization

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# Abbreviations

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| **AMR** | antimicrobial resistance |
| **AWeRe** | access, watch, reserve |
| **BPaLM** | bedaquiline, pretomanid, linezolid and moxifloxacin |
| **DALY** | disability-adjusted life-year |
| **GLASS** | Global Antimicrobial Resistance Surveillance System |
| **IPC** | infection prevention and control |
| **OECD** | Organisation for Economic Co-operation and Development |
| **PECO** | population, exposure, comparator, outcome |
| **PICO** | population, intervention, comparator, outcome |
| **STI** | sexually transmitted infection |
| **TB** | tuberculosis |
| **WASH** | water, sanitation and hygiene |

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# Glossary

**Antimicrobial resistance area**: research priorities are grouped into areas relevant to antimicrobial resistance (AMR): water, sanitation and hygiene (WASH); infection prevention and control (IPC); immunization; diagnosis and diagnostics; antimicrobial stewardship; antimicrobial use; antimicrobial medicines; epidemiology, burden and drivers of antimicrobial resistance; awareness and education; policies and regulations; prevention of drug-resistant tuberculosis (TB); diagnosis of people with drug-resistant TB; and treatment and care of people with drug-resistant TB.

**Antimicrobial use**: describes both medicines-level data on antimicrobial use (elsewhere known as "antimicrobial consumption" data) that provide information on the quantity and types of antimicrobials used and clinical-level data that can link antimicrobial use patterns with patient characteristics, clinical indication and treatment regimens, such as dose, route and duration.

**Knowledge gap**: a subject requiring further research as identified through a scoping review and an expert survey.

**Research Agenda Expert Group**: a group of global experts with expertise spanning research disciplines. Members were identified based on their peer-reviewed publication records and through the WHO Steering Group and regional advisers to attain gender balance, representation from low- and middle-income countries and from underrepresented areas such as paediatrics, mycology, WASH and policy and regulations related to AMR.

**Research disciplines**: field of research used to categorize expertise related to AMR: pharmacology and clinical disciplines; health economics; governance, regulations and legislation; epidemiology; and behavioural and social science.

**Research domains**: categories used to describe research topics. Four research domains are typically used in the Child Health and Nutrition Research Initiative to categorize research topics in a knowledge matrix: "descriptive" (characterizing the burden and drivers of AMR), "delivery" (providing ways to deliver existing interventions with better quality), "development" (improving existing interventions, reducing their costs or optimizing their implementation) and "discovery" (new interventions to prevent, treat and diagnose AMR).

**Research priority**: a subset of research topics with priorities set based on scoring from the Research Agenda Expert Group.

**Research topic**: a group of thematically related areas for further research formulated from consolidated knowledge gaps.

**Theme**: thematically related research priorities are grouped into five themes: prevention; diagnosis; treatment and care; a cross-cutting theme; and a focus theme on drug-resistant *Mycobacterium tuberculosis*.

**WHO bacterial priority pathogens**: bacterial families included in *Prioritization of pathogens to guide discovery, research and development of new antibiotics for drug-resistant bacterial infections, including tuberculosis* published by WHO in 2017.

**WHO fungal priority pathogens**: fungal pathogens that are critically important for AMR based on the *WHO fungal priority pathogens list to guide research, development and public health action* published in 2022.

**WHO secretariat**: staff members and consultants of the Antimicrobial Resistance Division at WHO headquarters coordinating the development of the agenda.

**WHO Steering Group**: WHO staff members across WHO divisions and departments with technical expertise spanning the various AMR areas. The Steering Group defined the objectives and scope of the agenda, guided the development of the criteria for setting priorities, supported the consolidation of research topics and the priority-setting process and contributed to writing area-specific sections of the report.

# Executive summary

Antimicrobial resistance (AMR) poses a considerable threat to human health, with an estimated 4.95 million deaths associated with bacterial AMR in 2019. A total of 410 000 new cases of rifampicin- and multidrug-resistant tuberculosis were estimated globally in 2022. Further, invasive fungal infections are increasing worldwide, and their management is challenged by antifungal resistance and difficulties in diagnosis. Low- and middle-income countries have disproportionately higher mortality from infections with resistant organisms compared with high-income countries.

Although AMR is recognized among the top 10 global threats requiring urgent action, over the past six years little progress has been made in improving awareness of AMR, monitoring and optimizing antimicrobial use and implementing infection prevention and control programmes. Efforts to address the inequitable impact of AMR across populations have been limited, challenged by the lack of data, including data disaggregated by age, sex, socioeconomic status and other factors.

The goal of this research agenda is to identify and give priority to the research topics with the greatest impact on mitigating AMR in the human health sector. A priority research agenda for AMR is critical in guiding policy-makers, researchers, funders, implementing partners, industry and civil society in generating new evidence to inform AMR policies and interventions. The research agenda is global in scope and focuses on AMR in the human health sector, especially infections caused by the WHO bacterial priority pathogens, including drug-resistant *Mycobacterium tuberculosis* and WHO fungal priority pathogens that are critically important for AMR (such as *Candida auris*, *Aspergillus fumigatus* and *Cryptococcus neoformans*). The research priorities apply to both adults and children.

The research agenda was developed through an adapted Child Health and Nutrition Research Initiative method in close collaboration with a multidisciplinary Research Agenda Expert Group on AMR. In the first phase, 2340 knowledge gaps were identified through a systematic search of peer-reviewed and grey literature, from screening of 8409 documents published in the past 10 years. In the second phase, with technical input from a multidisciplinary Research Agenda Expert Group and based on input from a global consultation, these knowledge gaps were further consolidated into 175 research topics.

In the final phase, the Research Agenda Expert Group was invited to assess each of the 175 research topics against five criteria: filling critical knowledge gaps; answerability and feasibility by 2030; potential for translation into policy; impact on mitigating AMR; and promoting health equity. A research priority score accounting for the opinion of all individual experts was calculated to identify the top scored 40 research priorities: 33 pertaining to AMR in bacteria and fungi and seven relating to drug-resistant *Mycobacterium tuberculosis* (Fig. E.1)

The research agenda aims to foster research by 2030 in accordance with the Sustainable Development Goals timeline and to catalyse scientific interest and investment among the scientific community and funders. The current list of research priorities should be further translated into tangible, concrete research proposals fundable by donors and implementable also in settings with limited resources.

**Fig. E1:** The forty research priorities of the WHO global research agenda for antimicrobial resistance in human health (abbreviated)

# Antimicrobial resistance research priorities

## Prevention

1. Investigate the impact and contribution of community WASH and waste management interventions on the burden and drivers of antimicrobial resistance
2. Investigate implementation strategies and the impact of WASH-related interventions in health-care settings on the burden of health care–associated infections and antimicrobial medicine prescribing
3. Identify (cost-)effective, acceptable and feasible multimodal IPC strategies and the relative effect of their components on reducing health care–associated infections
4. Assess the impact of vaccines on colonization and infection by resistant pathogens and on reducing the use of antimicrobial medicines, health-care encounters and health system costs

## Diagnosis

5. Investigate and evaluate rapid point-of-care tests to discriminate between bacterial versus non-bacterial infections
6. Investigate and evaluate diagnostic tests for detecting pathogens and antimicrobial susceptibility testing
7. Investigate and evaluate rapid antimicrobial susceptibility testing methods from blood cultures
8. Investigate and evaluate diagnostic tests for detecting fungal pathogens
9. Investigate the clinical and diagnostic value of phenotypic antifungal susceptibility testing
10. Investigate and evaluate novel rapid point-of-care assays and optimal testing approaches for (resistant) *Neisseria gonorrhoea*

## Treatment and care

11. Investigate antimicrobial stewardship interventions that are context specific, feasible, sustainable, effective and cost-effective in outpatient and inpatient settings
12. Identify feasible, effective and scalable pharmacist dispensing practices for antimicrobial medicines along with related regulatory frameworks to improve antimicrobial stewardship in the community, especially in low- and middle-income countries
13. Investigate criteria and strategies to optimize empirical antimicrobial therapy for the main infectious syndromes, especially in settings with limited access to medicine, diagnostic capacity and health-care services
14. Determine optimal methods, metrics and targets to monitor antimicrobial use
15. Determine the patterns and drivers of appropriate and inappropriate prescribing and use of antibiotics
16. Investigate approaches to effectively use data on antimicrobial use and AMR surveillance to inform antimicrobial stewardship and guidelines
17. Investigate antibiotic treatment regimens for infections, especially for extended-spectrum beta-lactamase–producing and carbapenem-resistant Enterobacterales
18. Investigate antibiotic treatment regimens for infections by drug-resistant typhoid and non-typhoidal salmonellae
19. Investigate empirical antibiotic treatments for gram-negative bacteria causing bloodstream infections among newborns and young children in settings with high AMR prevalence
20. Investigate antifungal regimens for infections caused by WHO fungal priority pathogens critically important for AMR
21. Investigate regimens for urogenital and extragenital STIs in the context of increasing AMR

## Cross-cutting

22. Investigate the epidemiology, mortality, morbidity and impact of infections caused by resistant WHO bacterial priority pathogens
23. Investigate the epidemiology, morbidity, mortality and impact of infections by resistant WHO fungal priority pathogens critically important for AMR
24. Investigate factors driving colonization and infection by resistant WHO bacterial priority and fungal pathogens
25. Identify optimal surveillance methods to generate accurate and reliable data on the epidemiology and burden of AMR
26. Assess how mass administration of antimicrobial medicines affects AMR
27. Evaluate how currently recommended syndromic STI management and treatment of people with asymptomatic STIs affect antibiotic prescribing and AMR
28. Determine the most (cost-)effective behavioural change interventions to mitigate the emergence and spread of AMR
29. Evaluate the implementation of AMR-related policies and regulations and how effective they are in mitigating AMR and improving health outcomes
30. Investigate implementation strategies for national policies, legislation and regulations to improve infection prevention, patient care and the use of antimicrobial medicines
31. Identify the most (cost-)effective interventions and an investment case to mitigate AMR globally and across countries
32. Investigate strategies to integrate AMR interventions into broader health, health financing, development and welfare structures and evaluate their impact
33. Investigate how regulatory frameworks, marketing incentives and financing models affect the sustainable development, availability, equitable access and use of new antimicrobial medicines

## Antimicrobial-resistant bacterial and fungal infections

### Drug-resistant TB

34. Investigate effective preventive TB vaccines that meet WHO preferred product characteristics criteria and demonstrate impact on preventing infection, disease and recurrence
35. Investigate how the diagnostic performance of molecular assays can be improved to detect drug resistance among people with extrapulmonary and pulmonary TB
36. Determine optimal diagnostic and treatment delivery models to improve the access, effectiveness, cost-effectiveness, feasibility and acceptability of drug-resistant TB treatment
37. Investigate better tolerated, optimally dosed, more effective and shorter combination regimens for treating people with all forms of drug-resistant TB
38. Determine the optimal, (cost-)effective, shortest duration and safest TB preventive treatment for the contacts of people with drug-resistant TB
39. Investigate strategies for improving treatment outcomes among people with drug-resistant TB who have known risk factors and conditions and among populations experiencing vulnerability
40. Investigate the programmatic effectiveness, safety and tolerability of currently used WHO-recommended treatment regimens for drug-resistant TB


ESCO Class II Biological Safety Cabinet
1. Start Up
2. Wipe Down
3. Material Placement
4. Check
5. Air Purge
6. Operating Guidelines
7. Purging and Wipe Down
8. Shut Down

# 1. Introduction

## 1.1 Background

Antimicrobial resistance (AMR) poses a considerable threat to human health, with an estimated 4.71 million deaths associated with bacterial AMR in 2021 *(1)*. Globally, there were an estimated 400 000 new cases of rifampicin- and multidrug-resistant tuberculosis (TB) in 2023 *(2)*. Invasive fungal infections are increasing worldwide *(3–5)*, and their management is challenged by difficulties in diagnosis and antifungal resistance. Low- and middle-income countries are disproportionately affected by AMR, with higher mortality rates caused by infections with resistant organisms than in high-resource settings *(1)*. In addition to its impact on health, AMR is also associated with substantial costs to the global economy, which may amount to US$ 100 trillion until 2050 if no action is taken *(6)*. Treating people with resistant bacterial infections may reach US$ 412 billion annually by 2035, with an additional US$ 443 billion per year in productivity losses *(7)*.

Since the Global Action Plan on antimicrobial resistance was developed in 2015 *(8,9)*, 178 countries published national action plans for AMR by the end of 2023 *(10)*. In accordance with the second objective of the Global Action Plan on Antimicrobial Resistance on strengthening the knowledge and evidence base through surveillance and research, in 2017 WHO published a bacterial pathogen priority list including 12 bacteria or bacterial groups classified into critical, high and medium priority according to the need for novel antibiotics (Table 1) *(11)*. The list aims to catalyse research and guide funding for developing new antibiotics. This list was updated in 2024 to include 24 pathogens from 15 families, including *Mycobacterium tuberculosis* *(12)*. Further, in 2022 WHO published a priority list for fungal pathogens, with the goal of strengthening surveillance, increasing awareness on their importance to public health and promoting research and development *(4)*.

Substantial knowledge gaps on AMR persist and hamper an effective response, illustrated by countries' stagnant progress in implementing their national action plans on AMR. For example, only 28% (49 of 177) countries reporting to the Tracking AMR Country Self-assessment Survey are actively implementing and monitoring their national action plans, of which almost two thirds (31 of 49) are low- and middle-income countries *(10)*. Over the past six years, survey data show little progress on improving awareness on AMR, monitoring and optimizing antimicrobial use and implementing infection prevention and control (IPC) programmes *(10)*. In addition, investments in AMR research have been inconsistent to date. Between January 2017 and September 2021, the Global AMR R&D Hub (https://globalamrhub.org) reported US$ 8.9 billion in investment across 12 093 projects funded by 214 organizations worldwide in AMR. Although this is still limited compared with other disease areas, 90% of the investment is directed to research and development for bacterial pathogens approximately with one third of the investment in priority bacterial pathogens (approximately 4.3 billion United States of America dollars) allocated toward development of new therapeutics. In comparison, only 12% was designated for vaccines, 6% for diagnostics and 1% for policy research. Fungal research across all sectors attracted only 6%

AMR is associated with an estimated 4.95 million deaths due to bacterial infections and substantial costs to the global economy which may amount to US$ 100 trillion until 2050 if no action is taken

**Left:** A laboratory technician processing bacterial cultures in a clinical laboratory in Khartoum, Sudan. © WHO / S Bertagnolio

of all investments. Investment in research and development of novel diagnostics or vaccines as well as policy research is lagging *(13)*.

More research is needed in these areas and in optimizing the use of current tools for more efficient use to support the implementation of evidence-informed policies and interventions for AMR, especially in low- and middle-income countries.

Research agendas are critical in guiding policy-makers, researchers, funders, the private sector and civil society in generating new evidence to inform policies and interventions and have been developed in other public health areas such as newborn health *(14)*, adolescents living with HIV *(15)*, dementia *(16)* and COVID-19 *(17)*. Previous initiatives have attempted to compile research gaps for resistant bacterial infections but have not adequately addressed key research priorities for human health *(18,19)*. Some have concentrated on specific aspects of AMR *(18,20–23)* or solely on the One Health interface *(24)*, and priorities specifically relevant to limited-resource settings have been neglected. A multidisciplinary research agenda on AMR with set priorities can play a critical role in directing investment by governments and funders and the attention of policy-makers, researchers and the private sector towards crucial knowledge gaps that require evidence, which in turn informs the effective implementation of AMR policies and interventions.

This work is the first comprehensive effort to outline the top research priorities, focusing on infections caused by drug-resistant bacteria and fungi using robust validated methods from a list of systematically identified research topics. This project is grounded in the Global Action Plan on Antimicrobial Resistance, a resolution endorsed by the 68th World Health Assembly in 2015 *(8,9,25)*, especially its second objective on strengthening knowledge and evidence through surveillance and research. Moreover, the resolution mandated WHO to develop a global public health research agenda for filling major gaps in knowledge on AMR, including methods to assess the health and economic burdens of AMR, cost–effectiveness of actions, mechanisms of development and spread of resistance and research to underpin the development of new interventions, diagnostic tools and vaccines and to monitor and report on implementation of the research agenda.

## 1.2 Purpose and scope of the research agenda

The purpose of this research agenda is to expand and enhance global knowledge on AMR in the human health sector. Its goal is to identify and give priority to the research topics with the greatest potential impact on mitigating AMR in the human health sector. The research agenda also aims to foster research by 2030, in accordance with the Sustainable Development Goals timeline and to catalyse scientific interest and investment among the scientific community and funders on the epidemiology and burden of resistant infections, on strategies to prevent infections and the emergence of resistance, on how to optimize and best deliver these in low- and middle-income countries and on optimized diagnostics and antimicrobial medicines. The current list of research priorities should be further translated into tangible, concrete research proposals fundable by donors and implementable also in settings with limited resources.

The research agenda is global in scope and focuses on AMR in the human health sector, especially infections caused by WHO bacterial priority pathogens *(11)*, WHO fungal priority pathogens that are critically important for AMR *(4)* and drug-resistant *M. tuberculosis*. The research agenda pertains to all income contexts and aims to serve both adults and children. Important research topics relevant to animal health, agriculture and the environment are out of scope and are addressed by the WHO One Health Priority Research Agenda for AMR, complementary to this work *(24)*. Detailed methods are described in Annex 1.

**Table 1:** Pathogens within the scope of the research agenda

| BACTERIAL PRIORITY PATHOGENS [a] |
|---|
| **PRIORITY 1: CRITICAL** |
| *Acinetobacter baumannii*, carbapenem-resistant<br>*Pseudomonas aeruginosa,* carbapenem-resistant<br>Enterobacterales, carbapenem-resistant, extended-spectrum beta-lactamase-producing |
| **PRIORITY 2: HIGH** |
| *Enterococcus faecium*, vancomycin-resistant<br>*Staphylococcus aureus*, methicillin-resistant, vancomycin-intermediate and resistant<br>*Helicobacter pylori*, clarithromycin-resistant<br>*Campylobacter* spp., fluoroquinolone-resistant<br>*Salmonella* spp., fluoroquinolone-resistant<br>*Neisseria gonorrhoeae*, cephalosporin-resistant, fluoroquinolone-resistant |
| **PRIORITY 3: MEDIUM** |
| *Streptococcus pneumoniae*, penicillin non-susceptible<br>*Haemophilus influenzae*, ampicillin-resistant<br>*Shigella* spp., fluoroquinolone-resistant |
| **DRUG-RESISTANT MYCOBACTERIUM TUBERCULOSIS [a]** |
| **FUNGAL PRIORITY PATHOGENS [b]** |
| *Candida* spp.<br>*Aspergillus fumigatus*<br>*Cryptococcus neoformans* |
| **OTHER** |
| *Mycoplasma genitalium*[c] |

a: Source: Prioritization of pathogens to guide discovery, research and development of new antibiotics for drug-resistant bacterial infections, including tuberculosis *(11)*.

b: Source: adapted from the WHO fungal priority pathogens list to guide research, development and public health action *(4)*.

c: An emerging cause of difficult-to-treat sexually transmitted infections.

## 1.3 Intended audience

The research agenda is cross-cutting and intended for a multidisciplinary audience including researchers, academia, public health professionals, funding agencies and donors, policy makers, the private sector and civil society across the world. Researchers working in all disciplines and undertaking different types of research, including basic science research, clinical research and implementation research are encouraged to use the agenda when drafting research questions, protocols and funding proposals. Research funders are encouraged to adopt priorities under this agenda when outlining AMR funding calls.

# 2. Global research priorities for AMR in human health

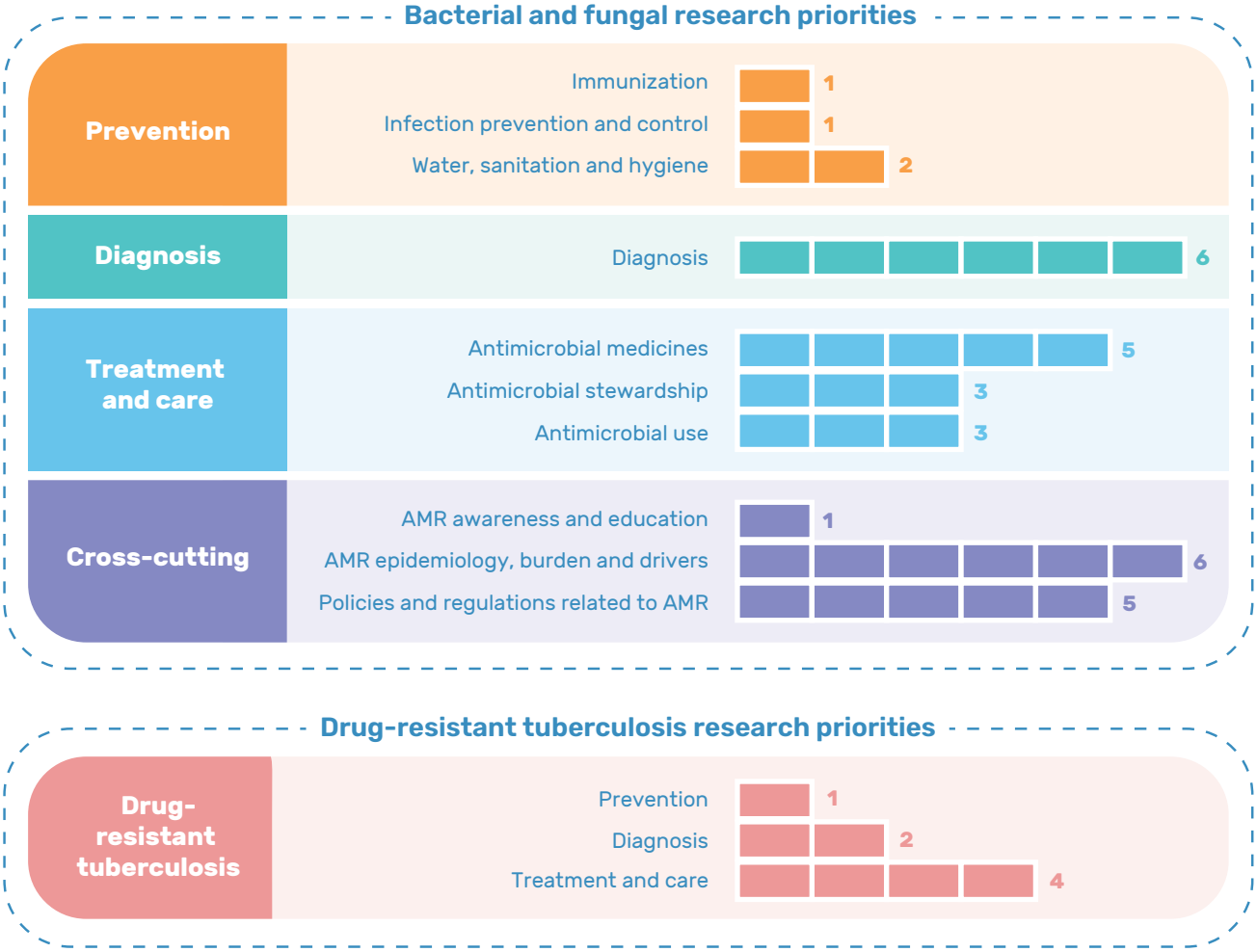
The WHO global research agenda for AMR in human health consists of 40 research priorities: 33 for bacterial and fungal infections and seven focused on drug-resistant TB (Table 2).

## 2.1 Overview

Including one or more priorities from all the AMR areas, the research agenda reflects the multidisciplinary and multifaceted diversity of AMR topics (Fig. 1). The research priorities are composite in nature, encompassing a variety of aspects related to the topic and likely requiring studies of different types to address. Nevertheless, each priority represents a discrete topic for holistic implementation.

Beyond the summary of research priorities outlined below, each priority is explored in detail in Section 2.2, aiming to illustrate the public health importance of the priority, showcase known advancements and areas lacking information, offer more detailed context for various aspects, propose specific research enquiries and suggest potential approaches to tackle the topic. They do not, however, provide comprehensive overviews of the subject.

**Fig. 1:** Number of research priorities by AMR area



The 33 research priorities for bacterial and fungal infections are grouped into four themes: prevention (four priorities), diagnosis (six priorities), treatment and care (11 priorities) and a cross-cutting theme (12 priorities). Further subgrouping by AMR area occurs for the themes of prevention (water, sanitation and hygiene (WASH), IPC and immunization), treatment and care (antimicrobial stewardship, antimicrobial use and antimicrobial medicines) and for the cross-cutting theme (AMR epidemiology, burden and drivers, AMR awareness and education, and policies and regulations related to AMR).

The seven research priorities for drug-resistant TB priorities are grouped into prevention (one priority), diagnosis (two priorities) and treatment and care (four priorities). The order in which the priorities are presented does not imply that priorities have been set within the list, and research priorities are numbered for ease of referencing.

## 2.1.1 Bacterial and fungal infections

The prevention theme comprises research priorities focusing on preventing infections with antimicrobial-resistant organisms. These include a research priority highlighting the need for investigating the impact, effectiveness and implementation strategies of WASH-related interventions within community and health-care settings, with the goals of reducing the burden and transmission of resistant organisms and reducing the use of antimicrobial medicines. A further research priority focused on the need for identifying optimal multimodal IPC strategies and the relative effect of their components for reducing health care–associated infections from antimicrobial-resistant pathogens. This theme also includes a research priority on vaccines and their role in preventing colonization and infection with resistant organisms and reducing antimicrobial use, health-care encounters and costs.

The diagnosis theme focuses on the need to improve diagnostics for bacterial and fungal infections *(26)*. Research priorities for diagnosis include point-of-care tests and diagnostic algorithms that can also be used in low- and middle-income countries for discriminating between bacterial and viral infections to aid treatment decisions. Other research priorities focus on methods for rapid pathogen detection and antimicrobial susceptibility testing directly from blood cultures, on the use of (near-) point-of-care and affordable molecular tests (including multiplexed and panel-based tests) for pathogen identification and resistance testing and for tests for detecting drug-resistant fungal infections. Another research priority addresses the need for investigating and evaluating tests for phenotypic antifungal susceptibility testing. Finally, one research priority focuses on novel point-of-care molecular and non-molecular tests and screening strategies for *Neisseria gonorrhoeae*, including detecting resistance.

The treatment and care theme includes research priorities on antimicrobial stewardship both within health-care settings and in community pharmacies. They cover the need for investigating stewardship interventions (such as implementing the WHO AWaRe antibiotic book) and adapting them to context; the need for improving pharmacists' dispensing practices within community pharmacies while accounting for regulatory frameworks and incentive mechanisms; and the need for optimizing empirical antimicrobial therapy for the main infectious syndromes. The research priorities on antimicrobial use include the need to identify the methods and metrics for measuring use and of targets for monitoring progress towards reducing inappropriate use; the need for determining the levels, patterns, trends and drivers of inappropriate use; and for determining the use of facility- and national-level data on antibiotic use as well as AMR surveillance data for informing stewardship programmes and treatment guidelines. The research priorities in this theme also cover

investigating treatment regimens for extended-spectrum beta-lactamase-producing and carbapenem-resistant Enterobacterales; the need for investigating safe and efficacious treatment options for drug-resistant typhoid and non-typhoidal salmonellae, fungal priority pathogens and drug-resistant STIs and the need for investigating optimal empirical treatment regimens for bloodstream infections among newborns and young children.

The cross-cutting theme focuses on three broad areas covering the epidemiology, burden and drivers of AMR: surveillance; AMR awareness and education; and policies and regulations related to AMR. Specifically, the area on AMR burden and drivers addresses the need for investigating the burden of community–acquired and health care–associated infections that are caused by resistant WHO priority bacterial and fungal pathogens; the impact of structural and health system factors on colonization and infection with resistant organisms; optimal surveillance methods for generating accurate and reliable data; the AMR impact of using antimicrobials within mass drug administration campaigns; and the benefits and effects of syndromic management for STIs. One research priority addresses the need for determining the optimal behaviour change interventions for mitigating AMR emergence and transmission, including among the public. Finally, five research priorities cover policies and regulations, including the need for identifying effective strategies for mitigating AMR and improving antimicrobial use, approaches for implementation, their integration within broader health and health financing structures and assessing how regulatory frameworks and marketing incentives affect the development of and access to new antimicrobial medicines.

### 2.1.2 Drug-resistant TB

The drug-resistant TB theme includes key priorities covering the development of new vaccines, improving diagnostic tests and testing strategies, and investigating better tolerated, effective and shorter treatment regimens for improving TB treatment outcomes. More specifically, one research priority addresses prevention using vaccines that meet the WHO target product profile characteristics and can affect preventing infection, disease and recurrence. Two research priorities focus on TB diagnostics: one on molecular assays for detecting resistance from non-respiratory samples and one on diagnostic and treatment delivery models for improving access and impact. Four research priorities address the treatment of people with drug-resistant TB: on investigating better-tolerated, shorter regimens; on optimal TB preventive therapy for contacts of people with drug-resistant TB; on strategies for improving outcomes among those at higher risk of unfavourable outcomes; and on the programmatic effectiveness (including drivers of treatment failure) of the new WHO-recommended treatment regimens.

**Table 2:** Forty priorities of the WHO global research agenda for antimicrobial resistance in human health

## Research priorities by antimicrobial resistance theme and area

| | | Research priority score [a] | Equity | Feasibility | Gaps | Impact | Policy |
|---|---|---|---|---|---|---|---|
| **PREVENTION OF BACTERIAL AND FUNGAL INFECTIONS** | | | | | | | |
| | **Water, sanitation, and hygiene (WASH)** | | | | | | |
| 1 | Investigate the impact, contribution, utility, effectiveness and cost-effectiveness of interventions to ensure safely managed WASH (including hand hygiene) and waste management practices in the community setting on reducing the burden and drivers of AMR, such as unnecessary antibiotic use for diarrhoeal diseases in low- and middle-income countries. | 0.90 [b] | 0.97 | 0.91 | 0.82 | 0.93 | 0.93 |
| 2 | Investigate implementation strategies of WASH-related interventions in health-care settings (including ensuring access to safely managed water and sanitation, safe hand hygiene, safe management of waste and environmental cleaning), and assess their impact, acceptability, equity and cost-effectiveness on the burden and transmission of resistant health care–associated infections and antimicrobial medicine prescribing across socioeconomic settings. | 0.89 [b] | 0.94 | 0.89 | 0.82 | 0.89 | 0.93 |
| | **Infection prevention and control** | | | | | | |
| 3 | Identify the most effective, cost-effective, acceptable and feasible multimodal IPC strategies (such as hand hygiene, contact precautions and patient isolation) and the relative effect of their components in reducing different types of health care–associated infections caused by multidrug-resistant pathogens across geographical and socioeconomic settings. | 0.90 [b] | 0.87 | 0.90 | 0.82 | 0.95 | 0.94 |
| | **Immunization** | | | | | | |
| 4 | Assess the impact of vaccines on preventing colonization and infection by resistant pathogens (whether specifically targeted by the vaccine or not) and on reducing the overall use of antimicrobial medicines, health-care encounters and health system costs among adults and children and across socioeconomic settings. | 0.94 [c] | 0.91 | 0.80 | 0.92 | 0.96 | 1 |

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**Table notes:**

**a.** Weighted as 10% for "feasibility" and "health equity" and 27% for "critical gaps", "impact" and "policy translation."

**b:** Research priority score fell within the top 20th percentile when considering all experts' responses

**c:** Research priority score fell within the top 20th percentile when considering only the responses of experts scoring with a low- and middle-income setting perspective.

Each of the 40 research priorities, grouped by theme and area, is explored in detail in Section 2.2.

| | | Research priority score [a] | Equity | Feasibility | Gaps | Impact | Policy |
|---|---|---|---|---|---|---|---|
| **DIAGNOSIS OF BACTERIAL AND FUNGAL INFECTIONS** | | | | | | | |
| | **Diagnosis and diagnostics** | | | | | | |
| 5 | Investigate and evaluate rapid point-of-care diagnostic tests (including biomarker-based tests) and diagnostic algorithms to discriminate between bacterial and viral infections and non-infectious syndromes that are feasible for use in limited-resource settings and among different subpopulations (including children and newborns), and how using these tests affects clinical outputs and outcomes. | 0.89 [b] | 0.72 | 0.93 | 0.88 | 0.94 | 0.90 |
| 6 | Investigate and evaluate diagnostic tests for isolating and identifying antimicrobial susceptibility testing and/or detecting resistance of bacterial pathogens (including multiplex panel–based tests and tests using novel technologies) that are rapid, (near) point of care, affordable, feasible for use in limited-resource settings and among different subpopulations and from a variety of specimen types, and how using these tests affects clinical outputs and outcomes. | 0.91 [b] | 0.85 | 0.78 | 0.96 | 0.97 | 0.87 |
| 7 | Investigate and evaluate phenotypic and genotypic methods of rapid antimicrobial susceptibility testing and resistance detection directly from positive blood culture bottles, especially for use in low- and middle-income countries, and how using these tests affects clinical outputs and outcomes. | 0.89 [b] | 0.82 | 0.90 | 0.92 | 0.91 | 0.85 |
| 8 | Investigate and evaluate rapid, (near) point-of-care diagnostic tests (including antigen and multiplex panel–based tests) for detecting WHO fungal priority pathogens that are critically important for AMR (such as *Candida auris*, *Aspergillus fumigatus* and *Cryptococcus neoformans*) and feasible for use in limited-resource settings and among different subpopulations, and how using these tests affects clinical outputs and outcomes. | 0.89 [b] | 0.86 | 0.80 | 0.92 | 0.92 | 0.88 |
| 9 | Investigate and evaluate the clinical utility and diagnostic accuracy of phenotypic antifungal susceptibility testing, including determining minimal inhibitory concentration breakpoints and testing for in vitro and in vivo synergy between antifungal medicines | 0.94 [c] | 079 | 0.98 | 0.93 | 1 | 0.93 |
| 10 | Investigate, assess the performance and evaluate the implementation of novel rapid point-of-care molecular and non-molecular assays and optimal testing and screening approaches (including self-testing) for *Neisseria gonorrhoeae* and AMR detection to reduce inappropriate antibiotic prescribing and emergence of AMR. | 0.90 [b] | 0.81 | 0.87 | 0.93 | 0.93 | 0.90 |

| | | Research priority score [a] | Equity | Feasibility | Gaps | Impact | Policy |
|---|---|---|---|---|---|---|---|
| **TREATMENT AND CARE OF BACTERIAL AND FUNGAL INFECTIONS** | | | | | | | |
| | **Antimicrobial stewardship** | | | | | | |
| 11 | Investigate antimicrobial stewardship interventions (such as implementing the WHO AWaRe antibiotic book, guidelines, clinical algorithms, education and training, audit and feedback), alone or in combination, that are context specific, feasible, sustainable, effective and cost-effective to avoid antimicrobial misuse in outpatient and inpatient settings, especially where diagnostic capacity may be limited. | 0.95 [b] | 0.92 | 0.88 | 0.93 | 0.98 | 0.97 |
| 12 | Identify feasible, effective and scalable pharmacist dispensing practices for antimicrobial medicines in community pharmacies, along with related regulatory frameworks (such as incentives and disincentives) to improve antimicrobial stewardship in the community, especially in low- and middle-income countries. | 0.90 [b] | 0.89 | 0.91 | 0.87 | 0.91 | 0.93 |
| 13 | Investigate criteria and strategies to optimize empirical antimicrobial therapy (such as antimicrobial spectrum, dose, timing of initiation, de-escalation and stopping), weighting the benefits (such as improving outcomes and reducing costs) versus potential harm (such as clinical failure, infection relapse, resistance emergence and adverse events) for main community and health care–associated infectious syndromes among adults and children, especially in settings with limited access to medicine, diagnostics and health-care services. | 0.92 [a] | 0.93 | 0.92 | 0.92 | 0.91 | 0.92 |
| | **Antimicrobial use** | | | | | | |
| 14 | Determine optimal (feasible, accurate and cost-effective) methods and metrics to monitor antimicrobial use in the community and health-care settings and appropriate targets to monitor progress in reducing inappropriate antimicrobial use. | 0.88 [b] | 0.80 | 0.97 | 0.88 | 0.83 | 0.94 |
| 15 | Determine the levels, patterns, trends and drivers of appropriate and inappropriate prescribing and use of access, watch and reserve antibiotics across countries and community and health-care settings, with data disaggregated by sex, age, socioeconomic status and subpopulations, including those experiencing vulnerability and with comorbidities (such as people living with HIV, people with TB and people with malaria). | 0.91 [b] | 0.88 | 0.92 | 0.90 | 0.92 | 0.92 |
| 16 | Investigate optimal approaches to effectively use facility- and/or national-level data on antimicrobial use and AMR surveillance to inform antimicrobial stewardship programmes and treatment guidelines. | 0.91 [b] | 0.77 | 0.96 | 0.87 | 0.92 | 0.97 |

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| | | Research priority score [a] | Equity | Feasibility | Gaps | Impact | Policy |
|---|---|---|---|---|---|---|---|
| | **Antimicrobial medicines** | | | | | | |
| 17 | Investigate efficacious and safe antibiotic treatment regimens based on old and new agents and combinations for infections, especially for extended-spectrum beta-lactamase–producing and/or carbapenem-resistant Enterobacterales, with minimum selection and transmission risk for AMR, especially among children and other subpopulations experiencing vulnerability. | 0.90 [b] | 0.82 | 0.91 | 0.93 | 0.88 | 0.90 |
| 18 | Investigate efficacious and safe antibiotic treatment regimens for infections by drug-resistant typhoid and non-typhoidal salmonellae (including for pathogens resistant to cephalosporins and fluoroquinolones) across socioeconomic settings. | 0.93 [c] | 0.90 | 0.90 | 0.92 | 0.97 | 0.93 |
| 19 | Investigate efficacious and safe empirical antibiotic treatment (drug choice, drug combination, route, dose and duration) for gram-negative bacteria causing bloodstream infections or sepsis among newborns and young children, especially in settings with high AMR prevalence and limited diagnostic capacity and antimicrobial medicine availability. | 0.90 [b] | 0.88 | 0.94 | 0.90 | 0.88 | 0.91 |
| 20 | Investigate antifungal regimens optimized for efficacy, cost, safety and duration for the treatment of infections caused by WHO fungal priority pathogens that are critically important for AMR (such as *Candida auris*, *Aspergillus fumigatus* and *Cryptococcus neoformans*) in settings with increasing or high prevalence of antifungal resistance. | 0.89 [b] | 0.72 | 0.90 | 0.92 | 0.86 | 0.93 |
| 21 | Investigate efficacious and safe regimens based on new or existing antimicrobial medicines for urogenital and extragenital STIs (such as resistant *N. gonorrhoeae* and resistant *Mycoplasma genitalium*) in the context of increasing AMR levels, including in populations experiencing vulnerability (such as people living with HIV, pregnant women and adolescents) | 0.89 [b] | 0.82 | 0.90 | 0.92 | 0.89 | 0.90 |

| | | Research priority score [a] | Equity | Feasibility | Gaps | Impact | Policy |
|---|---|---|---|---|---|---|---|
| | **CROSS-CUTTING AREAS** | | | | | | |
| | **Antimicrobial resistance epidemiology, burden and drivers** | | | | | | |
| 22 | Investigate the prevalence, incidence, mortality, morbidity and socioeconomic impact of community-acquired infections (respiratory tract infections, urinary tract infections and bloodstream infections) and health care–associated infections (bloodstream infections, urinary tract infections, surgical site infections and respiratory tract infections) caused by resistant WHO bacterial priority pathogens, with data disaggregated by sex, age, socioeconomic status and subpopulations (such as populations experiencing vulnerability or with comorbidities, including people living with HIV, people with TB and people with malaria) and across socioeconomic settings, especially in low- and middle-income countries. | 0.91 [b] | 0.91 | 0.96 | 0.93 | 0.88 | 0.90 |
| 23 | Investigate the prevalence, incidence, morbidity, mortality and socioeconomic impact and identify and quantify the routes and dynamic of infections by resistant WHO fungal priority pathogens that are critically important for AMR (such as *C. auris*, *A. fumigatus* and *C. neoformans*) across geographical and socioeconomic settings and in populations experiencing vulnerability. | 0.94 [c] | 0.86 | 0.90 | 0.94 | 0.96 | 0.98 |
| 24 | Investigate the association, contribution and impact of structural and health system factors (such as hospital microbiome, sanitation infrastructure, waste management, health expenditure, governance, distribution of resources, population displacement, conflict and disruptions in the care continuum) on colonization (selection, persistence and spread or loss of bacterial populations) and infection by WHO bacterial and fungal priority pathogens in subpopulations, including those experiencing vulnerability (such as migrants and refugees) and people with comorbidities, across socioeconomic settings. | 0.94 [b] | 0.88 | 0.92 | 0.94 | 0.97 | 0.95 |
| 25 | Identify optimal (efficient, effective and cost-effective) surveillance methods to generate accurate and reliable data on the epidemiology and burden of AMR among WHO bacterial and fungal priority pathogens (including determining the molecular mechanisms of resistance) in community and health-care settings and disaggregated by sex, age and subpopulations that are relevant and actionable at the local and national levels, especially in low- and middle-income countries. | 0.94 [b] | 0.90 | 0.91 | 0.95 | 0.95 | 0.96 |
| 26 | Assess how the programmatic use of antimicrobial medicines in mass administration affects AMR in the short and long term, focusing on subpopulations experiencing vulnerability in low-income settings. | 0.90 [b] | 0.92 | 0.84 | 0.89 | 0.89 | 0.93 |
| 27 | Evaluate the public health benefits, cost, impact on unnecessary or inappropriate antibiotic prescribing and potential AMR consequences of currently recommended syndromic STI management and treatment of people with asymptomatic STIs (including *N. gonorrhoeae*) in settings with variable diagnostic capacity. | 0.95 [c] | 0.89 | 0.93 | 0.96 | 0.96 | 0.96 |

continued...

| | | Research priority score [a] | Equity | Feasibility | Gaps | Impact | Policy |
|---|---|---|---|---|---|---|---|
| | **Antimicrobial resistance awareness and education** | | | | | | |
| 28 | Determine the most (cost-)effective behavioural change interventions to mitigate the emergence and spread of AMR by targeting and engaging the general public, young people, mass media, health-care workers and policy-makers across socioeconomic settings. | 0.94 [b] | 0.93 | 0.93 | 0.93 | 0.95 | 0.95 |
| | **Policies and regulations related to antimicrobial resistance** | | | | | | |
| 29 | Evaluate the implementation of AMR-related policies and regulations at the national level and how effective they are in mitigating AMR and improving health outcomes in the community and health-care settings across socioeconomic contexts. | 0.93 [c] | 0.95 | 0.79 | 0.97 | 0.96 | 0.92 |
| 30 | Investigate strategies for the sustainable and (cost-)effective implementation of national policies, legislation and regulations (including sustainable financing and optimal governance structures) to improve infection prevention and patient care practices and the use of antimicrobial medicines in the community and health-care settings across socioeconomic contexts. | 0.89 [b] | 0.90 | 0.86 | 0.84 | 0.91 | 0.94 |
| 31 | Identify the most (cost-)effective interventions to mitigate AMR in the human health sector, globally and within countries or regions, and determine the rationale, costs, benefits, feasibility, sustainability and potential returns on investment to achieve the greatest benefit. | 0.89 [b] | 0.88 | 0.80 | 0.89 | 0.92 | 0.91 |
| 32 | Investigate strategies to integrate AMR interventions into broader health, health financing, development, welfare structures and national policies and evaluate their impact on mitigating AMR, enhancing health system efficiency, reducing people's out-of-pocket expenses and improving equitable access to and use of diagnostics and antimicrobial medicines. | 0.96 [b] | 0.96 | 0.90 | 0.95 | 1 | 0.96 |
| 33 | Investigate how existing regulatory frameworks, marketing incentives (or their absence) and sustainable financing models affect the development and availability of new antimicrobial medicines and identify effective strategies to adapt these approaches to low-income settings to improve availability for adults and children. | 0.96 [c] | 0.96 | 0.89 | 0.96 | 1 | 0.92 |

| | | Research priority score [a] | Equity | Feasibility | Gaps | Impact | Policy |
|---|---|---|---|---|---|---|---|
| | **DRUG-RESISTANT TUBERCULOSIS** | | | | | | |
| | **Prevention** | | | | | | |
| 34 | Investigate effective preventive TB vaccines that meet WHO preferred product characteristics criteria and demonstrate impact on preventing infection, disease and recurrence (relapse or reinfection), thereby preventing or reducing the incidence of drug-resistant TB. | 0.89 [b] | 0.87 | 0.56 | 0.94 | 0.94 | 0.92 |
| | **Diagnosis** | | | | | | |
| 35 | Investigate how the diagnostic performance of molecular assays can be improved to detect drug resistance among people with extrapulmonary and pulmonary TB, from non-respiratory specimens, including among children and adolescents. | 0.94 [c] | 0.96 | 0.96 | 0.89 | 0.96 | 0.94 |
| 36 | Determine optimal diagnostic and treatment delivery models to improve the access, effectiveness, cost–effectiveness, feasibility and acceptability of drug-resistant TB testing and treatment across settings and subpopulations (such as people living with HIV, prisoners and children and adolescents) and evaluate their impact on reducing drug-resistant TB at the population level. | 0.90 [b] | 0.91 | 0.89 | 0.84 | 0.92 | 0.93 |
| | **Treatment and care** | | | | | | |
| 37 | Investigate better tolerated, optimally dosed, more effective and shorter combination regimens, using a stratified risk approach, for treating people with all forms of drug-resistant TB, including in populations experiencing vulnerability (such as children, pregnant and breastfeeding women and people living with HIV). | 0.92 [b] | 0.94 | 0.83 | 0.92 | 0.91 | 0.95 |
| 38 | Determine the optimal, (cost-)effective, shortest duration and safest TB preventive treatment for the contacts of people with drug-resistant TB, especially among people at high risk of TB infection and disease, as identified in WHO guidance, and eligible populations experiencing vulnerability (such as children, adolescents, people living with HIV and pregnant women). | 0.91 [b] | 0.92 | 0.86 | 0.91 | 0.89 | 0.94 |
| 39 | Investigate strategies for improving treatment outcomes among people with drug-resistant TB who have known risk factors and co-occurring conditions (such as HIV, undernutrition, diabetes mellitus, tobacco use, alcohol and other substance use and mental health disorders) and populations experiencing vulnerability (such as pregnant and breastfeeding women, children, adolescents and prisoners) in various geographical and socioeconomic settings. | 0.97 [c] | 0.98 | 0.94 | 0.94 | 0.96 | 1 |
| 40 | Investigate the programmatic effectiveness, safety and tolerability of currently used WHO-recommended treatment regimens for drug-resistant TB (including combinations with bedaquiline, delamanid and/or pretomanid) on patient outcomes and drug-resistant TB emergence across populations and settings and identify the drivers of treatment failure. | 0.95 [b] | 0.81 | 0.91 | 0.88 | 0.87 | 0.92 |


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# 2.2 The 40 research priorities

**Left:** Microbiology laboratory staff member in Dushanbe, Tajikistan.
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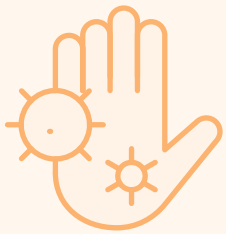
# 2.2.1 Prevention of bacterial and fungal infections



## Water, sanitation and hygiene

### **Priority #1.** Investigate the impact and contribution of community WASH and waste management interventions on the burden and drivers of antimicrobial resistance

Expanded version: Investigate the impact, contribution, utility, effectiveness and cost–effectiveness of interventions to ensure safely managed WASH (including hand hygiene) and waste management practices in the community setting on reducing the burden and drivers of AMR, such as unnecessary antibiotic use for diarrhoeal diseases in low- and middle-income countries.

Access to WASH can reduce the burden of infections and prevent the emergence and transmission of resistant pathogens within communities and overall reduce antimicrobial use. Sustainable Development Goal 6 aims to "ensure availability and sustainable management of water and sanitation for all" *(27)*. Despite improvements in access to safe water and sanitation over the past decade, an estimated 2.2 billion people were still lacking access to safe drinking-water in 2022, 3.5 billion lack sanitation systems that adequately collect and treat excreta and 2 billion lack basic handwashing services with soap and water in their household *(28)*. A recent modelling study estimated that ensuring access to high-quality WASH in LMIC could to prevent 247 800 AMR-associated deaths annually *(29)*.

Improving WASH in communities can have direct and indirect effects on AMR. More specifically, better WASH can directly prevent infections with resistant organisms while reducing overall infections, thereby decreasing antimicrobial use and selective pressure for resistance development. Safe drinking-water services can reduce exposure, and improved access to sanitation facilities and wastewater management can substantially decrease the load of resistant bacteria and AMR determinants released into the environment from humans and manufacturing sites *(30)*. A substantial body of evidence shows that simple interventions such as hand hygiene can reduce infections and potentially decrease antimicrobial use. WASH interventions decrease the risk of diarrhoea *(31,32)*, which is often inappropriately treated with antibiotics and remains one of the leading global causes of child mortality, with much of this burden occurring in low- and middle-income countries *(33,34)*. Improvements in WASH services would therefore directly reduce the burden of AMR by averting resistant infections, which is vital given the considerable mortality associated with AMR that results from pathogens spread through insufficient WASH *(1)*.

However, for interventions to be most effective, they need to be tailored to the context where they are implemented. Although there are numerous studies on a wide array of WASH interventions, few evaluate and compare them. Also, it is unclear whether single interventions or multimodal programmes can be more effective in reducing infection burden, AMR and the drivers of AMR, including antimicrobial use. In high-income settings, improvements in water and sanitation infrastructure have resulted in important reductions in the burden of infectious diseases in the past century. However, the impact of improving WASH systems and services on antibiotic use and emergence and transmission of AMR within communities and on at-risk populations (such as women and girls who often bear the responsibility of fetching water *(35)*) needs to be evaluated further. In particular, it is necessary to delineate the effects of reduced antibiotic prescriptions for diarrhoeal disease and the potential reduction in the rise of AMR in low- and middle-income countries.

This research priority highlights the need for studies exploring the impact of inadequate access to WASH and of improved water and sanitation infrastructure in complex urban environments (such as informal settlements) on driving the spread and burden of AMR and antibiotic use *(36)*. Studies investigating the cost–effectiveness of WASH interventions are also needed to ensure optimal resource allocation and investment *(23,37)*.


**Above:** Dr Oladele, a resident in clinical microbiology, rinses off excess Gram stain from a sample slide at the microbiology laboratory in the Department of Medical Microbiology and Parasitology at the Obafemi Awolowo University Teaching Hospitals, Nigeria.

## **Priority #2.** Investigate implementation strategies and the impact of WASH-related interventions in health-care settings on the burden of health care–associated infections and antimicrobial medicine prescribing

*Expanded version:* Investigate implementation strategies of WASH-related interventions in health-care settings (including ensuring access to safely managed water and sanitation, safe hand hygiene, safe management of waste and environmental cleaning), and assess their impact, acceptability, equity and cost–effectiveness on the burden and transmission of resistant health care–associated infections and antimicrobial medicine prescribing across socioeconomic settings.

The quality of WASH services in health-care facilities is defined by the availability of water, sanitation, waste management, environmental cleaning and the ability to perform hand hygiene at the point of care. An estimated 22% of health-care facilities globally in 2021 have limited or no basic water services, one in 10 is lacking sanitation services and half do not have adequate access to hand hygiene facilities at the point of care *(38)*. The lack of adequate facilities and staff shortages in busy clinics result in suboptimal compliance with hand hygiene practices, especially in limited-resource settings. Suboptimal hand hygiene facilitates pathogen transmission within health-care facilities and increases the risks of infections. Further, improper management of health-care waste puts personnel and patients at risk of infections and may lead to environmental contamination. Pathogens causing hospital-acquired infections have high levels of antibiotic resistance *(39)*. Additionally, in settings where health-care infections are common and WASH services inadequate, clinicians may resort to prescribing antibiotics to pre-empt infections, thus increasing the selection of resistant organisms.

Several WASH-related interventions can lead to reductions in the risk of health care-associated infections; however, their impact, cost–effectiveness, implementation and acceptability and equity need to be evaluated across settings and patient populations. More research is required to identify strategies to improve the implementation of WASH interventions in health-care facilities and to assess their impact on AMR. How improved WASH reduces the incidence of hospital-acquired infections and thereby affects the practice of pre-emptive antibiotic prescribing requires further study.

# Infection prevention and control

## **Priority #3.** Identify (cost-)effective, acceptable and feasible multimodal IPC strategies and the relative effect of their components on reducing health care–associated infections

Expanded version: Identify the most effective, cost-effective, acceptable and feasible multimodal IPC strategies (such as hand hygiene, contact precautions and patient isolation) and the relative effect of their components in reducing different types of health care–associated infections caused by multidrug-resistant pathogens across geographical and socioeconomic settings.

An estimated one in 10 patients admitted to hospital will develop a health care–associated infection, with critically ill patients being at highest risk *(40)*. According to recent estimates, 136 million cases of health care–associated antibiotic-resistant infections occur worldwide every year *(41)*, and IPC programmes could avoid an estimated 337 000 AMR-associated deaths in LMIC annually *(29)*. Health care–associated infections result in prolonged hospitalization, increased costs and excess deaths. Data from 2015 from the European Union and European Economic Area members indicated that 63% of cases of infections with antibiotic-resistant bacteria were associated with health care, resulting in 72% of deaths attributable to antibiotic resistance *(42)*. IPC programmes play a key role in preventing health care–associated infections and transmitting resistant pathogens in health-care facilities. WHO has developed recommendations on the core components for IPC, including having IPC programmes with dedicated personnel, the development of evidence-informed guidelines, education and training for all health and care workers, surveillance of hospital-acquired infections to detect their burden as well as outbreaks, multimodal improvement strategies for IPC interventions, monitoring, audit and feedback of IPC practices, ensuring that staff levels are sufficient and bed occupancy is not exceeded and that patient care is provided in suitable environments with sufficient WASH infrastructure and appropriate levels of materials needed for IPC *(43)*. Multimodal improvement strategies comprise several elements implemented together to achieve practice and improvements and are considered the most effective way to implement IPC interventions *(44)*. Critical elements of multimodal improvement strategies include system change, education, raising awareness, use of care bundles and checklists, monitoring and feedback, engaging leadership and positive reinforcement *(43)*.

Several studies have demonstrated the effectiveness of multimodal improvement strategies for IPC, especially for improving hand hygiene in health care and for reducing central-line associated bloodstream infections *(43)*. Stronger data are needed for other types of health care–associated infections, and research on the relative effectiveness of different elements on determining improvement in practices and reducing health care–associated infections, especially those caused by multidrug-resistant pathogens, is a high priority. Data are also still limited on the cost–effectiveness of multimodal improvement strategies and the acceptability and feasibility of their individual elements and of IPC interventions in general, especially in settings with limited resources. Additionally, further research is needed to identify the approaches that can facilitate the implementation and roll-out of multimodal improvement strategies at the national level. This research priority also addresses the need to identify optimal risk assessment strategies while considering their feasibility, clinical impact and cost–effectiveness.

# Immunization

## **Priority #4**. Assess the impact of vaccines on colonization and infection by resistant pathogens and on reducing the use of antimicrobial medicines, health-care encounters and health system costs

Expanded version: Assess the impact of vaccines on preventing colonization and infection by resistant pathogens (whether specifically targeted by the vaccine or not) and on reducing the overall use of antimicrobial medicines, health-care encounters and health system costs among adults and children and across socioeconomic settings.

Vaccines for adults and children represent a promising tool to mitigate AMR, by directly preventing infection and colonization with both antimicrobial-sensitive and -resistant pathogens and indirectly by reducing infections that may require antimicrobial use *(45–48)*. A modelling study estimated that vaccines for children could prevent 181 500 AMR-associated deaths by both directly preventing resistant infections and reducing antibiotic consumption *(29)*. The vaccine value profiles provide a holistic view on the health, economic and societal burden of pathogens with vaccines under development and include impact on AMR *(49,50)*.

Although the body of evidence around vaccines for preventing AMR is growing *(49,51,52)*, more research is needed to assess whether vaccines could reduce the overall burden of drug-resistant infections and prevent further transmission of resistance within communities and health-care settings. Evidence on how vaccines enhance the impact of other infection prevention and stewardship measures could be critical to inform interventions targeting infections caused by resistant pathogens for which treatment options are limited because of availability, access and costs. In addition, by reducing infections, vaccines may lead to reduced antibiotic use and reduce the selective pressure for AMR. More specifically, this priority addresses the need to evaluate how vaccines can be used to aid stewardship efforts and prolong the lifespan of antibiotics. Also, the impact of vaccines such as those for influenza, rotavirus and *Streptococcus pneumoniae* on antibiotic prescribing across settings and populations requires evaluation. In this context, it is critical to ensure that the impact of vaccines in reducing AMR is evaluated during clinical development while formulating policies and included as a criterion to inform the expansion of existing immunization programmes and introducing new vaccines.

## 2.2.2 Diagnosis of bacterial and fungal infections

### **Priority #5.** Investigate and evaluate rapid point-of-care tests to discriminate between bacterial versus non-bacterial infections

Expanded version: Investigate and evaluate rapid point-of-care diagnostic tests (including biomarker-based tests) and diagnostic algorithms to discriminate between bacterial and viral infections and non-infectious syndromes that are feasible for use in limited-resource settings and among different subpopulations (including children and newborns), and how using these tests affects clinical outputs and outcomes.

Almost half the population has limited or no access to diagnostics, and only 19% of people from low- and middle-income countries have access to simple diagnostic tests in primary care to guide prescriptions (excluding those for malaria and HIV) *(53)*. As such, antibiotic prescribing decisions are frequently based on clinical syndromes. Current diagnostic tools are too slow or unavailable to assist prescribers in deciding whether antibiotics are indicated. In many scenarios, decisions have to be made and actioned quickly, such as when managing critically ill people or in the outpatient setting. This is of great consequence since most antibiotic prescriptions are issued in the outpatient setting.

The roll-out of malaria and more recently SARS-CoV-2 rapid diagnostic tests have shown how point-of-care testing can be used for rapidly diagnosing infections and for guiding patient care. The 76th World Health Assembly also highlighted the importance of diagnostic testing through a resolution to strengthen diagnostic capacity and improve access to diagnostic services *(26)*.

Rapid diagnostic tests are needed to aid health-care workers in deciding whether an antibiotic prescription is needed. The lack of availability of and access to easy-to-use, accurate point-of-care tests hinders the ability to distinguish between bacterial, viral and other non-infectious syndromes. Diagnostic uncertainties result in antibiotic prescriptions that may not be necessary, which in turn drives AMR. This problem is especially crucial for children, who often develop viral respiratory infections and diarrhoeal diseases and are frequently given antibiotics they do not need. Additionally, rapid tests for monitoring treatment response have the potential to shorten therapy and reduce antibiotic use.

Studies from various geographical locations, income settings and people with different infectious syndromes have shown that using point-of-care alone or within management algorithms can result in a decrease in antibiotic prescriptions, although these findings have not been consistent across settings *(54)*. If we are to address the diagnostic gap, improve patient care and reduce unnecessary antibiotic prescriptions, rapid point-of-care tests and testing algorithms need to be evaluated across settings and populations to determine their accuracy, usability, cost and cost–effectiveness as well as challenges that might prevent

effective implementation and uptake. For example, the comparative performance and cost–effectiveness of procalcitonin versus other inflammation biomarkers (such as C-reactive protein) for various clinical syndromes and scenarios require further investigation. Such scenarios can include diagnosis of infection, differentiating between bacterial and viral causes, assessing severity and response to treatment. Additionally, algorithms, such as the Integrated Management of Childhood Illness algorithms *(55)*, need validation in different populations accounting for existing recommendations as well as local infection epidemiology. Further, it is critical to ascertain which tests, at which level of care and in which populations can affect patient-important outcomes.


**Above:** Like most of the babies in the ward at a neonatal hospital in Lagos, Nigeria, Ahamba had sepsis. Many had been born outside of a hospital, and limited medical supplies put them at greater risk of getting an infection.

## **Priority #6.** Investigate and evaluate diagnostic tests for detecting pathogens and antimicrobial susceptibility testing

Expanded version: Investigate and evaluate diagnostic tests for isolating and identifying antimicrobial susceptibility testing and/or detecting resistance of bacterial pathogens (including multiplex panel–based tests and tests using novel technologies) that are rapid, (near) point of care, affordable, feasible for use in limited-resource settings and among different subpopulations and from a variety of specimen types, and how using these tests affects clinical outputs and outcomes.

This priority highlights the need for better tests for pathogen identification and for antimicrobial susceptibility testing. Conventional bacteriology and mycology tests require complex laboratory infrastructure and expertise *(56)*. Molecular-based tests have low thresholds for pathogen detection and thus have the potential to reduce delays in instituting effective antimicrobial treatment but are still largely laboratory-based. Molecular tests done at the bedside or in a (near-) point-of-care scenario directly on clinical samples could expedite diagnosis. Rapid, accurate and affordable tests would ideally be developed to detect the presence of severe infections, such as bloodstream infections, directly from blood samples and also be able to rule out infections, thus reducing unnecessary antibiotics.

Within paediatrics, the type and amount of the sample are critical factors. The ideal diagnostic test should involve a minimal quantity of blood to mitigate the need for excessive blood draws from children. Minimizing the volume of blood required for testing from children is crucial to reduce discomfort and potential distress. Such an approach not only contributes to improving the patient experience but also enhances compliance with testing procedures. Another issue highlighted by this research priority is the need for developing innovative, inexpensive and easy-to-use methods for performing high-quality antimicrobial susceptibility testing in lower-level or outside laboratories, which is especially critical for limited-resource settings.

Research that spans multiple domains, including test development, clinical validation, implementation and into practice, is needed. Target product profiles of new tests should account for user requirements, targets assessed, sample processing, turnaround time and technologies used for detection *(57)*. Tests currently being developed are increasingly complex and can have many analytical targets *(58)*. With evolving and emerging AMR, tests would need evolving analytical targets, which may in turn increase resource demand. Translational aspects would need to address the evaluation and validation of the tests, their performance in relation to target product profiles and manufacturing capacity, upscaling and regulatory issues *(59)*. Finally, barriers to rolling out tests and their uptake, pricing and distribution should be considered.

# **Priority #7.** Investigate and evaluate rapid antimicrobial susceptibility testing methods from blood cultures

## Expanded version: Investigate and evaluate phenotypic and genotypic methods of rapid antimicrobial susceptibility testing and resistance detection directly from positive blood culture bottles, especially for use in low- and middle-income countries, and how using these tests affects clinical outputs and outcomes.

Bloodstream infections are associated with substantial mortality with an estimated 1.5 million deaths associated with AMR bacteria and directly causing an estimated 400 000 deaths in 2019 *(1,60)*. Rapid pathogen identification and treatment are critical for improving patient outcomes and the time to initiating appropriate therapy and are associated with survival among critically ill people. Although the time to bacterial identification and the availability of antimicrobial susceptibility testing results has been substantially reduced in recent years, these methods are not universally available and are usually lacking from laboratories in low- and middle-income countries. In 2019, the European Committee on Antimicrobial Susceptibility Testing published recommendations for conducting rapid antimicrobial susceptibility testing on positive blood cultures. which enables results after as little as four hours from blood culture positivity *(61)*. Further, novel phenotypic methods can provide full antimicrobial susceptibility testing results in less than 12 hours *(62)*. Molecular (usually multiplexed panels) tests have also been developed and can be used to detect selected resistance markers, but their price remains prohibitive, limiting their use in lower-level laboratories or in low- and middle-income countries. Further, these methods have not been widely evaluated in low- and middle-income countries, and their performance, usability, ease of result interpretation and challenges related to implementation in low- and middle-income countries have not been explored. Because some of these systems are easier to use than conventional microbiological methods, they may be especially suited for laboratories facing shortages of laboratory personnel, lead to decreased turnaround times and support microbiologists in providing high-quality results to health-care workers.

## **Priority #8.** Investigate and evaluate diagnostic tests for detecting fungal pathogens

Expanded version: Investigate and evaluate rapid, (near) point-of-care diagnostic tests (including antigen and multiplex panel–based tests) for detecting drug-resistant WHO fungal priority pathogens that are critically important for AMR (such as *Candida auris, Aspergillus fumigatus* and *Cryptococcus neoformans*) and feasible for use in limited-resource settings and among different subpopulations, and how using these tests affects clinical outputs and outcomes.

In 2022, WHO outlined a priority list for fungal pathogens, including those important for AMR, to guide research and the development of fungal diagnostics *(4)*. To date, few point-of-care tests are available to enable rapid diagnosis of fungal pathogens and the initiation of appropriate treatment, and access to these is still limited globally. This is especially challenging in limited-resource settings, where access to laboratory testing is generally inadequate *(63–66)*.

Microscopy for moulds is relatively widely available but lacks sensitivity, requires a high level of expertise and cannot be used to detect resistance. Cultures can be used for antimicrobial sensitivity testing but lack standardization, require expertise and laboratory infrastructure, are slow and have limited sensitivity. Following the COVID-19 pandemic, molecular test availability and utilization expanded substantially and can be leveraged to detect resistance. However, molecular methods can be prohibitively costly and are limited to some fungal species *(67)*. Multiplexed molecular assays for pathogen detection from positive blood cultures and other samples can also identify some fungal pathogens, but the spectrum is also limited to a few species and the tests do not usually include resistance detection for fungi. Biochemical assays for fungal identification are available, mainly for yeasts, and inexpensive, easy-to-use platforms are needed to identify filamentous fungi. Lateral flow and other rapid assays require relatively minimal infrastructure and technical requirements, but their global implementation remains limited. Thanks to other well-funded programmes, the cryptococcal antigen test has been extensively rolled out in many low- and middle-income countries *(68)*. However, this implementation is often on the backdrop of legacy agendas such as HIV programmes. Despite this progress, broader adaptation of similar diagnostic approaches with funding dedicated for fungal diseases is still needed. Overall, new tests and innovations are critically needed in this field. Lateral flow assays or similar simple tests with improved performance are needed for a broader range of fungal pathogens. More broadly affordable tests that can identify a broad range of invasive fungal pathogens directly from whole blood or other non-invasive samples without the requirement for culture are also needed. Another important challenge in diagnosing fungal infections is the frequent delays before fungal infections are suspected. Cheap, accurate (near-) point-of-care tests would have the potential to increase testing and reduce delays in initiating appropriate treatment.

# **Priority #9.** Investigate the clinical and diagnostic value of phenotypic antifungal susceptibility testing

## Expanded version: Investigate and evaluate the clinical utility and diagnostic accuracy of phenotypic antifungal susceptibility testing, including determining minimal inhibitory concentration breakpoints and testing for in vitro and in vivo synergy between antifungal medicines

A limited number of methods are available for performing antimicrobial susceptibility testing of fungal pathogens *(69)*. Reference methods exist for yeasts and moulds, but these are not commercial and are time-consuming. Breakpoints exist only for some of the *Candida* and *Aspergillus* species, and further breakpoints need to be developed. Methods using disk diffusion and gradient diffusion tests require less expertise and have variable costs. Commercial automated methods exist for yeasts, but they are expensive and do not have specific breakpoints. Correlation with other testing methods can be variable depending on the species and antifungal tested. Agar screening methods for moulds have also been developed, and the methods require confirmation using reference methods. Overall, antifungal susceptibility testing is not routinely performed in many settings, even in laboratories in high-income countries. Methods are mainly available for yeasts, and there are fewer methods for antifungal susceptibility testing in moulds. There are limited data on the availability and sustainability of these techniques in low- and middle-income countries and on the in vitro and in vivo correlation of antifungal susceptibility testing results. Methods assessing synergy between antifungals are not well developed, and the correlation with in vivo response needs further investigation *(4)*.

## **Priority #10.** Investigate and evaluate novel rapid point-of-care assays and optimal testing approaches for (resistant) *Neisseria gonorrhoea*

Expanded version: Investigate, assess the performance and evaluate the implementation of novel rapid point-of-care molecular and non-molecular assays and optimal testing and screening approaches (including self-testing) for *N. gonorrhoeae* and AMR detection to reduce inappropriate antibiotic prescribing and the emergence of AMR.

An estimated 82.4 million new *N. gonorrhoeae* infections occurred in 2020 among people aged 15-49 years old *(70)*. In the absence of diagnosis and treatment, infections can cause substantial morbidity among adolescents and adults and can negatively affect pregnancy and birth outcomes. Culture and antimicrobial susceptibility testing have long represented the gold standard for diagnosing *N. gonorrhoeae* infections, but these approaches require specialized technical expertise and laboratory settings and enhanced access to health-care services. More recently, molecular multiplexed tests have been developed for diagnosing STIs, but they typically operate within specialized laboratory settings, lead to delayed results and treatment and require costly equipment.

Syndromic management has been the cornerstone for STI diagnosis and treatment *(71)*, especially in low- and middle-income countries, where the availability and cost of diagnostic testing are challenging. However, many people with STIs are asymptomatic and are thus missed by a syndromic approach to diagnosis *(72)*. Novel rapid point-of-care tests have the potential to overcome this issue whenever they are easily accessible and at low cost *(73)*. Additionally, rapid tests that can provide results during the same clinic visit would prevent diagnostic delays and missed opportunities in people not returning after testing. Lateral-flow tests would be ideal in providing rapid diagnosis but currently lack sensitivity. Several molecular (near-) point-of-care tests for *N. gonorrhoeae* are currently in the pipeline but require further qualification evaluation. The additional detection of resistance would be critical in guiding optimal therapy given the increasing prevalence of resistance to third-generation cephalosporins, macrolides and fluoroquinolones globally. Additionally, this research priority considers novel screening approaches aimed at improving diagnosis and reducing transmission within communities at higher risk, including pregnant women. For example, self-testing could reduce stigma-related diagnostic barriers.

# 2.2.3 Treatment and care of bacterial and fungal infections

## Antimicrobial stewardship

### **Priority #11.** Investigate antimicrobial stewardship interventions that are context specific, feasible, sustainable, effective and cost-effective in outpatient and inpatient settings

Expanded version: Investigate antimicrobial stewardship interventions (such as implementing the WHO AWaRe antibiotic book, guidelines, clinical algorithms, education and training, audit and feedback), alone or in combination, that are context specific, feasible, sustainable, effective and cost-effective to avoid antimicrobial misuse in outpatient and inpatient settings, especially where diagnostic capacity may be limited.



Antimicrobial stewardship interventions are essential for patient care since they improve the quality of antimicrobial prescribing and antimicrobial use and ultimately patient outcomes *(74)*. WHO has published guidance and tools to support the implementation of antimicrobial stewardship. The AWaRe (access, watch, reserve) framework classifies antibiotics on the WHO Model List of Essential Medicines *(75,76)* into three groups – access, watch and reserve – based on how antibiotics affect AMR *(77)*. WHO has set a target that at least 60% of overall country-level antibiotic use should be from the access group *(78)*. The WHO AWaRe antibiotic book *(79)* provides guidance on managing common clinical infections among adults and children, considering antimicrobial stewardship principles and the AWaRe classification. WHO has also developed a toolkit for antimicrobial stewardship programmes, including the core elements for stewardship in hospitals for low- and middle-income countries *(74)*.

Although such guidance is crucial, availability alone does not ensure appropriate antibiotic prescribing and use. Existing evidence for the effectiveness of antimicrobial stewardship interventions largely derives from inpatient settings in high-income countries and often has methodological limitations. Further research is needed to identify, set priorities for, implement and evaluate effective antimicrobial stewardship interventions and their implementation in diverse settings, especially those with limited diagnostic capacity and primary care, where 90% of antibiotic prescriptions are dispensed *(80)*. Guidance for antibiotic audit and feedback for primary care has recently been published *(81)*, and the impact of these quality improvement interventions needs to be assessed in different settings and populations. A further key consideration for antimicrobial stewardship interventions is long-term sustainability. Investigating the cost–effectiveness of interventions across socioeconomic and geographical contexts is essential, considering their potentially broad impact.

This research priority underscores the importance of tailoring interventions to the unique circumstances and available resources of different contexts. It especially emphasizes the importance of appropriate antibiotic use in primary care and vulnerable populations and the need for antimicrobial stewardship to be implemented in low- and middle-income countries and limited-resource settings, where health system challenges have limited progress so far and where access to essential antibiotics also remains a key problem.

## **Priority #12.** Identify feasible, effective and scalable pharmacist dispensing practices for antimicrobial medicines along with related regulatory frameworks to improve antimicrobial stewardship in the community, especially in low- and middle-income countries

Expanded version: Identify feasible, effective and scalable pharmacist dispensing practices for antimicrobial medicines in community pharmacies, along with related regulatory frameworks (such as incentives and disincentives) to improve antimicrobial stewardship in the community, especially in low- and middle-income countries.



Community pharmacies are often the first point of contact with the health system and are a main source of health education and information, and of antibiotics, both with and without prescription. Although most countries have developed regulatory frameworks to prohibit over-the-counter sales of antibiotics, these are often not well implemented or enforced, especially in low- and middle-income countries. Worldwide, almost two thirds of antibiotics are dispensed without a prescription *(82)*. Factors leading to non-prescription use include customer demand and lack of knowledge, difficulties in accessing health care, financial gains for the pharmacies and permissive regulatory frameworks *(82)*. Antimicrobial stewardship interventions and related regulations at the pharmacy level are therefore expected to affect the volume and appropriateness of antibiotic use *(83)*.

The objective of this research priority is to identify viable, effective and scalable practices for pharmacists and pharmacy personnel in dispensing antimicrobials in community pharmacies. Understanding the knowledge, attitudes and practices of pharmacists and pharmacy personnel related to antimicrobial use, especially over-the-counter dispensing, and the socioeconomic context in which antibiotics are used and that drive dispensing without prescription, are key for implementing effective stewardship interventions in the community. This understanding is critical since pharmacists also act as community educators with the ability to dispel misconceptions about antibiotics and provide advice on how they should be accessed and used. It also highlights the need to examine regulatory frameworks (rules, policies and guidelines set by authorities to govern) and how these can be leveraged to promote responsible antimicrobial use in the community. The goal is to generate evidence to enhance antimicrobial stewardship within community pharmacies, especially those in low- and middle-income countries.

## **Priority #13.** Investigate criteria and strategies to optimize empirical antimicrobial therapy for the main infectious syndromes, especially in settings with limited access to medicine, diagnostic capacity and health-care services

Expanded version: Investigate criteria and strategies to optimize empirical antimicrobial therapy (such as antimicrobial spectrum, dose, timing of initiation, de-escalation and stopping), weighting the benefits (such as improving outcomes and reducing costs) versus potential harm (such as clinical failure, infection relapse, resistance emergence and adverse events) for main community and health care–associated infectious syndromes among adults and children, especially in settings with limited access to medicine, diagnostics and health-care services.

The vast majority of antimicrobials, especially in primary care, are prescribed empirically without identifying the pathogen and performing antimicrobial susceptibility testing. In low- and middle-income countries, where laboratory diagnostic capacity is limited or, where available, is underutilized or employed too late in the care cascade, empirical treatment plays an even larger role. This includes people with severe infections who are often treated without microbiological testing. When laboratory diagnostics are not available, antimicrobial therapy should nonetheless be optimized by having a clear clinical diagnosis of infection (based on history and examination), understanding the likely causative pathogens of the infectious syndrome and considering the prevalence of AMR. Further, treatment decisions should account for contextual and patient factors and adhere to basic antimicrobial stewardship principles. This approach aims to minimize unnecessary exposure to (broad-spectrum) antimicrobials and mitigate the risk of treatment failure and emergence of AMR.

There are several additional considerations for optimizing empirical regimens for children. Many antibiotics administered to children are prescribed off label, increasing risks such as reduced efficacy or heightened toxicity from under- or overdosing. This practice also increases the risk of AMR because of suboptimal dosing *(84)*. Ethical, logistical, regulatory and technical challenges inherent in conducting clinical trials within this age group also require special attention.

Overall, the purpose of this research priority is to provide criteria and strategies that can assist in optimizing empirical antimicrobial therapy to improve patient outcomes while promoting the appropriate use of antimicrobial medicines *(79,85)*. These criteria ensure that the chosen therapy is evidence informed and is tailored to the infectious syndrome, patient-specific factors and the broader epidemiological and access context.

More specifically, this priority highlights the need to identify a public health approach for empirical treatment informed by thresholds in the prevalence of AMR in the main pathogens causing infectious syndromes that would trigger a change in the antimicrobial choice for empirical therapy. Factors that need to be considered in treatment optimization include health-care setting, site of infection, infection severity, risk of further emergence or dissemination of resistance and patient population. In addition, effective strategies need to be identified, such as clinical scores, results from readily available tests and safety netting, to ultimately reduce unnecessary prescribing while maintaining patient safety and satisfaction for non-severe infections.

# Antimicrobial use

## **Priority #14.** Determine optimal methods, metrics and targets to monitor antimicrobial use

Expanded version: Determine optimal (feasible, accurate and cost-effective) methods and metrics to monitor antimicrobial use in the community and health-care settings and appropriate targets to monitor progress in reducing inappropriate antimicrobial use.



Global antimicrobial use increased by almost 40% between 2000 and 2015, partly because of improved access in limited-resource settings *(86)*. However, antimicrobial use in some low- and middle-income countries remains low, reflecting difficulty in access. Monitoring antimicrobial use and its appropriateness is crucial for understanding the factors contributing to developing AMR and implementing interventions to reduce its spread. Metrics are needed for quantifying antibiotic use and appropriateness and comparing them across settings and populations. These metrics can include defined daily doses, relative use of AWaRe antibiotic categories and the Access to Watch index *(87,88)*. Regarding data sources, some settings do not have accurate antibiotic use data and may need to use other approaches or implement systems that will enable accurate data collection. Methods that use and integrate various data collection systems at different levels of health care, such as electronic health records, pharmacy data and sales records, can be considered for measuring antimicrobial use. Further, special attention must be given to identifying the most suitable metrics for quantifying antibiotic use among children and newborns, since defined daily doses are normally assigned based on use among adults.

The goal of this research priority is to determine the most (cost-)effective methods and metrics for monitoring the use of antimicrobial drugs in both community and health-care settings. In addition, this priority aims to establish targets for monitoring progress in reducing inappropriate antimicrobial use. These targets will help to assess and track the effectiveness of interventions and strategies to mitigate AMR by enabling health-care systems and policy-makers to make informed decisions and implement evidence-informed interventions.

# **Priority #15.** Determine the patterns and drivers of appropriate and inappropriate prescribing and use of antibiotics

Expanded version: Determine the levels, patterns, trends and drivers of appropriate and inappropriate prescribing and use of access, watch and reserve antibiotics across countries and community and health-care settings, with data disaggregated by sex, age, socioeconomic status and subpopulations, including those experiencing vulnerability and with comorbidities (such as people living with HIV, people with TB and people with malaria).

This research priority aims to provide valuable insights into how access, watch and reserve antibiotics *(79)* are prescribed and used in various countries, communities, populations and health-care settings. It focuses on understanding the levels, patterns, trends and factors that influence both appropriate and inappropriate practices. Several factors need to be considered, including the indication for starting antibiotics (whether a bacterial infection is present, whether the organism isolated is colonizing the site or causing infection and the results of microbiological testing), the antibiotic prescription itself (whether it covers the most probable pathogens, its appropriateness for the severity of the disease and comorbidities, and whether antibiotics are prescribed at the optimal dose and route), its subsequent review (of the indication, antibiotic selection, possibility for oral switch and its compatibility with the results of microbiological testing) and the decision to stop (appropriate treatment duration for a particular indication and treatment response) *(89)*. However, when ascertaining appropriateness, the availability of and access to antibiotics and the context in which prescribing occurs should be carefully considered.

A significant focus of this research is to examine how potential determinants affect antibiotic utilization, including sex, age, socioeconomic status, comorbidities or other vulnerabilities and specific subpopulations. It aims to investigate disparities and specific trends that exist within demographic groups. The knowledge gained from this research can guide policy, target interventions, improve health-care delivery and ultimately contribute to more effective antibiotic stewardship efforts.

## **Priority #16.** Investigate approaches to effectively use data on antimicrobial use and AMR surveillance to inform antimicrobial stewardship and guidelines

Expanded version: Investigate optimal approaches to effectively use facility- and/or national-level data on antimicrobial use and AMR surveillance to inform antimicrobial stewardship programmes and treatment guidelines.

This research priority focuses on investigating effective approaches for using data on antimicrobial use and AMR surveillance at both the facility and national levels to drive action *(88)*. Its primary purpose is to leverage these data to inform the development of stewardship programmes and treatment guidelines and ultimately to improve patient care. The investigation requires a multidisciplinary approach and encompasses various aspects, including analysis techniques, interpretation approaches and strategies for disseminating the findings. By effectively utilizing antimicrobial use data, health-care facilities and national health systems can identify areas characterized by excessive or distorted antimicrobial use. This identification might enable the development of targeted stewardship interventions to promote appropriate antimicrobial use among adults and children. These data also play a crucial role in informing the development of context-specific treatment guidelines, considering local patterns of AMR and antimicrobial use. For example, AMR surveillance data could potentially be used to identify hotspots for resistance and predict areas of emerging resistance for specific pathogens or populations, thereby enabling prompt action and outbreak responses. New technologies and analysis approaches could be used to explore existing datasets and identify needs for stewardship interventions and changes in practice guidelines more efficiently. Integrating these findings enhances the ability of health-care systems to combat AMR by optimizing the effectiveness of antimicrobial therapy and bridging the gap between surveillance and daily practice.

# Antimicrobial medicines

## **Priority #17.** Investigate antibiotic treatment regimens for infections, especially for extended-spectrum beta- lactamase–producing and carbapenem-resistant Enterobacterales

Expanded version: Investigate efficacious and safe antibiotic treatment regimens based on old and new agents and combinations for infections, especially for extended-spectrum beta-lactamase–producing and/or carbapenem-resistant Enterobacterales, with minimum selection and transmission risk for AMR, especially among children and other subpopulations experiencing vulnerability.



*Escherichia coli* and *Klebsiella pneumoniae* are common causes of bacterial infections and are associated with substantial morbidity and mortality *(1,90)*. Resistance to third-generation cephalosporins is relatively prevalent in some regions and is commonly associated with resistance to other antibiotic classes. This is particularly problematic for settings in which carbapenems are inaccessible or unaffordable. Carbapenem resistance can further limit treatment options to toxic or very expensive antibiotics *(91,92)*.

The goal of this research priority is to identify treatment strategies that are both efficacious and safe for extended-spectrum beta-lactamase–producing and/or carbapenem-resistant Enterobacterales-resistant bacteria. It focuses on developing regimens that combine old and new antibiotics while exploring potential synergistic effects in laboratory settings and animal models and on conducting clinical trials. Another issue is optimizing dosing and administration of antimicrobials for pathogens that have higher minimal inhibitory concentrations and for which antimicrobials may still attain the desired effect. A key consideration in this research priority is to minimize the risk of selecting and transmitting AMR. Further, non-antibiotic alternatives, such as bacteriophages or bacteriophage-related products, require further evaluation for managing patients with multidrug-resistant organisms *(93,94)*. Oral therapies for extended spectrum beta-lactamase–producing bacteria remain a major gap *(95)*.

This research priority focuses especially on children, who currently face limited treatment options *(96)*. For example, for children younger than five years, *K. pneumoniae* accounted for an estimated 17.2 million disability-adjusted life-years (DALYs) in 2019, third only to malaria and *S. pneumoniae* *(90)*. Further, *K. pneumoniae* is a leading cause of neonatal sepsis in some settings in low- and middle-income countries; isolates are frequently resistant to third-generation cephalosporins *(97)*, and carbapenem resistance is increasing *(98)*. Antibiotics for newborns are often prescribed off label because of perceived or documented needs for empirical or targeted therapy against multidrug-resistant pathogens. Prescribing medication this way can lead to decreased effectiveness or higher risk of toxicity from incorrect dosing *(99)*, and it also raises the likelihood of developing AMR because of inadequate dose levels. Nevertheless, the current drug development and regulatory frameworks result in restricted and delayed access to approved drugs with labelling guidance for all children, especially newborns.

# **Priority #18.** Investigate antibiotic treatment regimens for infections by drug-resistant typhoid and non-typhoidal salmonellae

Expanded version: Investigate efficacious and safe antibiotic treatment regimens for infections by drug-resistant typhoid and non-typhoidal salmonellae (including for pathogens resistant to cephalosporins and fluoroquinolones) across socioeconomic settings.



An estimated 95 million cases of salmonella enterocolitis, 535 000 cases of invasive non-typhoidal salmonellosis and 14.3 million cases of enteric fever caused by *Salmonella* Typhi and *Salmonella* Paratyphi occurred in 2017 *(100,101)*. Non-typhoidal salmonellosis and enteric fever (caused by *S.* Typhi and *S.* Paratyphi) let to an estimated loss of 14.9 and 14.8 million DALYs, respectively, in 2019 *(90)*. Diarrhoeal disease strongly affects children. Although there have been widespread efforts to manage and prevent it, it remains the third most frequent cause of death for children younger than five years (not including newborn deaths), presenting a substantial global challenge and hitting low- and middle-income countries especially hard *(102)*.

AMR in salmonellae is increasingly limiting treatment options. Fluoroquinolones have represented the mainstay for enteric fever treatment because of their good oral bioavailability and low cost. However, reduced susceptibility and resistance to fluoroquinolones is prevalent in South-East Asia and is also increasingly being reported in Africa *(103)*. Further, some settings in South-East Asia have experienced outbreaks of third-generation cephalosporin resistant *S.* Typhi, further limiting treatment options, and azithromycin resistance has also been reported *(104)*.

Ineffective antibiotic treatment because of resistance is associated with poorer clinical outcomes and higher mortality. The goal of this research priority is to identify the treatment regimens that achieve the best outcomes for infections caused by drug-resistant typhoid and non-typhoidal salmonellae. The focus is on identifying regimens that are both effective and safe, considering various factors that can influence treatment outcomes, including the geographical context and the AMR patterns associated with different regions and regimens with early switch to oral administration.

# **Priority #19.** Investigate empirical antibiotic treatments for gram-negative bacteria causing bloodstream infections among newborns and young children in settings with high AMR prevalence

Expanded version: Investigate efficacious and safe empirical antibiotic treatment (drug choice, drug combination, route, dose and duration) for gram-negative bacteria causing bloodstream infections or sepsis among newborns and young children, especially in settings with high AMR prevalence and limited diagnostic capacity and antimicrobial medicine availability.

Globally in 2017, an estimated 20 million newborns and children younger than five years developed sepsis, resulting in 2.9 million deaths *(105)*. In this population, *K. pneumoniae* and *E. coli* were associated with 17.2 and 10.6 million lost DALYs, respectively, in 2019 *(90)*. Newborns and young children, especially those living in limited-resource settings, are highly susceptible to bloodstream infections and sepsis, making effective treatment crucial to improve their chances of survival and long-term health outcomes, combatting AMR, reducing health inequities and promoting public health. Empirical antibiotic treatment is crucial to initiate prompt therapy; however, limited AMR surveillance in many settings lacking access to diagnostic testing means the range of sepsis-causing pathogens and patterns of AMR is frequently unknown. The increasing prevalence of multidrug-resistant gram-negative bacteria limits the available treatment options and raises the risk of treatment failure.

Investigating new treatment approaches is vital to address this growing challenge. Studies are required to support the use of new and existing antibiotics at younger ages, including assessing safety, establishing appropriate dosing and administration, and initiating steps to obtaining regulatory approval *(84)*. Barriers to research include ethical issues, small sample sizes and heterogeneity in the study population. In settings with limited diagnostic capacity for bacterial identification and antimicrobial susceptibility testing, targeted treatment is often not possible. Consequently, understanding the most efficacious empirical treatment options is essential in these settings. The burden of gram-negative infections and sepsis disproportionately affects communities with limited access to health-care resources and higher rates of AMR. Research focused on optimizing treatment in these settings can help to bridge the gap and reduce health disparities, ensuring that populations experiencing vulnerability receive appropriate and effective care. There is a pressing need to develop alternative treatments to the current WHO-recommended empirical treatment for neonatal sepsis and possible serious bacterial infections among newborns and young infants in settings with a high prevalence of multidrug-resistant bacteria *(106,107)*.

## **Priority #20.** Investigate antifungal regimens for infections caused by WHO fungal priority pathogens critically important for AMR

Expanded version: Investigate antifungal regimens optimized for efficacy, cost, safety and duration for the treatment of infections caused by WHO fungal priority pathogens that are critically important for AMR (such as *Candida auris, Aspergillus fumigatus* and *Cryptococcus neoformans*) in settings with increasing or high prevalence of antifungal resistance.



The stalling investment into research and development of new antibiotics is widely recognized, but the situation for treating fungal infections is even more critical given the limited number of drug classes available and the rapid emergence of antifungal resistance. Antifungal resistance in *C. auris* and *A. fumigatus* leads to treatment failure, prolonged infections and unfavourable outcomes. The high cost of commonly prescribed antifungal drugs makes them inaccessible or unaffordable for certain populations or health-care systems. These challenges further limit the availability and effectiveness of therapies, especially in resource-limited settings. Addressing these issues requires collaborative research efforts to develop new antifungal agents, optimize treatment regimens and improve access to affordable and effective therapies *(108)*. Key aspects for research include comparing single versus combination regimens and their relative impact on antifungal resistance and whether shorter regimens with equal efficacy could reduce resistance. Determining how to integrate resistance endpoints built into clinical trials would be important to address these research questions.

Addressing this priority among children is equally important. Many of the existing data that support dosing approaches for the present antifungal agents for children come from research designed to achieve drug exposure levels parallel to those established as effective and secure among adults. Nevertheless, both the pathophysiology of fungal infection and pharmacokinetics differ clinically between children and adults. Achieving the best possible treatment for fungal infection in this unique population requires comprehensive understanding of these distinctions, prompting studies to explore the pharmacokinetics, safety and efficacy of antifungal therapies for newborns and children.

# **Priority #21**. Investigate regimens for urogenital and extragenital STIs in the context of increasing AMR

Expanded version: Investigate efficacious and safe regimens based on new or existing antimicrobial medicines for urogenital and extragenital STIs (such as resistant *N. gonorrhoeae* and resistant *Mycoplasma genitalium*) in the context of increasing AMR levels, including in populations experiencing vulnerability (such as people living with HIV, pregnant women and adolescents).



Effective treatment for *N. gonorrhoeae* infections is being challenged by the reduced susceptibility to third-generation cephalosporins, azithromycin and fluoroquinolones at the global level *(109,110)*. Moreover, few antibiotic drug classes are effective against *M. genitalium,* another sexually transmitted pathogen, and among these, doxycycline achieves low cure rates and azithromycin and fluoroquinolones resistance rates are increasing *(111)*. A few, but not nearly enough, novel antibiotics are currently being evaluated for treatment for *N. gonorrhoeae*. If proven effective, these antibiotics or antibiotic combinations need to be evaluated in different populations and settings. In addition, the effectiveness, optimal dose and antibiotic regimens for treating extragenital infections need to be explored because of differences in drug exposure and potential for acquiring resistance. This research priority aims to identify the most effective combinations of new or existing antimicrobial medicines while also considering the needs of the most severely affected populations. By addressing the unique challenges faced by these populations (such as people living with HIV, pregnant women and adolescents) in accessing health care, adhering to treatment regimens and potential drug–drug interactions because of coexisting conditions, health-care workers can improve the management of these infections and reduce their transmission and complications.

## 2.2.4 Cross-cutting areas

### Antimicrobial resistance epidemiology, burden and drivers

## **Priority #22.** Investigate the epidemiology, mortality, morbidity and impact of infections caused by resistant WHO bacterial priority pathogens

Expanded version: Investigate the prevalence, incidence, mortality, morbidity and socioeconomic impact of community-acquired infections (respiratory tract infections, urinary tract infections and bloodstream infections) and health care–associated infections (bloodstream infections, urinary tract infections, surgical site infections and respiratory tract infections) caused by resistant WHO bacterial priority pathogens, with data disaggregated by sex, age, socioeconomic status and subpopulations (such as populations experiencing vulnerability or with comorbidities, including people living with HIV, people with TB and people with malaria) and across socioeconomic settings, especially in low- and middle-income countries.

An estimated 4.71 million deaths were associated with bacterial AMR in 2021 *(1)*. However, the true burden of AMR is unknown because of the absence of reliable, comprehensive and representative surveillance data from many settings, especially low- and middle-income countries. In particular, more research is needed to investigate the AMR burden and the extent to which AMR contributes to increased morbidity and mortality in subpopulations experiencing vulnerability, those having limited access to health care or having comorbidities and who may be more susceptible to bacterial infections with resistant pathogens *(112)*. Understanding of the incidence, prevalence, burden and socioeconomic effects of community-acquired and hospital-acquired infections is also inadequate.

The scarcity of data can be attributed to several factors, including the limited availability of diagnostic tests, health-care financing models and effective national plans for conducting surveillance. One main objective of the Global Action Plan on Antimicrobial Resistance is to strengthen the knowledge and evidence base through surveillance and research to generate reliable estimates of the threat posed by AMR *(9)*. Robust studies are needed to characterize mortality, morbidity and cost attributable to AMR and to inform mathematical models to generate reliable estimates validated by empirical data *(113)*.

# **Priority #23.** Investigate the epidemiology, morbidity, mortality and impact of infections by resistant WHO fungal priority pathogens critically important for AMR

Expanded version: Investigate the prevalence, incidence, morbidity, mortality and socioeconomic impact and identify and quantify the routes and dynamic of infections by resistant WHO fungal priority pathogens that are critically important for AMR (such as *C. auris, A. fumigatus* and *C. neoformans*) across geographical and socioeconomic settings and in populations experiencing vulnerability.

Fungal infections have substantially increased in incidence, especially among immunocompromised people, such as those living with HIV, people with cancer, organ transplant recipients and critically ill people. In addition, the growing resistance of fungal pathogens to antifungals and limited access to effective and safe antifungals present a multifaceted challenge. Effectively addressing this challenge requires much better understanding of the epidemiology of fungal infections, the contribution of antifungal resistance to increased morbidity and mortality and the associated socioeconomic impact. Establishing robust surveillance systems globally might provide more comprehensive and representative data *(114)*, but lack of access to diagnostics will continue to result in underestimation of the incidence of fungal infections and the prevalence of antifungal resistance. Strengthening both diagnostics and surveillance is one of the three primary areas for action to address antifungal resistance outlined in the WHO fungal pathogen priority list, which further elaborates on various strategies to strengthen fungal surveillance *(4)*. Published in 2022, the document aims to catalyse scientific interest, increase resource allocation and gain support from policy-makers, and it assigns critical priority to pathogens with importance for AMR, including *C. auris*, *A. fumigatus* and *C. neoformans*.

## **Priority #24.** Investigate factors driving colonization and infection by resistant WHO bacterial priority and fungal pathogens

Expanded version: Investigate the association, contribution and impact of structural and health system factors (such as hospital microbiome, sanitation infrastructure, waste management, health expenditure, governance, distribution of resources, population displacement, conflict and disruptions in the care continuum) on colonization (selection, persistence and spread or loss of bacterial populations) and infection by WHO bacterial and fungal priority pathogens in subpopulations, including those experiencing vulnerability (such as migrants and refugees) and people with comorbidities, across socioeconomic settings.

This research priority seeks to improve understanding of the complex relationships between structural and health system factors and colonization and infection with antimicrobial-resistant pathogens across settings and populations, including those with comorbidities and those experiencing vulnerability. The priority highlights many factors that may contribute to colonization and subsequent infection with resistant organisms. Insufficient diagnostic services within health-care facilities results in inability to detect outbreaks, and ineffective or absent IPC programmes may result in transmission of resistant organisms. Insufficient training and staffing shortages can also lead to lapses in IPC practices, facilitating transmission. An estimated 1.7 billion people visit health facilities without basic water services, and only 21% of health-care facilities have basic sanitation *(38,115)*. The lack of water and sanitation services within health-care facilities further affects effective infection prevention and the acquisition of resistant organisms. The relative impact of each of these factors in different settings requires further study.

Overuse of antibiotics can select for resistant organisms and is recognized as one major driver of AMR *(116)*. System factors in the community that may contribute to overuse of antibiotics include lack of access to health care, leading to self-medication *(117)*. Other structural and system factors contributing to colonization or infection with AMR that are less well understood may include overcrowding, limited access to safe water and sanitation and contamination of the environment with resistant organisms or antibiotic residue because of inadequate waste disposal, extensive use in food production or natural disasters.

Research should focus particularly on populations that may be at increased risk of colonization and infection with resistant organisms. These include people with comorbidities (who use health care more frequently and may require antibiotic treatment more frequently) *(118)* and migrants, refugees and other displaced individuals who may be subject to overcrowding, lack of access to health care and inadequate access to water and sanitation services *(119)*.

Governance factors that may promote AMR include insufficient health expenditure, inadequate financing models for health-care systems and weak regulatory frameworks for antibiotic use, stewardship and IPC programmes *(120)*. However, each of these associations requires focused attention and better setting-specific data to drive policy changes and resource allocation.

# **Priority #25.** Identify optimal surveillance methods to generate accurate and reliable data on the epidemiology and burden of AMR

Expanded version: Identify optimal (efficient, effective and cost-effective) surveillance methods to generate accurate and reliable data on the epidemiology and burden of AMR among WHO bacterial and fungal priority pathogens (including determining the molecular mechanisms of resistance) in community and health-care settings and disaggregated by sex, age and subpopulations that are relevant and actionable at the local and national levels, especially in low- and middle-income countries.

In accordance with the Global Action Plan on Antimicrobial Resistance *(9)*, the Global Antimicrobial Resistance Surveillance System (GLASS) has set out to standardize data collection, analysis, interpretation and sharing across countries for a consolidated and effective response to AMR *(121)*. However, there is a need to go beyond laboratory-based surveillance and integrate epidemiological, clinical and population-level data and achieve better quality and representativeness of the data *(122)*. There are several important considerations to ensure the collection of high-quality, reliable data that can be translated into effective action. Among these, adequate diagnostic stewardship, which comprises ordering the right diagnostic tests for the right people at the right time, is critical to identify infections caused by antimicrobial-resistant organisms *(123)*. Limited resources and expertise for undertaking surveillance and conducting testing in some settings can introduce bias and compromise the representativeness and value of the observations. Examples include limited access to health care, lack of standardized knowledge and practices of health-care workers and inadequate health system financing. The design of a surveillance system, including methods for selecting surveillance units and choice of diagnostic tests, must therefore be tailored to the particularities and capacities of the setting and the specific objectives of the system for the data to be fit for purpose.

Molecular surveillance enables the tracking of specific resistance-conferring genes or variants, and genomic surveillance would enable more comprehensive genetic analysis and the tracking of resistant clones of bacteria *(124,125)*. Exploiting the full potential of genomic surveillance requires establishing how genotypic resistance predicts phenotypic resistance for all GLASS pathogens and ultimately all priority pathogens by establishing a comprehensive, standardized catalogue similar to the one developed by WHO for *M. tuberculosis* *(126)* and building on existing initiatives *(127,128)*.

## **Priority #26.** Assess how mass administration of antimicrobial medicines affects AMR

Expanded version: Assess how the programmatic use of antimicrobial medicines in mass administration affects AMR in the short and long term, focusing on subpopulations experiencing vulnerability in low-income settings.

Mass drug administration is a key strategy for controlling and eliminating several neglected tropical diseases and malaria. This strategy has benefits in reducing burden, morbidity and disability, especially in vulnerable populations from limited-resource settings *(129)*. Beyond targeted pathogen control programmes, mass administration of azithromycin may also improve children's survival by reducing the burden of other bacterial infections *(130–132)*. However, mass administration of antimicrobials may increase selective pressure and lead to acquiring and transmitting resistance *(133)*. Some evidence suggests that mass administration of azithromycin transiently increases the prevalence of macrolide resistance in *S. pneumoniae* and may be associated with resistance to other antibiotic classes *(134,135)*. Incorporating AMR as a primary outcome in randomized controlled trials that evaluate the clinical impact of mass administration of antimicrobials is therefore essential.

Further research is also needed on how programmatic use of antimicrobial medicines in mass administration affects the emergence, transmission and persistence of resistance in other pathogens important for AMR (such as *Salmonella enterica*, *Shigella* spp. and *Campylobacter* spp. in which fluoroquinolone resistance is increasing and *N. gonorrhoea*) and in subpopulations such as people living with HIV in the long term. This research priority also addresses the need to better understand the duration of these effects, the association with resistance in other antibiotic classes, the subsequent clinical impact of resistance and the best strategies that can be used for AMR surveillance when mass drug administration campaigns are implemented.

# **Priority #27.** Evaluate how currently recommended syndromic STI management and treatment of people with asymptomatic STIs affect antibiotic prescribing and AMR

Expanded version: Evaluate the public health benefits, cost, impact on unnecessary or inappropriate antibiotic prescribing and potential AMR consequences of currently recommended syndromic STI management and treatment of people with asymptomatic STIs (including *N. gonorrhoeae*) in settings with variable diagnostic capacity.

This expands on research priority #10, which highlights the urgent requirement to enhance diagnostic capability for STIs. Globally, STIs are widespread, with more than 1 million new cases occurring daily *(71)*. Rapid diagnosis of STIs and treatment are essential because untreated STIs may result in infertility, negative pregnancy outcomes, a higher likelihood of contracting additional infections such as HIV and increased spread of the STI. However, many STIs do not exhibit symptoms or present with symptoms that are not specific.

In low- and middle-income countries, a syndromic approach based on clinical algorithms is used for diagnosing STIs and treating the people who have them *(71,136)*. This approach bypasses the need for using laboratory tests in settings with limited access to laboratory services such as outreach activities or mobile clinics, and treatment can be offered on the same day. However, this approach is challenged by the risk of overtreatment and missed opportunities for treatment for those who are asymptomatic. Since diagnostics are either unavailable or inaccessible in many settings, syndromic management will continue to be used widely.

Syndromic management of STIs should not constitute the sole strategy for controlling STIs at the national level. STI surveillance should become an integral component of the syndromic approach, closely intertwined with periodic assessment of the AMR patterns of key pathogens. Sustained and strengthened STI surveillance efforts enable more robust data. Moreover, understanding of the root causes of emerging STIs syndromes needs to be improved through regular etiological studies conducted at sentinel sites, including through molecular assays. In addition, since STI complications significantly contribute to the overall disease burden, routine STI surveillance should incorporate the monitoring of these complications within STI management reporting systems.

To effectively address STIs, surveillance efforts must also encompass key populations, since their STI prevalence can be substantial. Consistent, systematic STI surveillance and screening within key populations are more pertinent than sporadic efforts, providing essential data for designing effective interventions.

# Antimicrobial resistance awareness and education

## **Priority #28.** Determine the most (cost-)effective behavioural change interventions to mitigate the emergence and spread of AMR

Expanded version: Determine the most (cost-)effective behavioural change interventions to mitigate the emergence and spread of AMR by targeting and engaging the general public, young people, mass media, health-care workers and policy-makers across socioeconomic settings.

The emergence of AMR has largely been driven by the inappropriate use of antimicrobial medicines across sectors *(137)*. In the context of human health, prescribers and dispensers of antimicrobial medicines, as well as the public, are frequently unaware of the risks associated with taking antimicrobial medicines or may focus more on their immediate benefits. Interventions such as public education campaigns can improve people's knowledge and awareness of appropriate antimicrobial use and AMR, but their success hinges on understanding different populations, their baseline knowledge, where they access information and other social factors that may drive inappropriate use and the patterns of behaviour that lead to the emergence of AMR. The behavioural insights approach can identify appropriate and feasible interventions to begin tackling AMR in various contexts *(138)*, but more information is needed on the long-term effectiveness of the interventions on reducing the inappropriate use of antimicrobial medicines. Social media and content platforms offer a key opportunity for raising awareness and influencing behaviour among the public, especially young people, and determining the optimal use of these platforms is a prime target for further investigation. For example, strategies might vary depending on the platform – content that works on one platform may not work on another. Video content platforms *(139)*, video games *(140)* and novel media technologies such as virtual and mixed reality should be investigated for their potential for immersive and effective dissemination of key messages, while acknowledging that people in low- and middle-income countries currently have less access to high-bandwidth media and expensive technology (see Vernet *(141)* as an example of a simple health-messaging virtual reality clip that can be viewed using a smartphone and inexpensive paper 3D glasses). A crucial element of engaging people on AMR is linking the abstract concept of AMR with the real experiences of people who have been affected by infections with resistant pathogens *(142)*, which might influence people's perception of their personal risk. Deployment of health communication models for AMR that are based on perceptions of risk and vulnerability to illness, such as the health beliefs model, requires further study *(143)*. Importantly, knowledge of how the different behaviour change models can be applied in different scenarios and sociocultural settings is needed.

# Policies and regulations related to antimicrobial resistance

## **Priority #29.** Evaluate the implementation of AMR-related policies and regulations and how effective they are in mitigating AMR and improving health outcomes

Expanded version: Evaluate the implementation of AMR-related policies and regulations at the national level and how effective they are in mitigating AMR and improving health outcomes in the community and health-care settings across socioeconomic contexts.

AMR policy decisions need to be informed by robust, timely evidence and best-practice recommendations regarding population-level interventions. Having a broader reach that can determine larger-scale effects on health is especially needed since most AMR research focuses on interventions attaining individual-level effects. However, despite the shared need for evidence on effective policy and regulatory interventions, relatively few high-quality evaluations are available *(21,144)*, and much of the available evidence is poorly conducted and reported *(145)*. More high-quality evaluations of population-level interventions are needed to reduce inappropriate antimicrobial use and prevent the spread of resistant pathogens *(146)*. In particular, more high-quality evaluations are needed for policies implemented in limited-resource settings, since policies that are effective in high-income countries may be inappropriate in other contexts because of the availability of human and financial resources, the socioeconomic and political context and differences in cultural drivers of antimicrobial use. Gaining regional understanding of the effectiveness of existing and novel policies will provide opportunities for shared learning among countries.

A wide range of policies target reducing the spread of resistant pathogens and inappropriate antimicrobial use and should be considered and assessed. These include guidelines, regulations, fiscal measures, legislation and policies on service provision, communication and environmental and social planning *(147)*. Recent funding initiatives such as that by the Canadian Institute of Health Research are trying to fill this space *(148)*, but further evidence is needed across settings and contexts.

This research priority highlights the need to assess the level of implementation and effectiveness of AMR-related policies and regulations on mitigating AMR and on improving health outcomes (such as increasing life expectancy and improving the quality of life) in the community and health-care settings. Research focusing on implementing policies and regulations is fundamental to developing effective, context-specific and sustainable strategies for combatting AMR. It ensures that policies are not only scientifically sound but also practical and adaptable to real-world conditions. Context-specific evidence is needed on strategies to effectively implement national AMR interventions, policies and programmes (such as IPC strategy and antimicrobial prescribing regulations) *(149)*. Such context-specific evidence can inform a more tailored approach to developing and implementing policy.

Current evaluation research is largely retrospective and driven by academia. Further research-policy collaborations to develop a priori evaluation plans for prospective policy interventions would be very helpful. This strategy would mitigate the risk of promoting ineffective interventions, thus optimizing resource use and reducing costs *(146)*. The development of a data repository for policy interventions could foster the sharing of data and learning *(146,150)*. In addition, exploring how policies implemented in other sectors affect human health would be important in a One Health context.


**Above:** Bilal, 22, has just been discharged from hospital after a bout of drug-resistant typhoid. Bilal' typhoid could be treated only with meropenem, which is reserved for the most serious infections and is sold at a price families like his struggle to afford.

## **Priority #30.** Investigate implementation strategies for national policies, legislation and regulations to improve infection prevention, patient care and the use of antimicrobial medicines

Expanded version: Investigate strategies for the sustainable and (cost-) effective implementation of national policies, legislation and regulations (including sustainable financing and optimal governance structures) to improve infection prevention and patient care practices and the use of antimicrobial medicines in the community and health-care settings across socioeconomic contexts.

The Global Action Plan on Antimicrobial Resistance urges Member States to put into place national action plans on AMR *(8,9)*. According to the Quadripartite Tracking AMR Country Self-assessment Survey, 177 countries had developed national action plans on AMR aligned with the Global Action Plan as of 2023, but only 27% are effectively implementing and monitoring their plans *(10)*. Studies have identified gaps and opportunities to strengthen current national-level governance and the implementation of national action plans on AMR *(149,151–153)*. A key finding is that having a plan or policy poorly correlates with a country's ability to respond to the threat of AMR, such as having a surveillance system in place or optimizing the use of antimicrobials *(149,154)*. Challenges to implementing national action plans include the lack of financing, accountability, feedback mechanisms, education and equitable access to diagnostics and antimicrobials *(154)*.

Anderson et al. developed a governance framework outlining indicators for assessing national action plans on AMR *(155)*. Key indicators included the existence of surveillance systems for AMR and antimicrobial use, antimicrobial stewardship programmes, IPC policies, educational programmes for health-care workers, public awareness campaigns and regulations on antimicrobial use. Although indicators proposed for evaluating national action plans for AMR were originally designed to have a binary application for their presence or absence, a more nuanced approach may be needed to increase granularity and provide a better representation of complexity when comparing settings and tracking progress *(154)*. Results of progress assessments should inform research on strategies to improve implementation. Further, engaging social science researchers on implementation strategies is especially important since they relate to the political, social and equity dimensions of implementation.

Another limitation that affects implementation and effectiveness is that national action plans in low- and middle-income countries are often developed based on examples and evidence from high-resource settings, thus not accounting for differences in infrastructure, resources and other setting-specific characteristics *(149)*. Finally, a critical gap remains in comprehensive monitoring and evaluation of the implementation of AMR interventions and the association with useful measures to assess their effectiveness in mitigating AMR.

There is a need to investigate whether policies for IPC (including immunization programmes) can be used in the context for which they are designed, are up to date based on the current evidence, are acceptable to health-care workers and patients and whether incentives and penalties exist for their implementation *(155)*. This research priority also includes the need for effective implementation of antimicrobial stewardship programmes and for policies and regulations on antimicrobial use and their enforcement and identifying setting-specific challenges to policy implementation, identifying specific needs such as limited governance structures and financial commitment and increasing the awareness and support of various stakeholders, including the general public *(156)*.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**Above:** In many countries antibiotics can still be obtained without a prescription despite existing legislations prohibiting the practice.

## **Priority #31.** Identify the most (cost-)effective interventions and an investment case to mitigate AMR globally and across countries

Expanded version: Identify the most (cost-)effective interventions to mitigate AMR in the human health sector, globally and within countries or regions, and determine the rationale, costs, benefits, feasibility, sustainability and potential returns on investment to achieve the greatest benefit.

According to a 2017 World Bank report, AMR would cause between 1.1% and 3.8% annual loss in the world's gross domestic product by 2050, amounting to between US$ 1 trillion and US$ 3.4 trillion shortfall in annual gross domestic product after 2030 *(157)*. Further, low- and middle-income countries are anticipated to be more severely affected, with larger reductions in economic growth than high-income countries, thus increasing inequalities *(157)*. Without effective interventions, AMR could also impact on the achievement of the Sustained Development Goals for 2030 *(27)* and may lead an additional 24 million people into extreme poverty by 2030 *(157)*. The multifaceted effects on health, the economy and society require coordinated global action and investment in research, health-care infrastructure, preventive measures and policy initiatives.

According to estimates by the Organisation for Economic Co-operation and Development (OECD), several interventions can be highly effective in mitigating AMR, and the costs of their implementation can be quickly recovered. These measures include improving hygiene in health-care facilities, stewardship programmes to reduce excessive antibiotic prescription, using rapid diagnostic tests for differentiating bacterial from viral infections, delayed prescriptions and public awareness campaigns *(158)*. These interventions are predicted to be financially self-sustaining within a year, yielding significant health and economic benefits. For instance, promoting handwashing and hygiene can halve mortality risk and reduce the health burden of AMR by 40% in OECD countries, with stewardship programmes showing comparable effectiveness *(158)*. Improving vaccination coverage is another AMR intervention that needs further evaluation. Another OECD study estimated that using an integrated One Health approach results in significant returns, with every United States of America dollar invested generating five United States of America dollars in economic benefits through decreased health expenditure and increased productivity *(159)*. Delineating interventions with the greatest impact is crucial to develop the investment case for AMR *(160)*.

Data from real-world observational studies and limited-resource settings are limited *(157–159)*. Granular information would also be needed on identifying the elements within interventions which are critical for their success. These components can be then customized for other settings while maintaining the core successful components. There is a need to explore whether AMR-specific investments and policies would be cost-effective and to identify opportunities to align them with action in other areas (such as immunizations and WASH). Further, assessing the impact from intervention in other One Health sectors is needed. WHO is currently compiling a report on modelled global and regional returns on investment that could potentially be derived from a One Health package of interventions that include improved AMR awareness, surveillance, IPC, WASH and antimicrobial stewardship and investment in new drugs, diagnostic tools and vaccines.

## **Priority #32.** Investigate strategies to integrate AMR interventions into broader health, health financing, development and welfare structures and evaluate their impact

Expanded version: Investigate strategies to integrate AMR interventions into broader health, health financing, development, welfare structures and national policies and evaluate their impact on mitigating AMR, enhancing health system efficiency, reducing people's out-of-pocket expenses and improving equitable access to and use of diagnostics and antimicrobial medicines.

This research priority addresses the need for more evidence on integrating AMR considerations into existing financing and health-care provision structures. Linking AMR interventions to wide-reaching frameworks such as primary health care and universal health coverage, pandemic prevention, child health and WASH programmes may be more effective and efficient. The rise of AMR may create increasing difficulty in achieving universal health coverage, in which everyone, everywhere can access the health services they require without encountering overwhelming costs *(161)*. However, universal health coverage provides opportunities to assist in mitigating AMR, such as health system strengthening, higher quality of services, increased emphasis on preventive measures, early diagnosis and appropriate treatment. Better quality of services can also reduce the incidence of health care–associated infections if facilities have sufficient access to WASH and IPC programmes. Better affordability can also ensure that people can access diagnostics and the antimicrobials they need, thus avoiding substandard medicines and enabling the required length of treatment for their infections *(161)*. More specifically, it is critical to identify effective strategies for promoting access to diagnostics and how best to integrate the goals of universal health coverage with antimicrobial stewardship to reduce unnecessary antimicrobial prescribing. Also relating to system integration, preventing outbreaks with resistant pathogens is listed in the draft WHO Pandemic Agreement under the article on pandemic prevention and public health surveillance *(162)*. An effective global surveillance system can enact early detection and appropriate action, preventing wider dissemination. Strengthening antimicrobial stewardship programmes can ensure that antimicrobials maintain their effectiveness and can be used in a pandemic situation should the need arise *(163)*.

Practical strategies and evidence for how countries can integrate AMR interventions into existing health system structures, such as antimicrobial prescription data collection or policies on antimicrobial shortages, can further ensure the efficient use of resources and the financial sustainability of the AMR response. Systems for collecting electronic data on AMR and antimicrobial prescriptions do not exist in many places. Other aspects of integration can include developing concerted health strategies, programmes and budgeting that account for the needs of mitigating AMR and ensure that measures are sustainable and resources (including human resources) are used efficiently *(164)*. This would include the existence of an adequate physical infrastructure for providing health-care services that can be easily accessed by patients, an adequate number of competent health-care workers, the availability of high-quality, affordable diagnostic services and medicines and mechanisms for reducing out-of-pocket expenditure and for ensuring financial protection *(164)*.

Research is needed on regional-specific strategies or strategies that need to be flexible enough to work with varying levels of data availability. Further, context-specific strategies for implementing *(165)* interventions and the opportunities for aligning AMR with broader development goals need to be identified and given priority.

## **Priority #33.** Investigate how regulatory frameworks, marketing incentives and financing models affect the sustainable development, availability, equitable access and use of new antimicrobial medicines

Expanded version: Investigate how existing regulatory frameworks, marketing incentives (or their absence) and sustainable financing models affect the development and availability of new antimicrobial medicines and identify effective strategies to adapt these approaches to low-income settings to improve availability for adults and children.



According to the WHO antibacterial pipeline review in 2023, 97 products (57 antibiotics and 40 non-traditional antibacterial agents) were in clinical development, of which 32 antibiotics targeted WHO bacterial priority pathogens and 19 drug resistant *M. tuberculosis*. Further, 244 agents were in preclinical development *(94)*. This is significantly fewer than products in the immuno-oncology pipeline, for example *(166)*, also considering that fewer than 3% of antimicrobials in the preclinical stage attain market approval *(167)*. Antimicrobial drug development is less profitable for the pharmaceutical industry than the development of drugs for noncommunicable diseases. This discrepancy results from a relatively restricted market for reserve antimicrobials and from the loss of effect through the emergence of AMR. Several strategies can be used for incentivizing the development of antimicrobials, such as push incentives in which public or philanthropical funding directly supports drug development or pull incentives that reward the successful development of a new drug *(168)*. Currently about US$ 500 million per year supports antimicrobial development through push mechanisms. Among key stakeholders are the United States National Institutes of Health, the Joint Programming Initiative on Antimicrobial Resistance, the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator and the Global Antimicrobial Research & Development Partnership *(169)*. Pull incentives include prize payments once the antimicrobials are developed, advance market commitments in which governments commit to buying certain quantities of antibiotics at a predetermined price, providing financial security to manufacturers and subscription models such as that proposed by the National Health Service in the United Kingdom *(170)*. This model helps to decouple revenue generation from the volume of antibiotics sold, encouraging new antimicrobial development without the traditional reliance on high sales volumes for profitability *(171)*. Other strategies can be determined by the regulatory authorities, such as prolonging market exclusivity or priority review vouchers that can be used to speed up regulatory approvals for bringing other potentially more lucrative drugs to market *(172)*.

Beyond research and development, equitable access needs to be ensured in limited-resource settings. Partnerships such as the Access to Medicine Foundation's AMR benchmarking initiative serve to align pharmaceutical strategies with global health priorities *(173)*. Emphasis on cost-sharing mechanisms, differential pricing and public–private collaborations may further facilitate the affordability and accessibility of antimicrobial medicines in low- and middle-income countries, thereby mitigating AMR. Regulatory hurdles such as complex and redundant approval processes hinder antimicrobial research and development. This could be addressed by regulatory harmonization aligning the requirements that drug developers must meet across various regulators, leading to expedited approvals and

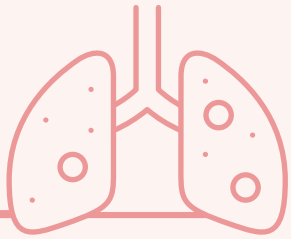
ensuring that antimicrobials are available sooner *(174,175)*. Another consideration would be enabling accelerated pathways for drug development and regulatory approvals, similar to those made for COVID-19 *(176)*, and considering new approaches for conducting clinical trials for new antimicrobials *(171)*. Although the development of new antimicrobial classes may surpass the timeline set forth in this agenda due to their extensive time to market, giving priority to research into novel antimicrobials is vital to secure effective treatment alternatives for the coming years.

This priority addresses the need to investigate how regulatory frameworks, market incentives and sustainable financing models can influence the development and availability of new antimicrobials and strategies on how to adapt these approaches to ensure access to vital antimicrobials in low- and middle-income countries. Another important area of policy research covers research and development incentives for antimicrobials. Solely relying on push incentives is considered inadequate for maintaining a robust pipeline *(169,177)*, with more research needed to evaluate the impact of regulatory frameworks, marketing incentives (including pull incentives) and sustainable financing models on antimicrobial research and development. Several projects have been underway to assess the feasibility, financial sustainability and prescribing incentives of various subscription-based reimbursement models for novel antimicrobials spearheaded by Sweden and the United Kingdom *(178–180)*. Robust evidence has the potential to inform policy regarding research and development incentives and strengthen the antimicrobial pipeline. Evidence on the feasibility of such arrangements for limited-resource settings and global equity-based frameworks could further bolster equitable access and prevent inappropriate antimicrobial use due to gaps in availability.


**Above:** For four years, after seeing multiple doctors, Autumn has been prescribed the strongest possible antibiotics but she still tests positive for drug-resistant urinary tract infections and has to self-administer antibiotics.

# 2.2.5 Drug-resistant tuberculosis

## Prevention



### **Priority #34.** Investigate effective preventive TB vaccines that meet WHO preferred product characteristics criteria and demonstrate impact on preventing infection, disease and recurrence

Expanded version: Investigate effective preventive TB vaccines that meet WHO preferred product characteristics criteria and demonstrate impact on preventing infection, disease and recurrence (relapse or reinfection), thereby preventing or reducing the incidence of drug-resistant TB.

An estimated one quarter of the world's population has been infected with *M. tuberculosis*, and 5–10% of those infected developing active disease over the course of their lives, usually within the first five years after infection *(181–183)*. The only licensed TB vaccine, Bacille Calmette-Guerin, provides moderate to good protection against severe forms of TB for infants and young children (averting thousands of deaths annually) but does not adequately protect adolescents and adults *(184)*. New effective TB vaccines that can be used to prevent all forms of TB, especially among adults and adolescents, would be needed to reach the WHO End TB Strategy targets of a 90% reduction in TB incidence and a 95% reduction in TB mortality by 2035 *(185)*. New vaccines may work in multiple ways, including by preventing the establishment of an initial infection (pre-exposure) or by preventing progression to disease (post exposure). A vaccine might also serve as an immunotherapeutic agent by shortening TB treatment or decreasing recurrence rates following treatment completion. Overall, an effective preventive vaccine would play an important role in tackling drug-resistant forms of TB, since new vaccines are likely to be equally effective against both drug-resistant and drug-susceptible strains. By preventing disease, vaccines would reduce the need for antibiotics, an essential step for curbing AMR. The WHO preferred product characteristics for new TB vaccines provide further guidance to the scientific community, vaccine developers and regulatory bodies on developing effective vaccine candidates *(186)*.

There is a strong economic and public health argument for new TB vaccines. A WHO-commissioned study estimates that, over 25 years, a vaccine that is 50% effective in preventing disease among adolescents and adults could avert up to 76 million new TB cases, 8.5 million deaths, 42 million courses of antibiotic treatment and US$ 41.5 billion in costs faced by TB-affected households *(187)*. Such a vaccine can generate significant longer-term economic benefits by improving public health, life expectancy and work performance, estimated to be US$ 1.6 trillion (gains in gross domestic product) between 2025 and 2080.

In 2023, at least 16 TB vaccine candidates were under clinical development *(188)*. These include subunit vaccines that pair different combinations of *M. tuberculosis* antigens with immune-modifying adjuvants, mRNA-based vaccines, viral-vectored vaccines and whole-cell vaccines based on genetically attenuated MTB or closely related mycobacterial species. As of today, only the M72/AS01E vaccine has preliminary results that meet the WHO preferred product characteristics *(189)*, and larger studies are planned to confirm these findings. Overall, very few candidate vaccine antigens have been identified in the last decade. Novel antigenic targets that can induce different and more effective immune characteristics, biomarkers that can serve as correlates or surrogates of protection and increased investment are needed to accelerate progress. In addition, countries, funders and relevant global and regional authorities should collaborate to facilitate timely manufacturing, procurement and equitable access to new TB vaccines once these are available.



**Above:** Shireen had drug-resistant tuberculosis. She tried different antibiotics until she finally started to feel better but she was still coughing.

# Diagnosis

## **Priority #35.** Investigate how the diagnostic performance of molecular assays can be improved to detect drug resistance among people with extrapulmonary and pulmonary TB

Expanded version: Investigate how the diagnostic performance of molecular assays can be improved to detect drug resistance among people with extrapulmonary and pulmonary TB, from non-respiratory specimens, including among children and adolescents.

The political declaration at the second United Nations High-level Meeting on the Fight to End Tuberculosis in 2023 included commitments by Member States that at least 90% of the estimated number of people who develop TB are reached with quality-assured diagnosis and treatment, with everyone diagnosed having been initially tested with WHO-recommended rapid molecular tests *(190)*.

WHO's End TB Strategy calls for the early diagnosis of TB and universal drug-susceptibility testing, highlighting the critical role of laboratories in rapidly and accurately detecting TB and drug resistance *(2)*. Of the 7.5 million new and relapse cases notified in 2022, 83% had pulmonary TB. Of these, 63% were bacteriologically confirmed, up from 55% in 2018. WHO-recommended rapid molecular tests were used as the initial diagnostic test in 47% of the cases only despite the recommendation to use it for everyone with signs and symptoms of TB *(2)*.

The microbiological detection of TB is critical because it enables people to be correctly diagnosed and start the most effective treatment regimen as early as possible. WHO has endorsed a range of new diagnostic technologies during the past 10 years. The amplification and detection of *M. tuberculosis* complex nucleic acids is a technology that has proven to be highly sensitive and specific to detect TB and drug resistance.

However, the diagnostic performance of these tests has not been fully optimized. For example, the sensitivity of all the available diagnostics is suboptimal in accurately defining TB disease among children and in paucibacillary samples *(191)*. The accuracy of WHO-recommended tests and the effectiveness of algorithms for diagnosing extrapulmonary TB need to be further evaluated. Comparison studies to determine which tests (or strategies) have better diagnostic accuracy and exploring strategies to improve the diagnostic yield of clinical specimens collected non-invasively, such as urine, are needed. Implementation research is required to build evidence and optimize access to screening and diagnostic tools to everyone at risk of TB and to better understand barriers to expanding access to WHO-recommended tests.

To ensure timely detection of drug resistance, the development of tests for drug susceptibility should be synchronized with the licensing and use of regimens that contain new or repurposed drugs. However, this has been challenging because of lag time in the availability of data on mutations known to result in changes in minimal inhibitory concentrations. WHO has incorporated molecular drug-susceptibility testing needs in its target regimen profiles for TB treatment to strengthen early collaboration between diagnostics and drug developers on molecular drug-susceptibility testing *(192)*. Further, WHO regularly publishes catalogues of mutations, which countries rely on for interpreting resistance *(126)*.

## **Priority #36.** Determine optimal diagnostic and treatment delivery models to improve the access, effectiveness, cost–effectiveness, feasibility and acceptability of drug-resistant TB treatment

Expanded version: Determine optimal diagnostic and treatment delivery models to improve the access, effectiveness, cost–effectiveness, feasibility and acceptability of drug-resistant TB testing and treatment across settings and subpopulations (such as people living with HIV, prisoners and children and adolescents) and evaluate their impact on reducing drug-resistant TB at the population level.

WHO uses the number of people diagnosed with TB and notified to public health reporting systems as a proxy indicator of access to TB diagnostic and treatment services. This number was 7.5 million in 2022, far below the estimated number of people who developed TB that year (10.8 million) *(2)*. There are two explanations for this gap: The first is underdiagnosis, either because people with TB do not reach health facilities (because of legal, social or economic barriers) or because they are not diagnosed when they do. The second is underreporting of people diagnosed with TB, especially in countries in which many private or public care providers are not closely linked to the national TB programme.

The use of WHO-recommended rapid molecular tests as the initial diagnostic test for TB was 47% in 2022 despite recommendation to use it for everyone with signs and symptoms of TB. Evaluation of means to improve the overall use, integration and optimization of diagnostic technologies in overall testing and care and in diagnostic pathways and algorithms is required to increase detection and linkage to care. Optimizing diagnostic delivery models also requires evaluating the impact of diagnostic technologies on clinical decision-making and outcomes that are important to patients (such as time to diagnosis, time to treatment initiation, cure and mortality) in all patient populations. Country-specific assessment of the cost–effectiveness and cost–benefit of WHO-recommended diagnostic tests can facilitate implementation and scale-up *(191)*.

This could be achieved by increasing effective population coverage and ensuring linkage to treatment across the care cascade. Effective population coverage is a function of the diagnostic test characteristics such as accuracy and yield, and access to passive and active case finding (ensuring that people who both seek care in health-care facilities and those who do not are diagnosed and start treatment). Recent studies have shown that people who are asymptomatic or have minimal symptoms can contribute substantially to transmission *(193)*. Strategies are needed to identify these people early to prevent disease progression and transmission. Access depends on feasibility, accessibility and costs. Qualitative research is needed across the diagnostic value cycle to better understand needs, feasibility and acceptability. Further, research on the diagnostic accuracy of tests and on the economic value and impact of diagnostic and treatment strategies is needed. Operational research that addresses all aspects of the care cascade and ensures linkage to treatment is also needed.

# Treatment and care

## **Priority #37.** Investigate better tolerated, optimally dosed, more effective and shorter combination regimens for treating people with all forms of drug-resistant TB

Expanded version: Investigate better tolerated, optimally dosed, more effective and shorter combination regimens, using a stratified risk approach, for treating people with all forms of drug-resistant TB, including in populations experiencing vulnerability (such as children, pregnant and breastfeeding women and people living with HIV).

Globally in 2022, an estimated 410 000 people developed TB resistant to at least rifampicin, one of the most effective drugs used to treat TB, of whom 175 650 were reported to have been enrolled in treatment, about two in five of those in need *(2)*. Effective treatment of TB, including its drug-resistant forms, relies on using several medicines administered in combination for an adequate duration. For many years, conventional treatment regimens for rifampicin-resistant TB and multidrug-resistant TB (defined as TB that is resistant to both rifampicin and isoniazid), collectively referred to as multidrug-resistant and rifampicin-resistant TB, were lengthy and arduous, and included painful injectable medicines. Compared with treatments for drug-susceptible forms of TB, the duration of treatment for rifampicin-resistant TB was about three times longer, with a much higher pill burden and a much higher risk of adverse events, both during treatment and after completion. Treatment was even more difficult for people with rifampicin-resistant TB and resistance to a fluoroquinolone, known as pre-extensively drug-resistant TB, and those with extensively drug-resistant TB (defined as pre-extensively drug-resistant TB plus resistance to at least one of either bedaquiline or linezolid).

WHO has endorsed the use of new all-oral six-month regimens, which shorten treatment duration and improve health outcomes, to treat people with rifampicin-resistant, multidrug-resistant and pre-extensively drug-resistant TB *(194)*. The evidence used as the basis for the new recommendations came from a randomized controlled trial: TB-PRACTECAL *(195)*. This trial showed much-improved treatment success rates with the six-month bedaquiline, pretomanid, linezolid and moxifloxacin (BPaLM) regimen (89%) compared with previous standard-of-care regimens (52%) and lower levels of treatment failure, death and loss to follow-up. A second trial, called ZeNiX-TB, randomized people with rifampicin-resistant TB to receive regimens of bedaquiline, pretomanid and daily linezolid at four different dosing schedules. Data from this trial as well as TB-PRACTECAL suggested that a linezolid dose of 600 mg maintains high efficacy but leads to fewer adverse events. There are some limitations to the use of the BPaLM/BPaL regimen. The lack of safety data on pretomanid for children younger than 14 years means that the recommendation currently applies only to adults and adolescents 14 years and older. Although the recommendation applies to all people, regardless of HIV status, some caution is needed when enrolling people with CD4 counts lower than 100 cells/mm3. The safety of pretomanid during pregnancy and breastfeeding is also unclear, and other treatment options should be used for pregnant and

breastfeeding women. The BPaLM/BPaL regimen is suitable for most forms of TB but is not recommended for extrapulmonary TB involving the central nervous system or osteoarticular and disseminated (miliary) TB. Overall, this underscores the message that research and development efforts should consider the needs of vulnerable people, including children, pregnant and breastfeeding women and people living with HIV as early as possible, while taking every precaution to minimize harm, in accordance with national and international ethical standards.

In 2023, WHO established a global BPaLM accelerator platform as a forum for information sharing and technical discussions to address challenges in implementing the BPaLM/BPaL regimen. Improving global access requires updating policy guidelines in countries and improving supply and access to the drugs central to these regimens.

In addition, research on and development of safer and shorter duration regimens must continue, together with strategies to optimize treatment through a stratified approach to TB treatment based on disease severity, optimal duration of treatment (based on previous treatment, baseline resistance patterns, site of disease and age), and while balancing the benefits and harm of regimen duration to increase the likelihood of positive treatment outcome. Safety should also be given priority by determining better ways to monitor for adverse events. This could be done, for example, by expanding the ability to monitor drug levels during treatment or identifying indirect markers associated with toxicity that are less expensive and more accessible. To shape product development in this space, WHO has developed target product profiles for minimum and optimum characteristics of tests for TB treatment monitoring and optimization *(192)*.

## **Priority #38.** Determine the optimal, (cost-)effective, shortest duration and safest TB preventive treatment for the contacts of people with drug-resistant TB

Expanded version: Determine the optimal, (cost-)effective, shortest duration and safest TB preventive treatment for the contacts of people with drug-resistant TB, especially among people at high risk of TB infection and disease, as identified in WHO guidance, and eligible populations experiencing vulnerability (such as children, adolescents, people living with HIV and pregnant women).

Some populations have an increased risk for developing active TB, such as people living with HIV and children who are household contacts of people with TB. Although WHO provides general guidance for treating people infected with drug-susceptible strains of *M. tuberculosis* and eligible for preventive treatment *(183)*, there are generally no clear recommendations for the contacts of people with drug-resistant TB considering the very limited evidence in this space. Adequately powered randomized controlled trials involving both adults and children and with at-risk populations such as people living with HIV are required to support policy decisions on preventive treatment for the contacts of people with multidrug-resistant TB or rifampicin-resistant TB. Ongoing studies are exploring various drugs and treatment regimens for prevention: these include delamanid and isoniazid or levofloxacin for the contacts of people with multidrug-resistant TB, including children *(188)*. The composition, dosage and duration of effective preventive treatment regimens for multidrug-resistant TB should be identified, and the potential role of newer agents with good sterilization properties should be investigated. Further evidence on the risk of contacts of people with multidrug-resistant TB for progression to active TB will be important to understand the benefits of preventive treatment. In the interim, WHO has issued recent guidance for the management of contacts of people with drug-resistant TB *(183)*.

Research on preventive therapies should be complemented by comprehensive appraisal of the cost–effectiveness of TB infection management stratified by population group, type of regimen or intervention. with parameters from different resource settings to enable better programmatic planning.

## **Priority #39.** Investigate strategies for improving treatment outcomes among people with drug-resistant TB who have known risk factors and conditions and among populations experiencing vulnerability

Expanded version: Investigate strategies for improving treatment outcomes among people with drug-resistant TB who have known risk factors and co-occurring conditions (such as HIV, undernutrition, diabetes mellitus, tobacco use, alcohol and other substance use and mental health disorders) and populations experiencing vulnerability (such as pregnant and breastfeeding women, children, adolescents and prisoners) in various geographical and socioeconomic settings.

Ending the drug-resistant TB crisis requires universal access to comprehensive TB services and treatment adherence for people with both drug-susceptible and drug-resistant TB. TB treatment coverage (a best estimate of 70% in 2022) needs to expand, especially for children 14 years and younger (49% in 2022) *(2)*. Improving access to appropriate treatment regimens for people with drug-resistant TB will also require accessible and affordable rapid and accurate point-of-care diagnostics, including for drug susceptibility testing.

Identifying interventions for patient support and treatment supervision or models of care that are best suited for people with drug-resistant forms of TB in low- and middle-income countries requires a multisectoral approach. WHO recommends the ambulatory model of care facilitated through decentralized health care (defined as care provided at non-specialized or peripheral health centres by community health workers or nurses, non-specialized doctors, community volunteers or treatment supporters) for scaling up treatment and care for people who are eligible for multidrug-resistant TB treatment *(196)*. The guideline also affirms that family-centred, integrated models of care may be used to deliver TB services for children and adolescents with signs and symptoms of TB and/or those exposed to TB, in addition to standard models of care. WHO also recommends that people with active multidrug-resistant TB and moderate undernutrition be provided with locally available nutrient-rich or fortified supplementary foods as necessary to restore normal nutritional status *(197)*.

However, further research is needed to optimize the models of care: the treatment success rate for drug-resistant TB was only 63% in the most recent patient cohort for which data are available *(198)*. According to national surveys, on average 49% of people with TB and their households faced total costs (including direct medical expenditures, direct non-medical payments and indirect costs such as lost income) that exceeded 20% of annual household income. The proportion is 83% for people with drug-resistant TB and their households. Member States adopted a new political declaration during the second United Nations High-level Meeting on the Fight to End Tuberculosis in September 2023, with a commitment to ensure access to health and social benefits packages to all eligible people with TB *(199)*.

# **Priority #40.** Investigate the programmatic effectiveness, safety and tolerability of currently used WHO-recommended treatment regimens for drug-resistant TB

Expanded version: Investigate the programmatic effectiveness, safety and tolerability of currently used WHO-recommended treatment regimens for drug-resistant TB (including combinations with bedaquiline, delamanid and/or pretomanid) on patient outcomes and drug-resistant TB emergence across populations and settings and identify the drivers of treatment failure.

The updated WHO guidelines published in 2022 have recommended shorter durations for the treatment of multidrug-resistant and rifampicin-resistant TB that can support with improving treatment outcomes *(200)*. Studies underpinning these changes showed that short, all-oral regimens are highly effective and relatively safe. However, data are needed on the programmatic implementation of these regimens across settings, populations and *M. tuberculosis* lineages. Especially important are data on effectiveness and safety outside trial conditions. In addition, the potential development of further drug resistance should be closely monitored to ensure that these drugs can be used for decades to come.

With respect to the BPaLM/BPaL regimen for treatment for rifampicin-resistant, multidrug-resistant or pre-extensively drug resistant TB, current data are limited or missing on the efficacy, safety and tolerability of the regimens across regions, countries and subpopulations, including children younger than 14 years, people with extrapulmonary TB, people living with HIV with CD4 counts less than 100 cells/mm$^3$ and pregnant and lactating women. These data are essential to expand the current recommendation to subpopulations and countries *(200)*. Overall, most programmatic data on the safety, efficacy and tolerability of regimens for treatment for drug-resistant TB come from one country (South Africa). The adverse event profile of newly recommended drugs such as pretomanid for humans is incomplete, including frequency, hepatotoxicity and reproductive toxicity. For delamanid, its role in multidrug-resistant TB regimens needs to be better understood, including for children (pharmacokinetics and pharmacodynamics), people living with HIV and pregnant women; mechanisms of development of drug resistance; and optimization of the duration for both adults and children. However, there are several drivers of treatment failure, including existing resistance, socioeconomic factors, weak health systems, limited access to high-quality medicines, stigma and discrimination. Multidisciplinary research is needed to support policy and practice with respect to care for people with drug-resistant TB.

**Right:** Mildred Fernando Pancho is a survivor of multi-drug resistant tuberculosis and a mother of two children. Today, she raises awareness about AMR through sharing the story of her 10-year treatment and struggles she and her family endured.
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# 3. Further considerations

## 3.1 Policy implications

The research agenda is expected to steer policy-makers, the global research community, industrial entities and funders in coordinating and aligning research efforts and investment on the most critical global knowledge gaps. An essential criterion for setting priorities was the ability to translate research output into policy, so that addressing the research priorities is likely to strongly affect AMR prevention practices, infection diagnosis, treatment and management and national and global policies.

The research agenda is set to play a key role in shaping and promoting the discourse, including actions regarding AMR at the United Nations General Assembly with the aim of filling essential knowledge gaps by 2030 and contributing to global strategies for containing and managing AMR. In addition, data from meticulously conducted, large-scale multidisciplinary studies on the research priorities for drug-resistant TB will help achieve the Member States' commitment to increase access to rapid diagnostic testing, treatment and TB preventive treatments to 90% and ensuring full health and social benefits for individuals with TB by the year 2027 *(201)*.

The agenda emphasizes the importance of research and development for vaccines, diagnosis and treatment methods, urging increased work on developing new treatments for Enterobacterales that produce extended-spectrum beta-lactamases or with carbapenem resistance and STIs. It also highlights the need to investigate how marketing incentives (or their absence) and sustainable financing models can affect the development and availability of new antimicrobial medicines, especially in low- and middle-income countries. The research topics given priority in this agenda underline the importance of not just sustaining investment in product-focused research and development but also of increasing funding throughout all research stages, encompassing descriptive research, delivery, development and discovery.

Implementing this research agenda could lead to a more equitable distribution of AMR research investment by balancing the development of new treatments with developing tools to diagnose infections rapidly and accurately, the need for data to inform policy decisions on cost-effective preventive measures and antimicrobial stewardship practices, implementing interventions and developing policies that are viable in limited-resource settings. This approach can ensure that countries are well equipped for addressing the complex challenges around AMR through a multidisciplinary approach.

## 3.2 Research priorities for children

Although the research agenda priorities pertain to all age groups, priority #9 specifically concerns empirical antibiotic regimens for gram-negative bacteraemia among children and newborns. Neonatal sepsis poses considerable challenges among the most vulnerable people in limited-resource settings and can be associated with very high mortality *(202)*. Drug development that accounts for the needs of children is a critical issue. Key aspects include the development of formulations for children for existing and novel antimicrobials *(84)*, conducting clinical trials for novel drugs involving children, harmonizing and facilitating the regulatory process for approvals and ultimately ensuring access.

Other priorities that explicitly mention relevance to children include priorities #4, #5, #17, #33 and #36–#39. The in-depth narratives for each of these priorities presented in Section 2 individually explore the considerations related to children relevant to the priority. For example, vaccines are typically administered to young children and are therefore a key population for priority #4. Differentiating bacterial infections from non-bacterial diseases is especially important for children who frequently receive antibiotics for viral respiratory tract and gastrointestinal illnesses (priority #5). Optimizing care for this population is critical because they are associated with substantial morbidity and mortality in low- and middle-income countries *(203)*.

To ensure that the most pressing AMR-related needs of children across the world were addressed in developing this agenda, we purposefully enriched the pool of participating paediatric experts. The number of experts applying an exclusively paediatric perspective during the priority-setting survey was 38, and each research topic received 30 or more scores from these experts. Although this number would be considered sufficient to power a separate paediatric research agenda, it is considerably lower than the median of 140 respondents per topic that informed the overall agenda. Further, several validation analyses were undertaken. The top-ranking research topics as determined by the responses of all experts and those of paediatric experts substantially overlapped (>70% of topics appeared in the top-ranked research topics in both lists), affirming the relevance of the overall agenda to children. However, since the 38 experts were mainly clinicians, the remaining additional topics were almost exclusively clinically oriented (treatment and care), resulting in an unbalanced agenda that did not consider important AMR areas such as epidemiology and policies and regulations. After thematical comparison of the additional topics, it was determined that the essential differences were the need to determine the causes of acute febrile illnesses (addressed partly in priority #5), a broader scope of pathogens for treatment regimen optimization and rationalization (*Acinetobacter baumannii, P. aeruginosa, Shigella* spp. and *Campylobacter* spp.), the need to investigate the efficacy and safety of generic antimicrobial medicines and the need to study the transmission pathways of AMR organisms between mothers, newborns and the environment. Being formidable AMR pathogens, especially in health-care facilities, *A. baumannii* and *P. aeruginosa* could arguably be considered critical priorities for all age groups. However, the ranking of the research topics addressing these two organisms (low- and middle-income countries rank = 40 for *P. aeruginosa* and low- and middle-income countries rank = 47 for *A. baumannii*) missed the cut-off for inclusion in the main agenda (rank ≤35). The discrepancy can likely be explained by the fact that most experts applying a paediatric perspective were hospital doctors.

## 3.3 Addressing inequalities in the burden of AMR

Low- and middle-income countries have the highest mortality from AMR and the highest burden of drug-resistant TB *(1,2)*, driven by a range of factors including limited access to high-quality health care, antimicrobials and diagnostics, a relatively small health workforce *(204)*, inadequate access to safe water, sanitation and other preventive services. This disparity is further exacerbated by economic constraints that limit the capacity to invest in research, education and infrastructure necessary to combat AMR effectively.

Setting was carefully considered in developing the research agenda for each topic. The primary setting that would benefit from evidence generation was defined, considering socioeconomic factors and especially acknowledging the needs of low- and middle-

income countries. The final list of research priorities was informed by experts from low- and middle-income countries or those focusing on low- and middle-income countries as well as in the priority-setting exercise (40% of experts had a low- and middle-income country perspective), by applying equal weight to research topics given priority by low- and middle-income country experts to those given priority by global experts (those having both a low- and middle-income country focus and high-income country focus) during the consolidation phase.

Beyond global inequalities, social inequalities within countries driven by social and cultural norms, disparities in income, education and access to health care further intensify the risks and consequences of AMR. Marginalized communities and people living in informal settlements have less access to health-care services, have increased pathogen exposure and face a higher risk of infections caused by resistant pathogens *(205)*. Geographical inequities also play a role, since individuals in remote or rural areas may encounter significant difficulties in accessing health care. In addition, the movement of people across borders, whether for economic migration or displacement by conflict and natural disasters, introduces further challenges in managing AMR equitably *(206)*. Biological sex and gender as a social construct also play a role in many contexts, driving differences in vulnerability and exposure to infection, antibiotic use, health-care access and decision-making likely influencing the AMR burden and outcomes *(207)*. Again, the research agenda carefully addressed these inequalities in the formulation of the research topics by specifying the need to study research priorities across geographical settings and among subpopulations.

## 3.4 Alignment with the One Health priority research agenda for AMR

This research agenda complements and is broadly aligned with the One Health priority research agenda for AMR *(24)*, which addresses the intricate interactions between humans, animals, plants and their shared environment and AMR. The One Health research agenda was developed through a collaborative effort of the Quadripartite, a partnership comprising WHO, the Food and Agriculture Organization of the United Nations, the United Nations Environment Programme and the World Organisation for Animal Health. The research agenda for AMR in human health complements critical knowledge gaps not in the scope of the One Health agenda and expands on the epidemiology, burden and drivers of drug-resistant bacterial, fungal and TB infections in the human health sector and the development of optimized diagnostics and antimicrobial treatment strategies.

## 3.5 Climate change

The wide array of consequences of climate change are important to consider for each of the priorities in this agenda as they begin to shift geographical contexts, disease epidemiology, social and clinical vulnerability and impact the economy. Global warming may expand the geographical distribution and increase the burden of infections *(208,209)*, rising temperatures can promote bacterial growth and transfer of resistance genes *(210)* and excessive rainfall can cause flooding, leading to environmental contamination and increasing the risk of exposure to antimicrobial-resistant pathogens *(208)*. Natural disasters can damage critical infrastructure, affecting water and sanitation service provision and access to health care. Hospitals may be overwhelmed by high patient numbers facilitating transmission of resistant pathogens within facilities. Droughts may compromise water supplies and result in food shortages, increasing the risk of infections.

Population displacement through natural disasters can lead to overcrowding and limited access to WASH and high-quality health services, thus increasing the risk of infection and transmission of resistant organisms *(211)*. Preventive programmes such as immunization can also be disrupted *(211)* resulting in increased susceptibility to infections and potentially higher antibiotic use. Low- and middle-income countries, which already have a higher burden of infectious diseases and more fragile health systems, are likely to be disproportionately affected *(212,213)*. Although the world is already experiencing many of the consequences of climate change, the most devastating effects are anticipated to occur over a timespan outside the scope of this agenda and will require increasing attention.

## 3.6 Emerging technologies

The rapid emergence of information technologies, notably those using large data sets, machine learning and artificial intelligence, is expected to revolutionize all aspects of modern life and health care, and AMR is no exception *(214,215)*. The potential (and risk) of these tools should be kept in mind to not only support research and evidence generation related to the priorities identified in this agenda but also as novel solutions to the problems the priorities aim to address *(216,217)*. Priority #25 addresses the genomic surveillance of AMR, but the potential of sequencing technologies for AMR may eventually extend beyond surveillance into clinical use *(191)*. It is important to lay a solid foundation for future use cases and their investigation by curating comprehensive globally representative databases of genomic and genetic data for all priority pathogens *(126)*.

# 4. Implementation and uptake of the research agenda

This research agenda will be implemented through several strategies. First, the agenda has been disseminated through multiple channels. A policy brief was released in June 2023 to facilitate early dissemination and to raise awareness of the 40 research priorities. The current report fully elucidates the methodological details, presents the quantitative results and qualitatively explores each of the research priorities. These topic narratives may serve to improve understanding and catalyse interest among readers unfamiliar with all the diverse AMR areas, researchers and non-researchers alike. Finally, a publication in an open-access academic journal will bring the agenda to a wide audience and enable the agenda to be indexed and cited as a peer-reviewed work *(218)*. All these outputs are freely available online.

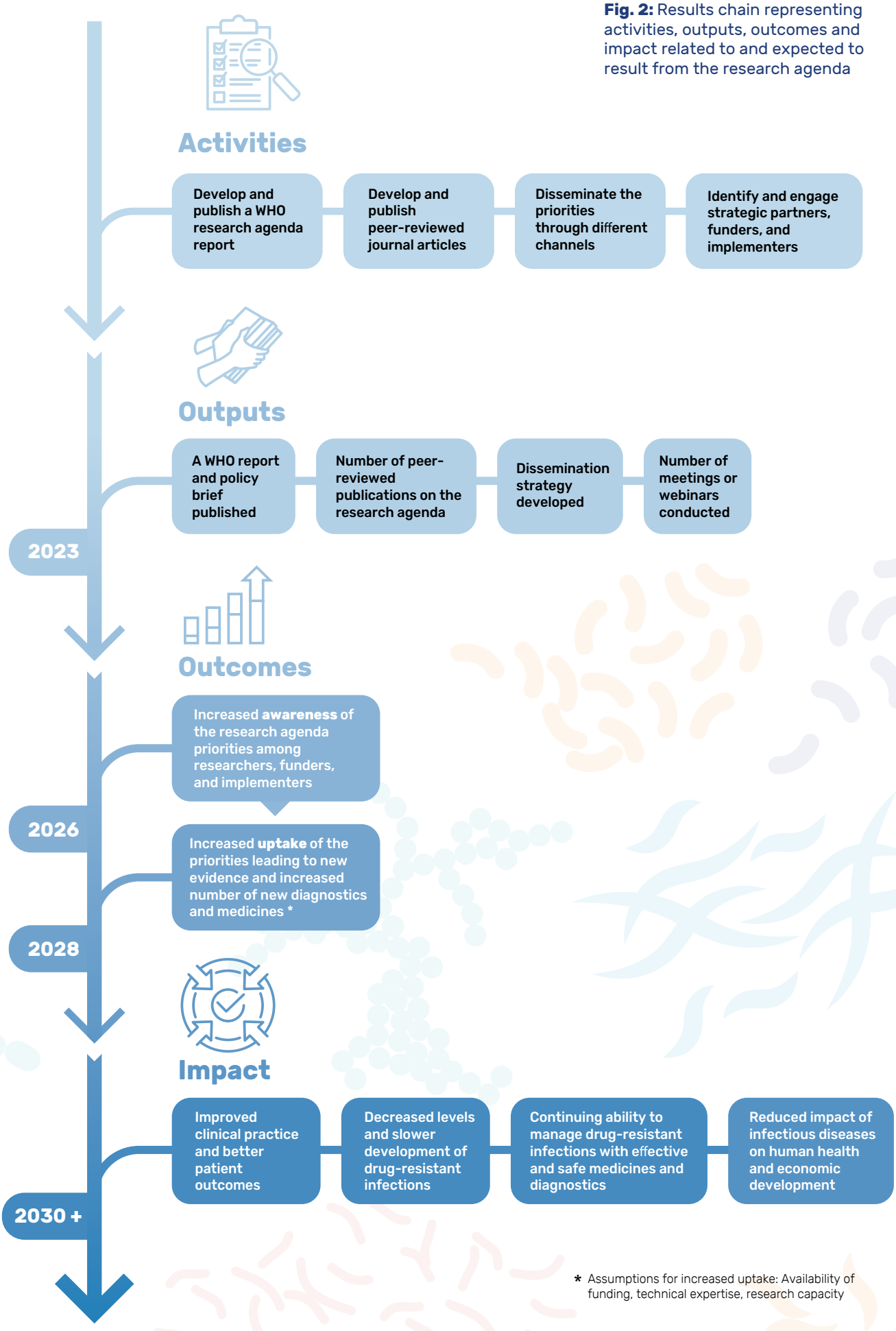
The research agenda will support WHO Member States in fulfilling their commitment to the 77th World Health Assembly resolution on accelerating the national and global responses to AMR, which urges Member States to support and promote basic, applied and implementation research on vaccines, IPC, diagnostics, therapeutics and antimicrobial stewardship by collaborating with academia, civil society and the private sector *(219)*. The impact of these initiatives would be maximized by focusing activities on the priorities identified in this agenda, with the agenda being adapted to align with the country's own public health needs, epidemiological context, available expertise and resources. This will ensure that generated evidence can be applied to the specific setting, resulting in more effective policies for addressing AMR at both the national and regional levels. Adapting the global agenda would avoid countries having to develop their own agendas, a labour-intensive and time-consuming process.

WHO calls on the global AMR research community and funders to intensify action and investments in research that is aligned with the research agenda's priorities.

## 4.1 Monitoring and evaluating the research agenda

A monitoring and evaluation plan adapted from the recommendations for conducting research priority-setting exercises *(220)* was developed for tracking awareness and uptake of the research agenda. Fig. 2 follows a results chain linking the activities and output of the research agenda to anticipated short- and medium-term outcomes, with the aim of ultimately achieving long-term impact on AMR. Proposed indicators for the research agenda address (1) awareness and dissemination of the research agenda through publications and other documents and (2) uptake by assessing funding for the research priorities and changes in diagnostic, treatment and vaccines pipelines (Table A2.1).

**Fig. 2:** Results chain representing activities, outputs, outcomes and impact related to and expected to result from the research agenda




* Assumptions for increased uptake: Availability of funding, technical expertise, research capacity

# References


1. Naghavi M, Vollset SE, Ikuta KS, Swetschinski LR, Gray AP, Wool EE et al. Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050. Lancet. 2024;404:1199-226. doi: 10.1016/s0140-6736(24)01867-1.
2. Global tuberculosis report 2024. Geneva: World Health Organization; 2024 (https://iris.who.int/handle/10665/379339, accessed 11 December 2024).
3. Fisher MC, Denning DW. The WHO fungal priority pathogens list as a game-changer. Nature Rev Microbiol. 2023;21:211–2. doi: 10.1038/s41579-023-00861-x.
4. WHO fungal priority pathogens list to guide research, development and public health action. Geneva: World Health Organization; 2022 (https://apps.who.int/iris/handle/10665/363682, accessed 12 August 2024).
5. Fisher MC, Alastruey-Izquierdo A, Berman J, Bicanic T, Bignell EM, Bowyer P et al. Tackling the emerging threat of antifungal resistance to human health. Nature Rev Microbiol. 2022;20:557–71. doi: 10.1038/s41579-022-00720-1.
6. Tackling drug-resistant infections globally: final report and recommendations. Review on Antimicrobial Resistance; 2016 (https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf, accessed 12 August 2024).
7. Towards specific commitments and action in the response to antimicrobial resistance: recommendations for consideration by UN Member States in the outcome document of the High-level Meeting on AMR in September 2024. Global Leaders Group on AMR; 2024 (https://www.amrleaders.org/resources/m/item/glg-report, accessed 12 August 2024).
8. Sixty-eighth World Health Assembly. Global action plan on antimicrobial resistance. Geneva: World Health Organization; 2015 (https://iris.who.int/handle/10665/253236, accessed 12 August 2024).
9. Global action plan on antimicrobial resistance. Geneva: World Health Organization; 2015 (https://iris.who.int/handle/10665/193736, accessed 12 August 2024).
10. Global Database for Tracking Antimicrobial Resistance (AMR) Country Self- Assessment Survey (TrACSS) [online database]. Geneva: World Health Organization; 2024 (https://amrcountryprogress.org/#/visualization-view, accessed 12 August 2024).
11. Prioritization of pathogens to guide discovery, research and development of new antibiotics for drug-resistant bacterial infections, including tuberculosis. Geneva: World Health Organization; 2017 (https://apps.who.int/iris/handle/10665/311820, accessed 12 August 2024).
12. WHO bacterial priority pathogens list, 2024: bacterial pathogens of public health importance, to guide research, development and strategies to prevent and control antimicrobial resistance. Geneva: World Health Organization; 2024 (https://iris.who.int/handle/10665/376776, accessed 12 August 2024).
13. Annual report 2021: the global AMR R&D funding landscape. Berlin: Global AMR R&D Hub; 2021 (https://globalamrhub.org/publications/annual-report-2021-now-available, accessed 12 August 2024).
14. Yoshida S, Martines J, Lawn JE, Wall S, Souza JP, Rudan I et al. Setting research priorities to improve global newborn health and prevent stillbirths by 2025. J Glob Health. 2016;6:010508. doi: 10.7189/jogh.06.010508.
15. Armstrong A, Nagata JM, Vicari M, Irvine C, Cluver L, Sohn AH et al. A global research agenda for adolescents living with HIV. J Acquir Immune Defic Syndr. 2018;78(Suppl. 1):S16–21. doi: 10.1097/QAI.0000000000001744.
16. Shah H, Albanese E, Duggan C, Rudan I, Langa KM, Carrillo MC et al. Research priorities to reduce the global burden of dementia by 2025. Lancet Neurol. 2016;15:1285–94. doi: 10.1016/S1474-4422(16)30235-6.
17. Polasek O, Wazny K, Adeloye D, Song P, Chan KY, Bojude DA et al. Research priorities to reduce the impact of COVID-19 in low- and middle-income countries. J Glob Health. 2022;12:09003. doi: 10.7189/jogh.12.09003.
18. Bulteel AJB, Larson EL, Getahun H. Identifying global research gaps to mitigate antimicrobial resistance: a scoping review. Am J Infect Control. 2021;49:818–24. doi: 10.1016/j.ajic.2020.11.024.

19. Containing antimicrobial resistance: review of the literature and report of a WHO Workshop on the Development of a Global Strategy for the Containment of Antimicrobial Resistance, Geneva, Switzerland, 4–5 February 1999. Geneva: World Health Organization; 1999 (https://iris.who.int/handle/10665/66157, accessed 12 August 2024).
20. Lacotte Y, Ardal C, Ploy MC, European Union Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections. Infection prevention and control research priorities: what do we need to combat healthcare-associated infections and antimicrobial resistance? Results of a narrative literature review and survey analysis. Antimicrob Resist Infect Control. 2020;9:142. doi: 10.1186/s13756-020-00801-x.
21. Rogers Van Katwyk S, Grimshaw JM, Nkangu M, Nagi R, Mendelson M, Taljaard M et al. Government policy interventions to reduce human antimicrobial use: a systematic review and evidence map. PLoS Med. 2019;16:e1002819. doi: 10.1371/journal.pmed.1002819.
22. Mitnick CD, Rodriguez CA, Hatton ML, Brigden G, Cobelens F, Grobusch MP et al. Programmatic management of drug-resistant tuberculosis: an updated research agenda. PLoS One. 2016;11:e0155968. doi: 10.1371/journal.pone.0155968.
23. WHO research agenda for hand hygiene in health care 2023–2030: summary. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/367527, accessed 12 August 2024).
24. WHO, FAO, UNEP, WOAH. A One Health priority research agenda for antimicrobial resistance. Geneva: World Health Organization; 2023 (https://apps.who.int/iris/handle/10665/370279, accessed 12 August 2024).
25. Global action plan on antimicrobial resistance. In: Sixty-eighth World Health Assembly. WHA68/2015/REC/1: resolutions and decisions. Geneva: World Health Organization; 2015 (https://apps.who.int/gb/or/e/e_wha68r1.html, accessed 12 August 2024).
26. Strengthening diagnostics capacity. In: Seventy-sixth World Health Assembly. Geneva: World Health Organization; 2023 (https://apps.who.int/gb/ebwha/pdf_files/WHA76/A76_R5-en.pdf, accessed 12 August 2024).
27. Transforming our world: the 2030 Agenda for Sustainable Development. New York: United Nations; ; 2015 (https://sdgs.un.org/2030agenda, accessed 12 August 2024).
28. WHO, UNICEF. Progress on household drinking water, sanitation and hygiene 2000–2022: special focus on gender. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/378150, accessed 10 September 2024).
29. Lewnard JA, Charani E, Gleason A, Hsu LY, Khan WA, Karkey A et al. Burden of bacterial antimicrobial resistance in low-income and middle-income countries avertible by existing interventions: an evidence review and modelling analysis. Lancet. 2024;403:2439–54. doi: 10.1016/S0140-6736(24)00862-6.
30. Fuhrmeister ER, Harvey AP, Nadimpalli ML, Gallandat K, Ambelu A, Arnold BF et al. Evaluating the relationship between community water and sanitation access and the global burden of antibiotic resistance: an ecological study. Lancet Microbe. 2023;4:e591–600. doi: 10.1016/S2666-5247(23)00137-4.
31. Wolf J, Hubbard S, Brauer M, Ambelu A, Arnold BF, Bain R et al. Effectiveness of interventions to improve drinking water, sanitation, and handwashing with soap on risk of diarrhoeal disease in children in low-income and middle-income settings: a systematic review and meta-analysis. Lancet. 2022;400:48–59. doi: 10.1016/s0140-6736(22)00937-0.
32. Preventing diarrhoea through better water, sanitation and hygiene: exposures and impacts in low- and middle-income countries. Geneva: World Health Organization; 2014 (https://iris.who.int/handle/10665/150112, accessed 12 August 2024).
33. Perin J, Mulick A, Yeung D, Villavicencio F, Lopez G, Strong KL et al. Global, regional, and national causes of under-5 mortality in 2000–19: an updated systematic analysis with implications for the Sustainable Development Goals. Lancet Child Adolesc Health. 2022;6:106–15. doi: 10.1016/s2352-4642(21)00311-4.
34. Araya P, Hug J, Joy G, Oschmann F, Rubinstein S. The impact of water and sanitation on diarrhoeal disease burden and over-consumption of antibiotics. London: London School of Economics and Political Science; 2016 (https://amr-review.org/sites/default/files/LSE%20AMR%20Capstone.pdf, accessed 12 August 2024).

35. UNICEF, WHO. Progress on household drinking water, sanitation and hygiene 2000–2022: special focus on gender. New York: UNICEF; 2023 (https://iris.who.int/handle/10665/378150, accessed 12 August 2024).
36. Nadimpalli ML, Marks SJ, Montealegre MC, Gilman RH, Pajuelo MJ, Saito M et al. Urban informal settlements as hotspots of antimicrobial resistance and the need to curb environmental transmission. Nature Microbiol. 2020;5:787–95. doi: 10.1038/s41564-020-0722-0.
37. WHO, FAO, WOAH. Technical brief on water, sanitation, hygiene and wastewater management to prevent infections and reduce the spread of antimicrobial resistance. Geneva: World Health Organization; 2020 (https://iris.who.int/handle/10665/332243, accessed 12 August 2024).
38. WHO, UNICEF. Progress on WASH in health care facilities 2000–2021: special focus on WASH and infection prevention and control. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/366657, accessed 10 September 2024).
39. Report on the burden of endemic health care–associated infection worldwide. Geneva: World Health Organization; 2011 (https://iris.who.int/handle/10665/80135, accessed 12 August 2024).
40. Global report on infection prevention and control. Geneva: World Health Organization; 2022 (https://iris.who.int/handle/10665/354489, accessed 12 August 2024).
41. Balasubramanian R, Van Boeckel TP, Carmeli Y, Cosgrove S, Laxminarayan R. Global incidence in hospital-associated infections resistant to antibiotics: an analysis of point prevalence surveys from 99 countries. PLoS Med. 2023;20:e1004178. doi: 10.1371/journal.pmed.1004178.
42. Cassini A, Hogberg LD, Plachouras D, Quattrocchi A, Hoxha A, Simonsen GS et al. Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis. Lancet Infect Dis. 2019;19:56–66. doi: 10.1016/S1473-3099(18)30605-4.
43. Guidelines on core components of infection prevention and control programmes at the national and acute health care facility level. Geneva: World Health Organization; 2016 (https://iris.who.int/handle/10665/251730, accessed 12 August 2024).
44. WHO, Patient Safety World Alliance. A guide to the implementation of the WHO multimodal hand hygiene improvement strategy. Geneva: World Health Organization; 2009 (https://iris.who.int/handle/10665/70030, accessed 12 August 2024).
45. Bacterial vaccines in clinical and preclinical development 2021: an overview and analysis. Geneva: World Health Organization; 2022 (https://iris.who.int/handle/10665/359172, accessed 12 August 2024).
46. Vaccines to tackle drug resistant infections: an evaluation of R&D opportunities. London: Wellcome Trust; 2018 (https://vaccinesforamr.org/wp-content/uploads/2018/09/Vaccines_for_AMR.pdf, accessed 12 August 2024).
47. Vekemans J, Hasso-Agopsowicz M, Kang G, Hausdorff WP, Fiore A, Tayler E et al. Leveraging vaccines to reduce antibiotic use and prevent antimicrobial resistance: a World Health Organization action framework. Clin Infect Dis. 2021;73:e1011–7. doi: 10.1093/cid/ciab062.
48. Product & delivery research [website]. Geneva: World Health Organization; 2024 (https://www.who.int/teams/immunization-vaccines-and-biologicals/product-and-delivery-research/anti-microbial-resistance, accessed 12 August 2024).
49. Hasso-Agopsowicz M, Sparrow E, Cameron AM, Sati H, Srikantiah P, Gottlieb S et al. The role of vaccines in reducing antimicrobial resistance: a review of potential impact of vaccines on AMR and insights across 16 vaccines and pathogens. Vaccine. 2024;42(19S1):S1–8. doi: 10.1016/j.vaccine.2024.06.017.
50. Giersing B, Karron R, Tufet-Bayona M, Trotter C, Lambach P, Jit M. Vaccine value profiles. Vaccine. 2023;41(Suppl. 2):S1–2. doi: 10.1016/j.vaccine.2023.06.083.
51. Kim C, Holm M, Frost I, Hasso-Agopsowicz M, Abbas K. Global and regional burden of attributable and associated bacterial antimicrobial resistance avertable by vaccination: modelling study. BMJ Glob Health. 2023;8:e011341. doi: 10.1136/bmjgh-2022-011341.
52. Buckley BS, Henschke N, Bergman H, Skidmore B, Klemm EJ, Villanueva G et al. Impact of vaccination on antibiotic usage: a systematic review and meta-analysis. Clin Microbiol Infect. 2019;25:1213–25. doi: 10.1016/j.cmi.2019.06.030.
53. Fleming KA, Horton S, Wilson ML, Atun R, Destigter K, Flanigan J et al. The Lancet Commission on diagnostics: transforming access to diagnostics. Lancet. 2021;398:1997–2050. doi: 10.1016/s0140-6736(21)00673-5.

54. Hermans LE, Centner CM, Morel CM, Mbamalu O, Bonaconsa C, Ferreyra C et al. Point-of-care diagnostics for infection and antimicrobial resistance in sub-Saharan Africa: a narrative review. Int J Infect Dis. 2024;142:106907. doi: 10.1016/j.ijid.2023.11.027.
55. Integrated management of childhood illness [website]. Geneva: World Health Organization; 2024 (https://www.who.int/teams/maternal-newborn-child-adolescent-health-and-ageing/child-health/integrated-management-of-childhood-illness, accessed 12 August 2024).
56. Landscape of diagnostics against antibacterial resistance, gaps and priorities. Geneva: World Health Organization; 2019 (https://apps.who.int/iris/handle/10665/326480, accessed 12 August 2024).
57. Target product profiles for antibacterial resistance diagnostics. Geneva: World Health Organization; 2020 (https://apps.who.int/iris/handle/10665/331054, accessed 12 August 2024).
58. Vasala A, Hytonen VP, Laitinen OH. Modern tools for rapid diagnostics of antimicrobial resistance. Front Cell Infect Microbiol. 2020;10:308. doi: 10.3389/fcimb.2020.00308.
59. van Belkum A, Bachmann TT, Ludke G, Lisby JG, Kahlmeter G, Mohess A et al. Developmental roadmap for antimicrobial susceptibility testing systems. Nat Rev Microbiol. 2019;17:51–62. doi: 10.1038/s41579-018-0098-9.
60. GBD Antimicrobial Resistance Collaborators. Global mortality associated with 33 bacterial pathogens in 2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2022;400:2221–48. doi: 10.1016/S0140-6736(22)02185-7.
61. Akerlund A, Jonasson E, Matuschek E, Serrander L, Sundqvist M, Kahlmeter G et al. EUCAST rapid antimicrobial susceptibility testing (RAST) in blood cultures: validation in 55 European laboratories. J Antimicrob Chemother. 2020;75:3230–8. doi: 10.1093/jac/dkaa333.
62. Kaprou GD, Bergspica I, Alexa EA, Alvarez-Ordonez A, Prieto M. Rapid methods for antimicrobial resistance diagnostics. Antibiotics (Basel). 2021;10:209. doi: 10.3390/antibiotics10020209.
63. Zhang SX, Babady NE, Hanson KE, Harrington AT, Larkin PMK, Leal SM Jr. et al. Recognition of diagnostic gaps for laboratory diagnosis of fungal diseases: expert opinion from the Fungal Diagnostics Laboratories Consortium (FDLC). J Clin Microbiol. 2021;59:e0178420. doi: 10.1128/JCM.01784-20.
64. Osaigbovo II, Rajasingham R. The urgent need to scale-up fungal diagnostics in Africa. Lancet Infect Dis. 2023;23:517–9. doi: 10.1016/s1473-3099(22)00682-x.
65. Lakoh S, Kamudumuli PS, Penney ROS, Haumba SM, Jarvis JN, Hassan AJ et al. Diagnostic capacity for invasive fungal infections in advanced HIV disease in Africa: a continent-wide survey. Lancet Infect Dis. 2022:S1473309922006569. doi: 10.1016/S1473-3099(22)00656-9.
66. Diagnostic surveys Africa. Diagnostics for fungal disease in Africa: a GAFFI survey 2022. Geneva: Global Action for Fungal Infections; 2022 (http://gaffi.org/africa-diagnostic-reports-2, accessed 12 August 2024).
67. Freeman Weiss Z, Leon A, Koo S. The evolving landscape of fungal diagnostics, current and emerging microbiological approaches. J Fungi. 2021;7:127. doi: 10.3390/jof7020127.
68. Ending cryptococcal deaths by 2030 – strategic framework. Geneva: Global Action for Fungal Infections; 2021 (https://dndi.org/wp-content/uploads/2021/05/EndCryptococcalMeningitisDeaths2030-StrategicFramework-EN-2021.pdf, accessed 12 August 2024).
69. Berkow EL, Lockhart SR, Ostrosky-Zeichner L. Antifungal susceptibility testing: current approaches. Clin Microbiol Rev. 2020;33:10.1128/cmr.00069-19. doi: 10.1128/cmr.00069-19.
70. Global progress report on HIV, viral hepatitis and sexually transmitted infections, 2021: accountability for the global health sector strategies 2016–2021: actions for impact. Geneva: World Health Organization; 2021 (https://iris.who.int/handle/10665/341412, accessed 12 August 2024).
71. Guidelines for the management of symptomatic sexually transmitted infections. Geneva: World Health Organization; 2021 (https://iris.who.int/handle/10665/342523, accessed 12 August 2024).
72. Sexually transmitted infections (STIs). Geneva: World Health Organization; 2024 (https://www.who.int/news-room/fact-sheets/detail/sexually-transmitted-infections-(stis), accessed 12 August 2024).
73. The diagnostics landscape for sexually transmitted infections. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/371498, accessed 12 August 2024).
74. Antimicrobial stewardship programmes in health-care facilities in low- and middle-income countries: a WHO practical toolkit. Geneva: World Health Organization; 2019 (https://apps.who.int/iris/handle/10665/329404, accessed 12 August 2024).

75. World Health Organization model list of essential medicines for children: 8th list (2021). Geneva: World Health Organization; 2021 (https://iris.who.int/handle/10665/345534, accessed 12 August 2024).
76. World Health Organization model list of essential medicines: 22nd list (2021). Geneva: World Health Organization; 2021 (https://iris.who.int/handle/10665/345533, accessed 12 August 2024).
77. The selection and use of essential medicines 2023: web annex C: WHO AWaRe (access, watch, reserve) classification of antibiotics for evaluation and monitoring of use, 2023. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/371093, accessed 12 August 2024).
78. Zanichelli V, Sharland M, Cappello B, Moja L, Getahun H, Pessoa-Silva C et al. The WHO AWaRe (access, watch, reserve) antibiotic book and prevention of antimicrobial resistance. Bull World Health Organ. 2023;101:290–6. doi: 10.2471/BLT.22.288614.
79. The WHO AWaRe (access, watch, reserve) antibiotic book. Geneva: World Health Organization; 2022 (https://apps.who.int/iris/handle/10665/365237, accessed 12 August 2024).
80. Antimicrobial consumption in the EU/EEA (ESAC-Net). Annual epidemiological report 2021. Stockholm: European Centre for Disease Prevention and Control; 2022 (https://www.ecdc.europa.eu/sites/default/files/documents/ESAC-Net_AER_2021_final-rev.pdf, accessed 12 August 2024).
81. Schwartz KL, Xu AXT, Alderson S, Bjerrum L, Brehaut J, Brown BC et al. Best practice guidance for antibiotic audit and feedback interventions in primary care: a modified Delphi study from the Joint Programming Initiative on Antimicrobial resistance: Primary Care Antibiotic Audit and Feedback Network (JPIAMR-PAAN). Antimicrob Resist Infect Control. 2023;12:72. doi: 10.1186/s13756-023-01279-z.
82. Li J, Zhou P, Wang J, Li H, Xu H, Meng Y et al. Worldwide dispensing of non-prescription antibiotics in community pharmacies and associated factors: a mixed-methods systematic review. Lancet Infect Dis. 2023;23:e361–70. doi: 10.1016/S1473-3099(23)00130-5.
83. The role of pharmacist in encouraging prudent use of antibiotics and averting antimicrobial resistance: a review of policy and experience. Copenhagen: WHO Regional Office for Europe; 2014 (https://iris.who.int/handle/10665/139702, accessed 12 August 2024).
84. Paediatric drug optimization (PADO) for antibiotics: meeting report, 30 November, 5–7 December 2022. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/366533, accessed 12 August 2024).
85. Auzin A, Spits M, Tacconelli E, Rodríguez-Baño J, Hulscher M, Adang E et al. What is the evidence base of used aggregated antibiotic resistance percentages to change empirical antibiotic treatment? A scoping review. Clin Microbiol Infect. 2022;28:928–35. doi: 10.1016/j.cmi.2021.12.003.
86. Klein EY, Van Boeckel TP, Martinez EM, Pant S, Gandra S, Levin SA et al. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. Proc Natl Acad Sci U S A. 2018;115:E3463–70. doi: 10.1073/pnas.1717295115.
87. Klein EY, Milkowska-Shibata M, Tseng KK, Sharland M, Gandra S, Pulcini C et al. Assessment of WHO antibiotic consumption and access targets in 76 countries, 2000–15: an analysis of pharmaceutical sales data. Lancet Infect Dis. 2021;21:107–15. doi: 10.1016/S1473-3099(20)30332-7.
88. Global Antimicrobial Resistance and Use Surveillance System (GLASS) report: 2022. Geneva: World Health Organization; 2022 (https://apps.who.int/iris/handle/10665/364996, accessed 12 August 2024).
89. Antimicrobial stewardship interventions: a practical guide. Copenhagen: WHO Regional Office for Europe; 2021 (https://iris.who.int/handle/10665/340709, accessed 12 August 2024).
90. IHME Pathogen Core Group. Global burden associated with 85 pathogens in 2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Infect Dis. 2024; 24:868–95. doi: 10.1016/S1473-3099(24)00158-0.
91. Paul M, Carrara E, Retamar P, Tängdén T, Bitterman R, Bonomo RA et al. European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines for the treatment of infections caused by multidrug-resistant gram-negative bacilli (endorsed by European Society of Intensive Care Medicine). Clin Microbiol Infect. 2022;28:521–47. doi: 10.1016/j.cmi.2021.11.025.
92. Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America 2023 guidance on the treatment of antimicrobial resistant gram-negative infections. Clin Infect Dis. 2023:ciad428. doi: 10.1093/cid/ciad428.
93. McCallin S, Drulis-Kawa Z, Ferry T, Pirnay J-P, Nir-Paz R. Phages and phage-borne enzymes as new antibacterial agents. Clin Microbiol Infect. 2023. doi: 10.1016/j.cmi.2023.10.018.

94. Analysis of the antibacterial pipeline. Geneva: World Health Organization; 2022 (https://www.who.int/observatories/global-observatory-on-health-research-and-development/analyses-and-syntheses/antimicrobial-resistance/analysis-of-the-antibacterial-pipeline, accessed 12 August 2024).
95. 2023 antibacterial agents in clinical and preclinical development: an overview and analysis. Geneva: World Health Organization; 2024 (https://iris.who.int/handle/10665/376944, accessed 12 August 2024).
96. Williams PC, Qazi SA, Agarwal R, Velaphi S, Bielicki JA, Nambiar S et al. Antibiotics needed to treat multidrug-resistant infections in neonates. Bull World Health Organ. 2022;100:797–807. doi: 10.2471/BLT.22.288623.
97. Okomo U, Akpalu ENK, Le Doare K, Roca A, Cousens S, Jarde A et al. Aetiology of invasive bacterial infection and antimicrobial resistance in neonates in sub-Saharan Africa: a systematic review and meta-analysis in line with the STROBE-NI reporting guidelines. Lancet Infect Dis. 2019;19:1219–34. doi: 10.1016/s1473-3099(19)30414-1.
98. Sands K, Carvalho MJ, Portal E, Thomson K, Dyer C, Akpulu C et al. Characterization of antimicrobial-resistant gram-negative bacteria that cause neonatal sepsis in seven low- and middle-income countries. Nat Microbiol. 2021;6:512–23. doi: 10.1038/s41564-021-00870-7.
99. Metsvaht T, Nellis G, Varendi H, Nunn AJ, Graham S, Rieutord A et al. High variability in the dosing of commonly used antibiotics revealed by a Europe-wide point prevalence study: implications for research and dissemination. BMC Pediatr. 2015;15:41. doi: 10.1186/s12887-015-0359-y.
100. GBD Non-Typhoidal Salmonella Invasive Disease Collaborators. The global burden of non-typhoidal salmonella invasive disease: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Infect Dis. 2019;19:1312–24. doi: 10.1016/S1473-3099(19)30418-9.
101. Celik IH, Hanna M, Canpolat FE, Pammi M. Diagnosis of neonatal sepsis: the past, present and future. Pediatr Res. 2022;91:337–50. doi: 10.1038/s41390-021-01696-z.
102. Villavicencio F, Perin J, Eilerts-Spinelli H, Yeung D, Prieto-Merino D, et al. Global, regional, and national causes of death in children and adolescents younger than 20 years: an open data portal with estimates for 2000-21. Lancet Glob Health 2024; 12(1): e16-e7. doi: 10.1016/S2214-109X(23)00496-5.
103. Carey ME, Dyson ZA, Ingle DJ, Amir A, Aworh MK, Chattaway MA et al. Global diversity and antimicrobial resistance of typhoid fever pathogens: Insights from a meta-analysis of 13,000 *Salmonella* Typhi genomes. Elife. 2023;12:e85867. doi: 10.7554/eLife.85867.
104. Disease outbreak news: Pakistan. Geneva: World Health Organization; 2018 (https://www.who.int/emergencies/disease-outbreak-news/item/27-december-2018-typhoid-pakistan-en, accessed 12 August 2024).
105. Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR et al. Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study. Lancet. 2020;395:200–11. doi: 10.1016/S0140-6736(19)32989-7.
106. Guideline: managing possible serious bacterial infection in young infants when referral is not feasible. Geneva: World Health Organization; 2015 (https://iris.who.int/handle/10665/181426, accessed 12 August 2024).
107. WHO recommendations on newborn health: guidelines approved by the WHO Guidelines Review Committee. Geneva: World Health Organization; 2017 (https://iris.who.int/handle/10665/259269, accessed 12 August 2024).
108. Gintjee TJ, Donnelley MA, Thompson GR 3rd. Aspiring antifungals: review of current antifungal pipeline developments. J Fungi (Basel). 2020;6:28. doi: 10.3390/jof6010028.
109. Unemo M, Lahra MM, Escher M, Eremin S, Cole MJ, Galarza P et al. WHO global antimicrobial resistance surveillance for *Neisseria gonorrhoeae* 2017–18: a retrospective observational study. Lancet Microbe. 2021;2:e627–36. doi: 10.1016/s2666-5247(21)00171-3.
110. Gonorrhea, chlamydia, and syphilis pipeline report 2019. New York: Treatment Action Group; 2020 (https://www.treatmentactiongroup.org/wp-content/uploads/2019/03/pipeline_gonorrhea_chlamydia_syphilis_final.pdf, accessed 12 August 2024).
111. Jensen JS, Cusini M, Gomberg M, Moi H, Wilson J, Unemo M. 2021 European guideline on the management of *Mycoplasma genitalium* infections. J Eur Acad Dermatol Venereol. 2022;36:641–50. doi: 10.1111/jdv.17972.

112. Olaru ID, Tacconelli E, Yeung S, Ferrand RA, Stabler RA, Hopkins H et al. The association between antimicrobial resistance and HIV infection: a systematic review and meta-analysis. Clin Microbiol Infect. 2021;27:846–53. doi: 10.1016/j.cmi.2021.03.026.
113. GLASS method for estimating attributable mortality of antimicrobial resistant bloodstream infections. Geneva: World Health Organization; 2020 (https://apps.who.int/iris/handle/10665/332457, accessed 12 August 2024).
114. Global Antimicrobial Resistance Surveillance System (GLASS): early implementation protocol for inclusion of *Candida* spp. Geneva: World Health Organization; 2019 (https://apps.who.int/iris/handle/10665/326926, accessed 12 August 2024).
115. WHO, UNICEF. Progress on WASH in health care facilities 2000–2021: special focus on WASH and infection prevention and control. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/366657, accessed 12 August 2024).
116. Holmes AH, Moore LS, Sundsfjord A, Steinbakk M, Regmi S, Karkey A et al. Understanding the mechanisms and drivers of antimicrobial resistance. Lancet. 2016;387:176–87. doi: 10.1016/S0140-6736(15)00473-0.
117. Denyer Willis L, Chandler C. Quick fix for care, productivity, hygiene and inequality: reframing the entrenched problem of antibiotic overuse. BMJ Glob Health. 2019;4:e001590. doi: 10.1136/bmjgh-2019-001590.
118. Confronting antimicrobial resistance 2024 to 2029. London: Government of the United Kingdom; 2024 (https://www.gov.uk/government/publications/uk-5-year-action-plan-for-antimicrobial-resistance-2024-to-2029/confronting-antimicrobial-resistance-2024-to-2029, accessed 12 August 2024).
119. Report on the health of refugees and migrants in the WHO European Region: No public health without refugee and migrant health: summary. Copenhagen: WHO Regional Office for Europe; 2018 (https://iris.who.int/handle/10665/311348, accessed 12 August 2024).
120. Collignon P, Beggs JJ, Walsh TR, Gandra S, Laxminarayan R. Anthropological and socioeconomic factors contributing to global antimicrobial resistance: a univariate and multivariable analysis. Lancet Planet Health. 2018;2:e398–405. doi: 10.1016/S2542-5196(18)30186-4.
121. GLASS manual for antimicrobial resistance surveillance in common bacteria causing human infection. Geneva: World Health Organization; 2023 (https://apps.who.int/iris/handle/10665/372741, accessed 12 August 2024).
122. Methodological principles of nationally representative surveys as a platform for global surveillance of antimicrobial resistance in human bloodstream infections. Geneva: World Health Organization; 2023 (https://apps.who.int/iris/handle/10665/366150, accessed 12 August 2024).
123. Diagnostic stewardship: a guide to implementation in antimicrobial resistance surveillance sites. Geneva: World Health Organization; 2016 (https://apps.who.int/iris/handle/10665/251553, accessed 12 August 2024).
124. GLASS whole-genome sequencing for surveillance of antimicrobial resistance. Geneva: World Health Organization; 2020 (https://apps.who.int/iris/handle/10665/334354, accessed 12 August 2024).
125. Global Antimicrobial Resistance Surveillance System (GLASS): molecular methods for antimicrobial resistance (AMR) diagnostics to enhance the Global Antimicrobial Resistance Surveillance System. Geneva: World Health Organization; 2019 (https://apps.who.int/iris/handle/10665/310993.
126. Catalogue of mutations in *Mycobacterium tuberculosis* complex and their association with drug resistance. 2nd ed. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/374061, accessed 12 August 2024).
127. Feldgarden M, Brover V, Gonzalez-Escalona N, Frye JG, Haendiges J, Haft DH et al. AMRFinderPlus and the Reference Gene Catalog facilitate examination of the genomic links among antimicrobial resistance, stress response, and virulence. Sci Rep. 2021;11:12728. doi: 10.1038/s41598-021-91456-0.
128. Alcock BP, Huynh W, Chalil R, Smith KW, Raphenya AR, Wlodarski MA et al. CARD 2023: expanded curation, support for machine learning, and resistome prediction at the Comprehensive Antibiotic Resistance Database. Nucleic Acids Res. 2023;51:D690–9. doi: 10.1093/nar/gkac920.
129. Trachoma. Geneva: World Health Organization; 2022 (https://www.who.int/news-room/fact-sheets/detail/trachoma, accessed 12 August 2024).

130. Rolfe RJ, Shaikh H, Tillekeratne LG. Mass drug administration of antibacterials: weighing the evidence regarding benefits and risks. Infect Dis Poverty. 2022;11:77. doi: 10.1186/s40249-022-00998-6.
131. Keenan JD, Bailey RL, West SK, Arzika AM, Hart J, Weaver J et al. Azithromycin to Reduce childhood mortality in sub-Saharan Africa. N Engl J Med. 2018;378:1583–92. doi: 10.1056/nejmoa1715474.
132. WHO guideline on mass drug administration of azithromycin to children under five years of age to promote child survival. Geneva: World Health Organization; 2020 (https://iris.who.int/handle/10665/333942, accessed 12 August 2024).
133. Ramblière L, Guillemot D, Delarocque-Astagneau E, Huynh BT. Impact of mass and systematic antibiotic administration on antibiotic resistance in low- and middle-income countries? A systematic review. Int J Antimicrob Agents. 2021;58:106364. doi: 10.1016/j.ijantimicag.2021.106364.
134. Doan T, Worden L, Hinterwirth A, Arzika AM, Maliki R, Abdou A et al. Macrolide and nonmacrolide resistance with mass azithromycin distribution. N Engl J Med. 2020;383:1941–50. doi: 10.1056/nejmoa2002606.
135. O'Brien KS, Emerson P, Hooper PJ, Reingold AL, Dennis EG, Keenan JD et al. Antimicrobial resistance following mass azithromycin distribution for trachoma: a systematic review. Lancet Infect Dis. 2019;19:e14–25. doi: 10.1016/S1473-3099(18)30444-4.
136. WHO implementation tool for pre-exposure prophylaxis (PrEP) of HIV infection: module 13: integrating STI services. Geneva: World Health Organization; 2022 (https://iris.who.int/handle/10665/362227, accessed 12 August 2024).
137. Mathew P, Sivaraman S, Chandy S. Communication strategies for improving public awareness on appropriate antibiotic use: bridging a vital gap for action on antibiotic resistance. J Family Med Prim Care. 2019;8:1867–71. doi: 10.4103/jfmpc.jfmpc_263_19.
138. The TAP manual: an in-depth guide for planning and implementing tailoring antimicrobial resistance programmes. Copenhagen: WHO Regional Office for Europe; 2022 (https://iris.who.int/handle/10665/363136, accessed 12 August 2024).
139. WHO Taskforce of AMR Survivors. AMR is invisible, I am not. Geneva: World Health Organization; 2024 (https://www.who.int/campaigns/world-amr-awareness-week/2024/amr-is-invisible-i-am-not#, accessed 12 August 2024).
140. Martin P, Chapoton B, Bourmaud A, Dumas A, Kivits J, Eyraud C et al. Health promotion in popular web-based community games among young people: proposals, recommendations, and applications. JMIR Serious Games. 2023;11:e39465. doi: 10.2196/39465.
141. Vernet V. "I dream of an empty ward": end polio now virtual reality [video]. 2017 (https://www.youtube.com/watch?v=EPYJOSBVhDw, accessed 12 August 2024).
142. WHO Taskforce of AMR Survivors. Meaningful engagement of patients, survivors and carers in addressing antimicrobial resistance. Geneva: World Health Organization; 2024 (https://www.who.int/publications/m/item/meaningful-engagement-of-patients--survivors-and-carers-in-addressing-antimicrobial-resistance, accessed 12 August 2024).
143. Haller DM, Sanci LA, Sawyer SM, Patton G. Do young people's illness beliefs affect healthcare? a systematic review. J Adolesc Health. 2008;42:436–49. doi: 10.1016/j.jadohealth.2007.09.013.
144. Dar OA, Hasan R, Schlundt J, Harbarth S, Caleo G, Dar FK et al. Exploring the evidence base for national and regional policy interventions to combat resistance. Lancet. 2016;387:285–95. doi: 10.1016/S0140-6736(15)00520-6.
145. Rogers Van Katwyk S, Grimshaw JM, Nkangu M, Mendelson M, Taljaard M, Hoffman SJ. Study reporting quality among interventions to reduce antibiotic use is a barrier to evidence-informed policymaking on antimicrobial resistance: systematic review. J Antimicrob Chemother. 2020;75:1091–8. doi: 10.1093/jac/dkz540.
146. Rogers Van Katwyk S, Hoffman SJ, Mendelson M, Taljaard M, Grimshaw JM. Strengthening the science of addressing antimicrobial resistance: a framework for planning, conducting and disseminating antimicrobial resistance intervention research. Health Res Policy Syst. 2020;18:60. doi: 10.1186/s12961-020-00549-1.
147. Michie S, van Stralen MM, West R. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. Implement Sci. 2011;6:42. doi: 10.1186/1748-5908-6-42.

148. Operating grant: evaluation of population-level interventions to reduce AMR. Ottawa: Canadian Institutes of Health Research; 2022 (https://www.researchnet-recherchenet.ca/rnr16/vwOpprtntyDtls.do?prog=3772&language=E, accessed 12 August 2024).
149. Charani E, Mendelson M, Pallett SJC, Ahmad R, Mpundu M, Mbamalu O et al. An analysis of existing national action plans for antimicrobial resistance – gaps and opportunities in strategies optimising antibiotic use in human populations. Lancet Glob Health. 2023;11:e466–74. doi: 10.1016/s2214-109x(23)00019-0.
150. Evidence for action on antimicrobial resistance. London: Wellcome Trust; 2016 (https://wellcome.org/sites/default/files/evidence-for-action-on-antimicrobial-resistance-wellcome-sep16.pdf, accessed 12 August 2024).
151. Chua AQ, Verma M, Hsu LY, Legido-Quigley H. An analysis of national action plans on antimicrobial resistance in Southeast Asia using a governance framework approach. Lancet Reg Health West Pac. 2021;7:100084. doi: 10.1016/j.lanwpc.2020.100084.
152. Willemsen A, Reid S, Assefa Y. A review of national action plans on antimicrobial resistance: strengths and weaknesses. Antimicrob Resist Infect Control. 2022;11:90. doi: 10.1186/s13756-022-01130-x.
153. Situation analysis on antimicrobial resistance in the South-East Asia Region: report 2016. New Delhi: WHO Regional Office for South-East Asia; 2017 (https://iris.who.int/handle/10665/272873, accessed 12 August 2024).
154. Patel J, Harant A, Fernandes G, Mwamelo AJ, Hein W, Dekker D et al. Measuring the global response to antimicrobial resistance, 2020–21: a systematic governance analysis of 114 countries. Lancet Infect Dis. 2023;23:706–18. doi: 10.1016/s1473-3099(22)00796-4.
155. Anderson M, Schulze K, Cassini A, Plachouras D, Mossialos E. A governance framework for development and assessment of national action plans on antimicrobial resistance. Lancet Infect Dis. 2019;19:e371–84. doi: 10.1016/s1473-3099(19)30415-3.
156. Antimicrobial resistance: national action plans IACG discussion paper. Geneva: Interagency Coordination Group on Antimicrobial Resistance; 2018 (https://cdn.who.int/media/docs/default-source/antimicrobial-resistance/iacg-amr-national-action-plans-110618.pdf, accessed 12 August 2024).
157. Drug-resistant infections: a threat to our economic future (Vol. 2): final report. Washington (DC): World Bank Group; 2017 (http://documents.worldbank.org/curated/en/323311493396993758/final-report, accessed 12 August 2024).
158. Stemming the superbug tide. Paris: Organisation for Economic Co-operation and Development; 2018 (https://www.oecd-ilibrary.org/content/publication/9789264307599-en, accessed 12 August 2024).
159. Embracing a One Health framework to fight antimicrobial resistance. Paris: Organisation for Economic Co-operation and Development; 2023 (https://www.oecd-ilibrary.org/content/publication/ce44c755-en, accessed 12 August 2024).
160. Building the investment case for action against antimicrobial resistance. Geneva: Global Leaders Group on Antimicrobial Resistance; 2024 (https://www.amrleaders.org/docs/librariesprovider20/glg/annex-to-the-glg-report.pdf, accessed 12 August 2024).
161. Preventing antimicrobial resistance together: why we should leverage universal health coverage to address AMR. Geneva: UHC2030; 2023 (https://www.uhc2030.org/news-and-events/news/preventing-antimicrobial-resistance-together-why-we-should-leverage-universal-health-coverage-to-address-amr, accessed 12 August 2024).
162. Seventh meeting of the intergovernmental negotiating body to draft and negotiate a WHO convention, agreement or other international instrument on pandemic prevention, preparedness and response. Proposal for negotiating text of the WHO Pandemic Agreement. Geneva: World Health Organization; 2023 (https://apps.who.int/gb/inb/pdf_files/inb7/A_INB7_3-en.pdf, accessed 12 August 2024).
163. Ruckert A, Lake S, Van Katwyk SR. Developing a protocol on antimicrobial resistance through WHO's pandemic treaty will protect lives in future pandemics. Glob Health. 2024;20:10. doi: 10.1186/s12992-024-01015-1.

164. People-centred approach to addressing antimicrobial resistance in human health: WHO core package of interventions to support national action plans. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/373458, accessed 12 August 2024).
165. Khurana MP, Essack S, Zoubiane G, Sreenivasan N, Cordoba GC, Westwood E et al. Mitigating antimicrobial resistance (AMR) using implementation research: a development funder's approach. JAC Antimicrob Resist. 2023;5:dlad031. doi: 10.1093/jacamr/dlad031.
166. The growing crisis in antibiotic R&D: opportunities for G20 member action to support sustainable innovation. London: Wellcome Trust; 2020 (https://wellcome.org/sites/default/files/the-growing-crisis-for-antibiotic-r-and-d.pdf, accessed 12 August 2024).
167. Anderson M, Panteli D, Mossialos E. How can the EU support sustainable innovation and access to effective antibiotics? Policy options for existing and new medicines. Copenhagen: WHO Regional Office for Europe; 2023 (https://iris.who.int/handle/10665/369638, accessed 12 August 2024).
168. Overcoming resistance. Ottawa: Council of Canadian Academies; 2023.
169. Global AMR R&D Hub, WHO. Incentivising the development of new antibacterial treatments. Geneva: Global AMR R&D Hub; 2023 (https://globalamrhub.org/wp-content/uploads/2024/10/g7progress_2024_hub_who.pdf, accessed 12 August 2024).
170. Antimicrobial products subscription model: guidance on commercial arrangements. London: NHS England; 2023 (https://www.engage.england.nhs.uk/survey/the-antimicrobial-products-subscription-model/user_uploads/antimicrobial-products-subscription-model--guidance-on-commercial-arrangements--1.pdf, accessed 12 August 2024).
171. McDonnell A, Dissanayake R, Klemperer K, Toxvaerd F, Sharland M. The economics of antibiotic resistance. Washington (DC): Center for Global Development; 2024 (https://www.cgdev.org/sites/default/files/economics-antibiotic-resistance.pdf, accessed 12 August 2024).
172. Tropical disease priority review voucher program. Washington (DC): United States Food and Drug Administration; 2024 (https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/tropical-disease-priority-review-voucher-program, accessed 12 August 2024).
173. 2021 antimicrobial resistance benchmark. Amsterdam: Access to Medicine Foundation; 2021 (https://accesstomedicinefoundation.org/resource/2021-antimicrobial-resistance-benchmark, accessed 12 August 2024).
174. Rogers Van Katwyk S, Weldon I, Giubilini A, Kirchhelle C, Harrison M, McLean A et al. Making use of existing international legal mechanisms to manage the global antimicrobial commons: identifying legal hooks and institutional mandates. Health Care Anal. 2023;31:9–24. doi: 10.1007/s10728-020-00393-y.
175. Improving regulatory practices to sustain antibiotic innovation. Washington (DC): Duke-Margolis Center for Health Policy; 2024 (https://healthpolicy.duke.edu/sites/default/files/2024-02/Webinar%20Takeaways_Regulatory%20Practices%20to%20Sustain%20Antibiotic%20Innovation_2023-12-12.pdf, accessed 12 August 2024).
176. Coronavirus Treatment Acceleration Program (CTAP). Washington (DC): United States Food and Drug Administration; 2023 (https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap, accessed 12 August 2024).
177. 2021 antibacterial agents in clinical and preclinical development: an overview and analysis. Geneva: World Health Organization; 2022 (https://iris.who.int/handle/10665/354545, accessed 12 August 2024).
178. Outterson K, Rex JH. Global pull incentives for better antibacterials: the United Kingdom leads the way. Appl Health Econ Health Policy. 2023;21:361–4. doi: 10.1007/s40258-023-00793-w.
179. Ardal C, Rottingen JA, Opalska A, Van Hengel AJ, Larsen J. Pull incentives for antibacterial drug development: an analysis by the Transatlantic Task Force on Antimicrobial Resistance. Clin Infect Dis. 2017;65:1378–82. doi: 10.1093/cid/cix526.
180. Ardal C, Lacotte Y, Ploy MC. Financing pull mechanisms for antibiotic-related innovation: opportunities for Europe. Clin Infect Dis. 2020;71:1994–9. doi: 10.1093/cid/ciaa153.
181. Behr MA, Edelstein PH, Ramakrishnan L. Is *Mycobacterium tuberculosis* infection life long? BMJ. 2019;367:l5770. doi: 10.1136/bmj.l5770.
182. Emery JC, Richards AS, Dale KD, McQuaid CF, White RG, Denholm JT et al. Self-clearance of *Mycobacterium tuberculosis* infection: implications for lifetime risk and population at-risk of tuberculosis disease. Proc Biol Sci. 2021;288:20201635. doi: 10.1098/rspb.2020.1635.

183. WHO consolidated guidelines on tuberculosis: module 1: prevention: tuberculosis preventive treatment. Geneva: World Health Organization; 2020 (https://iris.who.int/handle/10665/331170, accessed 12 August 2024).
184. World Health Organization. BCG vaccines: WHO position paper – February 2018. Wkly Epidemiol Rec. 2018;93:73–96.
185. The end TB strategy. Geneva: World Health Organization; 2015 (https://iris.who.int/handle/10665/331326, accessed 12 August 2024).
186. WHO preferred product characteristics for new tuberculosis vaccines. Geneva: World Health Organization; 2018 (https://iris.who.int/handle/10665/273089, accessed 12 August 2024).
187. An investment case for new tuberculosis vaccines. Geneva: World Health Organization; 2022 (https://iris.who.int/handle/10665/365230, accessed 12 August 2024).
188. WHO launches the TB research tracker, an online platform to track progress in TB research. Geneva: World Health Organization; 2023 (https://www.who.int/news/item/05-06-2023-who-launches-the-tb-research-tracker--an-online-platform-to-track-progress-in-tb-research, accessed 12 August 2024).
189. Tait DR, Hatherill M, Van Der Meeren O, Ginsberg AM, Van Brakel E, Salaun B et al. Final analysis of a trial of M72/AS01(E) vaccine to prevent tuberculosis. N Engl J Med. 2019;381:2429–39. doi: 10.1056/NEJMoa1909953.
190. United Nations General Assembly. Resolution 78/5: Political Declaration of the High-level Meeting of the General Assembly on the Fight against Tuberculosis. New York: United Nations; 2023 (https://undocs.org/Home/Mobile?FinalSymbol=A%2FRES%2F78%2F5&Language=E&DeviceType=Desktop&LangRequested=False, accessed 12 August 2024).
191. WHO consolidated guidelines on tuberculosis: module 3: diagnosis: rapid diagnostics for tuberculosis detection. 3rd ed. Geneva: World Health Organization; 2024 (https://iris.who.int/handle/10665/376221, accessed 12 August 2024).
192. Target regimen profiles for tuberculosis treatment, 2023 update. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/373790, accessed 12 August 2024).
193. Frascella B, Richards AS, Sossen B, Emery JC, Odone A, Law I et al. Subclinical tuberculosis disease – a review and analysis of prevalence surveys to inform definitions, burden, associations, and screening methodology. Clin Infect Dis. 2021;73:e830–41. doi: 10.1093/cid/ciaa1402.
194. WHO consolidated guidelines on tuberculosis: module 4: treatment: drug-resistant tuberculosis treatment. 2022 update ed. Geneva: World Health Organization; 2022 (https://iris.who.int/handle/10665/365308, accessed 12 August 2024).
195. New treatment for drug-resistant tuberculosis. Geneva: World Health Organization; 2023 (https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2023/featured-topics/new-treatment-tb, accessed 12 August 2024).
196. WHO consolidated guidelines on tuberculosis care and support. Geneva: World Health Organization; 2022 (https://www.who.int/publications/i/item/9789240047716, accessed 12 August 2024).
197. Guideline: nutritional care and support for patients with tuberculosis. Geneva: World Health Organization; 2013 (https://iris.who.int/handle/10665/94836, accessed 12 August 2024).
198. WHO consolidated guidelines on tuberculosis: module 4: treatment: tuberculosis care and support. Geneva: World Health Organization; 2022 (https://iris.who.int/handle/10665/353399, accessed 12 August 2024).
199. United Nations General Assembly. Resolution 78/5: Political Declaration of the High-level Meeting of the General Assembly on the Fight against Tuberculosis. New York: United Nations; 2023 (https://undocs.org/A/RES/78/5, accessed 12 August 2024).
200. WHO consolidated guidelines on tuberculosis, Module 4: treatment – drug-resistant tuberculosis treatment. Geneva: World Health Organization; 2022 (https://www.who.int/publications/i/item/9789240063129, accessed 12 August 2024).
201. United Nations General Assembly. Political Declaration of the High-level Meeting on the Fight against Tuberculosis: draft resolution. New York: United Nations; 2023 (https://digitallibrary.un.org/record/4022582/files, accessed 12 August 2024).
202. Fleischmann C, Reichert F, Cassini A, Horner R, Harder T, Markwart R et al. Global incidence and mortality of neonatal sepsis: a systematic review and meta-analysis. Arch Dis Child. 2021;106:745–52. doi: 10.1136/archdischild-2020-320217.

203. Levels & trends in child mortality: report 2023. New York: United Nations Inter-agency Group for Child Mortality Estimation; 2023 (https://childmortality.org/wp-content/uploads/2024/03/UNIGME-2023-Child-Mortality-Report.pdf, accessed 12 August 2024).
204. Boniol M, Kunjumen T, Nair TS, Siyam A, Campbell J, Diallo K. The global health workforce stock and distribution in 2020 and 2030: a threat to equity and "universal" health coverage? BMJ Glob Health. 2022;7:e009316. doi: 10.1136/bmjgh-2022-009316.
205. Chandler CIR, Nayiga S. Antimicrobial resistance in cities: an overlooked challenge that requires a multidisciplinary approach. Lancet. 2023;401:627–9. doi: 10.1016/S0140-6736(22)02351-0.
206. Fourth WHO global evidence review on health and migration stresses that equitable access to and appropriate use of antibiotics for refugees and migrants is essential to tackling antimicrobial resistance. Geneva: World Health Organization; 2022 (https://www.who.int/news/item/19-09-2022-fourth-who-global-evidence-review-on-health-and-migration-stresses-that-equitable-access-to-and-appropriate-use-of-antibiotics-for-refugees-and-migrants-is-essential-to-tackling-antimicrobial-resistance, accessed 12 August 2024).
207. Gautron JMC, Tu Thanh G, Barasa V, Voltolina G. Using intersectionality to study gender and antimicrobial resistance in low- and middle-income countries. Health Policy Plan. 2023;38:1017–32. doi: 10.1093/heapol/czad054.
208. Semenza JC, Ko AI. Waterborne diseases that are sensitive to climate variability and climate change. N Engl J Med. 2023;389:2175–87. doi: 10.1056/NEJMra2300794.
209. Seidel D, Wurster S, Jenks JD, Sati H, Gangneux JP, Egger M et al. Impact of climate change and natural disasters on fungal infections. Lancet Microbe. 2024;5:e594–605. doi: 10.1016/S2666-5247(24)00039-9.
210. MacFadden DR, McGough SF, Fisman D, Santillana M, Brownstein JS. Antibiotic resistance increases with local temperature. Nat Clim Chang. 2018;8:510–4. doi: 10.1038/s41558-018-0161-6.
211. Antimicrobial resistance and the climate crisis. Geneva: Global Leaders Group on Antimicrobial Resistance; 2021 (https://www.amrleaders.org/docs/librariesprovider20/default-document-library/amr-and-the-climate-crisis.pdf, accessed 12 August 2024).
212. Mendelson M, Laxminarayan R, Limmathurotsakul D, Kariuki S, Gyansa-Lutterodt M, Charani E et al. Antimicrobial resistance and the great divide: inequity in priorities and agendas between the Global North and the Global South threatens global mitigation of antimicrobial resistance. Lancet Glob Health. 2024;12:e516–21. doi: 10.1016/S2214-109X(23)00554-5.
213. Tol RS. The economic impacts of climate change. Rev Environ Econ Policy. 2018;12:4–25.
214. Lv J, Deng S, Zhang L. A review of artificial intelligence applications for antimicrobial resistance. Biosaf Health. 2021;3:22–31. doi: 10.1016/j.bsheal.2020.08.003.
215. Branda F, Scarpa F. Implications of artificial intelligence in addressing antimicrobial resistance: innovations, global challenges, and healthcare's future. Antibiotics. 2024;13:502. doi: 10.3390/antibiotics13060502.
216. Ethics and governance of artificial intelligence for health: WHO guidance: executive summary. Geneva: World Health Organization; 2021 (https://apps.who.int/iris/handle/10665/350567, accessed 12 August 2024).
217. Generating evidence for artificial intelligence-based medical devices: a framework for training, validation and evaluation. Geneva: World Health Organization; 2021 (https://apps.who.int/iris/handle/10665/349093, accessed 12 August 2024).
218. 218. Bertagnolio S, Dobreva Z, Centner CM, Olaru ID, Donà D, Burzo S et al. WHO global research priorities for antimicrobial resistance in human health. Lancet Microbe. 2024:100902. doi: 10.1016/s2666-5247(24)00134-4.
219. Seventy-seventh World Health Assembly. Agenda item 11.8 Antimicrobial resistance: accelerating national and global responses. Geneva: World Health Organization; 2024 (https://apps.who.int/gb/ebwha/pdf_files/WHA77/A77_ACONF1-en.pdf, accessed 12 August 2024).
220. A systematic approach for undertaking a research priority-setting exercise: guidance for WHO staff. Geneva: World Health Organization; 2020 (https://iris.who.int/handle/10665/334408, accessed 12 August 2024).

# Annex 1. Developing the research agenda

## 1. Overview

The research priorities of this agenda were compiled through a multistage process (Fig. A1.1). The WHO secretariat convened a Steering Group, comprising staff across WHO headquarters departments and regional offices with technical expertise spanning the AMR subject areas, to assist with defining the objectives and scope and to guide the development of the agenda.

A scoping review was conducted to identify knowledge gaps in AMR. The knowledge gaps were then consolidated into a list of broader research topics. This list was reviewed by members of the Research Agenda Expert Group who were identified through a review of publication records and referrals and through a global online consultation open to the wider research community. Both activities enabled experts and researchers to amend research topics or propose new ones.

These proposals were then consolidated to generate a revised list of research topics. The list was distributed to members of the Research Agenda Expert Group, who individually assessed each research topic against predefined criteria, based on which a final list of 40 research priorities was generated.

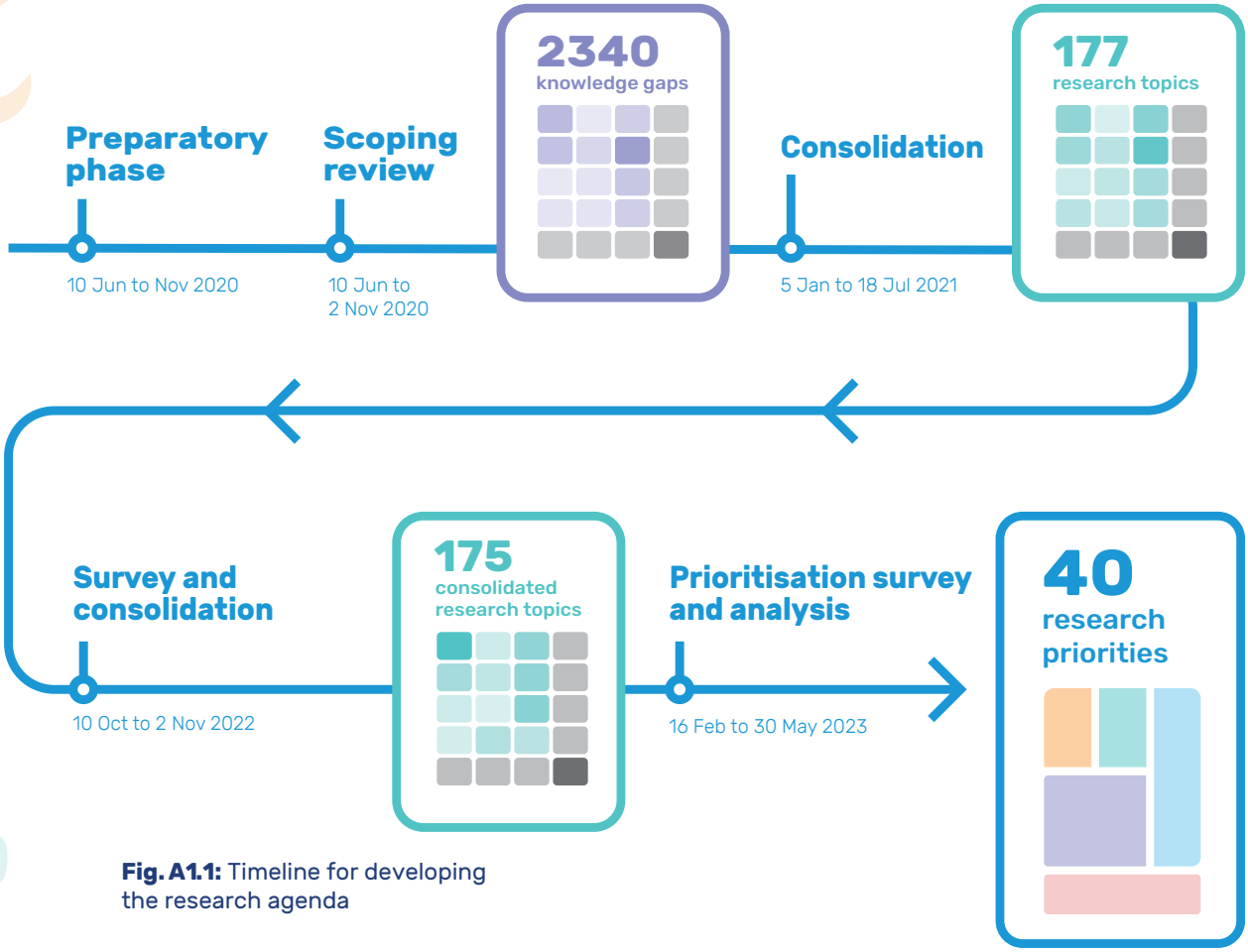



**Fig. A1.1:** Timeline for developing the research agenda

# 2. Preparation

## 2.1 Defining governance, objectives and scope

A WHO Steering Group comprising WHO staff with expertise in the key AMR areas was established to provide strategic guidance at critical points in the decision-making process, to provide technical guidance across AMR areas and to oversee the development of the research agenda. This process included defining the research agenda's objectives, scope, population, geographical focus, time frame, AMR areas and research investment strategies (Box A1.1).

Box A1.1

### Framework for developing the research agenda

#### Objectives

The research agenda has two objectives: (1) to advance the evidence on AMR by identifying and setting priorities for research topics encompassing prevention, diagnosis, treatment and care, the burden and determinants of AMR and optimizing intervention delivery and (2) to catalyse investment and scientific interest among researchers, donors, and public health professionals.

#### Scope and focus

The research agenda focuses on AMR in the human health sector and specifically on infections caused by WHO bacterial priority pathogens, WHO fungal priority pathogens with critical importance for AMR and resistant *Mycobacterium tuberculosis*. Other pathogens such as drug-resistant HIV and malaria are out of scope.

#### Population

The research agenda addresses research priorities applicable to the general population, including children and people experiencing vulnerability.

#### Geographical context

Although the research agenda is global in scope, it especially focuses on identifying knowledge gaps and giving priority to research topics that are relevant for limited-resource settings.

#### Time frame

In accordance with the Sustainable Development Goals, the research agenda aims to catalyse research by 2030.

#### Research investment strategy

The research agenda aims for investment in AMR research to be balanced and diversified across the priority research topics (not focusing on one or a few high-risk and/or expensive research ideas) and encompassing the four domains of research (descriptive, delivery, discovery and development).

## 2.2 Choice of methods

The research agenda was developed following the Child Health and Nutrition Research Initiative (CHNRI), a well-established method for setting priorities for research from a large pool of research topics *(1–3)*. CHNRI is a metric-based approach that enables the research topics in a given area to be identified and formulated, followed by systematically setting priorities based on collective opinion. Compared with alternative consensus-based approaches, CHNRI offers a systematic, transparent and reproducible method for setting priorities. Based on the standard CHNRI method, the initial pool of research topics for setting priorities is derived from experts' ideas. In the development of this research agenda, this step was preceded by an extensive scoping review to identify knowledge gaps from the literature.

Box A1.2

### Scoring criteria

#### Filling critical knowledge gaps

Is the research likely to fill critical knowledge gaps on AMR?


#### Answerability and feasibility by 2030

Can a research study be designed and carried out by 2030 to address at least some components of the research topic? (Availability of funding should not be considered)

#### Potential for translation into policy

Do findings have the potential to lead to evidence-informed policy and practices aimed at mitigating the public health impact of AMR?

#### Impact to mitigate AMR

Is the research likely to result in an intervention that is effective, efficacious and/or efficient in mitigating the impact of AMR? (Effective: producing a desired effect in a real-world environment; efficacious: providing a desired effect in a controlled environment; efficient: providing highest value for the available resources)

#### Promoting health equity

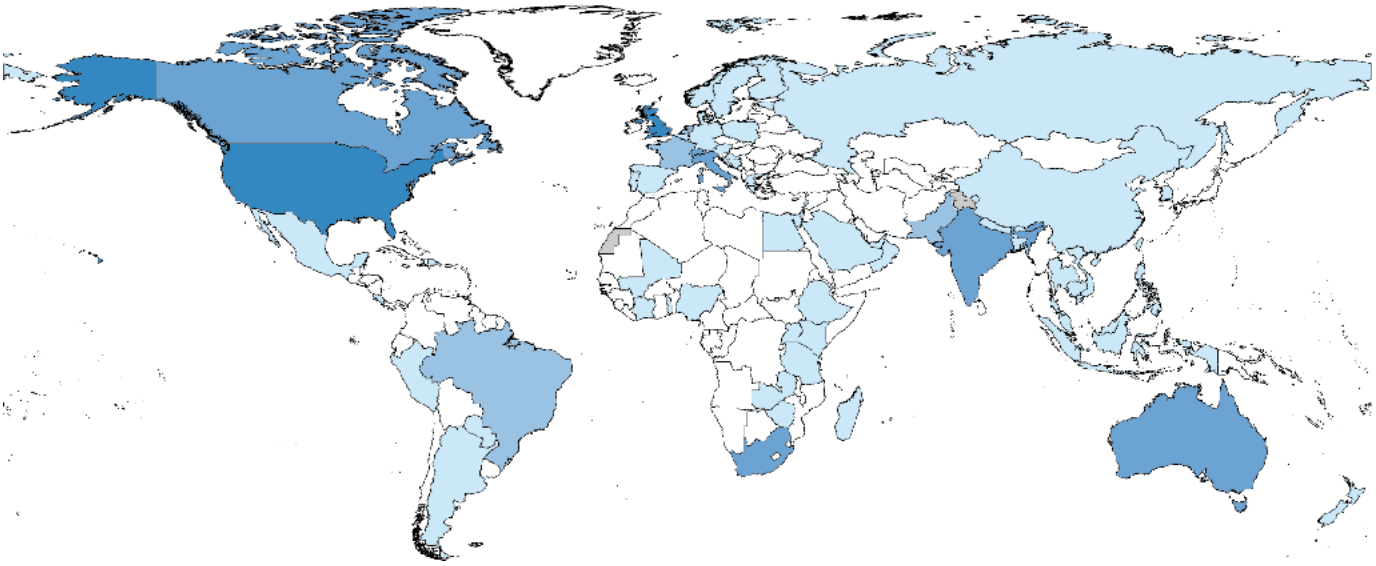
Is the research likely to promote health equity: leading to interventions that will reduce the inequitable impact of AMR across diverse socioeconomic contexts and underprivileged populations?

## 2.3 Convening the Expert Group

A global Research Agenda Expert Group was established through a systematic review of publication records and referrals. In the first step, the top 125 experts within five research disciplines and 14 vertical AMR areas were identified based on their scientific production in the Web of Science *(4)*. To ensure wide representation within the Expert Group across geographical areas, income settings, subpopulations, research domains and AMR areas and inclusion of a sufficient number of experts focusing on children, tuberculosis and mycology, the Expert Group was supplemented through referrals and recommendations by members of the Steering Group and WHO regional offices.

A total of 562 experts were invited, and 261 participated in developing the research agenda by completing one or both of two surveys. Experts were based in 69 countries from all WHO regions: European Region (41%), Region of the Americas (24%), African Region (15%), Western Pacific Region (8%), South-East Asia Region (7%) and Eastern Mediterranean Region (4%). The countries with the highest number of experts were the United Kingdom, United States of America, South Africa, Switzerland, Canada, India, Brazil and Australia. Experts in all AMR areas and across research disciplines were represented; 49% self-identified as women (Fig. A1.2).

**Fig. A1.2:** Number of experts by country.



Key:

- 0
- 1 to <5
- 5 to <10
- 10 to <20
- 30
- Not applicable

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data source: World Health Organization
Map production: WHO Health Emergencies Programme

**Fig. A1.3:** Number of experts by research discipline.

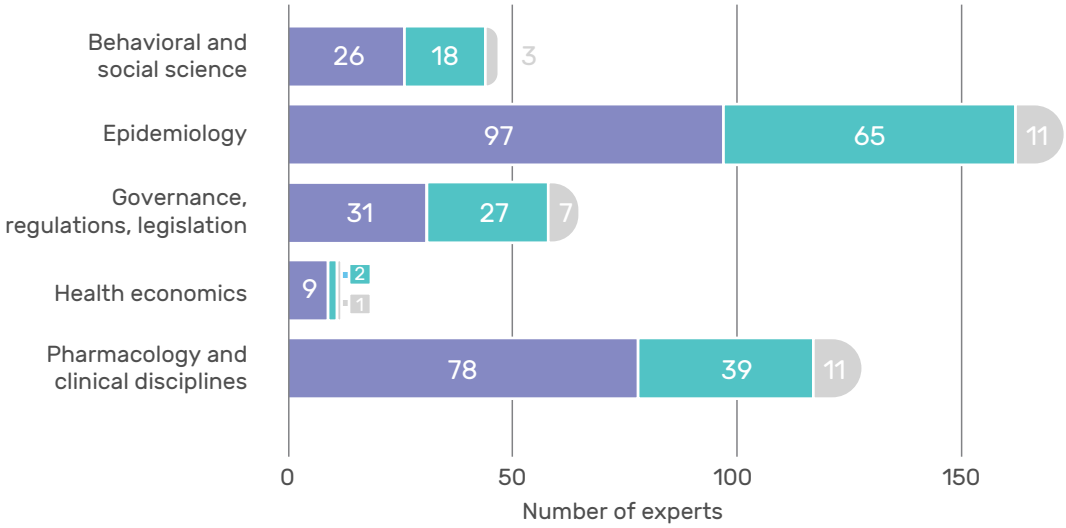
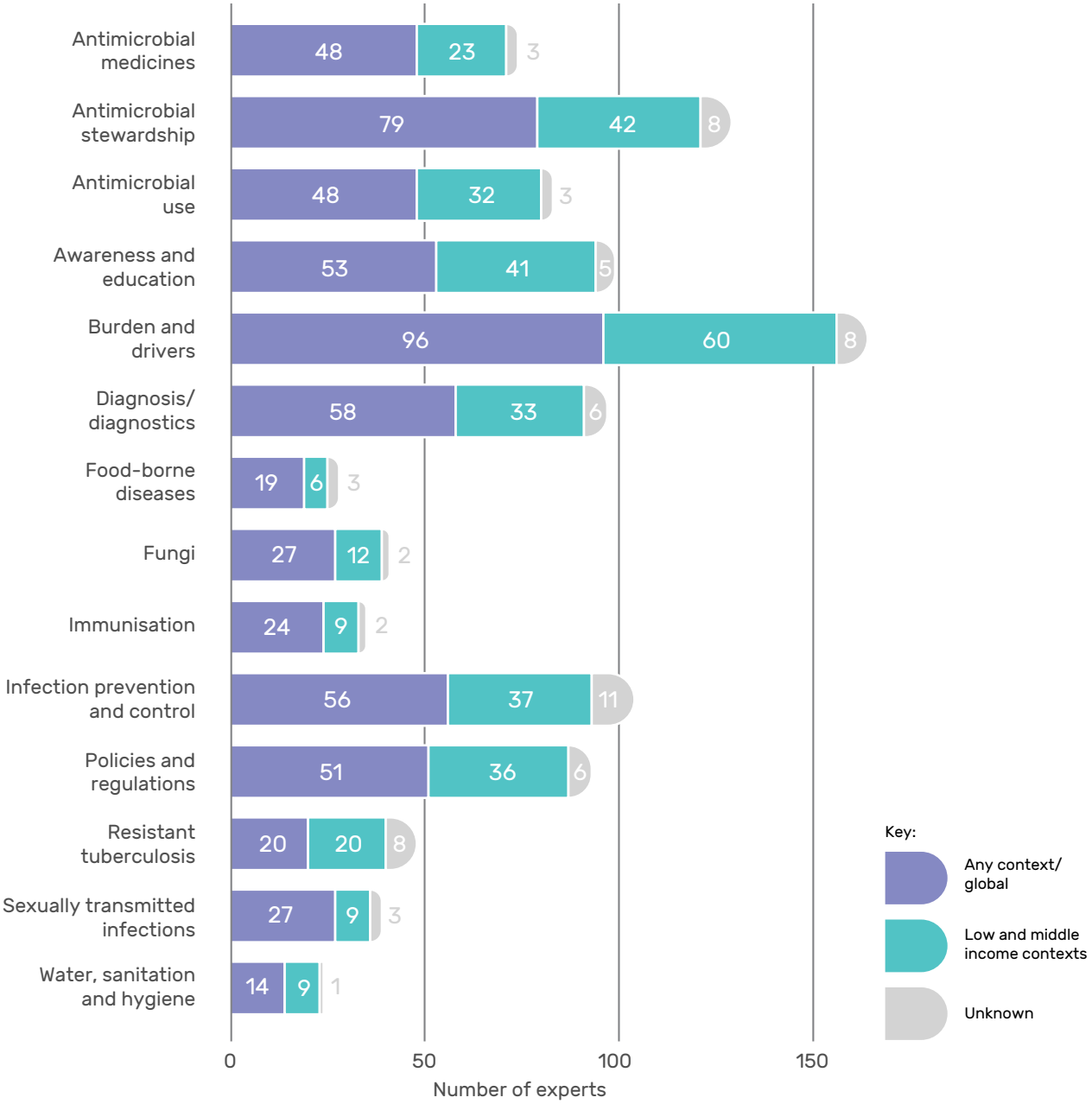



**Fig. A1.4:** Number of experts based on reported area of expertise.



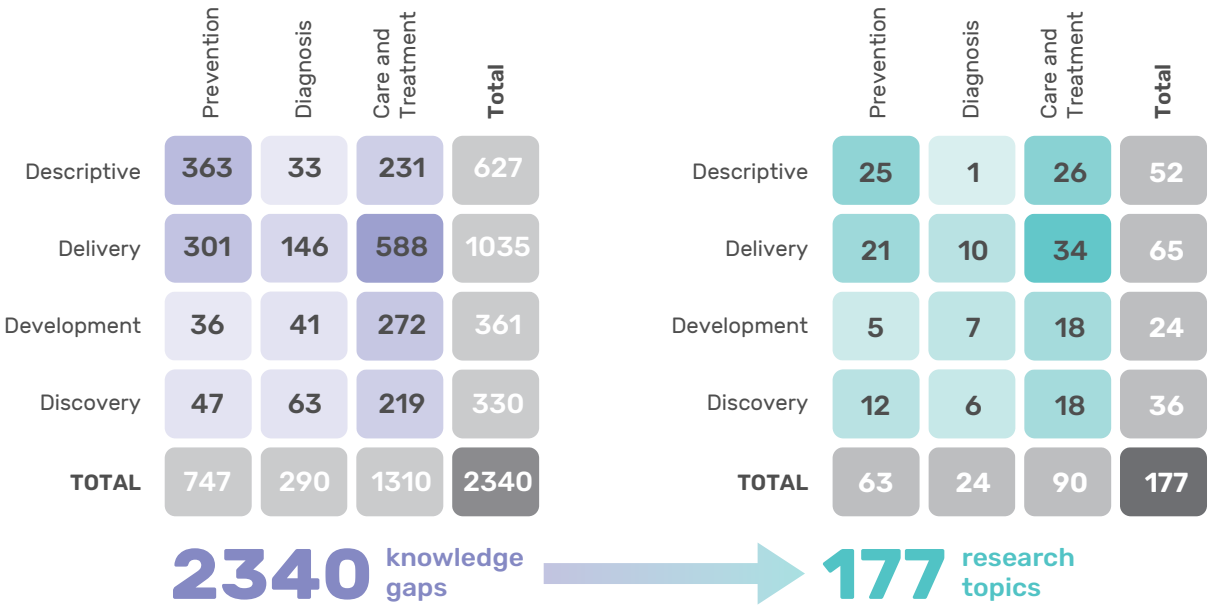
# 3. Scoping review to identify knowledge gaps

A systematic search of the peer-reviewed and grey literature covering a 10-year period (2012–2021) was undertaken to identify knowledge gaps in AMR *(5,6)*. The literature included WHO documents such as guidelines, grey literature relevant to AMR, systematic reviews on AMR research gaps and priorities and additional documents suggested by the WHO Steering Group. Since the scoping review aimed to identify and compile knowledge gaps rather than individual research findings, the search strategy focused on reports, guidelines and systematic reviews rather than individual original research studies.

Identified research gaps and topics were categorized into a knowledge matrix according to the four CHNRI research domains: descriptive (have greater understanding of antimicrobial burden and drivers), delivery (provide ways to deliver existing interventions with better quality), development (improve existing interventions, reduce their costs or optimize their implementation) and discovery (new interventions for AMR prevention, treatment and diagnosis) and the three themes of the WHO people-centred approach to AMR *(3,7)* (Fig. A1.3). The search found 1156 unique documents screened from 8409 publications and from which 2340 knowledge gaps were identified. These originated from 68 countries and included 225 (20%) publications originating from low- and middle-income countries.

The knowledge gaps were subsequently reformulated and consolidated into higher-level thematic research topics by removing duplicates, merging thematically similar ones and removing those that did not meet the scope (such as not focusing on human health or one of the pathogens in scope). This process yielded 177 research topics in a population, intervention, comparator and outcomes (PICO) or population, exposure, comparator and outcomes (PECO) format.

**Fig. A1.5:** Knowledge matrix categorizing knowledge gaps (left) and research topics (right) according to the four CHNRI research domains and three themes of the WHO people-centred approach for AMR.



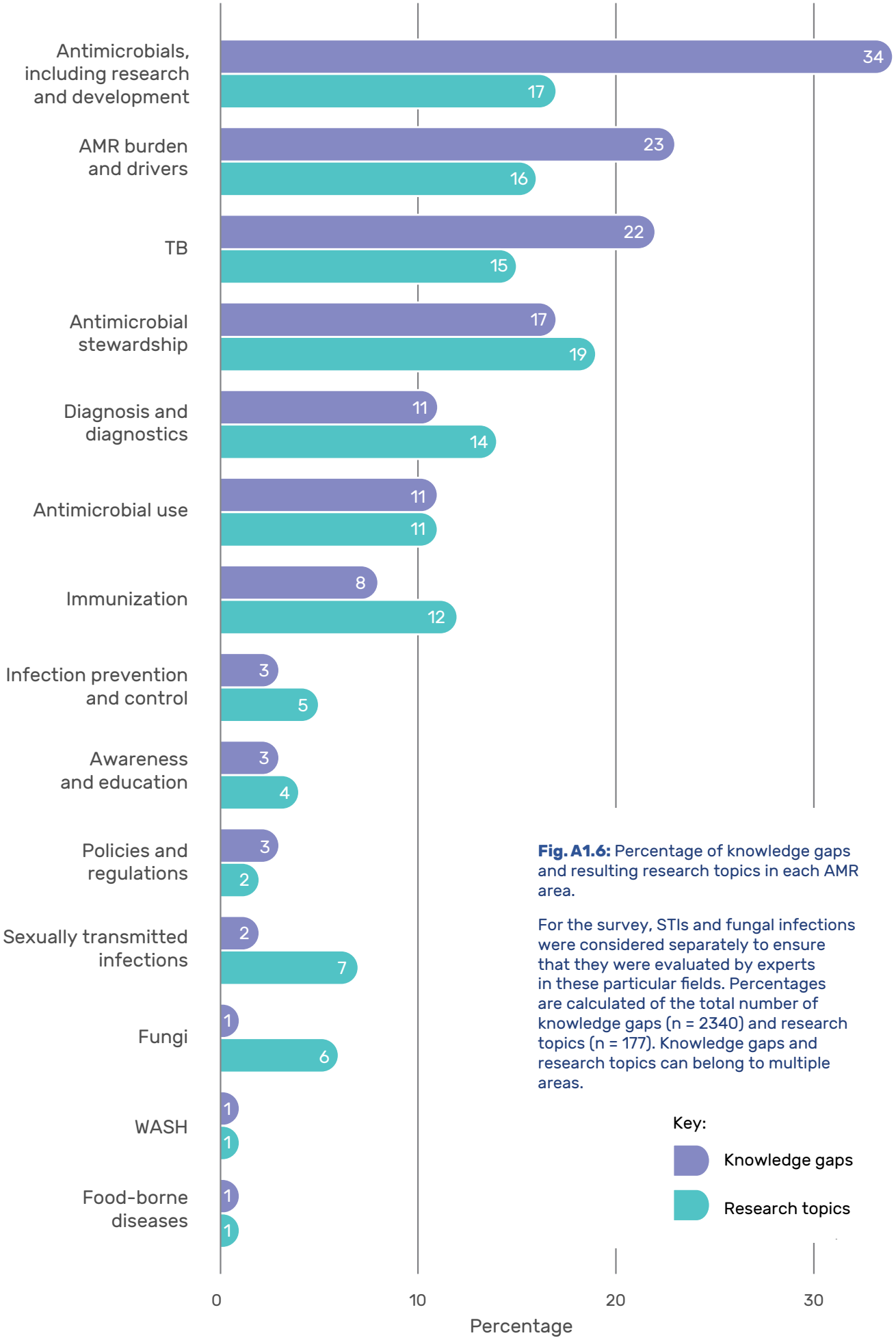



**Fig. A1.6:** Percentage of knowledge gaps and resulting research topics in each AMR area.

For the survey, STIs and fungal infections were considered separately to ensure that they were evaluated by experts in these particular fields. Percentages are calculated of the total number of knowledge gaps (n = 2340) and research topics (n = 177). Knowledge gaps and research topics can belong to multiple areas.

# 4. Developing the list of research topics for prioritization

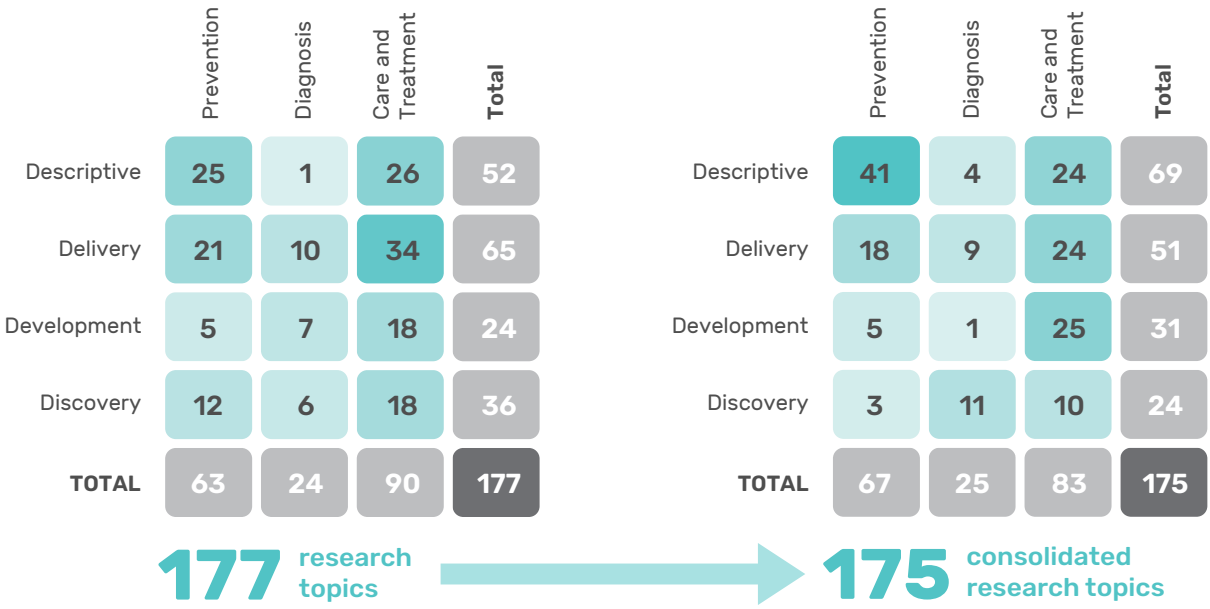
An Expert Group survey and online consultation were undertaken to review and supplement the list of research topics.

## 4.1 Expert Group survey and open call

A total of 257 experts agreed to participate in the Research Agenda Expert Group and were invited to review the 177 research topics through an online survey. Experts could agree to include the topic, suggest text improvements and mark individual topics for removal. The topics could be marked for removal if the expert considered that the topic met any of the three exclusion criteria: (a) the topic does not concern a critical gap in the current knowledge on AMR in the human health sector (evidence already exists to address the research topic); (b) evidence generated from the topic would result in evidence that is unlikely to inform and be translated into health policies and/or AMR evidence-informed interventions; or (c) a research study cannot be designed, carried out and evidence generated to address the research topic by 2030. Experts could also propose up to two new topics they considered relevant to the scope of the agenda that address a critical knowledge gap on AMR.

Of the 257 experts invited, 156 (61%) provided feedback in the survey and proposed 158 new topics. In parallel, an open global consultation calling for feedback on the same list of research topics was posted on the WHO website, allowing the global research community to propose additional research topics for inclusion *(8)*. Eighteen people participated in the open call, proposing seven additional research topics. In total, 165 new topics were proposed in addition to the 177 identified through the scoping review.

**Fig. A1.7:** Knowledge matrix categorizing research topics sent for review by the Expert Group (left) and research topics after consolidation of the received feedback (right).



## 4.2 Consolidating feedback

During the consolidation step, the topics underwent a rigorous iterative review based on a semistructured decision-making process. Two independent members of the WHO secretariat reviewed each proposed research topic addition or removal and considered whether the proposed topic was within the scope of the agenda; whether multiple experts suggested the removal of the topic and their justification; whether the topic was already covered by another topic included in the agenda and the degree of overlap; whether the topic could be considered a subtopic; whether the topic could be merged with another topic in the agenda or could be considered sufficiently unique to stand alone; whether the topic was sufficiently balanced between broadness and granularity; and whether the topic could be reformulated into a PICO/PECO format. Based on this, the proposal was either rejected or accepted or the topic was merged with or made a subtopic of an existing topic. Reviewers had to provide rationale for their decisions, and any disagreements were discussed by the secretariat and a final decision was made jointly. Further, all Expert Group comments and feedback were considered, whereby any relevant inputs were incorporated in the rephrasing of the research topics. Subject area experts in the WHO Steering Group were consulted to provide inputs on the acceptance or removal of each newly proposed research topic, as well as suggest additional topics. This exercise resulted in a list of 175 consolidated research topics (110 from the original scoping review and 65 new topics).


**Above:** A biosafety cabinet in a clinical laboratory in Khartoum, Sudan.

# 5. Prioritizing the research topics

## 5.1 Expert group prioritization survey

In the prioritization survey, 328 experts were invited to score the 175 research topics. For each research topic, experts were asked to answer "Yes", "No", or "Don't know" on whether they thought that a specific research topic fulfilled each of five scoring criteria: fills critical knowledge gaps, answerability and feasibility by 2030, potential for translation into policy, impact to mitigate AMR and promoting health equity (Box A1.2). The scoring criteria were adapted from several other initiatives *(9–13)* with input from the Strategic and Technical Advisory Group for Antimicrobial Resistance *(14)*. Experts specified whether they applied primarily a high-income, a low- and-middle-income or an all-income-levels perspective and whether they considered an adult, children or whole-population perspective in their overall scoring of the research topics. Of the invited experts, 234 (71%) completed the prioritization survey, of whom 129 had also participated in the research topic review survey. Fifty-five (23%) experts applied a high-income perspective when evaluating the research topics, 93 (40%) applied a low- and middle-income perspective and 86 (37%) considered all income settings. Seventy-eight (33%) experts focused on adults only, 38 (16%) on children only and 118 (50%) considered all age groups in their evaluation.

## 5.2 Analysis of survey results and priority-setting process

For each combination of criterion and research topic, 1 point was assigned for "Yes" and 0 points for "No". The sum of scores was divided by the total number of experts voting on that combination ("Don't know" and blank responses were excluded from the analysis) to produce an "intermediate score". A research priority score was calculated for each topic by weighting and then summing the intermediate scores for each criterion. The weight distribution was as follows: 10% for "feasibility" and "health equity" and 27% for "critical gaps", "impact" and "policy translation" *(4)*. The median number of experts scoring each topic was 140 using the five criteria. Overall, 130 research topics (74% of the total) had a research priority score of 0.80 or more, and the median research priority score was 0.85, with a range between 0.62 and 0.95.

The research topics were ranked in descending order of the research priority score, and the topics ranked in the upper 20th percentile were used to populate two separate lists: one representing the scores of all experts and one representing the scores of experts who applied a low- and middle-income country perspective in the prioritization survey. The two lists were merged, and deduplication resulted in a consolidated list of 40 research priorities. This approach was used to enhance the agenda's focus on low- and middle-income countries.

# References

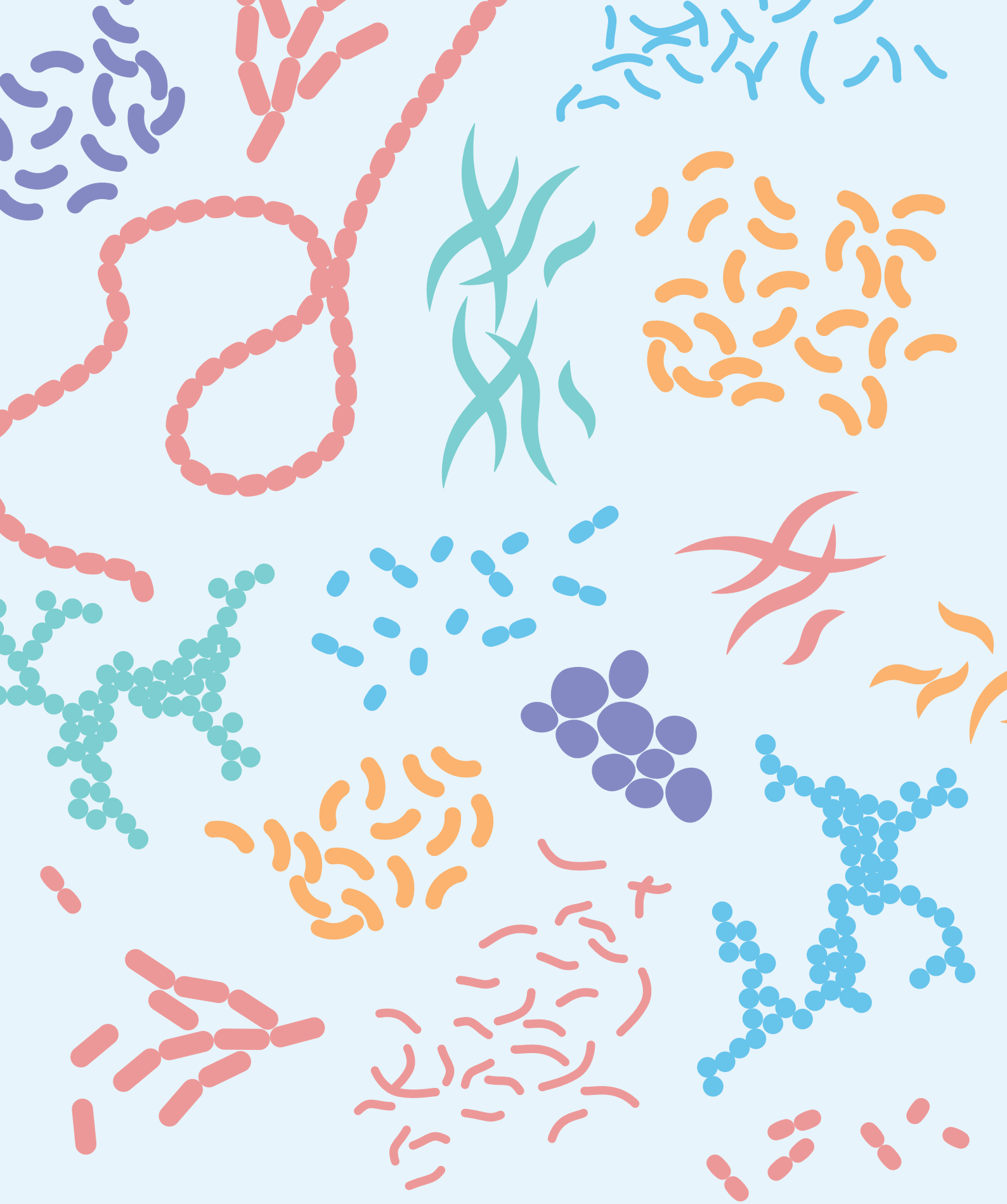

1. A systematic approach for undertaking a research priority-setting exercise: guidance for WHO staff. Geneva: World Health Organization; 2020 (https://iris.who.int/handle/10665/334408, accessed 12 August 2024).
2. Rudan I, Gibson JL, Ameratunga S, El Arifeen S, Bhutta ZA, Black M et al. Setting priorities in global child health research investments: guidelines for implementation of CHNRI method. Croat Med J. 2008;49:720–33. doi: 10.3325/cmj.2008.49.720.
3. Rudan I. Setting health research priorities using the CHNRI method. IV. Key conceptual advances. J Glob Health. 2016;6:010501. doi: 10.7189/jogh.06.010501.
4. Bertagnolio S, Dobreva Z, Centner CM, Olaru ID, Donà D, Burzo S et al. WHO global research priorities for antimicrobial resistance in human health. Lancet Microbe. 2024:100902. doi: 10.1016/s2666-5247(24)00134-4.
5. Hamers RL, Cassini A, Asadinia KS, Bertagnolio S. Developing a priority global research agenda for antimicrobial resistance in the human health sector: protocol for a scoping review. BMJ Open. 2022;12:e060553. doi: 10.1136/bmjopen-2021-060553.
6. Hamers RL, Dobreva Z, Cassini A, Tamara A, Lazarus G, Asadinia KS et al. Global knowledge gaps on antimicrobial resistance in the human health sector: a scoping review. Int J Infect Dis. 2023;134:142–9. doi: 10.1016/j.ijid.2023.06.004.
7. People-centred approach to addressing antimicrobial resistance in human health: WHO core package of interventions to support national action plans. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/373458, accessed 12 August 2024).
8. Global antimicrobial resistance (AMR) research agenda in human health: a call for expert contributions. Geneva: World Health Organization; 2022 (https://www.who.int/news-room/articles-detail/global-antimicrobial-resistance-research-agenda-in-human-health-a-call-for-expert-contributions, accessed 12 August 2024).
9. WHO fungal priority pathogens list to guide research, development and public health action. Geneva: World Health Organization; 2022 (https://apps.who.int/iris/handle/10665/363682, accessed 12 August 2024).
10. Armstrong A, Nagata JM, Vicari M, Irvine C, Cluver L, Sohn AH et al. A global research agenda for adolescents living with HIV. J Acquir Immune Defic Syndr. 2018;78(Suppl. 1):S16–21. doi: 10.1097/QAI.0000000000001744.
11. Yoshida S, Rudan I, Lawn JE, Wall S, Souza JP, Martines J et al. Newborn health research priorities beyond 2015. Lancet. 2014;384:e27–9. doi: 10.1016/S0140-6736(14)60263-4.
12. COVID-19 Research Prioritization Group on MNCAH. Global research priorities on COVID-19 for maternal, newborn, child and adolescent health. J Glob Health. 2021;11:04071. doi: 10.7189/jogh.11.04071.
13. Polasek O, Wazny K, Adeloye D, Song P, Chan KY, Bojude DA et al. Research priorities to reduce the impact of COVID-19 in low- and middle-income countries. J Glob Health. 2022;12:09003. doi: 10.7189/jogh.12.09003.
14. WHO Strategic and Technical Advisory Group for Antimicrobial Resistance (STAG-AMR): report of the second meeting, 14–16 June 2022. Geneva: World Health Organization; 2022 (https://iris.who.int/handle/10665/366191, accessed 12 August 2024).

# Annex 2. Indicators for monitoring and evaluating the research agenda

**Table A2.1.** Overview of indicators for monitoring and evaluating the research agenda

| Results statement | Indicator | Indicator definition | Means of verification | | Comments |
|---|---|---|---|---|---|
| | | | Data source | Frequency | |
| Outcome: Increased awareness of the research agenda priorities among researchers, funders and implementers | | | | | |
| Research agenda references in WHO publications | Number of WHO references to the research agenda | Count of WHO documents that explicitly mention the research agenda or the research agenda publications. WHO documents include guidance, reports and press releases | Number of WHO documents that explicitly reference the research agenda identified from the WHO website | Once near 2030 | |
| Research agenda references in non-WHO publications | Number of research agenda references in non-WHO publications | Count of journal publications and other non-WHO documents that explicitly reference the research agenda via comprehensive literature search by key terms of the titles of the publications directly associated with the research agenda | References in the academic and grey literature of the research agenda: publications in the academic and grey literature that explicitly reference the research agenda | Once near 2030 | |
| Access to the research agenda document and publication | Number of clicks and downloads of the research agenda documents and publications | Record and analyse the number of clicks and downloads for the research agenda and associated documents and publications | Research agenda web page, journal web page for the associated publications | Once near 2030 | |

| Results statement | Indicator | Indicator definition | Means of verification | | Comments |
|---|---|---|---|---|---|
| | | | Data source | Frequency | |
| Outcome: Increased uptake of the priorities leading to new evidence and increased number of novel diagnostics and medicines | | | | | |
| Increased funding for the top research priorities | Amount of funding for the research priorities | This indicator will identify the funding amount and time trends for the research priorities | Number of funded studies and amount of funding addressing the top research priorities. Studies will be identified by searching the websites of major funders. Data obtained from the Global Observatory on Health and Development, other data repositories for research funding, funders' websites | Multiple timepoints until 2030 | Depending on the availability of data, can be done according to area, domain, discipline, topic, country or region etc. |
| Generation of evidence to fill research gaps and support the development and implementation of policies | Percentage of experts who consider that the research priorities have been sufficiently addressed | This indicator will determine whether the experts consider that enough evidence has been generated to fill the research gaps and whether the evidence generated was also translated into policy and implemented | Brief survey with experts, in depth interviews with a small number of experts | Once near 2030 | Baseline: none of the research priorities have been adequately addressed to date |
| Advances in the development of diagnostic tests, therapeutics and vaccines | Number of new diagnostics, medicines and vaccines developed to address the research priorities | Desk review of diagnostic, therapeutic and immunization pipelines to determine the landscape of tests, therapeutics, and vaccines available or under development that relate to the priorities identified by the research agenda | Pipeline reports, websites of organizations supporting diagnostic test development, test developers; and pipeline reports for therapeutics and vaccines | Once near 2030 | Baseline: products developed after 2023 will be considered |



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