Comprehensive Review of the WHO Global Action Plan on Antimicrobial Resistance

Volume 1: Report

September 2021

World Health Organization

WHO Evaluation Office

Acknowledgements

The Evaluation Office was supported in this review by an independent consultant, Dr Roger Drew, and his contribution is much appreciated. The review team would like to thank the Antimicrobial Resistance Division and other WHO stakeholders at the three levels of the Organization for sharing their valuable insights and perspectives to inform the review. In addition, the important contributions of current and former members of the Strategic and Technical Advisory Group for Antimicrobial Resistance, members of the Interagency Coordination Group on Antimicrobial Resistance, and representatives of United Nations agencies, academia, civil society organizations and other partners are also acknowledged.

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This report is supported by a separate volume of six annexes the content of which is as follows:

Annexes (separate volume)

List of Acronyms

ABR	Antibiotic Resistance
ACORN	A Clinically-Orientated AMR Surveillance Network
ADG	Assistant Director-General
AFR	African Region (WHO)
AGISAR	Advisory Group on Integrated Surveillance of Antimicrobial Resistance
AIDS	Acquired Immunodeficiency Syndrome
AMC	Antimicrobial Consumption
AMR	Antimicrobial Resistance
AMR	Region of the Americas (WHO/PAHO)
AMU	Antimicrobial Use
ARC	Antimicrobial Research Collaborative
AST	Antimicrobial Susceptibility Testing
ATCC	American Type Culture Collection
ATLASS	Antimicrobial Resistance Surveillance System
AWaRe	Access, Watch, Reserve
BCA	Biennial Collaborative Agreement
CAESAR	Central Asian and European Surveillance of Antimicrobial Resistance
CARB-X	The Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator
CC	Collaborating Centre
CCS	Country Cooperation Strategy
CDC	Centers for Disease Control and Prevention
CO	Country Office
COVID 19	Coronavirus Disease 2019
CPA	Commonwealth Pharmacist Association
CwPAMS	Commonwealth Partnerships for Antimicrobial Stewardship Programme
DNDi	Drugs for Neglected Diseases Initiative
EAR	Emerging Antimicrobial Resistance Reporting
EARS-Net	European Antimicrobial Resistance Surveillance Network
ECDC	European Centre for Disease Control and Prevention
EGASP	Enhanced Gonococcal Antimicrobial Surveillance Programme
EMR	Eastern Mediterranean Region (WHO)
EQA	External Quality Assessment
ESBL	Extended-Spectrum β-Lactamase
ESBL-EC	Extended-Spectrum β-Lactamase producing E Coli
EU	European Union
EUR	European Region (WHO)
EURO	Regional Office for Europe (WHO)
FAO	Food and Agriculture Organization of the United Nations
FAOLEX	Database of the Food and Agriculture Organization of the United Nations
FAOSTAT	Food and Agriculture Organization Corporate Statistical Database
GAP	Global Action Plan
GARDP	Global Antibiotic and Research Partnership
GCP	Global Coordination and Partnership
GDP	Gross Domestic Product
GLAAS	Global Analysis and Assessment of Sanitation and Drinking-Water
GLASS	Global Antimicrobial Resistance and Use Surveillance System
GPW	General Programme of Work (WHO)
GRAM	Global Research on Antimicrobial Resistance Project
GS	Graduated Scoring

HCAI	Health Care-Associated Infection
HIC	High-Income Countries
HIV	Human Immunodeficiency Virus
HQ	Headquarters
IACG	Inter-Agency Coordination Group
IDEA	Innovation + Design Enabling Access Initiative
ID-IRI	Infectious Diseases International Research Initiative
IHME	International Health Metrics and Evaluation
IHR	International Health Regulations
IPC	Infection Prevention and Control
JEE	Joint External Evaluation
JPIAMR	Joint Programming Initiative on Antimicrobial Research
KII	Key Informant Interview
LIC	Low-Income Countries
LMIC	Lower-Middle-Income Countries
M&E	Monitoring and Evaluation
MDR-TB	Multidrug-Resistant Tuberculosis
MERS	Middle East Respiratory Syndrome
MF	Monitoring Framework
MPTF	Multi-Partner Trust Fund
NAP	National Action Plan
NCC	National Coordination Centre
NGO	Non-Governmental Organization
NHS	National Health Service (UK)
NRL	National Reference Laboratory
OECD-DAC	Organisation for Economic Cooperation and Development – Development Assistance Committee
OIE	World Organisation for Animal Health
PAHO	Pan American Health Organization
PHCC	Primary Healthcare Corporation (Qatar)
PLISA	Health Information Platform for the Americas
PVS	Performance of Veterinary Services
R&D	Research and Development
ReLAVRA	Latin American Network for Antimicrobial Resistance Surveillance
RO	Regional Office
SARS	Severe Acute Respiratory Syndromes
SDG	Sustainable Development Goal
SEAR	South-East Asian Region (WHO)
SORT IT	Structured Operational Research and Training Initiative
SPC	Surveillance, Prevention and Control
STAG	Strategic and Technical Advisory Group
STAR-IDAZ	International Research Consortium on Animal Health
TB	Tuberculosis
TDR	The Special Programme for Research and Training in Tropical Diseases
THET	Tropical Health and Education Trust
TISSA	Tripartite Integrated Surveillance System on Antimicrobial Resistance/Antimicrobial Use
TrACSS	Tripartite AMR Country Self-Assessment Survey
UHC	Universal Health Coverage
UK	United Kingdom
UMIC	Upper-Middle-Income Countries
UN	United Nations
UNDP	United Nations Development Programme

UNEP	United Nations Environment Programme
UNICEF	United Nations Children's Fund
URL	Uniform Resource Locator
USAID	United States Agency for International Development
WASH	Water, Sanitation and Hygiene
WHA	World Health Assembly
WHO	World Health Organization
WPR	Western Pacific Region (WHO)
WPRACSS	Western Pacific Regional Antimicrobial Consumption Surveillance System
WR	WHO Representative

Executive Summary

Background

S1 In 2015, the Sixty-eighth World Health Assembly (WHA) endorsed the Global Action Plan (GAP) on Antimicrobial Resistance (AMR). The plan was further endorsed by the World Assembly of the World Organisation for Animal Health (OIE) Delegates in May 2015 and by the Food and Agriculture Organization of the United Nations (FAO) Conference in June 2015. The GAP AMR provides a framework of actions across five objectives for three stakeholder groups (Member States, the Secretariat and national/international partners) to take over the next five to ten years, and for countries to develop national action plans (NAPs).

S2 The mandate to conduct a comprehensive review of the Global Action Plan on Antimicrobial Resistance derives from paragraph 4.1 of resolution WHA72.5 of the Seventy-second World Health Assembly in 2019. This in turn is captured in the Evaluation Office's 2020-21 biennial evaluation workplan approved by the Executive Board.

S3 The overall purpose of this comprehensive review was to enhance current work on AMR. Based on the five primary objectives of the GAP AMR (see Box S1), the review documents successes, challenges and best practices, and provides lessons learned and recommendations for use by WHO and other GAP AMR stakeholders to guide future implementation of the GAP AMR and to inform decision-making on AMR.

Box S1: GAP AMR objectives
Objective 1: Improve awareness and understanding of antimicrobial resistance through effective communication, education and training
Objective 2: Strengthen the knowledge and evidence base through surveillance and research
Objective 3: Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures
Objective 4: Optimize the use of antimicrobial medicines in human and animal health
Objective 5: Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions

S4 The review has four objectives, namely:

- To document successes, challenges and gaps in the implementation of the GAP AMR since its adoption in 2015;
- To review how efficiently AMR activities are being implemented across the three levels of WHO: Headquarters (HQ), Regional Offices (ROs) and Country Offices (COs);
- To review how well AMR activities are coordinated, including with relevant United Nations (UN) agencies and other relevant stakeholders;
- To provide lessons learned and recommendations to improve the implementation of the GAP AMR at all three levels of WHO.

S5 As a comprehensive review, its scope was set by the scope of the GAP AMR. The GAP has a section on scope which explains that it covers antimicrobial not just antibiotic resistance, that support for tackling antimicrobial resistance was multisectoral and that the GAP provides the framework for national AMR plans, which outline actions for three groups of stakeholders across the five objectives of the GAP. More specifically, in terms of actors, the review considered all stakeholders identified in the GAP AMR through a WHO lens. In practice this meant that the review considered:

- Actions taken by WHO Member States to implement the GAP AMR, for example through developing and implementing their own National AMR Action Plans.
- Actions taken by the three levels of the WHO Secretariat to implement the GAP AMR.
- Actions taken by national and international partners to implement the GAP AMR. In line with the WHO lens taken for this review, the focus here was on coordination by WHO with national and international partners and this is illustrated in Figure S1 with particular focus on FAO and OIE. The green areas are those on which the review focused, i.e. the work of WHO and its interactions with other national and international partners including FAO and OIE.

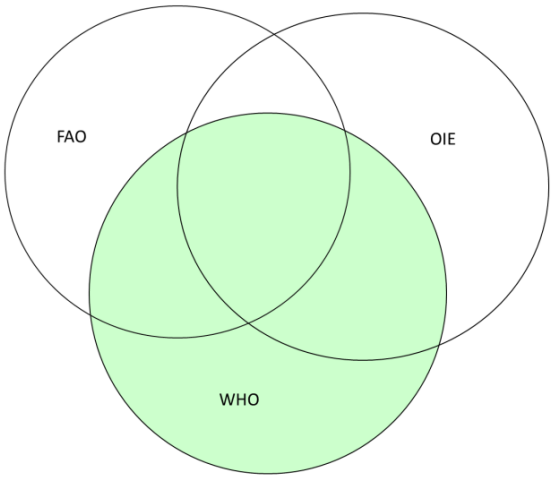


Figure S1: Scope of the comprehensive review

S6 The review focused mainly on what has been achieved through the GAP AMR and how this was achieved. As a result, the review did not have a major focus on the outcomes and impact of the GAP AMR. Based on its mandate, the review considered how efficiently AMR activities are being implemented across WHO. The time frame considered within the scope of the review was from the endorsement of the GAP AMR by the World Health Assembly in May 2015 until completion of the review. The review aimed to be forward-looking and sought to provide useful and actionable recommendations to facilitate future policy and decision-making.

S7 Four main review questions were identified based on three of the objectives of the review.

- Review Objective 1: To document successes, challenges and gaps in the implementation of the GAP AMR since its adoption in 2015;
  - What are the successes and challenges in the implementation of the five primary objectives of GAP AMR since 2015?
- Review Objective 2: To review how efficiently AMR activities are being implemented across the three levels of WHO: HQ, ROs and COs;
  - What have been the main internal and external factors influencing WHO's ability to implement the GAP AMR in the most efficient manner?
  - To what extent have AMR activities been implemented efficiently across the three levels of WHO?
- Review Objective 3: To review how well AMR activities are coordinated, including with relevant United Nations agencies and other relevant stakeholders;
  - To what extent have AMR activities been well coordinated with other United Nations agencies and relevant stakeholders?

Methodology

S8 The overall process and methodological approach followed the principles set forth in the WHO evaluation practice handbook and the United Nations Evaluation Group Norms and Standards for Evaluation and Ethical Guidelines for Evaluation. The initial inception phase of the review focused on refining the review's design and was concluded by April 2021. Data collection was divided into two phases. The first focused on identifying and reviewing existing secondary data which involved reviewing more than 600 documents. This review was structured around the GAP AMR's monitoring and evaluation (M&E) framework focusing on data reported by Member States over four rounds of the Tripartite AMR Country Self-Assessment Survey (TrACSS) and other data sources including the Global Antimicrobial Resistance and Use Surveillance System (GLASS), progress reports, Country Cooperation Strategies (CCSs), Biennial Cooperative Agreements (BCAs) and Joint External

Evaluations (JEEs). The second data collection phase collected additional primary data through more than 100 semi-structured interviews with key informants identified from a range of stakeholder groups. All WHO Regional Offices were interviewed and all WHO Country Offices were either interviewed or given opportunity to respond in writing to a small number of review questions. All interviews were conducted remotely. Given that WHO Member States already report annually to WHO on progress on AMR, and in keeping with a principle of reducing reporting burden on Member States and in view of the current pandemic, the review relied on available secondary data from Member States rather than requesting completion of a further survey.

Key Findings

S9 This section considers findings for the GAP AMR overall before considering findings for each of its objectives and for a number of crosscutting issues.

GAP AMR Overall

S10 While recognizing the importance of understanding progress towards the GAP AMR's expected outcomes, objectives and goals, the review notes that this is currently difficult because there is a lack of a shared understanding as to what the expected outcomes of the GAP AMR are and what would constitute success. Although the GAP AMR's M&E framework seeks to address this by identifying a number of outcome indicators, progress toward these is not yet being systematically tracked and reported by the WHO Secretariat. It may be difficult to do this, not least because of the number of outcome indicators identified. While the framework identifies 18 outcome indicators, the review counted these as 34 once compound indicators were separated out. Of these, the review found that three (9%) were incompletely defined, more than half (19, 55%) appeared to lack any data and a further seven (21%) had insufficient data for the purposes of outcome monitoring.

S11 The review was able to assess implementation progress across four of the five GAP AMR objectives using TrACSS data and analyzing this using implementation scores. The results of this analysis are shown in Table S1. The biggest improvements are seen in relation to multi-sector and One Health working arrangements (+18) and national action plans (+20) with little change seen in infection prevention and control in human health (+2) and optimizing antimicrobial use in animal health (+1).

Table S1: Implementation scores across GAP AMR indicators for Member States reporting through TrACSS (n=187)
Colour coding for scores – amber 0-40; yellow 41-60; light green 61-80; dark green >80 for change – amber 0-10; yellow 11-20; light green >21

	Indicator	Baseline	Performance	Change
Core	Multi-sector and One Health working arrangements	27	45	+18
	National action plan	38	58	+20
Objective 1	Awareness and understanding of AMR risks and response (human health)	43	55	+12
	Awareness and understanding of AMR risks and response (animal health, plant health, food production, food safety and environment)	29	31	+3
	Training and professional education on AMR in the human health sector	43	48	+5
	Training and professional education on AMR in the veterinary sector	32	39	+7
	Training and professional education on AMR in farming sector, food production, food safety and the environment	17	19	+2
	Progress with strengthening veterinary services	34	41	+7
Objective 2	National monitoring system for consumption and rational use of antimicrobials in human health	34	41	+7
	National monitoring system for antimicrobials intended to be used in animals	29	39	+10
	National monitoring system for antimicrobial use in plant production	13	22	+9
	National surveillance system for AMR in humans	44	53	+9
	National surveillance system for AMR in animals	33	43	+11
	National surveillance system for AMR in food (animal and plant origin)	37	40	+3
Objective 3	Infection prevention control in human health care	47	49	+2
	Good health, management and hygiene practices to reduce the use of antimicrobials and minimize development and transmission of AMR in animal production	29	35	+6
	Good management and hygiene practices to reduce the development and transmission of AMR in food processing	32	36	+5

Objective 4	Optimizing antimicrobial use in human health	34	45	+11
	Optimizing antimicrobial use in animal health (terrestrial and aquatic)	37	37	+1
	Laws or regulations on prescription and sale of antimicrobials for human use	77	86	+9
	Laws or regulations on prescription and sale of antimicrobials for animal use	61	65	+4
	Laws or regulations that prohibit the use of antibiotics for growth promotion	41	50	+9

S12 Figure S2 shows the mean overall implementation score across the indicator set. Overall, the mean implementation score was 44.3% as compared to 36.7% at baseline. In general, the highest mean implementation score is seen in WHO's European Region (EUR) and the lowest in WHO's African Region (AFR). There is marked variation in mean implementation scores between low-income countries (LIC) (24.8) and high-income countries (HIC) (60.9) and this difference is statistically significant (p<.001). Figure S3 shows the mean change in overall implementation score from baseline to performance data. The highest change in implementation score occurred in WHO's South East Asia Region (SEAR). There was no clear pattern by country income group (p=.86).

S13 Figure S4 shows the improvement in mean implementation score which has occurred between baseline and performance data. This shows that the increase is highest for core indicators, i.e. the main improvement that has occurred is the introduction of multisectoral coordination mechanisms and national action plans, and lowest for objective 3 relating to infection prevention and control.

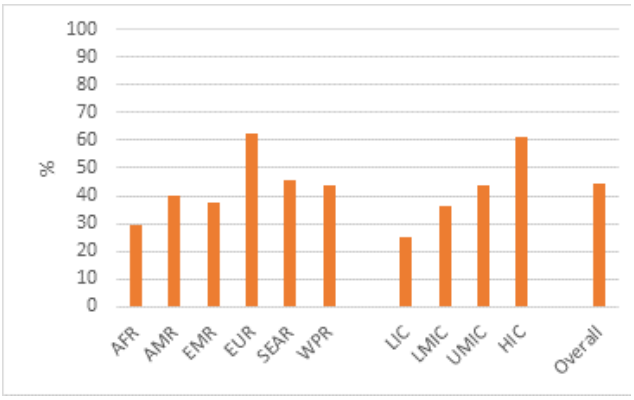


Figure S2: Mean overall implementation score by WHO region, country income group and overall

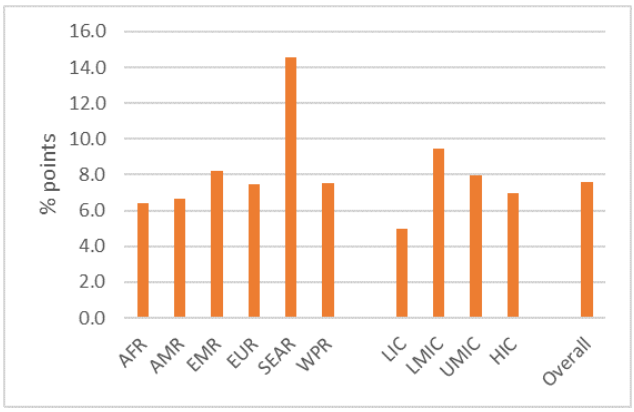


Figure S3: Mean change in overall implementation score from baseline to performance data by WHO region, country income group and overall

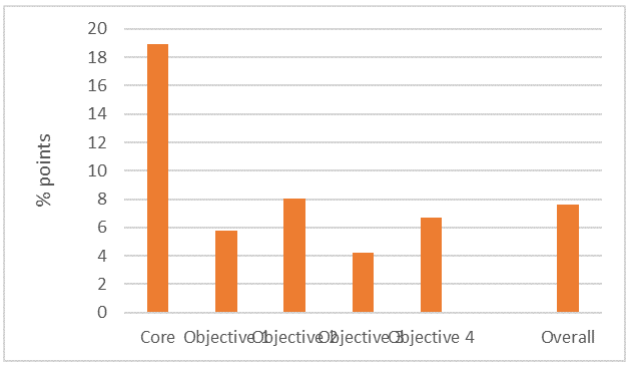


Figure S4: Change in mean implementation score between baseline and performance data across core indicators and indicators for four objectives of GAP AMR

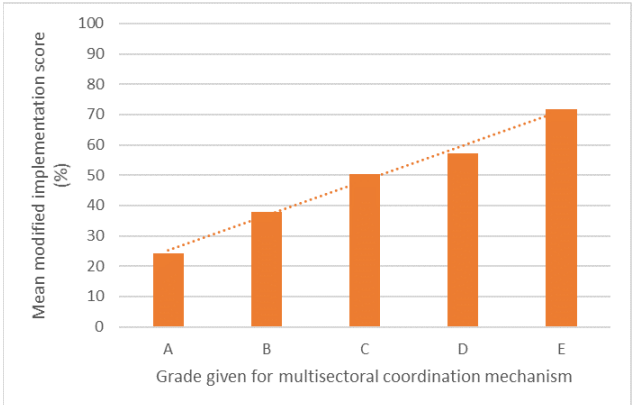


Figure S5: Is there an association between the grade a country gives for its multisectoral coordination mechanism and mean modified implementation score?

S14 Some respondents were concerned that the main progress made was in terms of plans and coordination mechanisms leading to questions as to what benefits this had for people. The review has shown that performance and improvement on these has a statistical association with performance and improvement in overall implementation scores. Figure S5 illustrates this for having a multisectoral coordination mechanism in place and overall modified implementation score. This association is statistically significant (p<.001). Similar

associations are seen for changes in scores and when national action plans are considered in place of multisectoral coordination mechanisms.

S15 However, there was a great deal of variation between countries with many having higher implementation scores than might be expected, for example, based on country income level. The review has sought to identify, with WHO Country Offices, possible explanations for these variations and these are illustrated in Figure S6. First, because TrACSS data is self-reported, there will be situations where higher scores do not reflect higher levels of performance but rather reflect more positive reporting. Possible ways to verify TrACSS data might include:

- Through other data sources, such as joint external evaluations (JEE). The review conducted statistical analysis across all countries in which a JEE could be identified. There was a statistically significant positive correlation (p<.001) between both (i) the overall score on JEE and (ii) the JEE score on AMR and the performance score on GAP AMR based on TrACSS data.
- By understanding the processes used to generate TrACSS reports in a particular country. Where those processes are inclusive and consultative, the findings are more likely to be robust.
- Through the views of other stakeholders, such as civil society and development partners.

S16 The central square box of Figure S6 shows areas where countries have made particular progress (national action plans; coordination mechanisms; surveillance) but also shows that there may be other areas where opportunities may have been missed and less progress made, e.g. on infection prevention and control (IPC). Several WHO Country Offices were able to identify specific pieces of data which had served as a type of "*eye opener*" in terms of how serious AMR was as a problem in a particular country. Linked to this was the willingness to recognize where there were challenges and difficulties, and then seek to address them. Political support was recognized as important as was the role of AMR champions. There was recognition that many countries had needed external financial and technical support for the progress they had made, and that this had come from a range of sources including WHO. In terms of WHO Country Offices being able to provide support, respondents recognised the need to have a staff member for whom AMR was their job (or part of it) and who received support from the WHO Representative (WR) and the Regional Office. Finally, there was recognition of the importance of good coordination between different actors including government ministries and development partners. Where they existed, pre-existing One Health structures had been helpful. Despite apparent progress that these countries may have made, there were concerns that some of the progress might be fragile and could be undermined if there were changes in circumstance.

S17 The review found a statistically significant positive association between a country having a CCS or BCA that mentioned AMR and a country's performance score (p<.001) or improvement in performance score (p=.03). This does not establish causality. One possible explanation is that WHO technical support, provided on the basis of the CCS, is contributing to countries' performance on GAP AMR. It is clear that WHO has provided considerable technical support to countries on AMR and this report presents qualitative evidence of this throughout. However, there could be other explanations. There could be common causal factors, for example, country income level or another unrecognized factor, such as government political commitment to AMR which might mean that the government would wish for AMR to be included in the CCS or BCA. Also, it is possible that there could be causal factors other than WHO technical assistance, for example, if other development partners were more likely to provide financial and technical assistance to a country on AMR if both the national government and WHO recognized AMR as a priority in the country. These possible causal mechanisms are illustrated in Figure S7.

S18 On balance, it seems likely that causality is multifactorial and that the exact balance of causality probably varies from country to country. However, this finding along with the qualitative findings of this review suggest that WHO technical support provided to countries on the basis of an agreed CCS or BCA may contribute to the country's performance on GAP AMR.

Figure S6: Factors that may enable a country to improve its performance on AMR regardless of income level

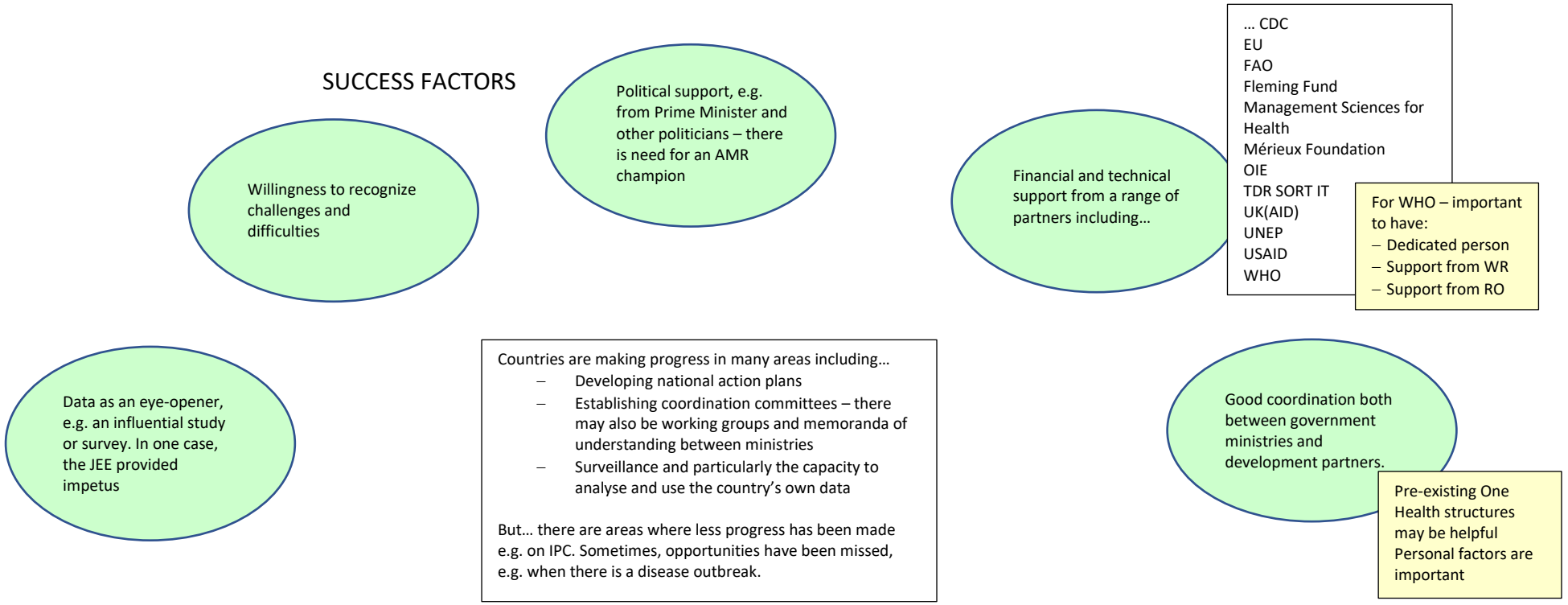
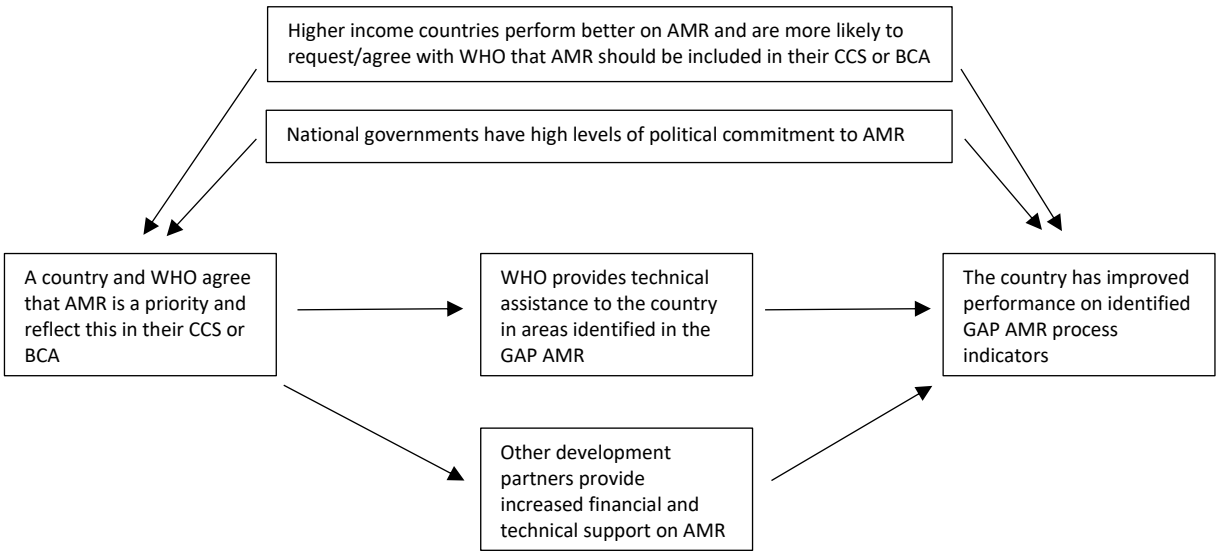


Figure S7: Possible causal mechanisms explaining the association between whether a CCS or BCA mentions AMR and a country's performance on GAP AMR



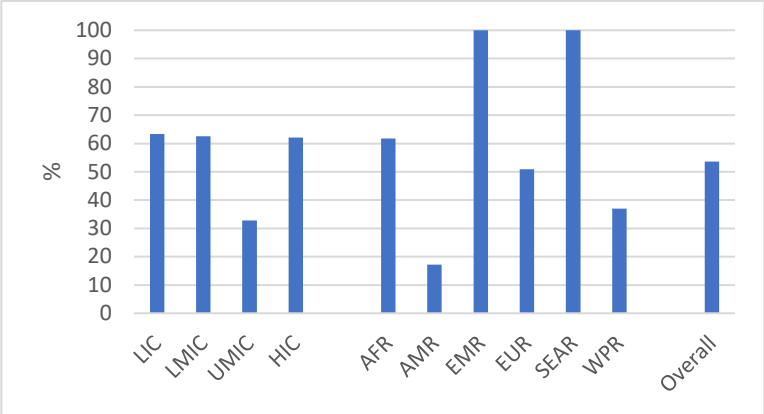
Objective 1: Improve awareness and understanding of antimicrobial resistance through effective communication, education and training

S19 There is a lack of clarity in this objective as to precisely what awareness and understanding needs to be improved, by whom and for what purpose. In the absence of this clarity, it is difficult to assess the progress or added values of activities under this objective, such as the annual celebration of World Antimicrobial Awareness Week. The outcome indicator for this objective is not fully defined and "*awareness of key groups*" currently constitutes little more than an indicator title. There have been efforts to collect outcome data but, to date, these have been sporadic and fragmented. A recent study which looked at World Antibiotic Awareness Weeks from 2015 to 2020 using Google Trends Analysis suggested that these weeks "*did little to improve the public awareness of AMR in… selected countries…*". TrACSS has collected data on key activities under this objective, such as awareness campaigns and training and professional education on AMR in different sectors and this provides useful insights. The WHO Secretariat has contributed to this objective by supporting the implementation of AMR-related events globally, transforming the world awareness week from focusing solely on antibiotics to a broader focus on all antimicrobials, developing guidance and toolkits for countries, and consistently raising the importance of addressing AMR in high-level political settings.

Objective 2: Strengthen the knowledge and evidence base through surveillance and research

S20 Although this objective concerns both surveillance and research, there has been much more emphasis and progress on the former than the latter. Clearly, one of the major initiatives under this objective has been the development and expansion by the WHO Secretariat of the Global Antimicrobial Resistance and Use Surveillance System (GLASS). GLASS has expanded considerably over time, both in terms of the number of countries enrolled and the range of topics (modules) covered. As of April 2021, the WHO Secretariat reported that 109 WHO Member States were enrolled in either the GLASS module for AMR or the newer module for Antimicrobial Consumption (AMC). Based on this, Figure S8 shows the percentage of WHO Member States enrolled in GLASS AMR overall and by WHO region and country income group, as of April 2021. Overall, more than half (104, 54%) of WHO Member States are enrolled in GLASS. This percentage is highest in WHO's South East Asia Region (SEAR) (11 of 11, 100%) and WHO's Eastern Mediterranean Region (EMR) (21 of 21, 100%) but lowest in the Region of the Americas (AMR) (6 of 35, 17%). There is no clear pattern by country income group although enrolment rates are lowest among upper-middle-income countries (UMIC) (19 of 58, 33%) (see Figure S8).

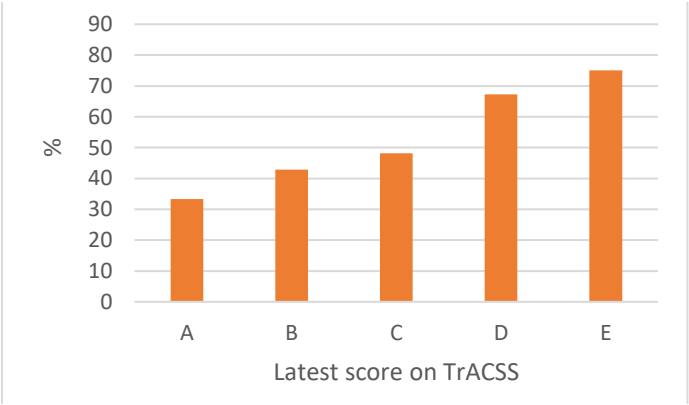
Figure S8: Percentage of WHO Member States (n=194) enrolled in GLASS AMR by country income group, WHO region and overall (as of April 2021)



S21 Countries also report through TrACSS a self-assessment of their national surveillance systems, not only for human health but also in animals and plant production. Overall, there are slightly more Member States that report having a national surveillance system for AMR in humans to TrACSS than are enrolled in GLASS AMR (126 as compared to 104). But, this pattern is reversed in low-income and lower-middle-income countries where more countries are enrolled in GLASS than report having national surveillance systems for AMR in humans to TrACSS. Across the regions, more Member States are enrolled in GLASS than report having national surveillance systems for AMR in humans to TrACSS in AFR, EMR and SEAR. But, this pattern is reversed in EUR, WPR and particularly in AMR.

S22 Figure S9 shows a positive correlation between the percentage of WHO Member States that reported a particular level (A-E) for their AMR surveillance system in humans in their last TrACSS report that are currently enrolled in GLASS. While only one third of Member States (4 of 12, 33%) that reported that they had no capacity for generating data and reporting on antibiotic resistance (level A) are enrolled in GLASS, this figure is three quarters for those Member States (15 of 20, 75%) that reported that the national AMR surveillance system integrates surveillance of AMR across sectors and generates regular reports covering at least one common indicator (level E). The enrolment of countries in GLASS that report not having a national AMR surveillance system in humans represents a development opportunity but provides a cautionary note on the likely quality of surveillance data reported through GLASS, at least from those countries. Also, the fact that less than two thirds of Member States (76 of 126, 60%), that reported having a national AMR surveillance system for humans (level C or above) in their last TrACSS report, are currently enrolled in GLASS represents a missed opportunity to collect AMR surveillance data through GLASS.

Figure S9: Percentage of WHO Member States (n=187) that reported a particular level of national surveillance system for AMR in humans in their last TrACSS report that are enrolled in GLASS



S23 While GLASS is identified as the data source for a number of indicators identified in the GAP AMR M&E framework, this review finds that GLASS is not currently able to provide representative outcome data. While it is possible that GLASS may be able to provide representative antimicrobial consumption data, issues of highly variable laboratory capacity and different clinical testing practices mean that it is extremely unlikely that any system based on sentinel surveillance could provide representative and comparable antimicrobial resistance data in the foreseeable future. This has been recognized in a recent review of GLASS which produced an outcome statement which reaffirmed the participants' commitment to GLASS but also requested

WHO to "*develop complementary approaches such as surveys to enable all countries to report on SDG indicators in the short and medium term*".

S24 One concern raised by respondents is whether countries are using surveillance data for national decision-making. In 2019/20, surveillance data was reportedly most used nationally in relation to human health (88 of 128, 69%) and least in relation to plant health (20 of 106, 19%) and the environment (12 of 106, 11%). Rates of reported use of surveillance data nationally increased from 2018/19 to 2019/20 for both human and animal health. However, almost half of countries enrolled in GLASS did not report using surveillance data to amend national strategy and/or to inform decision making nationally in 2019/20.

S25 Respondents expressed concern that there had been much less emphasis on research under this objective. Indeed, there was confusion as some consider research to be covered under objective 5 but this is limited to product research and development. Some have described this by saying that *current research in AMR is inequitably focused on new drug development*". While the GAP mandated the WHO Secretariat to "*consult Member States and other multisectoral stakeholders for the development of a global public health research agenda for filling major gaps in knowledge on antimicrobial resistance*", it does not appear that this has yet been done although some work on this is reported to be underway. There were also concerns that while a focus on surveillance may imply the need to strengthen and develop laboratory capacity, this was not explicitly recognized in the GAP nor was the need for adequate laboratory capacity to ensure appropriate clinical management which is a key part of optimizing antimicrobial use.

Objective 3: Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures

S26 The main issue for this objective is that measures for infection prevention and control are much broader than AMR only as they address all aspects of pathogen transmission in community and healthcare settings. This presents an opportunity because initiatives taken to prevent a particular infection may have benefits on preventing or reducing AMR. But, it brings its own challenges. Infection prevention and control may be seen as not being specific to AMR so may receive less emphasis than other objectives of the GAP AMR. There is a risk that infection prevention and control may be seen as everyone's responsibility with it not being "*owned*" by specific diseases or issues, such as AMR. There is also a risk that some of the issues, such as sanitation and hygiene, may be seen as so huge that they risk consuming entire AMR programmes and budgets. According to respondents, many countries address IPC as part of the International Health Regulations (IHR) Preparedness agenda and do not fully associate infection prevention and control with AMR. The breadth and cross-cutting nature of both AMR and IPC are challenging for countries to implement and integrate as they both include a wide variety of workstreams and sectors.

S27 In addition, IPC remains affected by a lack of infrastructure and limited resources, both human and financial, to implement and monitor infection prevention and control measures in some low-income settings. Overall, there is concern about limited progress being made on water and sanitation globally.

S28 One specific area of IPC of particular relevance to AMR is the prevention of healthcare-acquired infections, including following surgery. The GAP AMR M&E framework includes an outcome indicator on the incidence of surgical site infections but this overlooks other important types of healthcare-acquired infections and does not appear to be being actively monitored. Many of the other outcome indicators either lack data or lack clarity as to how data would be used and interpreted. It is difficult to relate the data available through TrACSS to the output indicators as defined in the GAP AMR framework. Nevertheless, analysis carried out by the WHO Secretariat and for this review shows that there was little, if any, progress on IPC from the time the GAP/AMR was adopted to 2019/2020. There have been developments on IPC as a result of the COVID-19 pandemic (see from paragraph S47, p xiv).

S29 The WHO Secretariat has contributed to this objective through coordinating crosscutting work across the WHO Secretariat, by developing normative guidance and educational materials on IPC, conducting global campaigns and establishing an infection prevention and control global unit within the Secretariat. WHO has worked with FAO and OIE to establish linkages between IPC, WASH, AMR and related environmental components.

Objective 4: Optimize the use of antimicrobial medicines in human and animal health

S30 There are concerns that this objective appears to be limited to the use of antimicrobials in human and animal health, overlooking areas such as food, plants and the environment. Although there have been considerable efforts, including by WHO, to guide the prescription of antibiotics and to support national regulatory authorities, respondents noted that the implementation of recommended guidance to optimize the use of antibiotics is challenged by structural barriers, particularly in low- and middle-income countries. Such barriers include weak national regulatory authorities, lack of capacity for accurate diagnosis and lack of available data. In many cases, laws and policies requiring a prescription for antibiotics are in place but they are not enforced. Respondents were concerned that the GAP and the implementation of it frame the issue of optimal use in human health more in terms of excess use of antibiotics rather than difficulties in accessing antibiotics when their use is indicated. There are also concerns about the ongoing use of antibiotics, particularly those of critical importance for human health, in animal growth promotion and crop protection.

S31 There has been ongoing work to develop an AMR stewardship framework. Based on Inter-Agency Coordination Group recommendations, the Tripartite organizations published a review of International Instruments on the Use of Antimicrobials across the Human, Animal and Plant Sectors in 2020 and this process was reported to WHO's Executive Board in December 2020. The WHO Secretariat report that, following consultations with Member States, there are no longer plans to negotiate a specific AMR stewardship framework but it is expected that AMR would be reflected in the proposed pandemic treaty.

S32 Some of the outcome indicators in the M&E framework for this objective are being seen as potentially useful outcome indicators for the GAP AMR as a whole, e.g. the proportion of total human consumption of antibiotics for systemic use that are Access antibiotics. However, while there is potential for collecting good quality, comparable data on this, data availability currently remains limited. TrACSS data for this objective shows that many countries have laws or policies in place relating to human or animal use of antimicrobials but this may not be translated into optimal antimicrobial use in those sectors.

S33 The WHO Secretariat has contributed to this objective by supporting the rational use of antimicrobials through the development of key normative products to help ensure the responsible use of safe antimicrobials, including the Essential Medicines List, the Access, Watch, Reserve (AWaRe) Classification Database of Antibiotics for evaluation and monitoring of use, the Priority Pathogens List , List of Critically Important Antimicrobials for Human Medicine, guidance on controlling effluents from manufacturing processes, guidance on integrated antimicrobial stewardship activities and a practical toolkit for antimicrobial stewardship programmes in health-care facilities in low- and middle-income countries.

Objective 5: Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions

S34 While this objective has two distinct elements, much of the focus (e.g. in indicators and progress reports) has been on the second element. This is highly problematic as the initial enthusiasm for AMR both globally and nationally, as evidenced by the development of national action plans, has often not translated into provision of resources needed to implement planned actions. One problem with the GAP AMR is that there is little, if anything, purposive in the plan to go beyond raised awareness of AMR to sustained political commitment with allocation and/or raising of funding although the need for this has been recognized in the recently-published priorities of the Global Leaders Group. There is also little clarity about what funding is needed globally or in

different national settings or how this might be calculated. There is little guidance about what to prioritize when funding is limited. There is however, a high degree of consensus that funds raised so far, for example, for the Multi-Partner Trust Fund (MPTF) fall far short of what is needed. The lack of available data on AMR disease burden and details of how this might be calculated are obstacles to developing a compelling economic case for AMR although there have been some efforts to do this, for example, in the UK's Review on Antimicrobial Resistance and work by the World Bank and the Organisation for Economic Cooperation and Development (OECD). However, these analyses do not appear to have been used to set or track fundraising targets for AMR investment globally.

S35 In contrast, much of the focus of implementing this objective has been on the second element namely increasing investment, particularly in medicines. Examples of key initiatives supported by WHO include the establishment of the Global Antibiotic Research and Development Partnership and the AMR Action Fund, provision of reports on the antibiotic pipeline, development of a priority list of bacterial pathogens for new drug development and production of target product profiles for antibacterial agents and diagnostics.

S36 While there is recognition of the progress being made on developing new antimicrobial treatments, some respondents were concerned that any new antimicrobials may only be available for high-income countries. Respondents also expressed concern that other areas of research and innovation might be overlooked under this objective and may not be adequately covered under objective 2. In addition, many countries have found it difficult to see how they would apply this objective in their national action plan. In some cases, countries have omitted objective 5 from their national action plan covering any elements of research and innovation under objective 2. In others, objective 5 has been used to address research, innovation and other issues more broadly.

International and national partners

S37 While the objective-by-objective sections have focused on what Member States and the WHO Secretariat have contributed to particular GAP AMR objectives, there are many other partners who have played key roles. OIE and FAO feature prominently in the GAP and in its implementation. In 2021, FAO published an evaluation of their work on AMR. In contrast, the UN Environment Programme (UNEP) does not feature prominently in the GAP but there is now increasing recognition of the need for greater inclusion of environmental matters in GAP AMR implementation. For example, priority six of the Global Leaders Group focuses on advocating for better understanding of environmental pathways to the development and transmission of AMR. Overall, there is relatively little recognition in either the GAP AMR or progress reports of the role played by multilaterals, other than OIE and FAO, including UN agencies. Similarly, progress reports on GAP implementation make little mention of the contribution of other sectors, e.g. civil society or the private sector.

Coordination

S38 The importance of effective coordination is recognized in the GAP AMR and it is reflected in the objectives of this review. The basis of this is the concept of One Health but this is not clearly defined in the GAP AMR or elsewhere. Crucial elements of the concept include focusing on consequences, responses and actions at the animal-human-ecosystem interface and having interdisciplinary collaboration at its heart. In the Tripartite Strategic Framework, to be published in September 2021, One Health is described as a collaborative, multisectoral, and trans-disciplinary approach recognizing the interconnections between people, animals, plants and their shared environment. In terms of GAP AMR implementation, the main issues related to One Health are not conceptual but practical. For example, does it mean that everything needs to be done together or is there need to identify what needs to be done jointly and what can be done separately and by whom? Many of the challenges encountered around One Health are not unique but are seen wherever groups or organizations seek to work together. Many of the solutions are not unique either but include tried and trusted ways of working collaboratively including building trust, understanding others concerns and

priorities, identifying potential flashpoints, identifying solutions that benefit all, avoiding stepping on toes and surprises, agreeing approaches to communication and having a recognized way of solving problems when/if they arise. There are also specific issues that arise because of differences in size and capacity between partners.

S39 In principle, the growing emphasis on Tripartite cooperation is welcomed although some respondents have concerns including the implication of this approach for areas of agencies' work that might fall outside the scope of joint actions, for example healthcare-acquired infections. There are also concerns about limited financial resources and how these will be shared and whether the amount consumed in coordination efforts is justified. Many respondents consider that more emphasis needs to be placed on the environment and that the Tripartite should be extended to a Quadripartite to include UNEP. Some multilateral agencies outside the Tripartite are concerned that it does not represent fully the multisectoral nature of AMR.

S40 One area of particular focus of the review is the extent of coordination with other multilateral agencies, including UN agencies. The political declaration of the UN General Assembly high-level meeting requested the UN Secretary General to establish an ad hoc inter agency coordination group (IACG) to provide practical guidance for approaches needed to ensure sustained effective global action to address antimicrobial resistance and then report to the seventy third session of the General Assembly including on options to improve coordination. In its report, the IACG recommended establishing a One Health Global Leadership Group on Antimicrobial Resistance, an Independent Panel on Evidence for Action against Antimicrobial Resistance in a One Health context and a constituency-based partnership platform. Two years later, the progress on establishing these structures has been mixed despite the fact that senior management meetings of the Tripartite organisations have been held every two months since January 2020 to seek to expedite the implementation of the recommendations of the IACG including the governance structures. The Global Leaders Group has been established and two meetings have been held. Priorities were established for the group in the form of a rolling action plan in July 2021. There was a consultation on the draft terms of reference for the proposed Independent Panel on Evidence for Action against Antimicrobial Resistance and this generated extensive feedback. A report was submitted by the Tripartite organizations to the UN Secretary General in February 2021 outlining the final terms of reference and proposed next steps. However, a response is awaited from the Secretary General and that report has not been made public nor shared with the review team. Based on publicly-available documentation, there appears to have been least progress on establishing the partnership platform. However, the Joint Tripartite Secretariat is organising a meeting of Member States to discuss the draft terms of reference for the platform. This meeting is being hosted by WHO and is scheduled for 30 September 2021. According to the draft terms of reference, there will be five representative clusters with other technical action groups.

S41 However, it is difficult to see how the proposed structures, even if operationalized, are going to meet the need for technical coordination across multilateral agencies, including UN agencies, beyond the agencies that are part of the Tripartite and potentially UNEP. Multilateral agencies were not explicitly identified as part of the stakeholder platform proposed by the IACG and are not one of the five representative clusters that appear to be proposed. This is problematic now and respondents expressed concern that there seems little focus from the Tripartite organizations on including other multilaterals, such as the Global Fund to Fight AIDS, Tuberculosis and Malaria, Gavi, the World Bank and other UN agencies, particularly the United Nations Development Programme (UNDP) and the United Nations Children's Fund (UNICEF).

S42 While the proposed stakeholder platform does include civil society, the long delay between the IACG report and establishment of this platform means that there has been a hiatus in relationships between WHO and other Tripartite organizations and civil society, meaning that gains that were previously made in this area have been or risk being lost. Respondents also wanted to see dedicated space to engage with Member States. Some respondents have existing concerns about the level of private sector influence regarding AMR. These respondents cite concerns about the profits of pharmaceutical companies and the practices of some

agricultural companies. They are therefore concerned about involving private sector in the stakeholder platform, even though this was part of the IACG proposal, and would want stringent safeguards, in terms of avoiding conflicts of interest, if that part does proceed.

S43 While it is difficult to assess details of how they interact among themselves and with other mechanisms, and the anticipated cost, it does seem that there could be a risk of the global governance and coordination mechanisms being too cumbersome, bureaucratic and costly. It is also unclear if there would need to be similar structures regionally. While it is difficult to comment on coordination mechanisms at country level, presumably it is this level which will be the most important. Where countries have functioning multisectoral coordination mechanisms, it may be that these incorporate the need for coordination among Tripartite, organizations, UNEP and other multilaterals. If not, how is coordination happening? Would it be through existing UN country teams? How would they include OIE given that they are not a UN agency and may lack in-country presence? If there are separate in-country structures for Tripartite organizations and UNEP, how do they involve other multilateral/UN agencies? Is there any role for the UN Resident Coordinator?

Equity and inclusion

S44 There is some consideration of equity in the GAP AMR, the political declaration of the UN General Assembly high-level meeting and the report of the Inter-Agency Coordination Group. The WHO Secretariat published guidance on enhancing the focus on gender and equity in national efforts to respond to AMR. The WHO Secretariat was instrumental in establishing the Global Antibiotic Research and Development Partnership (GARDP) and part of GARDP's role is to ensure sustainable access to treatments and affordability to all in need. However, a recent internal audit concluded that there had been insufficient analysis and attention to mainstreaming gender, equity and human rights. Also, some respondents are concerned that there has been more focus on limiting excessive use of antibiotics rather than on more equitable access to antibiotics. Other areas where respondents argued for greater focus on equity and inclusion included setting priorities for AMR responses, ensuring equitable access to new medicines when they are developed and ensuring communications reach beyond elites, e.g. in capital cities.

Health Systems

S45 The GAP AMR recognizes that countering AMR needs long-term investment in strengthening health systems in developing countries, and that this applies to animal as well as human health systems. The review has identified issues and actions related to a number of health systems building blocks including:

- *Service delivery* – laboratory services are crucial to delivering clinical services to people who may have antimicrobial-resistant infections. Yet, they often lack capacity, particularly in low- and middle-income countries and the importance of building such capacity is not an explicit focus of the GAP AMR. Particular barriers affecting laboratories included limited capacity of laboratory staff, difficulties in procurement and supply of laboratory reagents and equipment, limited funding and limitations in the regulatory framework.

- *Health workforces* - some countries lack policies and mechanisms to identify gaps in technical skills and training for health workers and many countries have limited pre- and in-service training programmes. There are difficulties attracting and retaining suitable qualified health workers, e.g. microbiologists and many of these problems are underpinned by a lack of financial resources.

- *Information systems* – although appropriate information is a crucial need for effective AMR responses, many countries face significant challenges in this area including lacking M&E systems for national AMR action plans, lacking national strategic plans for AMR surveillance and lacking data management systems for AMR surveillance. One overarching issue is the risk of creating another parallel system if

links are not made between AMR monitoring and surveillance systems and overall health management information systems.

- *Medical products, vaccines and technologies* – countries may lack appropriate regulations on access to antimicrobials in different sectors. Perhaps even more commonly, at least in the human health sector, laws and regulations are not enforced. In many low-and middle-income countries, lack of access to health services, including antibiotics is a major challenge.

- *Financing* – this is perhaps the key issue in many low- and middle-income countries as financial resources are inadequate to implement even basic plans in many countries. Where funds are available, they are often provided by donors and earmarking of these may skew priorities.

- *Leadership and governance* – many countries have experienced difficulties in establishing and operating multisectoral AMR coordination mechanisms. Countries have also faced challenges in operationalizing a One Health approach in practice. One concern raised from the health systems perspective relates to the risk of establishing another coordination mechanism, particularly if this is based on a one-size fits all approach.

WHO internal structures and systems

S46 The review has identified issues and actions related to WHO internal structures and systems including:

- *Leadership, strategy and vision on AMR in the WHO Secretariat* – respondents welcomed the leadership provided by having an ADG on AMR. However, there were concerns that WHO does not have a strategy or workplan to guide and monitor its own activities, e.g. as other Tripartite organizations might have.

- *Structures* – respondents welcomed the creation of an AMR Division but some questioned the rationale for having two departments in the division and how the work was divided between them. Because of the nature of AMR, there is need to coordinate extensively with other organizations outside WHO; with other divisions, e.g. on IPC; across the two departments of the AMR Division; and within teams and groups of a particular department. There were concerns that sometimes the WHO Secretariat culture seemed to encourage competition rather than cooperation. In general, there has been good coordination between the different levels of the Secretariat although there have been some issues between headquarters' approach to surveillance and some regions.

- *Staffing* – there are concerns about the availability of staff to work on AMR. These issues are particularly severe in WHO Country Offices and with national governments and in UNEP and some Tripartite organizations, such as OIE.

- *Linking to broader WHO priorities including the SDGs* – while there has been some focus on contributing to the SDGS including, for example, successfully advocating for the inclusion of a specific AMR indicator within the SDG indicators, the review found that AMR was still insufficiently framed within the 2030 Agenda hindering a clearer, more visual understanding of the socio-economic, health and environmental impacts of AMR.

COVID-19

S47 While this was not a review of COVID-19 responses, the review did take place at a time when the world was experiencing a COVID-19 pandemic. It affected the review, for example, meaning that all interviews were conducted remotely. More significantly, COVID affected actions on GAP AMR in a number of ways. It displaced

focus away from AMR to the pandemic and disrupted some planned activities. Many activities which might have been conducted face-to-face were conducted virtually.

S48 The COVID-19 pandemic emphasized the importance of diagnostic testing and of laboratories to allow testing to take place. However, some laboratories found that they were repurposed to focus exclusively on COVID-19. The pandemic also focused attention on issues of infection, prevention and control but there are concerns about a narrow focus on respiratory viruses and a lack of clarity over how sustainable any changes are. There were also concerns that the WHO Secretariat and others had failed to capitalize on the opportunity provided by COVID-19 to emphasize the wider benefits of better infection prevention and control. Another issue highlighted by the COVID-19 pandemic is the role played by health-care settings in transmitting infection and, in some cases, acting as epidemic amplifiers.

S49 COVID-19 has had a mixed effect on levels of human antibiotic use with possible mixed effects on levels of AMR. In many hospital settings, there has been an increase in the use of antibiotics, even in the absence of evidence of their value. Conversely, in many community settings, as COVID-19 infections rose and lockdown measures were imposed, the number of people attending health services for other conditions fell, in some cases dramatically. As a result of this, rates of antibiotic prescription and use fell in these contexts.

S50 Another lesson from the COVID-19 response has been increased understanding of how quickly therapeutics and vaccines can be developed when there is an imperative to do so and it also highlighted deficiencies in the current mechanisms for reimbursing medicine research and development based solely on use. The COVID pandemic provided a stark object lesson on what a pandemic is and its potential consequences, particularly in the absence of effective medical countermeasures, especially therapeutics. It also illustrated the importance of having diagnostic tests that can be made available quickly, at the point-of-care and at sufficient scale. Given that COVID-19 is considered to have spread to humans from animals, it has increased public recognition and understanding that the health of humans, animals, and the environment are intricately connected. Given these and potentially other points, there is probably justification for a lesson learning exercise from COVID-19 for the benefit of responses to AMR. This could take the form of a review.

Conclusions

S51 The review has drawn a number of conclusions and these are summarized here and are the basis for recommendations in the section that follows. They follow the same structure as the findings, namely considering the GAP AMR overall, each of the five objectives and then a number of crosscutting issues.

GAP AMR Overall

C1. It is very difficult to assess overall progress towards outcomes as these are not clearly defined. While the M&E framework provides a menu of possible outcome indicators for the GAP AMR, a smaller number is needed that can be actively monitored and tracked. While performance in terms of GAP implementation by Member States is statistically-associated with country income level, there are countries that have managed to achieve higher levels of implementation than might be expected based on country income level. Identified success factors include using data as an "*eyeopener*"; being willing to recognize and respond to challenges and difficulties; high level political support and the role of AMR champions; financial and technical support; and effective coordination often based on existing mechanisms. There is some evidence that WHO support has contributed to levels of and improvements in country performance in terms of GAP AMR implementation. While the biggest areas of improvement have been in core areas, such as developing national action plans and multisectoral coordination, there is evidence that these elements are associated with improved performance overall. While performance on human health indicators is stronger than in other areas, there is a statistically-significant positive association between improvements in human health indicators and improvements in other areas.

C2. The review has highlighted a number of deficiencies in the GAP AMR which need to be addressed in the short-term through strengthening guidance and application of the current GAP and in the medium- to longer-term through revising and updating the GAP. These areas include:

- The current GAP was originally conceived as a WHO document which other partners, FAO and OIE, later adopted. The STAG has agreed that any future revised GAP would need to be a Tripartite (plus UNEP) document.

- Unlike other Tripartite organizations, such as FAO, the WHO Secretariat lacks a detailed workplan for its own contribution to the GAP AMR. Such a plan is needed and should contain clear milestones which could be monitored to assess progress.

- Developing a tool or tools which allow prioritization of responses, particularly in contexts where resources are limited.

- The need for a clearer focus on how raised political awareness is translated into practical political commitment and provision of resources globally, regionally and nationally, for example as reflected in the recently-published priorities of the Global Leaders Group.

- The need for a more practical M&E framework with clearer indicators and targets which are actively tracked and reported on.

- The need to reflect the importance of research and innovation beyond product research and development.

- The need to recognize the importance of laboratory capacity not only for surveillance purposes but also for diagnosis of AMR for clinical management purposes.

- The need within product research and development to emphasise the importance of diagnostics and vaccines.

- Greater emphasis on the importance of plant health, food production, food safety and the environment, for example in the area of optimizing antimicrobial use.

Objective 1: Improve awareness and understanding of antimicrobial resistance through effective communication, education and training

C3. Clearly, the GAP AMR has raised awareness of AMR globally and, in many countries. It has become the recognized reference document for responses to AMR. But, this has largely not been translated into increased financial resources available to the AMR response, not least because there is no clear purposive plan of action for how this should be achieved globally or in country although the recently-published priorities of the Global Leaders Group (particularly priorities 1 and 4) do focus on these issues. It is very difficult to assess progress towards objective 1 because of a lack of a clear and shared understanding of what awareness and understanding are to be promoted, among whom and for what purpose. The current outcome indicator is currently little more than a title. What efforts there have been to collect data at outcome level have been sporadic and fragmented.

Objective 2: Strengthen the knowledge and evidence base through surveillance and research

C4. Clearly, there has been a strong commitment to developing the Global Antimicrobial Resistance and Use Surveillance System (GLASS) and this has expanded the number of countries enrolled and the number of areas or modules covered. GLASS has provided support and incentives to many countries to develop or strengthen their AMR surveillance systems. However, there are still many countries, that report having national AMR surveillance systems that are not part of GLASS and this is particularly an issue in some regions. One of the main issues with GLASS is that it is not currently able to provide representative and comparable data on AMR across countries and it is unlikely that any system based on sentinel surveillance could do this in the foreseeable future because of differences in laboratory capacity and clinical testing practices. The recent review of GLASS concluded that there was a need to develop complementary approaches, such as prevalence surveys. Much of the focus on surveillance has been on human health. Integration of surveillance across sectors remains a challenge. Many countries reportedly lack a One Health approach to surveillance due to technical, financial and coordination constraints. There has been much less focus on research under this objective and, in practice, research activities under the GAP are mainly focused on product research and development.

Objective 3: Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures

C5. The main challenge with this objective is the breadth of infection prevention and control measures and that they benefit a wide range of other diseases and issues apart from AMR. As a result, the AMR Division does not have direct control and responsibility for this objective so needs to work with others to make progress. This has proved difficult. Analysis by the WHO Secretariat and for the review shows that there had been little progress in this area in many countries as of 2020.

Objective 4: Optimize the use of antimicrobial medicines in human and animal health

C6. There are concerns that this objective focuses only on human and animal health, so excludes important areas, such as plant health, food production, food safety and the environment. There are many barriers to optimal use of antimicrobials, not least limited data on how antimicrobials are currently being used. There are also concerns that the GAP AMR and its implementation may be focusing more on excessive use of antimicrobials rather than ensuring access to appropriate antibiotics when they are needed. There has been extensive work on a stewardship framework for AMR but the WHO Secretariat report that, following consultations with Member States, there are no longer plans to negotiate a specific AMR stewardship framework but it is expected that AMR would be reflected in the proposed pandemic treaty. Some of the initiatives taken by the WHO Secretariat, for example, the development of the AWaRe classification, revision of Essential Medicines List, development of the priority pathogens list and development of the List of Critically Important Antimicrobials are considered to have been particularly influential.

Objective 5: Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions

C7. Relatively little has been done on the first part of this objective not least because of a lack of information on the disease burden caused by AMR globally, regionally and in particular countries. While some organizations have done work on the economic case globally, this has not been used to advocate for or track global resources available to respond to AMR or to provide guidance and support for countries in terms of identifying resources available to their national action plan. While the development of the MPTF is a welcome development, it is of concern that it is currently only very partially funded. There has been much more progress on the second element of the objective with the WHO Secretariat playing a key role in many important initiatives including

establishing the Global Antibiotic Research and Development Partnership, establishing the AMR Action Fund, providing valued reports on the antibiotic pipeline, developing a priority list of bacterial pathogens for new product development and developing a number of target product profiles for antibacterial agents and diagnostics.

Coordination with international and national partners

C8. The importance of coordination is emphasized in the GAP AMR and a One Health approach is widely accepted as the way to achieve this. However, there is no clear shared understanding of what the definition of One Health is or what this means in practice, including at country level. The Tripartite collaboration is perhaps the clearest expression of this coordination/collaboration. In the Tripartite Strategic Framework, to be published in September 2021, One Health is described as a collaborative, multisectoral, and trans-disciplinary approach recognizing the interconnections between people, animals, plants and their shared environment. OIE and FAO are key international partners and the importance of their role is recognized both in the GAP AMR and in progress reports. Respondents would like to see more focus on environmental issues within the GAP AMR and more inclusion of UNEP, for example by expanding the Tripartite to be a Quadripartite. The IACG recommended the establishment of a number of global governance structures but, two years on, progress with implementation has been limited despite regular meetings of Tripartite organizations senior management since January 2020 to try to expedite progress. The Global Leaders Group has been established, has had two meetings and published its priorities in July 2021. However, although there was a consultation about the proposed Independent Evidence Panel and many comments were received, it is currently unclear to external stakeholders what the status of this panel is. A report was submitted by the Tripartite organizations to the UN Secretary General in February 2021 outlining the final terms of reference and proposed next steps. However, a response is awaited from the Secretary General and that report has not been made public nor shared with the review team. Finally, the partnership platform is being taken forward by the Tripartite organizations and the Tripartite Joint Secretariat is organising a meeting of Member States on 30 September 2021 to discuss the draft terms of reference and this meeting is being hosted by WHO. It is unclear how all these structures will fit together with each other and with existing structures. In the absence of costs, it is difficult to assess whether or not these are justified. What is clear is that the current proposals are unlikely to meet the coordination needs of other multilaterals, including UN agencies, working on AMR, whereas a simpler inter-agency coordination group or task force as conceived in other areas, such as non-communicable diseases might. The important roles of other multilaterals and UN agencies in responding to AMR are largely overlooked in the GAP AMR and in progress reports. Similarly, there is little systematic progress reporting of the contribution of other sectors including civil society and the private sector. In addition, presumably the main need for coordination is probably at country level and it is unclear how this might operate in a way which brings in various development partners and maximizes use of existing structures, e.g. the UN country team.

Equity and inclusion

C9. While the importance of equity and inclusion is recognized in the GAP AMR, and in subsequent publications, there are concerns, not least in the recent audit, that GAP AMR implementation is not sufficiently focused on gender, inclusion and human rights. The WHO Secretariat has provided guidance to Member States as to how they might enhance the focus on gender and equity in national efforts to respond to AMR but more thought and analysis are probably needed to identify how a greater focus on equity and inclusion could be ensured in other areas of GAP AMR implementation.

Health Systems

C10. Weak laboratory services are a major barrier to effective programmes to respond to AMR but these are not explicitly recognized in the GAP AMR. Other elements of health systems building blocks are also extremely relevant to responses to GAP AMR. It is unclear how things envisaged in response to AMR fit into a wider systems view. For example, will AMR multisectoral coordination mechanisms and AMR surveillance data systems end up being yet another vertical or parallel system or are there ways of integrating them into existing governance systems and health management information systems? One particular complexity is that AMR is not limited to the human health sector but it also involves other sectors including animal health, plant health, food production, food safety and the environment.

WHO internal structures and systems

C11. Overall, WHO has signalled its commitment to AMR by establishing an AMR Division and providing some allocated funding and personnel. The appointment of an ADG for AMR has increased the visibility and profile of AMR both within and outside of the Organization. There are severe staffing shortages in a number of organizations in relation to AMR including WHO Country Offices, national government ministries, UNEP and some Tripartite organizations, particularly OIE. While links between AMR and broader WHO objectives, e.g. the health SDGs exist, these could be emphasized more.

COVID-19

C12. There are many lessons which can be learned from the COVID-19 pandemic and the response to it of relevance to AMR. Not only did COVID-19 cause many AMR responses and programmes to be disrupted or adapted but there were many issues of relevance to COVID-19 which were also of relevance to AMR and there were opportunities for enhanced action which may or may not have been taken. Such issues included the importance of diagnostic testing and laboratory capacity, the need for infection prevention and control and the important role of health-care settings as amplifiers of infectious diseases. In addition, COVID-19 responses may have had effects on levels of antibiotic use and, through that, on levels of AMR. These effects may have been mixed and may have differed in different contexts. COVID-19 has demonstrated very clearly what a pandemic can be like particularly in the absence of effective medical countermeasures. It has also raised awareness and understanding of the connection between the health of humans, animals and the environment. COVID-19 also highlighted the deficiencies of some accepted approaches to research and development, e.g. relying on price and volume of sales to reimburse research and development costs of antimicrobials with the potential to prevent outbreaks becoming pandemics. It also showed what is possible, e.g. in terms of developing vaccines and therapeutics, when there is sufficient imperative.

Recommendations

S52 The review has identified the following recommendations. They follow the same structure as the findings and the conclusions, namely considering the GAP AMR overall, each of the five objectives and then a number of crosscutting issues.

GAP AMR Overall

R1. **WHO Secretariat and Member States to determine how best to strengthen the current GAP AMR both in the short-term and in the medium- and longer term.** Specifically:

In the short-term

- WHO Secretariat to provide guidance on how Member States might prioritize in low-resource settings, for example by identifying "*best buys*".

- WHO Secretariat to provide more support and guidance on how raised political awareness of AMR might be translated into practical political commitment and provision of resources globally, regionally and nationally.

- WHO Secretariat to develop a detailed workplan as to what it will do to implement the GAP AMR. This should include some form of M&E framework including, for example, tangible milestones.

- WHO Secretariat to identify a sub-set of clear indicators and targets which will be used to monitor progress of the GAP AMR overall and which the WHO Secretariat will actively track and report progress against.

- WHO Secretariat to provide guidance on how research and innovation will be promoted through the GAP AMR. This might include an overarching AMR global research agenda and guidance to countries on how they might reflect research and innovation in their national action plans.

In the medium- and longer term

- Member States and the WHO Secretariat to determine when the GAP AMR should be revised and updated to fully reflect a One Health approach covering aspects of human health, animal health, plant health, food production, food safety and the environment, jointly owned by Tripartite organizations and UNEP. One option would be to revise and update the GAP more in line with the recently-published priorities of the Global Leaders Group.

Objective 1: Improve awareness and understanding of antimicrobial resistance through effective communication, education and training

R2. **WHO Secretariat and Member States to clarify understanding and scope of this objective.** Specifically:

- WHO Secretariat to develop a theory of change covering awareness and understanding of what, by whom and for what purpose. This should be based on available evidence.

- WHO Secretariat to propose a clear indicator for the expected outcome of this objective including plans for how they will actively monitor this.

Objective 2: Strengthen the knowledge and evidence base through surveillance and research

R3. **WHO Secretariat and Member States to maintain support to GLASS and to supplement with methods to collect accurate, representative, comparable AMR data nationally, regionally and globally.** Specifically:

- WHO Secretariat and Member States to further expand enrolment in GLASS particularly among those Member States who have reported through TrACSS that they have a national AMR Surveillance system but are not yet enrolled in GLASS.

- WHO Secretariat to propose ways in which prevalence surveys can be conducted to supplement availability of representative, comparable AMR data nationally, regionally and globally.

- WHO Secretariat and Member States to identify ways in which use of surveillance data national can be increased and enhanced.

- WHO Secretariat to identify ways in which research and innovation, beyond product research and development, can be encouraged and promoted through the GAP, perhaps under this objective.

Objective 3: Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures

R4. **WHO Secretariat and Member States to identify ways in which effective sanitation, hygiene and infection prevention measures can be promoted in ways which reduce AMR.** Specifically:

- WHO Secretariat and Member States to explore ways in which effective infection prevention and control can be reflected in national AMR action plans.

- WHO Secretariat to review how parts of the Secretariat working on AMR and those working on IPC can work more effectively together.

- WHO Secretariat to review whether gains made on IPC related to COVID-19 responses are sustained and their effect on antimicrobial use and AMR.

- WHO Secretariat to develop plans to more effectively include AMR in any future plans to strengthen IPC in the light of a specific disease outbreak.

Objective 4: Optimize the use of antimicrobial medicines in human and animal health

R5. **WHO Secretariat and Member States to consider how progress under this objective can be expanded and monitored more effectively.** Specifically:

- WHO Secretariat to propose how this objective could include plant health, food production, food safety and the environment in the short-term.

- WHO Secretariat to continue with plans to track effectively antimicrobial consumption and use, particularly in the human health sector.

- WHO Secretariat to clarify the importance of appropriate clinical management of people with infections as a key part of optimal use of antimicrobials. This could take the form of guidance, including a focus on the importance of good laboratory services.

Objective 5: Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions

R6. **WHO Secretariat to explain how the economic case for investment in AMR responses will be made and used to advocate for the resources needed including globally, regionally and nationally.** Specifically:

- WHO Secretariat with others, including the Tripartite organizations, UNEP and others who have worked in this field, e.g. the World Bank and OECD, to develop a clear economic case for investment in responses to AMR. This will include clear, credible data on the disease burden posed by AMR globally, regionally and in different countries.

- WHO Secretariat to develop clear plans and guidance as to how the economic case (above) can be used to advocate for sustained political commitment to and greater financial resources for AMR responses.

- WHO Member States to consider ways in which the increased financial resources needed to respond to AMR can be made available, not least through more Member States providing funds to the MPTF.

R7. **Member States and the WHO Secretariat to sustain and expand progress made on research and development for products.** Specifically:

- Member States to identify ways in which they can finance product research and development in ways which are delinked from cost and volume of sales.

- Member States, the WHO Secretariat and others to continue efforts to maximize the benefits of existing antimicrobial agents.

- WHO Secretariat to continue efforts to expand research and development efforts to also include diagnostics and vaccines.

Coordination with international and national partners

R8. **The WHO Secretariat and other Tripartite organizations to identify ways in which coordination can be enhanced and the contribution of other actors recognized and maximized.** Specifically:

- WHO Secretariat, FAO and OIE to identify organizations, such as UNEP and other multilateral agencies, and sectors, such as civil society and the private sector that are making important contributions to AMR and to identify ways in which their contributions can be maximized and recognized, e.g. in progress reports.

- WHO Secretariat to cooperate with FAO, OIE and UNEP to develop guidance on the One Health approach. While this could include a working definition of One Health, it needs to focus mostly on the practical implications of what the One Health approach does (and does not) mean for AMR approaches globally, regionally and nationally.

- WHO Secretariat, FAO and OIE to work with UNEP to expand the current Tripartite arrangement to a Quadripartite.

- The Tripartite Joint Secretariat and Global Leaders Group to develop a framework to monitor and report on progress towards the Global Leaders Group's six priorities, key performance indicators and 2021 deliverables. This might include more detailed descriptions of the key performance indicators and how these will be measured, when particular deliverables might be expected in 2021 and how these plans fit with other monitoring and reporting efforts, e.g. for the GAP AMR, SDGs and GPW13.

- The Tripartite organisations to follow up with the UN Secretary General to determine the response to the proposal submitted six months ago. The Tripartite Joint Secretariat to explain to stakeholders the nature of the platform once a response has been received and to explain how this panel will fit with other AMR structures.

- The Tripartite Joint Secretariat to update stakeholders on the status of the proposed partnership platform following the planned meeting with Member States on 30 September 2021 to discuss the draft terms of reference.

- The WHO Secretariat, OIE, FAO and UNEP to identify ways in which work with other multilaterals, including UN agencies, can be more effectively coordinated. This could involve the establishment of an inter-agency task force.

- The WHO Secretariat, OIE, FAO and UNEP to produce guidance as to how coordination on AMR between development partners at country level might work. This should include relationships with national AMR multisectoral coordination mechanisms and links to existing structures including the UN country team and Resident Coordinator.

Equity and inclusion

R9. **Member States and the WHO Secretariat to identify ways in which equity and inclusion can be better reflected in AMR programmes and responses.** Specifically:

- WHO Secretariat to produce guidance as to how equity and inclusion can be better reflected in AMR responses globally and regionally in a similar way to the guidance produced for national AMR action plans.

Health Systems

R10. **Member States and the WHO Secretariat to identify ways in which the importance of an approach based on understanding of health systems can be incorporated more effectively into AMR responses.** Specifically:

- WHO Secretariat to produce guidance on laboratory strengthening as part of responses to AMR recognizing the importance of laboratories in delivery of clinical services and surveillance.

- WHO Secretariat to produce guidance on how AMR responses might fit with a broader health systems approach, for example, using existing systems where possible.

- WHO Secretariat to work with OIE, FAO and UNEP to provide guidance on what a health systems approach looks like in a One Health context, i.e. how can a health systems approach consider not only human health but also animal health, plant health, food production, food safety and the environment.

WHO internal structures and systems

R11. **Member States and the WHO Secretariat to review WHO internal structures and systems to ensure they are able to support effectively AMR responses.** Specifically:

- WHO Secretariat to identify ways in which effective coordination can be achieved and strengthened on AMR across organizations, WHO levels, divisions, departments, teams and groups.

- Member States and the WHO Secretariat to cooperate with OIE, FAO and UNEP to better understand the level of resourcing needed to ensure optimal staffing levels across responses to AMR.

- WHO Secretariat to identify ways in which AMR responses can be more effectively linked to overall organizational priorities, for example, the health SDGs.

COVID-19

R12. **The WHO Secretariat to conduct a review of lessons learned relating to AMR responses as a result of the COVID-19 pandemic.** Specifically, this should include:

- Understanding the disruptions and adaptations that took place in AMR responses because of COVID-19.
- The opportunities that were created for AMR responses by the COVID-19 pandemic and responses to it and the extent to which these were or were not maximized.
- Better understanding of the effects of COVID-19 on antibiotic use and levels of AMR.
- Understanding how AMR responses can use increased public understanding of pandemics, the need for effective medical countermeasures and the links between human health, animal health and the environment to promote better understanding of and commitment to AMR responses.
- Lessons learned for product research and development.

1. Introduction

1. In 2015, the World Health Assembly (WHA) endorsed the Global Action Plan (GAP) on Antimicrobial Resistance (AMR).[1] The plan was further endorsed by the World Assembly of the World Organisation for Animal Health (OIE) Delegates in May 2015 and by the Food and Agriculture Organization of the United Nations (FAO) Conference in June 2015. The GAP AMR provides a framework of actions across five objectives for three stakeholder groups (Member States, the Secretariat[2] and national/international partners[3]) to take over the next five to ten years, and for countries to develop national action plans (NAPs).

2. The mandate to conduct a comprehensive review of the World Health Organization (WHO) Global Action Plan on Antimicrobial Resistance[4] derives from paragraph 4.1 of resolution WHA72.5 of the World Health Assembly.[5] This in turn is captured in the Evaluation Office's 2020-21 biennial evaluation workplan approved by the Executive Board.

3. Terms of reference for the review overall are presented in Annex 1.[6] The review's purpose, objectives and scope are stated in the terms of reference and are also discussed in the review's inception report and in this introduction. The inception report and this introduction also explore who are the expected users of, and audiences for, this review.

4. The overall *purpose* of this comprehensive review is to enhance current work on AMR. Based on the five primary objectives of the GAP AMR (see Box 1), the review documents successes, challenges and best practices, and provides lessons learned and recommendations for use by WHO and other GAP AMR stakeholders to guide future implementation of the GAP AMR and to inform decision-making on AMR.

Box 1: GAP AMR objectives
Objective 1: Improve awareness and understanding of antimicrobial resistance through effective communication, education and training
Objective 2: Strengthen the knowledge and evidence base through surveillance and research
Objective 3: Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures
Objective 4: Optimize the use of antimicrobial medicines in human and animal health
Objective 5: Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions

[1] World Health Assembly, Resolution WHA68.7, https://apps.who.int/gb/ebwha/pdf_files/WHA68-REC1/A68_R1_REC1-en.pdf#page=27 (accessed 16 July 2021).
[2] However, the GAP AMR does not clearly define "*the Secretariat*". Following the adoption of the GAP AMR in 2015, a Secretariat for AMR was established in the Office of the Director General which was intended to coordinate the work on AMR across the WHO secretariat (Headquarters, Regional Offices and Country Offices). However, since then an AMR Division was established within WHO as part of the global transformation agenda – see https://www.who.int/groups/strategic-and-technical-advisory-group-on-antimicrobial-resistance (accessed 16 July 2021). In addition, in 2019, a tripartite secretariat was established between WHO, FAO and OIE, hosted by WHO – see https://www.who.int/docs/default-source/antimicrobial-resistance/amr-gcp-tjs/tjs-tor-final-october-2019.pdf?sfvrsn=bbd8a3fe_0 (accessed 16 July 2021). In terms of this review, the term "*the Secretariat*" is understood in terms of the WHO secretariat (at the three levels of Headquarters, Regional Offices and Country Offices), in contrast to the other two main groups of stakeholders, i.e. Member States and international and national partners.
[3] A wide range of international and national partners are identified in the GAP AMR including professional organizations and societies, accreditation bodies, intergovernmental organizations (such as OIE, FAO and the World Bank), civil society organizations, trade and industry bodies, employee organizations, foundations with an interest in science education, the media, the international research community (in both the public and private sector including the pharmaceutical industry), global health donors, philanthropic organizations, international development bodies, aid and technical agencies, research funding organizations and foundations, health insurance providers and other payers, and partners in the finance and economic sectors. WHO more broadly is also sometimes referred to as an international partner.
[4] Global Action Plan on Antimicrobial Resistance, World Health Organization, 2015, https://www.who.int/publications/i/item/9789241509763 (accessed 16 July 2021).
[5] WHA72.5, Resolution on Antimicrobial resistance, https://apps.who.int/gb/ebwha/pdf_files/WHA72-REC1/A72_2019_REC1-en.pdf#page=1 (accessed 16 July 2021).
[6] Please note that annexes are provided as a separate volume of this report.

5. The review has four *objectives*, as stated in the terms of reference (see Annex 1), namely:
   - To document successes, challenges and gaps in the implementation of the GAP AMR since its adoption in 2015;
   - To review how efficiently AMR activities are being implemented across the three levels of WHO: Headquarters (HQ), Regional Offices (ROs) and Country Offices (COs);
   - To review how well AMR activities are coordinated, including with relevant United Nations (UN) agencies and other relevant stakeholders;
   - To provide lessons learned and recommendations to improve the implementation of the GAP AMR at all three levels of WHO.

6. According to its mandate, this is a comprehensive review, and therefore the *scope* of the review is set by the scope of the GAP AMR as it was adopted by WHO in 2015. The GAP has a section on scope (#5) which explains that it covers antimicrobial resistance and not just antibiotic resistance, that support for tackling antimicrobial resistance was multisectoral and that the GAP provides the framework for national AMR plans, which outline actions for three groups of stakeholders across the five objectives of the GAP.

7. More specifically, in terms of actors covered by this review, the team considered all stakeholders identified in the GAP AMR through a WHO lens.[7] In practice this meant that the review considered:

   - Actions taken by WHO Member States to implement the GAP AMR, for example through developing and implementing their own National AMR Action Plans.

   - Actions taken by "*the Secretariat*" to implement the GAP AMR. As explained in footnote 2 and in line with the WHO "*lens*" taken for this review, the actions considered here were not limited to a particular AMR secretariat but included all actions of the WHO secretariat (at three levels) including actions of structures taken subsequent to the GAP AMR being adopted.

   - Actions taken by national and international partners to implement the GAP AMR. In line with the WHO "*lens*" taken for this review, the focus here was on coordination by WHO with national and international partners, including FAO and OIE, whose roles are particularly emphasized and highlighted in the GAP AMR. It is important to stress that this was not a performance review of any national or international partner beyond WHO. Nevertheless, the review recognized and reflected the multisectoral efforts needed to address AMR and which are central to the GAP AMR. Figure 1 illustrates the WHO lens that the review took particularly in relation to FAO and OIE as key international partners identified in the GAP AMR. This shows that the review's focus was on WHO and its cooperation and collaboration with others in seeking to implement the GAP AMR.

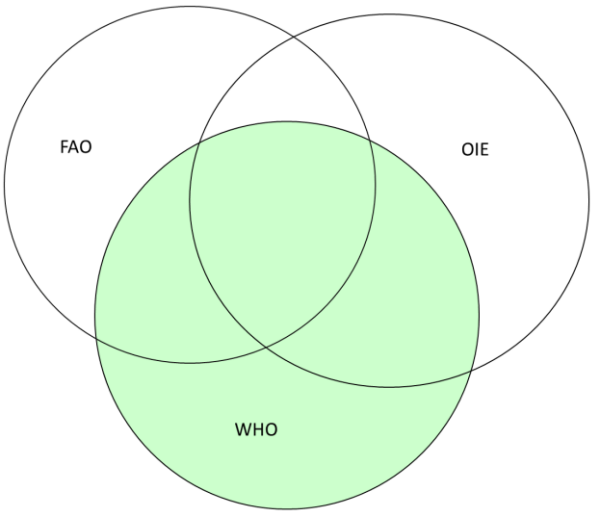


Figure 1: Figure based on Venn diagram shared by WHO AMR Division – this figure shows how work of three agencies intersects and it highlights, in green, the areas on which the review focused, i.e. the work of WHO and its interactions with other national and international partners including FAO and OIE.

[7] Given that this is a review by WHO's Evaluation Office of a WHO global action plan.

8. The review focused mainly on what has been achieved through the GAP AMR and how this was achieved. As a result, the review did not have a major focus on the outcomes and impact of the GAP AMR.

9. Based on its mandate, the review considered how efficiently AMR activities are being implemented across WHO. To date, WHO does not have an agreed way of measuring or assessing such efficiency. The review considered multiple ways of assessing this including through review of WHO budgetary allocations, deployment of staff and through qualitative consultation with key stakeholders. This element of review of efficiency included consideration of any structures or processes established within or involving WHO to take forward GAP AMR implementation.

10. The time frame considered within the scope of the review was from the endorsement of the GAP AMR by the World Health Assembly in May 2015 until completion of this review. The review aims to be forward-looking and seeks to provide useful and actionable recommendations to facilitate future policy and decision-making.

11. Four main review questions have been identified based on three[8] of the objectives of the review (see paragraph 5) and these are included in the terms of reference (see Annex 1).

- Review Objective 1: To document successes, challenges and gaps in the implementation of the GAP AMR since its adoption in 2015;
    - What are the successes and challenges in the implementation of the five primary objectives of GAP AMR since 2015?

- Review Objective 2: To review how efficiently AMR activities are being implemented across the three levels of WHO: HQ, ROs and COs;
    - What have been the main internal and external factors influencing WHO's ability to implement the GAP AMR in the most efficient manner?
    - To what extent have AMR activities been implemented efficiently across the three levels of WHO?

- Review Objective 3: To review how well AMR activities are coordinated, including with relevant United Nations agencies and other relevant stakeholders;
    - To what extent have AMR activities been well coordinated with other United Nations agencies and relevant stakeholders?

12. These questions have been discussed with the WHO AMR division. Table 1 presents these questions and analyses how they relate to the evaluation criteria of relevance, effectiveness, efficiency, impact, sustainability and coherence.

[8] The fourth is "*to provide lessons learned and recommendations to improve the implementation of the GAP AMR at all three levels of WHO*". While this does not have a specific question to answer for data collection purposes, it is a focus of analysis and reporting.

Table 1: Main review questions

	Relevance	Effectiveness	Efficiency	Impact	Sustainability	Coherence
1. What are the successes and challenges in the implementation of the five primary objectives of GAP AMR since 2015?		✓✓		✓		
2. What have been the main internal and external factors influencing WHO's ability to implement the GAP AMR in the most efficient manner?		✓	✓✓		✓	
3. To what extent have AMR activities been implemented efficiently across the three levels of WHO?			✓✓		✓	
4. To what extent have AMR activities been well coordinated with other United Nations agencies and relevant stakeholders?		✓			✓	✓✓

13. Question 1 is largely about how effectively the GAP AMR has been implemented. While it does touch on contribution to impact and outcomes of the GAP AMR, this was not the main focus of the review. Questions 2 and 3 focus mainly on efficiency although question 2 touches on issues of effectiveness and both include elements of how any progress made under the GAP AMR might be sustained. Question 4 mainly focuses on how well-coordinated WHO's activities have been with others and this covers elements of coherence, effectiveness and sustainability. While issues of relevance are not explicitly covered in the four main evaluation questions, these issues are covered in the forward-looking lessons learned and recommendations of the review.

2. Method

14 A more detailed description of method is contained in Annex 4. In the absence of an agreed theory of change for the GAP AMR, the review was based around the results chain outlined in the M&E framework. The review's analysis and this report are structured around the GAP AMR's five objectives with an initial overview section. In addition, the findings section concludes with consideration of a number of crosscutting issues. A review matrix was developed which identified the review's main questions, issues that were to be covered, the basis on which these were to be answered and relevant data sources, incorporating methods of data collection. Additional data was only collected when it was going to be used for analysis and generation of findings. This was done by structuring and focusing data collection around the review's main questions. Data collected from different sources, e.g. from document review, key informant interviews and other methods for each question was compared and used to produce a written report of findings. Quality and reliability of data was ensured by triangulating and comparing data of different types and from different sources.

15 The review was divided into four phases – inception; review of secondary data; primary data collection; analysis and reporting. Inception took place in March and April 2021 and focused on identifying and describing how the review would be conducted, providing a clear and actionable plan for that. A separate report of the inception phase was produced. Some minor changes were made from the terms of reference and inception report during implementation and these are described in detail in Annex 4.

16 The review of secondary data focused on assessing progress, in relation to the indicators in the M&E framework.[9] It was carried out in April 2021 and a report of this process was produced which is included as Annex 6. Other elements of secondary data review, e.g. review of CCSs, JEEs and BCAs were conducted later June and these were incorporated into the main report of the secondary data review. Details of all the main data sources used in the secondary data review (TrACSS, GLASS, progress reports, CCSs, JEEs and BCAs) are included in Annex 4. Details of how performance scores were calculated using TrACSS data are also included in Annex 4. One major challenge facing the review was the absence of any clear baseline data. This was addressed by taking a country's first report to TrACSS on a particular question as their baseline and this approach is described in more detail in Annex 4. A large number of documents were provided, particularly by the WHO Secretariat, but also by other informants. A full list of all these documents is given as Annex 2.[10] The primary data collection phase ran from May to July 2021. The main method for primary data collection was through semi-structured interviews with identified key informants. And details of these are provided in Annex 4. The groups of stakeholders interviewed included WHO Secretariat staff in headquarters, all regional offices and a number of country offices, current and former members of the STAG, and a number of identified partners. All WHO country offices that were not offered an interview were invited to respond to a short set of questions sent by email. More than 100 interviews were conducted and details are provided in Annex 3.

17 Following the data collection phases, on 13 July 2021, the review team met virtually to review and summarize the evaluation's main findings and to begin to identify key conclusions and recommendations. These were consolidated into a summary and main report (this document). Throughout this analysis process, comparisons were made between quantitative and qualitative data from different sources in order to answer and address the agreed evaluation questions. The reports were then shared with WHO's Evaluation Office. Details of limitations of the review are included in Annex 4. However, while there were some limitations to the evaluation and its processes, efforts were made to mitigate these producing a robust, rigorous and high-quality review of the GAP AMR.

[9] WHO, FAO and OIE (2019) *Monitoring and Evaluation of the Global Action Plan on Antimicrobial Resistance: Framework and Recommended Indicators* available on https://apps.who.int/iris/bitstream/handle/10665/325006/9789241515665-eng.pdf?ua=1 (accessed 16 July 2021). For a detailed description of this framework, please see Annex 4.

[10] Where specific documents are referred to in the report's narrative, details are given as a footnote. Where possible, URLs have been provided to aid the reader to quickly access referred material. A note of caution is needed here. The review coincided with a major revamp of the WHO website. Every effort has been made to ensure working links are provided and a date is provided as to when the team last checked this. However, given the ongoing work to revamp the WHO website and the experience of the team, it is likely that some links may not operate fully in future.

3. Findings

18 The findings of this review are presented as follows. First, there is an overview assessment of progress overall. This is then followed by sections which look at progress objective by objective. Each of these sections follows a similar format looking first at progress overall within the objective then looking specifically at identified indicators, focused mainly on progress by Member States, and then concluding with consideration of WHO Secretariat's contribution to the objective.[11] Following these objective-by-objective sections, there is a section looking at the contribution of other actors and then a section on a number of crosscutting issues.

3.1 Overview

Progress towards outcomes, objectives and goals

19 One option when looking at GAP AMR implementation is to look at progress made towards identified outcomes, objectives and goals. However, caution is needed in any such approach as there is unlikely to be a simple causal relationship between GAP AMR actions and outcomes. Many other factors may be at play. Nevertheless, tracking progress made towards outcomes will be important if contribution of GAP AMR (beyond activities and outputs) is to be understood. At worst, outcome data provides useful contextual understanding.

20 One challenge facing GAP AMR implementation is that there does not appear to be a shared understanding of what the desired outcomes are or what success might look like. The GAP itself[12] does not use the term outcome. The plan's goal is described in quite general terms as "*to ensure, for as long as possible, continuity of successful treatment and prevention of infectious diseases with effective and safe medicines that are quality-assured, used in a responsible way, and accessible to all who need them*". The GAP AMR M&E framework[13] identifies a large number[14] of indicators to be tracked at overarching goal, goal and outcome level. The review team attempted to identify data for these indicators given that data on these is not currently being systematically tracked and monitored by the AMR Division, although there are plans to establish an AMR data portal to attempt to address this issue. Currently, of the 34 outcome indicators identified, three (9%) appear to be incompletely defined while more than half (19, 55%) seem to lack any data.[15] A further seven (21%) have some data but this is considered insufficient for outcome monitoring at a country level while only four (12%)[16] have country-level data available, including baseline data.[17] It is therefore currently difficult to do much, if any, analysis at the outcome level. There are too many outcome indicators and most of them have insufficient data for analytical purposes. If this assessment is correct, it is likely that any data portal will have limited success in making outcome data available for analysis as the approach appears to be based on the assumption that the data is available somewhere.

21 One option would be to focus attention on a smaller number of key outcome indicators. Possibilities include:

- *Burden of disease caused by AMR* – currently, the indicator at goal level is burden of infectious disease.[18] However, the detailed indicator descriptions explains that more work is needed to define this indicator

[11] A detailed analysis of progress on all expected Secretariat actions, as described in the GAP, is included as Annex 5.
[12] See https://www.who.int/publications/i/item/9789241509763 (accessed 20 July 2021)
[13] See https://www.who.int/publications/i/item/monitoring-and-evaluation-of-the-global-action-plan-on-antimicrobial-resistance (accessed 20 July 2021) and https://www.who.int/antimicrobial-resistance/global-action-plan/monitoring-evaluation/AMR-M-E-indicator-reference-sheets-web-high-December-2019.pdf (accessed 20 July 2021). Please note that the link within the M&E framework to Annex 3 no longer works following WHO's revamp of its website.
[14] There are 18 numbered outcome indicators but many of these are compound and the review team found that there are 34 outcome indicators contained within the framework.
[15] It is possible that the review may have overlooked some data sources. It would be helpful if the indicator metadata had clear links to available data sets and reports (where available).
[16] Three of these are SDG indicators and the fourth relates to levels of resistant TB.
[17] The basis for this assessment is contained in Annex 1 of the secondary data review conducted for the review.
[18] Defined as "*key bacterial infections plus HIV, TB and malaria*".

and the data source cited is IHME's generic Global Burden of Disease website.[19] According to its 2021 report,[20] GLASS has introduced a module on estimating the AMR burden and this focuses on a method for estimating attributable mortality of AMR bloodstream infections[21] and its prospective use by ACORN in selected countries in Africa and South-East Asia. However, many others are working in this space[22] [23] and it is difficult to get an idea of how all these initiatives fit together. It is clear that getting data on the burden of disease caused by AMR is both crucial and difficult.

- *Prevalence of blood-stream infections caused by specific pathogens*[24] - these indicators are included in the M&E framework, as SDG indicators and within GPW13. Data on these is collected by GLASS but there are problems with the quality, representativeness and comparability of data not least because of the highly variable capacity and sampling policy of sentinel surveillance networks in different countries.[25] Getting data for a global estimate of these indicators is likely to need a different approach, such as the use of point-prevalence surveys, at least in the short-term.[26]

- *Antibiotic consumption* – there are indicators on total consumption of antibiotics for systemic use and the proportion of these that are "*access*" antibiotics in the M&E framework. The latter indicator is included within GPW13. While stakeholders are optimistic that this can be measured, the review was unable to find little evidence that data has yet been collected. There is an expectation that GLASS will collect such data. While the latest GLASS report[20] contained a strong focus on the AMC module, it appeared to cover very few countries and did not appear to report actual data. An earlier report of surveillance of antibiotic consumption[27] in 2018 did contain a data table showing estimates of total consumption of antibiotics for 65 countries. However almost three quarters of these (46 of 65, 71%) were from EUR. While this report did refer to the AWaRe classification, it did not appear to analyse antibiotic use using that classification.

22 Given these issues, and its nature and timing, this review does not focus on progress towards outcomes but focuses more on processes and outputs. However, while this is reasonable for this review, it is unlikely to be the case for subsequent reviews and evaluations, not least because of reporting imperatives, e.g. relating to GPW13 and the SDGs.

Implementation progress overall

23 One way of getting an overview of GAP AMR implementation is through the use of an implementation score based on aggregating results across a number of output-level indicators.[28] Such an implementation score was

[19] See http://www.healthdata.org/gbd/2019 (accessed 20 July 2021)
[20] See https://www.who.int/publications/i/item/9789240027336 (accessed 20 July 2021)
[21] See https://www.who.int/publications/i/item/9789240000650 (accessed 20 July 2021)
[22] Including, for example, the GRAM project implemented by IHME and the University of Oxford with funding from the Fleming Fund, the Wellcome Trust and the Bill and Melinda Gates Foundation – see http://www.healthdata.org/gram (accessed 20 July 2021)
[23] See also Cassini et al. (2019) *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* https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(18)30605-4/fulltext (accessed 26 July 2021) and OECD (2018) *Stemming the Superbug Tide: Just a Few Dollars More* available on https://www.oecd.org/health/stemming-the-superbug-tide-9789264307599-en.htm (accessed 27 July 2021)
[24] In particular, Methicillin-resistant S aureus and ESBL-producing E Coli.
[25] Although there are published comparisons across countries, e.g. OECD (2018) *Stemming the Superbug Tide: Just a Few Dollars More* available on https://www.oecd.org/health/stemming-the-superbug-tide-9789264307599-en.htm (accessed 27 July 2021)
[26] Even if surveys do generate data for these two indicators, there may still be questions about whether these are the right indicators in all contexts and for the foreseeable future. Some stakeholders argue that the pathogens of concern vary by setting and over time. In addition, it is not clear what success in this area might look like. Some stakeholders argue that there needs to be a target, such as a 10% reduction but setting such a target in the absence of baseline data, including some understanding of current trends, is problematic. For example, if rates are rapidly increasing, slowing those rates may be more realistic than a somewhat arbitrary reduction target that may prove unrealistic.
[27] See https://www.who.int/publications/i/item/who-report-on-surveillance-of-antibiotic-consumption (accessed 20 July 2021)
[28] A similar approach is taken by the 2021 AMR Preparedness Index – see https://globalcoalitiononaging.com/wp-content/uploads/2021/06/GCOA-AMR-Preparedness-Index_FINAL.pdf (accessed 21 July 2021). This considers data for 11 countries across seven areas – national strategy for AMR; awareness and prevention; innovation; access; appropriate and responsible use; AMR and the environment; and collaborative environment. In each area, scores are generated out of 100 using a combination of qualitative and quantitative data. Data is drawn from a range of sources including TrACSS and GLASS. While the

calculated in the report of the second round of TrACSS.[29] Relatively limited analysis was done in that report (p20) including a graph of country scores across all indicators and across human and non-human indicators (Figure 9). It does not appear that this approach was used in subsequent rounds of reporting on TrACSS.[30] WHO's Evaluation Office has used this approach in evaluations of other global action plans, for example on non-communicable diseases.[31] This review used two methods for calculating overall implementation score (C+ and GS) and these are described in detail in Annex 4.

24 Table 2 presents data for the two ways of calculating implementation scores across all included indicators. Numbers presented are the mean across all Member States that submitted at least one response to TrACSS (n=187). Baseline data reflects the first data set reported by a Member State on a particular indicator and performance data reflects the last data set so reported. The change is the mean difference between these two figures. Data is similar between the two calculation methods.[32] The biggest improvements are seen in relation to multisectoral coordination and national action plans with little if any change seen in infection prevention and control in human health and optimizing antimicrobial use in animal health.

Table 2: Implementation scores across GAP AMR indicators

Colour coding

- *for scores – amber 0-40; yellow 41-60; light green 61-80; dark green >80*
- *for change – amber 0-10; yellow 11-20; light green >21*

Indicator	Baseline		Performance		Change	
	GS	C+	GS	C+	GS	C+
Multi-sector and One Health working arrangements	27	20	45	45	18	25
National action plan	38	48	58	75	20	27
Awareness and understanding of AMR risks and response (human health)	43	49	55	78	12	28
Awareness and understanding of AMR risks and response (animal health, plant health, food production, food safety and environment)	29	29	31	47	3	17
Training and professional education on AMR in the human health sector	43	60	48	71	5	11
Training and professional education on AMR in the veterinary sector	32	33	39	50	7	17
Training and professional education on AMR in farming sector, food production, food safety and the environment	17	16	19	19	2	3
Progress with strengthening veterinary services	34	39	41	52	7	13
National monitoring system for consumption and rational use of antimicrobials in human health	34	41	41	47	7	6
National monitoring system for antimicrobials intended to be used in animals	29	33	39	51	10	18
National monitoring system for antimicrobial use in plant production	13	18	22	33	9	15
National surveillance system for AMR in humans	44	53	53	67	9	14
National surveillance system for AMR in animals	33	38	43	55	11	18
National surveillance system for AMR in food (animal and plant origin)	37	53	40	60	3	7
Infection prevention control in human health care	47	61	49	61	2	0
Good health, management and hygiene practices to reduce the use of antimicrobials and minimize development and transmission of AMR in animal production	29	31	35	33	6	2
Good management and hygiene practices to reduce the development and transmission of AMR in food processing	32	38	36	44	5	6
Optimizing antimicrobial use in human health	34	44	45	67	11	24
Optimizing antimicrobial use in animal health (terrestrial and aquatic)	37	44	37	44	1	0
Laws or regulations on prescription and sale of antimicrobials for human use	77	77	86	86	9	9
Laws or regulations on prescription and sale of antimicrobials for animal use	61	61	65	65	4	4
Laws or regulations that prohibit the use of antibiotics for growth promotion	41	41	50	50	9	9

scores and rankings do vary between the scoring method used in this review and the AMR Preparedness Index, there is a statistical association between the two scoring methods (p=.009). It is likely that this link is mediated through country income levels as both performance scores have a positive association with country income level. For example, although the AMR Preparedness Index only has 11 data points, there is a statistical association between scores and GNI per capita (p=.002).

[29] See https://apps.who.int/iris/handle/10665/273128 (accessed 20 July 2021)

[30] See https://www.who.int/publications/i/item/monitoring-global-progress-on-antimicrobial-resistance-tripartite-amr-country-self-assessment-survey-(tracss)-2019-2020 (accessed 20 July 2021)

[31] See https://cdn.who.int/media/docs/default-source/documents/about-us/evaluation/ncd-gap-final-report.pdf?sfvrsn=55b22b89_22&download=true (accessed 20 July 2021).

[32] In general, the scores are slightly higher in the C+ method. This is essentially because this system does not distinguish between C and higher levels of performance. The GS system effectively sets the bar higher as full marks are only given to a score of E. In general, the change scores are higher for the C+ method than for GS. This reflects changes from B (or below) to C (or above). In a few cases, the change score is higher in the GS method, i.e. when changes do not cross the B to C threshold, e.g. a change from A to B or from C to D or E. For full details of the scoring system, please see Annex 4.

25 Figure 2 shows the mean overall implementation score across the indicator set for both calculation methods. This shows that the two methods produce similar results although the C+ method produces consistently higher results. Overall, the mean implementation score on the C+ method was 52.9% as compared to 41.0% at baseline. The mean implementation score on the GS method was 44.3% as compared to 36.7% at baseline. In general, the highest mean implementation score is seen in EUR and the lowest in AFR. There is marked variation in mean implementation scores between low-income countries (C+ 26.9, GS 24.8) and high-income countries (C+ 72.2, GS 60.9) and this difference is statistically significant for both methods (p<.001). Figure 3 shows the mean change in overall implementation score from baseline to performance data again using both methods. Again, the change documented with the C+ method (+12.0) was higher than for the GS method (+7.6). The highest change in implementation score occurred in SEAR. There was no clear pattern by country income group (for C+ method p=.80; for GS method p=.86).

Figure 2: Mean overall implementation score (both methods) by WHO region, country income group and overall

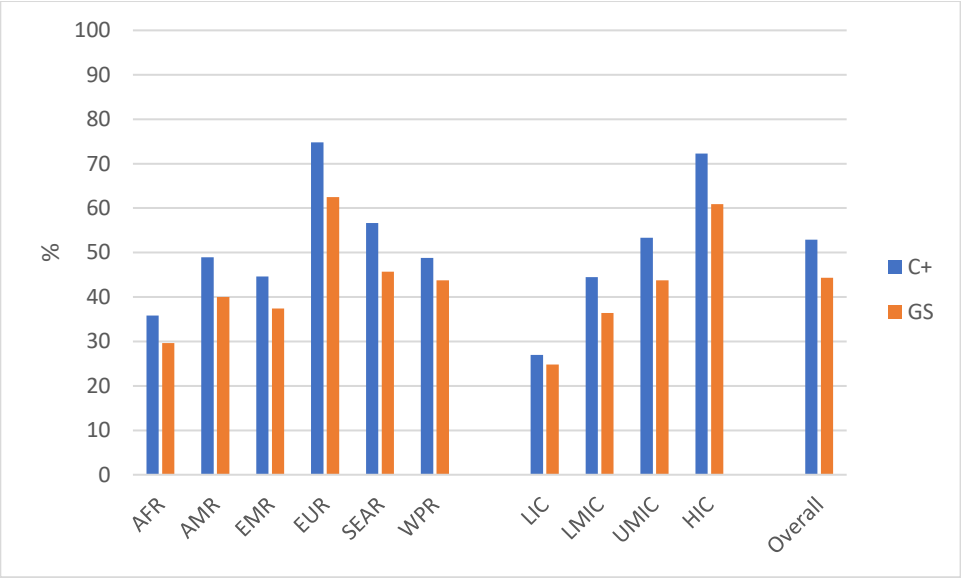
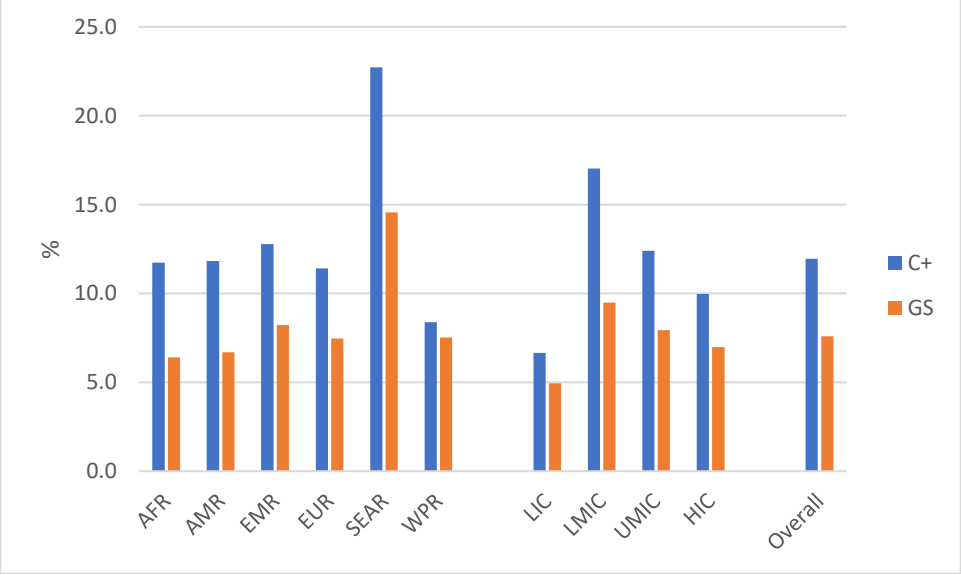


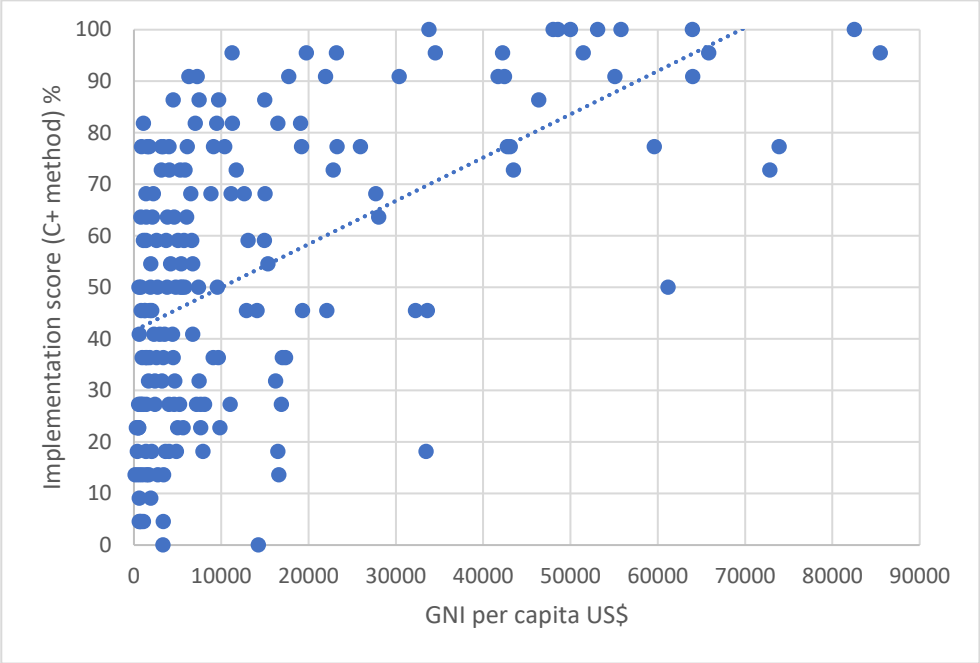
Figure 3: Mean change in overall implementation score from baseline to performance data (both methods) by WHO region, country income group and overall



26 There is a statistically significant association between performance score and income level. Figure 4 shows this in a different way by plotting the mean implementation score (C+ method) against GNI per capita. This

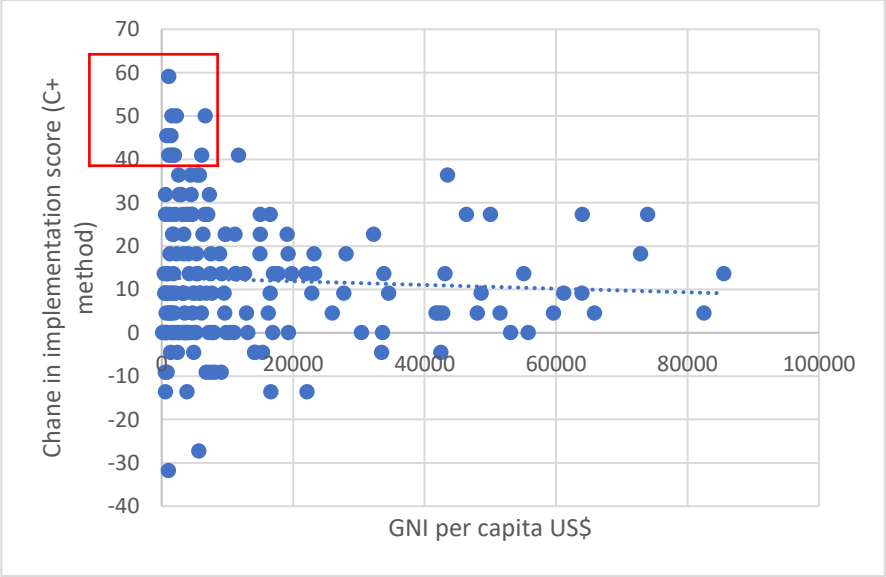
shows the same pattern, namely that mean implementation score increases as GNI per capita rises. This change is statistically significant (p<.001). However, there is substantial variation in performance scores among low-income countries with some countries achieving higher implementation scores based on their reports than might be expected for their level of GNI per capita. This variation was used as one of the selection criteria for which WHO Country Offices to interview (see Annex 4).

Figure 4: Mean overall implementation score (C+ method) compared to GNI per capita



27 Figure 5 shows a similar graph but this time it plots change in implementation score (C+ method) between baseline and performance data by GNI per capita. This shows that change in implementation score is largely independent of GNI per capita.[33] However, the countries with the highest increases all have GNI per capita below US$12,000. This variation was used as one of the selection criteria for which WHO Country Offices to interview (see Annex 4)

Figure 5: Change in implementation score (C+ method) between baseline and performance data by GNI per capita



[33] There is a slight negative association but this is not statistically significant (p=0.80).

28 Figure 6 shows the mean implementation score across core indicators and indicators for four of the objectives of GAP AMR. The highest mean score is for objective 4 (C+ 62%; GS 57%) and for the core areas of multisectoral collaboration and national action plans (C+ 60%; GS 51%). Scores for the other three objectives are similar. Figure 7 shows the improvement in mean implementation score which has occurred between baseline and performance data. This shows that the increase is highest for core indicators, i.e. the main improvement that has occurred is the introduction of multisectoral coordination mechanisms and national action plans (C+ increase of 26 percentage points; GS increase of 19 percentage points), and lowest for objective 3 relating to infection prevention and control.

Figure 6: Mean implementation score (both methods) across core indicators and indicators for four objectives of GAP AMR

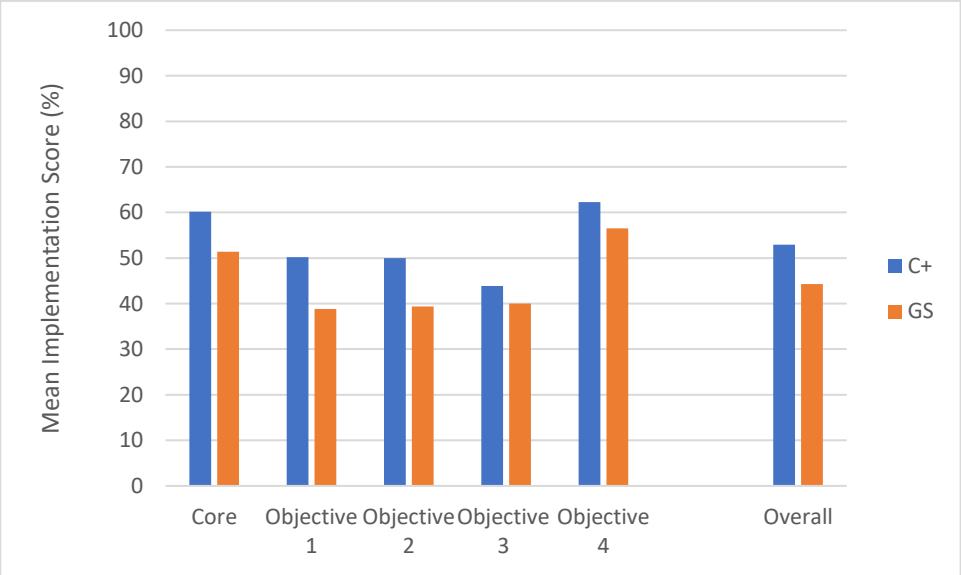
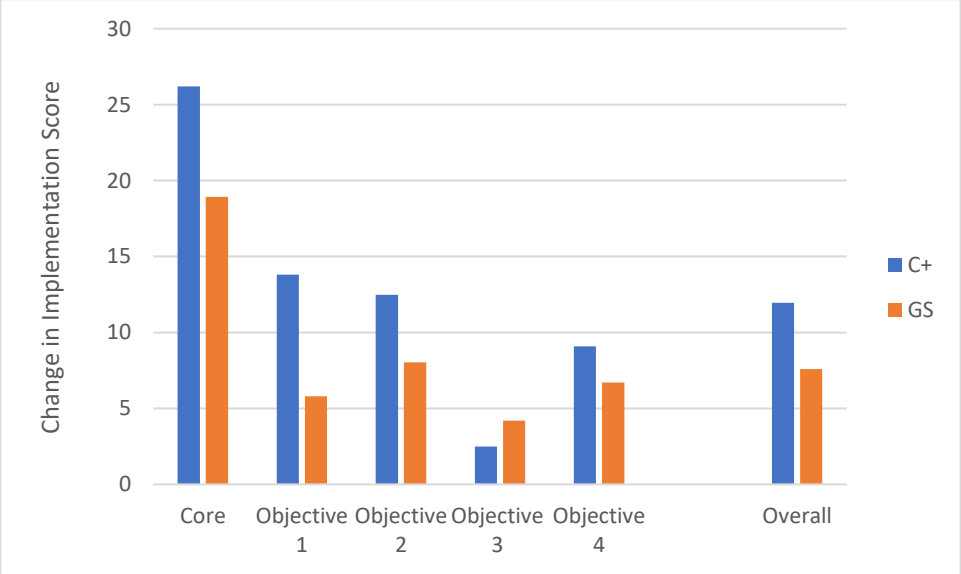


Figure 7: Change in mean implementation score (both methods) between baseline and performance data across core indicators and indicators for four objectives of GAP AMR



29 This could perhaps be viewed negatively, i.e. that the main changes that have occurred in countries following the adoption of the GAP AMR have been in relation to multisectoral coordination and national action plans. For example, some might argue that it is all very well having plans and coordination mechanisms but what difference do they make on the ground. Others might counter that they are the necessary first step in

producing desired change. Figure 8 perhaps provides some evidence for the latter argument. This shows that there is a positive association between having a multisectoral coordination mechanism and overall modified[34] implementation score. This association is statistically significant (p<.001 for both methods). There is also a statistically significant positive association (p=.01 for C+ method and <.001 for GS method) between improvement in multisectoral coordination mechanism between baseline and performance data and improvement in modified implementation score (see Figure 9). It should be noted that the numbers of countries at the extreme ends of this graph are small (see Figure 10) and this may explain the somewhat anomalous findings in those groups. Almost all countries (90%) fall in the range of 0 to 3. Only eight countries (4%) recorded negative changes.

Figure 8: Is there an association between the grade a country gives for its multisectoral coordination mechanism and mean modified implementation score

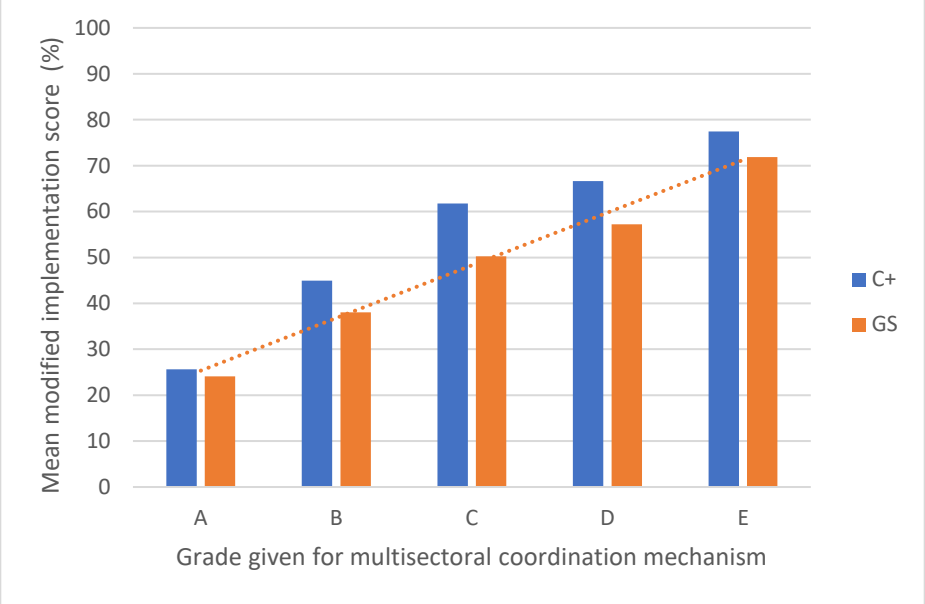
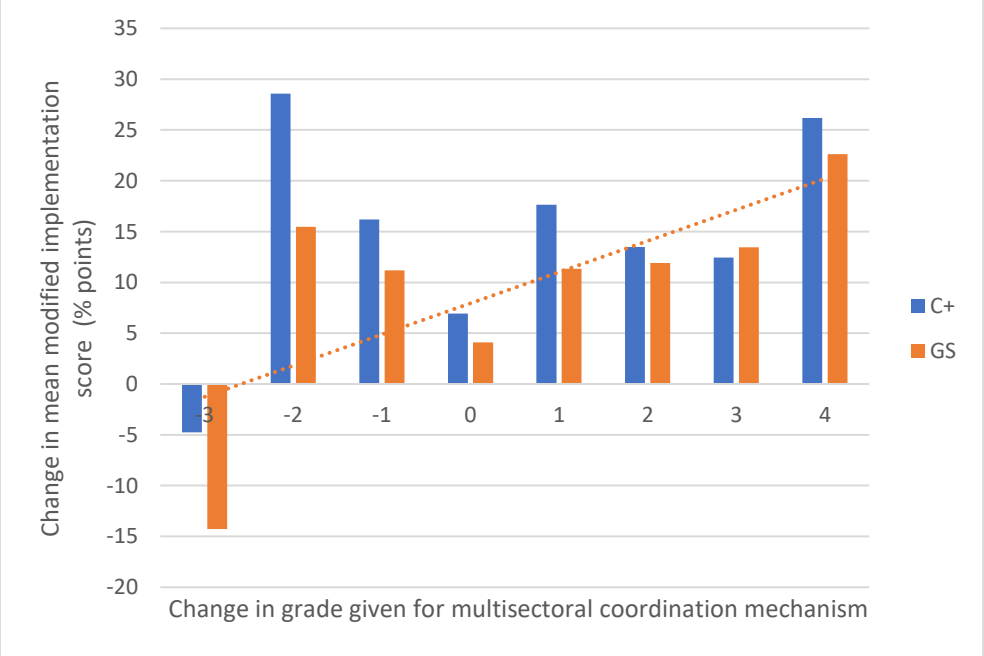
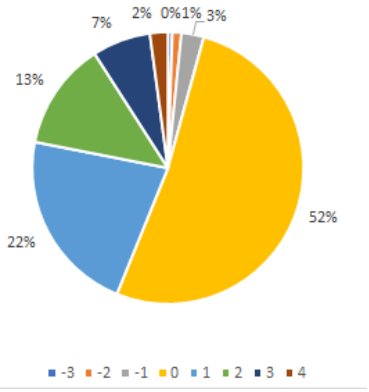


Figure 9: Is there an association between change in the grade a country gives for its multisectoral coordination mechanism between baseline and performance data and change in mean modified implementation score



[34] The modification is that the score for the particular indicator being considered is deducted from the implementation score, in this case the score for the multisectoral coordination mechanism.

Figure 10: Percentage of Member States that recorded different levels of changes in scores for multisectoral coordination commissions between baseline and performance data



30 Figure 11 also shows that there is a positive association between having a national action plan in place and overall modified[35] implementation score. This association is statistically significant (p<.001 for both methods). There is also a statistically significant positive association (p<.001 for both methods) between improvement in national action plans between baseline and performance data and improvement in modified implementation score (see Figure 12).

Figure 11: Is there an association between the grade a country gives for its national action plan and mean modified implementation score

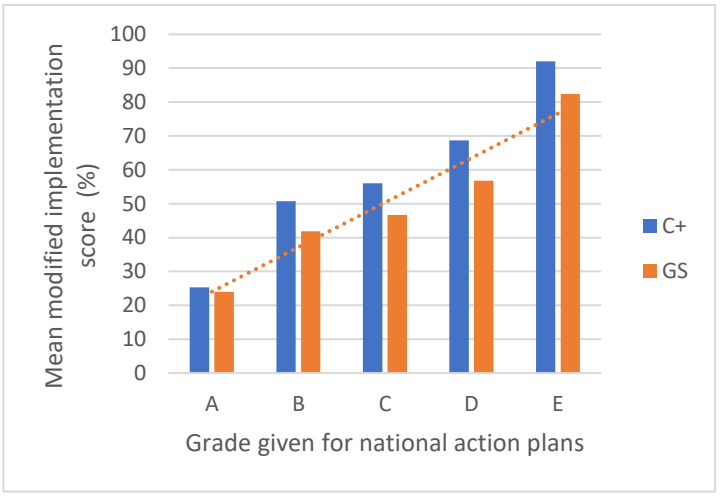
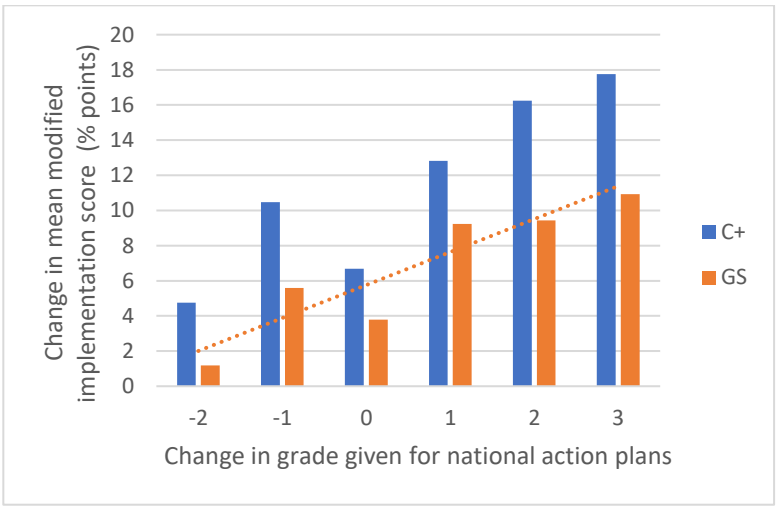


Figure 12: Is there an association between change in the grade a country gives for its national action plan between baseline and performance data and change in mean modified implementation score

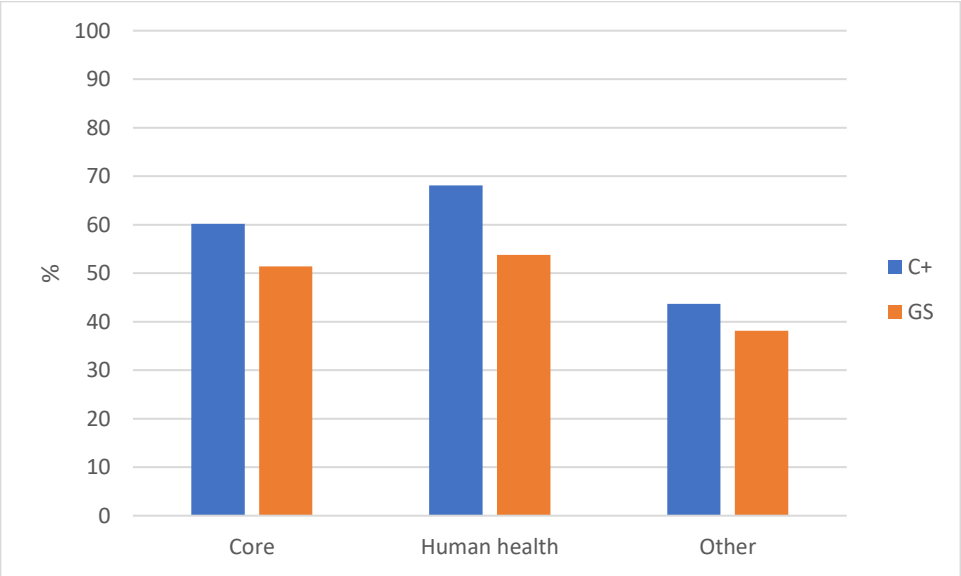


[35] The modification is that the score for the particular indicator being considered is deducted from the implementation score, in this case the score for the national action plan.

31 One issue that is commonly referred to is that many national action plans are not budgeted or funded.[36] A commonly cited figure is that around only one in five countries had identified funding sources.[37] On one level, given that many countries model their national action plan on the GAP, this is unsurprising given that there is no budget for the GAP and no funding sources are explicitly identified (see paragraph 144). It seems that the data for this assertion comes from TrACSS reporting. Over the four rounds of TrACSS, only those countries scoring the highest level (E) were considered to have identified funding sources. To qualify as level E, other criteria also needed to be met. For all rounds, these criteria included being implemented and having monitoring in place. From round 2, the criteria also included having relevant sectors involved and having an evaluation process in place. It is not clear but presumably if a country had a national action plan in place, with funding sources identified, but lacking one or more of these criteria, it would not be possible to respond E on this question. This might mean that data from this source may underestimate the number of NAPs with funding sources identified. In addition, in the 4th round, criterion D was modified so it was no longer sufficient to have an operational plan for the NAP but that operational plan had to be budgeted. According to 2019/20 TrACSS data, one fifth (27 of 136, 20%) of countries responding had national action plans that were classified as level E, that is they had funding sources identified, were being implemented and had relevant sectors involved with a defined M&E process in place. It should be noted that this figure had increased from 4% (6 of 151) in 2016/17. In addition, a further 40% (55 of 136) of countries responding had national action plans that were classified as level D, that is they were approved by government, reflected GAP objectives, had a budgeted operational plan and had monitoring arrangements. This means that, in 2019/20, well over half the countries (82 of 136, 60%) reporting to TrACSS reported a national action plan that either had a budgeted operational plan or had funding sources identified. This compared to less than one fifth (29 of 151, 19%) in 2016/17.[38]

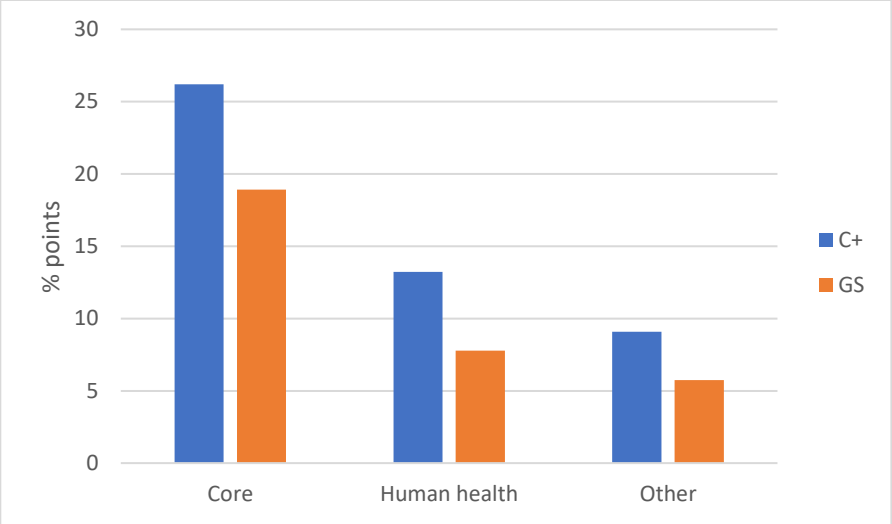
32 Finally, in this section, Figure 13 shows that the mean implementation scores are higher for indicators of human health (C+ 68%; GS 54%) than for other areas (C+ 44%; GS 38%). Figure 14 shows similar levels of change in indicators of human health and other areas.[39] The gap is not narrowing and, if anything, is potentially widening.

Figure 13: Mean implementation scores for core indicators, indicators related to human health and other indicators



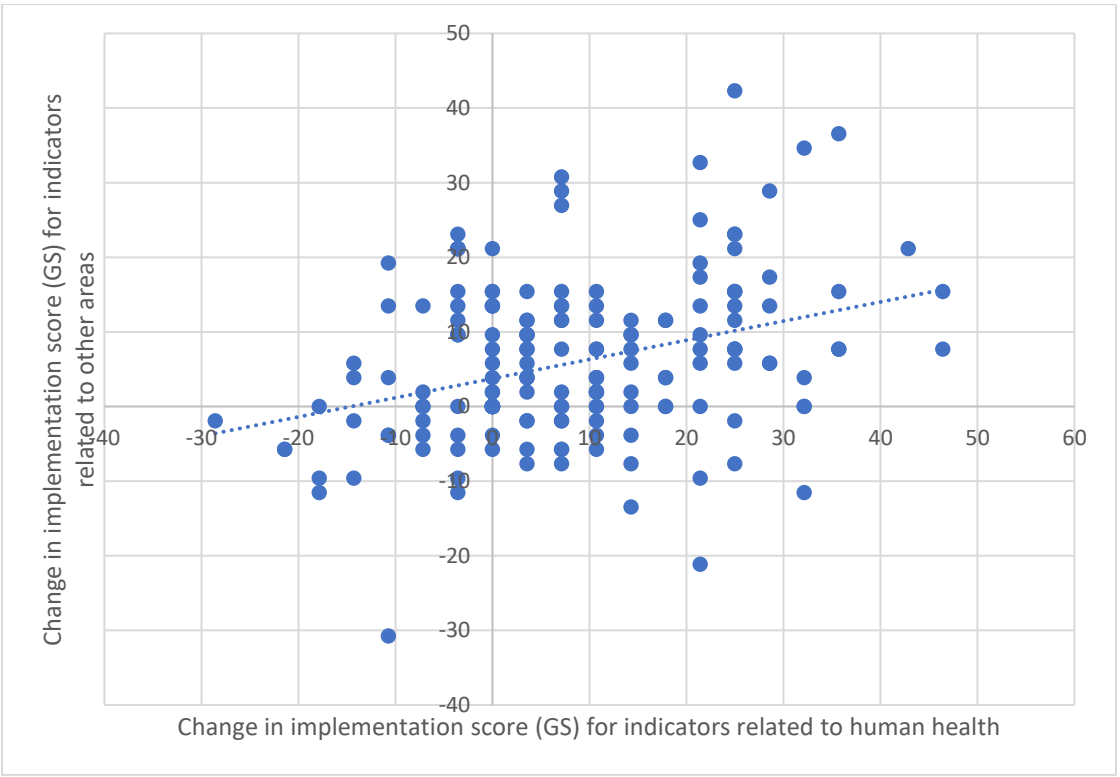
[36] See https://www.thelancet.com/action/showPdf?pii=S2666-7762%2821%2900138-1 (accessed 21 July 2021).
[37] See https://www.ignitetheidea.org/whoeb-amrbriefing (accessed 21 July 2021).
[38] And the criteria for that year just required an operational plan to achieve level D, it did not need to be budgeted.
[39] As noted before, the biggest change is in core indicators, i.e. relating to national action plans and multisectoral coordination mechanisms

Figure 14: Change in mean implementation scores for core indicators, indicators related to human health and other indicators between baseline and performance data



33 Figure 15 compares improvements on implementation scores related to human health indicators and indicators in other areas. There is a statistically significant positive association (p<.001), that is countries that improve their score on human health are also improving their score on other elements of health.[40] This variation was used as one of the selection criteria for which WHO Country Offices to interview (see Annex 4).

Figure 15: Change in mean implementation scores for indicators of human health compared to change in mean implementation scores for indicators in other areas



34 Box 2 briefly summarizes the main findings from this section concerning GAP implementation overall.

[40] Although there are exceptions.

Box 2: Review findings concerning overall GAP implementation

Calculating an overall implementation score based on country TrACSS reports is useful and shows:

- A statistical association between performance and country income level. However, there are exceptions and some possible explanations as to why a country might perform better than expected from income level are considered in Figure 16.
- Improvement in performance level during the period of GAP implementation is not associated with country income level. There have been particular improvements in some regions, e.g. SEAR, and some of the biggest improvements have been seen in low- and middle-income countries.
- The biggest areas of improvement have been in core indicators related to developing national action plans and establishing multisectoral coordination mechanisms. There has been little, if any, improvement in some areas, e.g. infection prevention and control.
- Reported strengths of a country's national action plan and multisectoral coordination mechanism are both associated with levels of performance in relation to AMR. Countries that have improved their national action plan or multisectoral coordination mechanism have also improved other areas of their AMR performance.
- In general performance in relation to human health is stronger than in other areas of health. During the period of the GAP, there is little evidence of greater improvement in other areas of health than in human health and it is possible that the gap is widening. However, where countries have improved in relation to human health there has often been similar improvement in other areas.

35 Based largely on input from WHO Country Offices, Figure 16 seeks to identify why it is that certain countries may be doing better in terms of responding to AMR than might be expected based on their income level. It is worth recognising first that because TrACSS data is self-reported, there will be a few cases where higher scores do not reflect higher levels of performance but rather reflect more positive reporting. Possible ways to verify TrACSS data include:

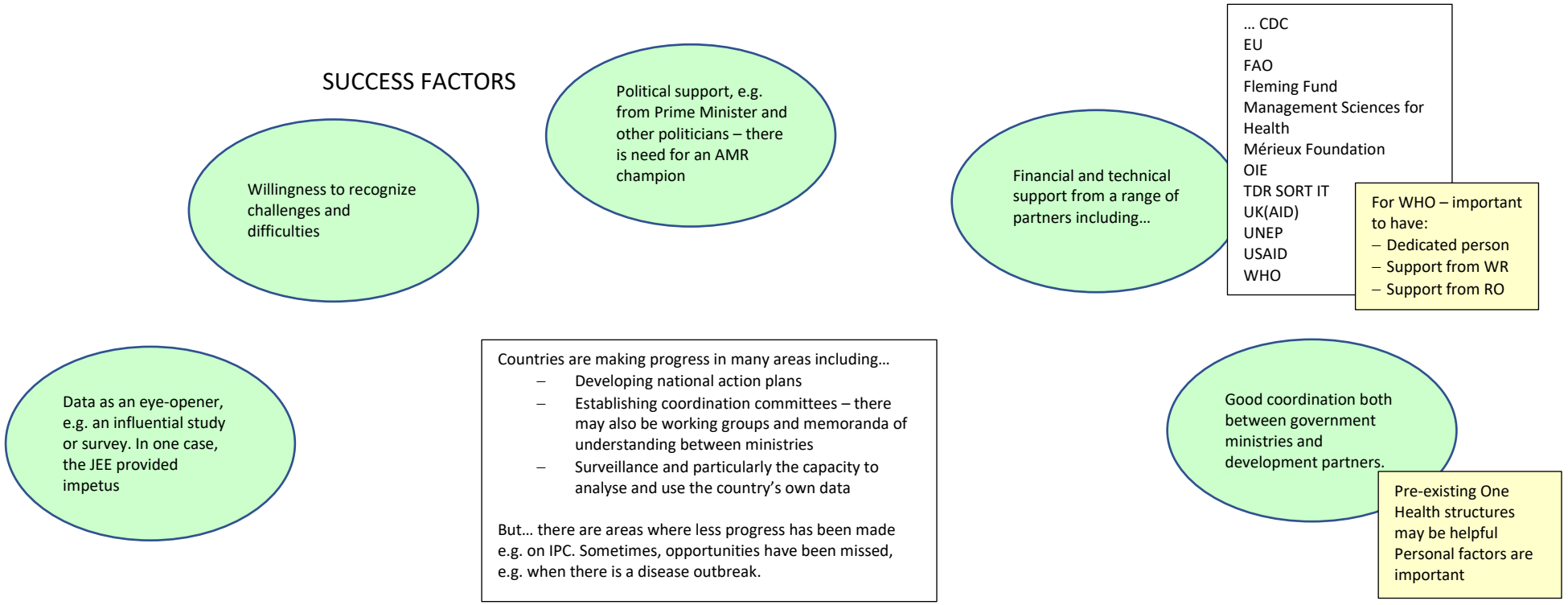
- Through other data sources, such as joint external evaluations. The review conducted statistical analysis across all countries in which a JEE could be identified. There was a statistically significant positive correlation ($p<.001$) between both (i) the overall score on JEE and (ii) the JEE score on AMR and the performance score on GAP AMR based on TrACSS data. For more details, see Annex 4.
- By understanding the processes used to generate TrACSS reports. Where those processes are inclusive and consultative, the findings are more likely to be robust
- Through the views of other stakeholders, such as civil society and development partners

36 Nevertheless, there are many examples of countries that are performing better on AMR than would be expected given the country's income level. The central square box of Figure 16 shows areas where many of those countries have made progress (national action plans; coordination mechanisms; surveillance) but also shows that there may be other areas where opportunities may have been missed and less progress made, e.g. on infection prevention and control.

37 Several WHO Country Offices were able to identify specific pieces of data which had served as a type of "*eye opener*" in terms of how bad AMR was as a problem in a particular country. These might be from a particular study or survey. In one case, a Joint External Evaluation was considered to have given particular impetus to a country. Linked to this was the willingness to recognize where there were challenges and difficulties, and then seek to address them. Political support, e.g. from the Prime Minister and other politicians was recognized as important as was the role of AMR champions. There was recognition that many countries had needed external financial and technical support for the progress they had made, and that this had come from a range of sources not just WHO. In terms of WHO being able to provide support, respondents recognised the need to have a staff member for whom AMR was their job (or part of it) and who received support from the WR and the Regional Office. Finally, there was recognition of the importance of good coordination between different actors including government ministries and development partners. Where they exist, pre-existing One Health structures may be helpful, and respondents recognised the important of personal or inter-personal factors.

38 Despite apparent progress that these countries may have made, there were concerns that some of the progress might be fragile and it could be undermined if there were changes in circumstance (see examples in Figure 16). There were some doubts as to whether progress on processes would be reflected in improved outcomes.

Figure 16: Factors that may enable a country to improve its performance on AMR regardless of income level



Has the WHO Secretariat contributed to progress and achievements of Member States?

39 The review considered whether having a WHO Country Cooperation Strategy (CCS) or Biennial Collaborative Agreement (BCA) that mentioned AMR was associated with a country's performance score or improvement in performance score (see Table 3). The calculations presented compare overall performance scores[41] and improvement in that score with whether a country has a CCS or BCA that mentions AMR, the number of CCSs or BCAs that mention AMR and the proportion of CCSs or BCAs that mention AMR. There is a statistically significant association between having a CCS or BCA which mentions AMR and overall performance score on GAP AMR and (to a lesser degree) improvement in GAP AMR performance score. While this is seen among all countries that mention AMR in their CCS or BCAs, the association is stronger if the number or proportion of CCSs or BCAs that mention AMR is taken onto account.

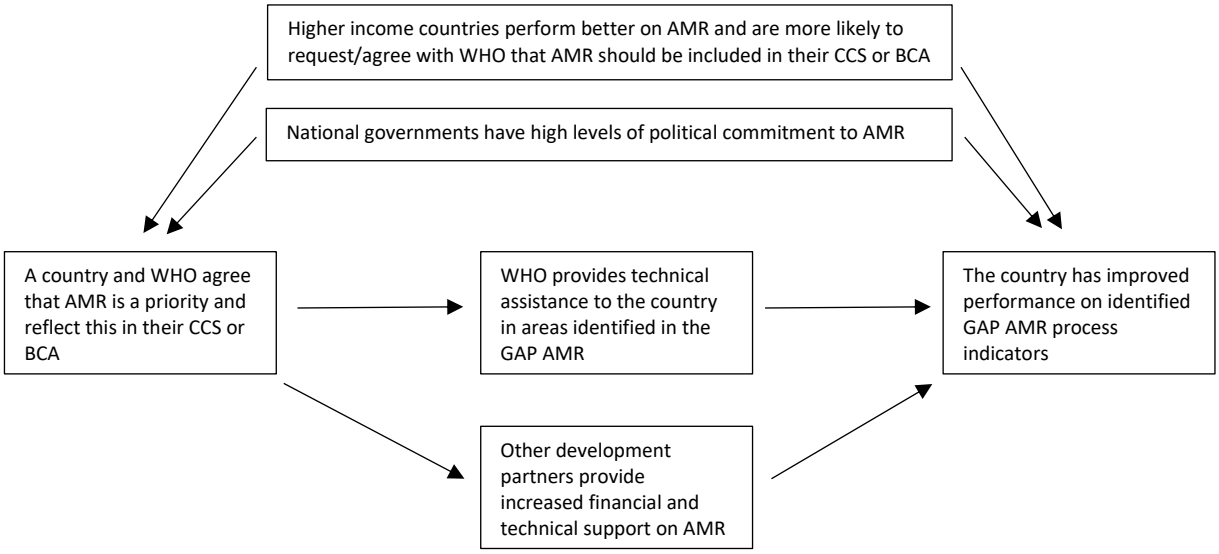
Table 3: Is performance score and improvement in performance score on GAP AMR associated with having a CCS or BCA that mentions AMR?

	Having a CCS/BCA that mentions AMR	Number of CCSs/BCAs that mentions AMR	Proportion of CCSs/BCAs that mention AMR
GAP AMR performance score (GS method)	*p<.001*	*p<.001*	*p<.001*
Improvement in GAP AMR performance score (GS method)	*p=.03*	*p=.004*	*p=.02*
Country income level	*p=.002*	*p=.01*	*P<.001*

40 This does not establish causality. One possible explanation is that WHO technical support, provided on the basis of the CCS, is contributing to countries' performance on GAP AMR. It is clear that WHO has provided considerable technical support to countries on AMR and this review report presents qualitative evidence of this throughout. However, there could be other explanations. There could be common causal factors affecting both GAP AMR performance and whether or not a CCS/BCA mentions AMR, for example, country income level. The review has shown (see paragraphs 25-26, p9) that GAP AMR performance is statistically associated with country income level and there is a similar association between whether or not a CCS or BCA mentions AMR and country income level. However, there is no association between change in GAP AMR performance and country income level. So, while country income level might explain the link between a CCS or BCA mentioning AMR and overall performance on GAP AMR, it is unlikely to explain the link with change in performance on GAP AMR. However, there could be another unrecognized factor that is affecting both performance on GAP AMR and whether a CCS or BCA mentions AMR. For example, if a country government had strong political commitment to AMR, it might be more likely that progress would be made on AMR and that the government would wish for AMR to be included in the CCS or BCA. Also, it is possible that there could be causal factors other than WHO technical assistance. If, for example, other development partners were more likely to provide financial and technical assistance to a country on AMR if both the national government and WHO recognized AMR as a priority in the country, it could be this additional financial and technical support that is contributing to improved performance on GAP AMR. These possible causal mechanisms are illustrated in Figure 17.

[41] Using the GS method.

Figure 17: Possible causal mechanisms explaining the association between whether a CCS or BCA mentions AMR and a country's performance on GAP AMR



41 On balance, it seems likely that causality in this case is multifactorial and that the exact balance of causality probably varies from country to country. However, this finding along with the qualitative findings of this review suggest that WHO technical support provided to countries on the basis of an agreed CCS or BCA may contribute to the country's performance on GAP AMR

3.2 Objective 1: Improve awareness and understanding of antimicrobial resistance through effective communication, education and training

42 This objective appears to have two desired outcomes (improved awareness of AMR and improved understanding of AMR) and three means for achieving those (effective communication, effective education and effective training). These three means are specified in more detail:

- *Communication* means public communication programmes that target different audiences in human health, animal health and agricultural practice as well as consumers.
- *Education* means including the use of antimicrobial agents and resistance in school curricula.
- *Training* means making antimicrobial resistance a core component of professional education, training, certification, continuing education and development in the health and veterinary sectors and agricultural practice.

43 However, these elements are not presented as an overall theory of change explaining how these different elements might be expected to contribute to improved awareness and understanding of AMR and how this improved awareness and understanding might be expected to contribute to the expected overall goal of the GAP, namely to ensure, for as long as possible, continuity of successful treatment and prevention of infectious diseases with effective and safe medicines that are quality-assured, used in a responsible way, and accessible to all who need them. It appears that this objective hypothesizes that if the general public, school students and relevant professionals are more aware of AMR and understand it, certain changes would occur which would contribute to the goal expressed above. What are those changes? Are there underlying assumptions that need to be in place for those expected changes to happen?

44 These matters are not clearly explained in the GAP and it is apparent from documents and discussion with stakeholders that there are very different understandings of them. For example, in 2019, the IACG[42] recognized that this GAP objective was key to secure political commitment and to further the implementation of NAPs, overall contributing to achieving impact against antimicrobial resistance. However, the GAP is not explicit that raising awareness and understanding is intended to secure political commitment and increase the implementation of national action plans. Also, there are some actions in the GAP's framework for action for this objective, e.g. promoting and supporting the establishment of multisectoral coalitions to address AMR, which do not immediately seem to fit into the means and outcomes explained above. There has been a great deal of discussion over whether there should be a shift away from a focus on awareness and knowledge to a focus on behaviour change and this term is reflected in the statement of outcome for this objective in the M&E framework, even though the term is not mentioned explicitly in the GAP. The IACG identified supporting behaviour change as one of the five components needed to improve strategic communication on AMR. Respondents also pointed to behaviour change as key to conducting targeted and useful campaigns, and adapting materials developed to help the implementation of objective 1 to specific audiences and resource settings. For example, research on targeted campaigns for children and youth would be helpful in designing behaviour change and communication campaigns for this specific group. WHO held two AMR Behaviour Change Expert consultations in 2017[43] and 2018,[44] with the participation of civil society and academia representatives, which resulted in a series of recommended next steps. There are also some examples of programmes working with communities on AMR.[45] However, some respondents are concerned that an

[42] See https://www.who.int/antimicrobial-resistance/interagency-coordination-group/IACG_final_report_EN.pdf?ua=1 (accessed 16 April 2021).
[43] Antimicrobial Resistance Behaviour Change First informal technical consultation, 6-7 November, 2017, Geneva Meeting Report. https://www.who.int/antimicrobial-resistance/AMR-Behaviour-Change-Consultation-Report_6-and-7-Nov-2017.pdf?ua=1 (accessed 18 May 2021)
[44] Antimicrobial Resistance Behaviour Change Second informal technical consultation 6-7 June 2018, Geneva Meeting Report, https://www.who.int/antimicrobial-resistance/Second-Behaviour-Change-Expert-Consultation-Meeting-Report-June-2018.pdf (accessed 18 May 2021)
[45] Mathew P (2021) *Working with Communities to Stimulate AMR Action* a presentation as part of a civil society meeting attended by the review team.

excessive focus on individual behaviour and change of that behaviour may inadvertently blame poor and excluded people for actions that are affected by underlying structural and economic factors. For example, people living in informal settlements may lack access to clean water, toilets and formal health care services. As a result, they may get sick frequently and may then buy antibiotics from informal sources. Should the focus be on changing their behaviour or on addressing the social and economic determinants of that behaviour?

45 Some stakeholders expressed concern that, in the absence of a theory of change for this objective, it was difficult to assess whether the activities being conducted were being (the most) effective. For example, the worldwide celebration of World Antibiotic Awareness Week was widely-praised but concern was expressed that the expected outcome(s) of hosting these events is/(are) not described. A recent study which looked at World Antibiotic Awareness Weeks from 2015 to 2020 using Google Trends Analysis suggested that these weeks "*did little to improve the public awareness of AMR in… selected countries*[46]*…*"[47] Additionally, there are concerns that World Antibiotic Awareness Week celebrations may be held mostly in capital cities greatly reducing the proportion of the population reached. However, other stakeholders acknowledge that World Antibiotic Awareness Week served as a useful focal point and that materials produced for that could be used at other times and in other locations.

46 It is also worth noting that the M&E framework restates this objective in terms of the following outcome – improved awareness of AMR and behaviour change among policy-makers, farmers, veterinary and health workers, food industry and the general public.[48]

47 The M&E framework identifies "*awareness of key groups*" as the outcome indicator for this objective. However, this indicator is little more than a title as the relevant metadata/indicator description in Annex 3 of the M&E framework is largely blank with a commitment that a methodology will be published at a later (unspecified) stage. This is also potentially a compound indicator as it covers multiple key groups.[49] Also, the indicator description does not specify what type of knowledge, understanding, awareness or behaviour would be measured. The M&E framework states that *"… while improved public awareness and understanding are vital, the costs of tracking progress against this outcome in a meaningful way at the global level are considered disproportionately challenging at this stage."* It is unclear why the M&E framework would include indicators that it is considered not feasible to measure.

48 There have been some attempts to collect relevant outcome data, but these attempts have been rather sporadic and fragmented. In 2015, WHO published the results of a public awareness survey conducted in 12 countries.[50] Box 3 summarizes some of the indicators/metrics that were included in that survey. WHO has been working with London School of Hygiene and Tropical Medicine to conduct a survey of healthcare workers' awareness of antibiotic resistance.[51]

[46] Japan, the United Kingdom and the United States.
[47] See https://doi.org/10.1016/j.ijid.2021.08.018 (accessed 30 August 2021).
[48] This differs from the objective in the GAP in that it refers to behaviour change rather than understanding and it mentions some additional stakeholder groups – policy-makers, farmers, food industry and does not highlight school children.
[49] The framework specifies human and animal workers, prescribers, farmers and food processing workers but these appear to be examples and not a definitive list. A definitive list would be needed if this indicator is/these indicators are to be tracked.
[50] See http://apps.who.int/iris/bitstream/handle/10665/194460/9789241509817_eng.pdf;jsessionid=A4957D2EB7734E11619FB45C202CD61D?sequence=1) (accessed 21 July 2021).
[51] See WHO (undated) *Antibiotic Resistance (ABR) Healthcare Workers Awareness Survey: Concept Note*. This concept note specifically references objective 1 of the GAP but notes that awareness-raising activities, such as participating in the World Antibiotic Awareness Week, do not always correlate to acquired knowledge. The concept note also refers to data from the survey being used to report against outcome 1 of the M&E framework. The concept note (Appendix 1) contains 23 agree/disagree statements for healthcare workers to respond to. There is also a separate tool entitled *Antibiotic Resistance Awareness Survey for Health Care Workers.* This contains the 23 statements mentioned above plus some introductory questions.

Box 3: Indicators/metrics included in WHO 2015 antibiotic resistance multi-country public awareness survey

Age (group)

Percentage of respondents having taken antibiotics in (i) the past month (ii) in the past two months

Place where respondents get their antibiotics (doctor or nurse; pharmacy or medical store)

Percentage of respondent who think it is acceptable to use antibiotics that were given to a friend or family member, as long as they were used to treat the same illness

Percentage of respondents who think it is acceptable to buy the same antibiotic, or request these from a doctor, if they are sick and antibiotics helped then get better when they had the same symptoms before

Percentage of respondents who think that they should stop taking antibiotics when they feel better

Percentage of respondents who think the following conditions can be treated with antibiotics – (i) bladder/urinary tract infection; (ii) skin/wound infections; (iii) colds and flu

Percentage of respondents who identified that the following actions could (help) address the problem of AMR – (i) regular handwashing; (ii) only using antibiotics when prescribed

Percentage of respondents who reported that there is not much that people like them can do to stop antibiotic resistance

Percentage of respondents who believe (i) that many infections are becoming increasingly resistant to treatment by antibiotics; (ii) that antibiotic resistance occurs when their body becomes resistant to antibiotics; (iii) that antibiotic resistance is only a problem for people who take antibiotics regularly

49 The M&E framework has two output indicators for this objective. One relates to strengthened veterinary services.[52] The other is entitled targeted awareness raising and relates to nationwide, government-supported AMR awareness campaign targeting priority stakeholder group(s) in six sectors.[53] The data source for these is TrACSS.[54] In addition, TrACSS has questions about training and professional education on AMR in (i) the human health sector; (ii) the veterinary sector; and (iii) other sectors.[55] However, these questions do not seem to translate into indicators in the M&E framework.[56]

50 Table 4 summarizes the implementation scores for six output indicators[57] under objective 1. The strongest performance is seen in relation to the two indicators pertaining to human health and the biggest improvement is seen in one of these – awareness and understanding of AMR risks and response (human health). The weakest performance and least improvement are seen in relation to the indicator on training and professional education on AMR in farming sector, food production, food safety and the environment.[58]

Table 4: Implementation scores for output indicators within objective 1
Colour coding for scores – amber 0-40; yellow 41-60; light green 61-80; dark green >80; for change – amber 0-10; yellow 11-20; light green >21

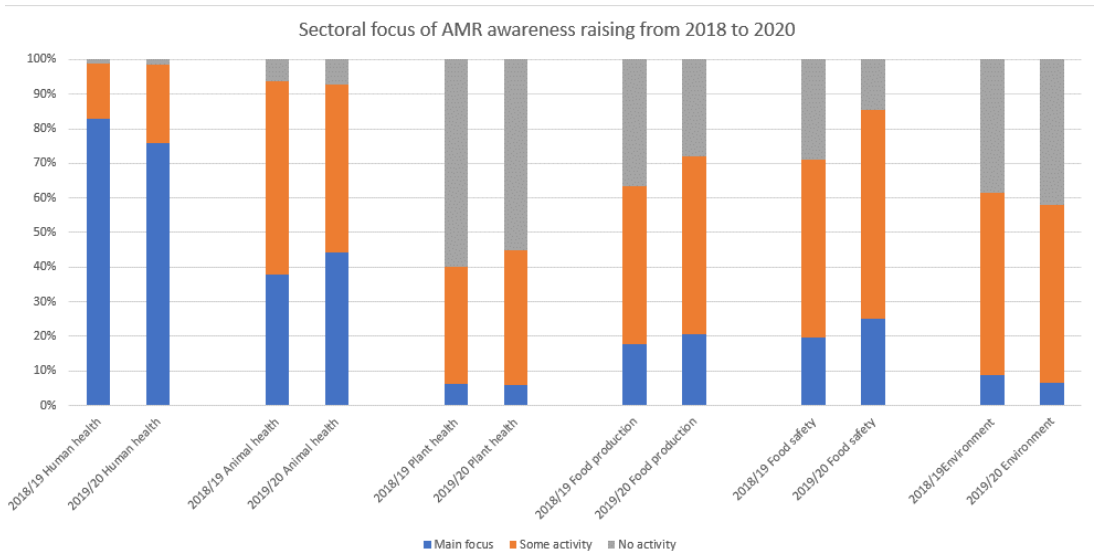
Indicator	Baseline		Performance		Change	
	GS	C+	GS	C+	GS	C+
Awareness and understanding of AMR risks and response (human health)	43	49	55	78	12	28
Awareness and understanding of AMR risks and response (animal health, plant health, food production, food safety and environment)	29	29	31	47	3	17
Training and professional education on AMR in the human health sector	43	60	48	71	5	11
Training and professional education on AMR in the veterinary sector	32	33	39	50	7	17
Training and professional education on AMR in farming sector, food production, food safety and the environment	17	16	19	19	2	3
Progress with strengthening veterinary services	34	39	41	52	7	13

[52] The data source for this is the OIE Performance of Veterinary Services. This indicator is not considered further in this review. However, there is a question in TrACSS on progress with strengthening veterinary services and this has been considered by the review.
[53] Human health, animal health, plant health, food production, food safety and environment.
[54] In the first two rounds of TrACSS, there were separate questions on human health and other aspects of health. In the first round, those other aspects covered animal health and food production. In the second round, these were expanded to include plant health, food safety and environment. In rounds three and four, these two questions were combined with supplementary questions about whether the six sectors specified were main focus, some activity or no activity. In round 3, WASH was specified as part of environment and, in round 4, as part of human health.
[55] Farming, food production, food safety and the environment. This question has only been in TrACSS since round 2.
[56] They do, however, reflect a specified area of activity in the GAP AMR. The same is not true of whether or not AMR is included in school curricula. This is stated in the GAP but is not reflected in the TrACSS questionnaire or the M&E framework.
[57] These are referred to as output indicators as these reflect what TrACSS measured. They do not exactly correspond to the indicators in the M&E framework.
[58] One possible explanation for this is that this question was only introduced in the second round of TrACSS meaning that baselines may be later for this indicator than for others. However, this is unlikely to be the whole explanation and, while it could be a factor in levels of change observed, it would not explain lower levels of overall performance.

51 By way of example, Figure 18 shows data[59] for awareness and understanding of AMR risks and response (human health). This shows that average score varies by country income group and by region. Improvements have occurred in all country income groups and across all regions, particularly SEAR. Figure 19 shows that while human health remained the main focus of AMR awareness raising in many countries from 2018 to 2020, the number of countries making animal health a main focus rose as did the number of countries focusing on other areas including plant health, food production and food safety (but not environment).

Figure 18: Implementation scores (using GS method) for awareness and understanding of AMR risks and response (human health)

Figure 19: Percentage of countries reporting different levels of focus on a particular sector in AMR awareness raising activities: 2018/19-2019/20



[59] Using the GS method.

52 Respondents noted that while some countries have included education and/or pre- and in-service training in AMR in their NAPs, only a limited number of countries have begun implementing or implemented these elements in their national plans. Political commitment and multi-sector financing and collaboration[60] are necessary conditions to ensure the translation of this objective into country-level changes. However, limited national financial resources and a reported limited understanding of the actual steps to be taken to implement objective 1 remain a barrier to its implementation.

53 The WHO Secretariat has contributed to this objective by supporting the implementation of AMR-related events globally, developing guidance and toolkits for countries, and consistently raising the importance of addressing AMR in high-level political settings.[61] Box 4 briefly summarizes the WHO Secretariat's contributions to this objective.

Box 4: WHO Secretariat contributions to the GAP AMR Objective 1 – improve awareness and understanding of antimicrobial resistance through effective communication, education and training

The WHO Secretariat successfully worked to raise AMR as a priority in the global health agenda and has contributed strongly to building momentum for AMR among high-level political and health settings. The WHO Secretariat played a leading role in building momentum and securing political buy-in during the process of developing the GAP by convening meetings and consultations between Member States and other international partners. The GAP, now a reference document for key actors in AMR, helped raise awareness and set an agenda for policy-makers and international organizations.

WHO, in just over five years, has successfully established itself as a leading global organization on AMR. AMR is now a recurring theme in high-level political meetings related to health, including the G7 and G20. The WHO Secretariat also helped maintain momentum around AMR by providing progress reports to governing bodies, including the WHO Executive Board, the World Health Assembly and the United Nations General Assembly. WHO also reports on this objective through reports based on TrACCS data. However, such reports have not been produced after each round of TrACSS reporting.

The WHO Secretariat has helped raise awareness of AMR by supporting countries to run communication campaigns and programmes. World Antibiotic Awareness Week has provided a focal point for awareness-raising activities and has been held annually, in November, since 2015. In 2019, 122 countries celebrated World Antibiotic Awareness Week, supported by the Tripartite organizations, to raise awareness through the dissemination of materials, guidelines and multimedia communications. The WHO Secretariat transformed the world awareness week away from just antibiotics to include all antimicrobials. This broadened its scope and engaged those working in other areas, such as HIV, TB etc., in spreading awareness about drug resistance. WHO and FAO also initiated the regional "*Smartphone for Change*" campaign. in WHO's Eastern Mediterranean region, to empower key national actors to promote a rational use of antibiotics.

The WHO Secretariat has developed targeted guidance documents, toolkits and training materials, including a competency framework and a curricula guide for health workers, to help countries in the training and education of health workers. Some countries have integrated education and/or pre- and in-service training in AMR into their national action plans, recognizing that inclusion in a plan does not necessarily mean that this education is taking place.

3.3 Objective 2: Strengthen the knowledge and evidence base through surveillance and research

54 This objective appears to have two desired outcomes (strengthened knowledge base and strengthened evidence base) and two means for achieving those (surveillance and research). The GAP emphasizes the importance of knowledge of benefit and cost-effectiveness of actions and investments to tackle AMR. It also identified a number of gaps in knowledge which needed to be addressed including a number of specific research gaps.

55 Respondents identified that there had been considerable focus on AMR surveillance since the GAP was approved. Indeed, many commented that this was the objective of GAP where there had been most focus and progress. Clearly, one of the major initiatives under this objective has been the development and expansion of the Global Antimicrobial Resistance and Use Surveillance System (GLASS). Details of this have been discussed in the methodology section of this report (see Annex 4), given the importance of GLASS as a major data source for the review. Elements covered there include the objectives of GLASS, country enrolment rates,

[60] United Nations General Assembly, High-Level Interactive Dialogue on Antimicrobial Resistance Summary, 29 April 2021, https://www.un.org/pga/75/wp-content/uploads/sites/100/2021/06/PGA-letter-Summary-of-High-Level-Interactive-Dialogue-on-Antimicrobial-Resistance-AMR.pdf, (accessed 5 May 2021)

[61] For example, the G7 Health Ministers' Meeting - see https://www.gov.uk/government/publications/g7-health-ministers-meeting-june-2021-communique/g7-health-ministers-meeting-communique-oxford-4-june-2021 (accessed 10 June 2021) – and the G20 Health Ministers' Meeting on Fighting Antimicrobial Resistance – see https://www.oecd.org/germany/g20-health-ministers-meeting-fighting-antimicrobial-resistance.htm (accessed 10 June 2021).

modules, reports, data types, ability to generate outcome data, the recent review of GLASS and identified strengths and weaknesses.

56 However, respondents expressed concern that, in practice, while surveillance had been given strong emphasis, there had been much less emphasis on research under this objective. Indeed, there is concern that some consider research to be covered under objective 5 of the GAP and that it is limited to product research and development. Some have described this by saying that *current research in AMR is inequitably focused on new drug development*".[62] Excluding research from this objective is not in line with the fact that the GAP identified research gaps under this objective and mandated the WHO Secretariat to "*consult Member States and other multisectoral stakeholders for the development of a global public health research agenda for filling major gaps in knowledge on antimicrobial resistance.*" It does not appear that the Secretariat has done this but, in June 2021, a group of academics published an interdisciplinary consensus on key priorities for research in relation to optimising antimicrobial use in humans.[62] [63] It identifies four main research themes – policy and strategic planning; medicines management and prescribing systems; technology to optimise prescribing; and context, culture and behaviours. It also identifies three crosscutting issues – public engagement,[64] capacity building and the impact of the COVID-19 pandemic. The paper also identifies three broad roles from a research policy perspective – technical,[65] financial and foresight. The WHO Secretariat also report that work is beginning, staff are engaged and there is a work programme on the human and One Health aspects. Specifically, both departments within the AMR Division are addressing the need for evidence generation. GCP is developing a One Health research agenda with tripartite partners, and SPC is developing a Human Health operational/implementation research agenda to support evidence generation at country level for the introduction and evaluation of (new) tools and interventions activities under national action plans. The Control and Response Strategies Unit is tasked with research and related policy development.

57 Respondents also raised some concerns about barriers and obstacles to effective national AMR surveillance. The first of these relates to the need to strengthen national laboratory and diagnostic capacity,[66] an issue which received little emphasis in the GAP. This capacity is needed both for surveillance purposes[67] and also for effective clinical management. However, many countries face critical capacity issues, for example, some do not have adequate water or electricity supplies needed for functional laboratories (see paragraph 136). Additionally, respondents pointed to gaps in laboratory staff capacity at country-level, including limited skills for testing, detection and diagnosis and laboratory personnel with limited training (see paragraph 138).[68] Respondents noted that the use of different protocols for surveillance by some regional offices or donor programmes has created issues in harmonizing data, systems and tools for donor reporting and for analysis purposes. At country-level, there are challenges in linking and integrating antimicrobial resistance, usage and consumption surveillance data from the human and animal sectors. Reported issues in data sharing and collaboration constitute barriers to a One Health approach to AMR surveillance.

58 The M&E framework does not identify any additional outcome indicators for objective 2 beyond those already developed for the goal level (see Annex 4 and paragraph 21, p6). The M&E framework identifies nine output indicators for this objective and TrACSS is identified as the relevant data source for some of them. However,

[62] See Charani et al, 2021 *Optimising Antimicrobial Use in Humans – Review of Current Evidence and an Interdisciplinary Consensus on Key Priorities for Research* – available on https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(21)00138-1/fulltext#%20 (accessed 21 July 2021).
[63] It is recognized that this does not cover the entire GAP but part of one objective (#4).
[64] And concerns that existing communication and engagement initiatives often leave behind the most vulnerable and those at the most negative risks of AMR.
[65] While previously this role was largely fulfilled mainly by WHO, including through regional offices, the paper identifies that regional and other organizations are now playing such a role also and that the role of developing international norms and standards might in future fall to the most relevant agency with an interest in One Health rather than only to WHO.
[66] This issue is considered in more detail in this report's section on health systems.
[67] Iskandar et al (2021) *Surveillance of Antimicrobial Resistance in Low- and Middle-Income Countries: A Scattered Picture* available on https://doi.org/10.1186/s13756-021-00931-w (accessed 22 July 2021)
[68] The Fleming Fund focuses some of its grant activities on establishing laboratory capacity for AMR surveillance. Some of the Fund's activities include: development of Standard Operating Procedures and protocols for laboratories, quality management systems, laboratory refurbishments, biosecurity and biosafety, data systems and coordination. More information can be found at https://www.flemingfund.org/our-approach/our-activities/ (accessed 8 July 2021)

it is difficult to reconcile what the M&E framework says should be available from TrACSS and what is available.[69] Table 5 seeks to compare what the M&E framework expects to be available from TrACSS and what is available.

Table 5: Data source for output indicators for outcome 2: Expectations of M&E framework compared to what is available from TrACSS

Indicator number	Description	Data source specified in M&E framework	Is data available from TrACSS?[70]	Data used in calculating performance scores for this review?
2a	Data on AMR and AMU in humans	GLASS[71]	Yes from Q7.1 (consumption and use) and 7.4 (AMR)	Yes from TrACSS but data from GLASS is also cited in this report
2b	Data on AMU in animals	OIE AMU database	Yes from Q7.2	Yes from TrACSS
2c	Data reporting on AMU in animals	OIE AMU database		
2d	Data on AMU in plants	TrACSS	Yes from Q7.3	Yes
2e	Food and agriculture AMR laboratory network	ATLASS reports/TrACSS	Yes from 7.7a-d – this question was only included from round 3	No
2f	AMR surveillance data in animals and food	TrACSS	Yes – 7.5a/b for animals and 7.5c/d for plants	Yes from 7.5a for animals and 7.5c for plants
2g	Prevalence of ESBL-producing indicator E coli in animals	TrACSS	Yes – from the fourth part of 7.5b – from round 3	No
2h	Use of AMR surveillance data	TrACSS	Yes – from round 4 only	No
2i	Authority and capability of veterinary services to manage AMU and AMR	OIE PVS pathway	No	No

59 This is perhaps one of the areas where the TrACSS questionnaire has changed the most with multiplication of questions, variation of scoring systems[72] and contingent questions.[73] To maximize simplicity and consistency over rounds, the review included in the performance score questions on whether a country had a surveillance system for (i) AMR and (ii) AMC/AMU in three sectors – humans, animals and plants, i.e. six questions/ indicators overall.

60 Table 6 summarizes the implementation scores for these six output indicators. The strongest performance is seen in relation to national surveillance systems for AMR in humans but achievement of a national monitoring system for consumption and rational use of antimicrobials in human health is lagging behind this and the gap is not closing although this may change now that GLASS is using its AMC module. Based on TrACSS data, the weakest performing area relates to national monitoring systems for antimicrobial use in plant production, but this area improved more than some other areas including national monitoring systems for consumption and rational use of antimicrobials in human health and national surveillance systems for AMR in food (animal and plant origin).

Table 6: Implementation scores for output indicators within objective 2
Colour coding for scores – amber 0-40; yellow 41-60; light green 61-80; dark green >80; for change – amber 0-10; yellow 11-20; light green >21

Indicator	Baseline		Performance		Change	
	GS	C+	GS	C+	GS	C+
National monitoring system for consumption and rational use of antimicrobials in human health	34	41	41	47	7	6
National monitoring system for antimicrobials intended to be used in animals	29	33	39	51	10	18
National monitoring system for antimicrobial use in plant production	13	18	22	33	9	15
National surveillance system for AMR in humans	44	53	53	67	9	14
National surveillance system for AMR in animals	33	38	43	55	11	18
National surveillance system for AMR in food (animal and plant origin)	37	53	40	60	3	7

[69] One particular challenge is that the M&E framework gives TrACSS question numbers but these have changed over time. It appears that the framework is referring to question numbers in the 2019/20 questionnaire.
[70] Note that all TrACSS question numbers cited here are for 2019/20 except if explicitly stated
[71] Data on this is available, particularly for AMR. The module on antimicrobial consumption is newer and fewer countries are reporting currently but information on that number is available.
[72] Q7.3 is scored on an A-D scale.
[73] Which the respondent only answers if they answer an earlier question in a particular way.

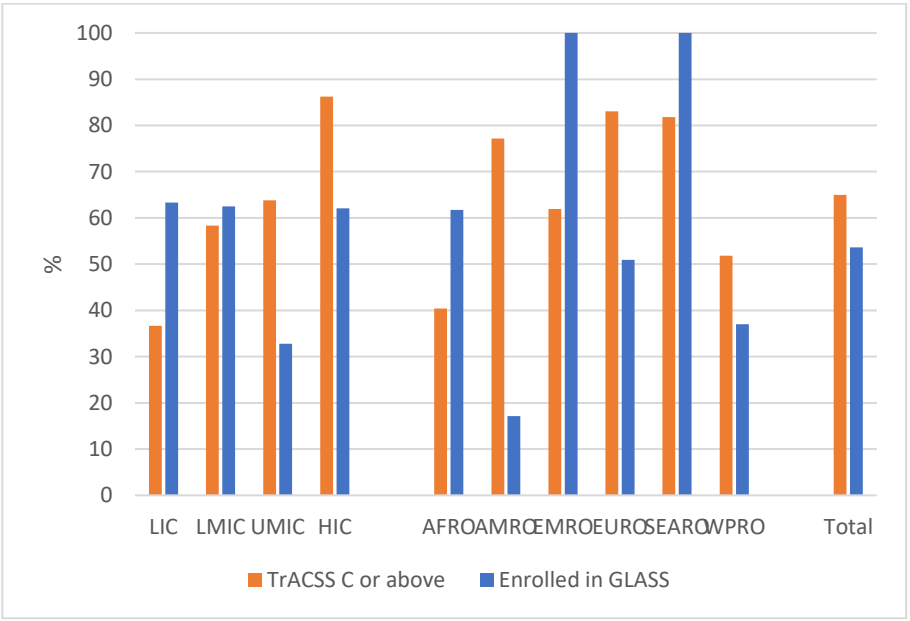
61 One question that arises is whether it is possible to compare figures on national surveillance systems for AMR between GLASS and TrACSS. This is difficult as they are not measuring the same thing. The data from GLASS relates to how many countries are enrolled in GLASS whereas TrACSS data relates to national self-assessment of surveillance systems. The review compared the number of countries enrolled in GLASS at any given point (see Annex 4) with the number of countries that scored their response to TrACSS on the national surveillance system for AMR in humans as C or higher.[74] Table 7 presents this analysis. This shows that the number of countries reporting to TrACSS that they have a national surveillance system has been consistently higher than the numbers enrolled in GLASS but the gap is narrowing as the numbers enrolled in GLASS rise and the number reporting a national AMR surveillance system to TrACSS plateaus.

Table 7: Number of countries enrolled in and reporting to GLASS: 2016-2019 compared to number of countries reporting having a national surveillance system to TrACSS

	2016	2016/17	2017	2017/18	2018	2018/19	2019	2020
Enrolled in GLASS AMR	31	42	51	69	71	82	88	94
Reporting C+ to TrACSS		82		105		107		101

62 It is also possible to compare data reported to TrACSS with number of countries enrolled in GLASS regionally and across income levels. Figure 20 compares these figures for all WHO Member States based on latest report to TrACSS and current GLASS enrolment status as reported to the review team by the WHO Secretariat. Overall, there are slightly more Member States that report having a national surveillance system for AMR in humans to TrACSS (C or higher) than are enrolled in GLASS (126 as compared to 104). But, this pattern is reversed in low-income and lower-middle-income countries where more countries are enrolled in GLASS than report having national surveillance systems for AMR in humans to TrACSS. Across the regions, more Member States are enrolled in GLASS than report having national surveillance systems for AMR in humans to TrACSS in AFR, EMR and SEAR. But, this pattern is reversed in EUR, WPR and particularly in AMR.

Figure 20: Comparison of latest report to TrACSS on AMR surveillance in humans and latest figures for enrolment in GLASS for all WHO Member States (n=194) by country income level, WHO region and overall



63 Figure 21 shows the percentage of WHO Member States that reported a particular level (A-E) for their AMR surveillance system in humans in their last TrACSS report that are currently enrolled in GLASS. Unsurprisingly, there is a positive correlation. While only one third of Member States (4 of 12, 33%) that reported that they

[74] The definition of criterion C changed slightly between rounds 2 and 3 of TrACSS. The changes were dropping the words are in place, changing pathogens to infections, dropping the requirement to link patient information with susceptibility testing and adding the need to follow national standards. Common features were national surveillance activities with a national reference laboratory that participates in external quality assurance.

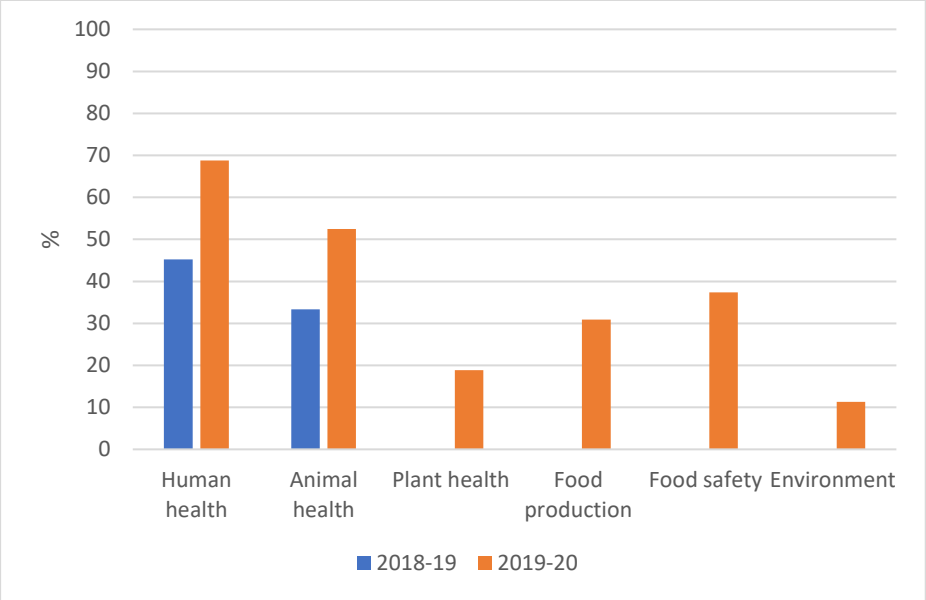
had no capacity for generating data and reporting on antibiotic resistance (level A) are enrolled in GLASS, this figure is three quarters for those Member States (15 of 20, 75%) that reported that the national AMR surveillance system integrates surveillance of AMR across sectors and generates regular reports covering at least one common indicator (level E). The enrolment of countries in GLASS that report not having a national AMR surveillance system in humans represents a development opportunity but provides a cautionary note on the likely quality of surveillance data reported through GLASS, at least from those countries.[75] In addition, the fact that less than two thirds of Member States (76 of 126, 60%), that reported having a national AMR surveillance system for humans (level C or above) in their last TrACSS report, are currently enrolled in GLASS represents a missed opportunity to collect AMR surveillance data.[76] Of those countries that reported the highest level of capacity to TrACSS, only three quarters (15 of 20) are enrolled in TrACSS.

Figure 21: Percentage of WHO Member States (n=187) that reported a particular level of national surveillance system for AMR in humans in their last TrACSS report that are enrolled in GLASS

64 One concern raised by respondents is whether countries are using surveillance data for national decision-making. TrACSS did ask questions about this in 2018/19 and 2019/20.[77] Figure 22 shows that, in 2019/20, surveillance data was reportedly most used nationally in relation to human health (88 of 128, 69%) and least in relation to plant health (20 of 106, 19%) and the environment (12 of 106, 11%). Rates of reported use of surveillance data nationally increased from 2018/19 to 2019/20 for both human and animal health.[78] Countries that reported to TrACSS that they had a national AMR surveillance system for humans were more likely (75 of 126, 60%) to use surveillance data nationally than those that did not (13 of 61, 21%). The same was true for those that were enrolled in GLASS (53 of 104, 51% as compared to 35 of 104, 39%). However, the difference is less marked for those enrolled in GLASS[79] and almost half of countries enrolled in GLASS did not report using AMC/AMU/AMR surveillance data to amend national strategy and/or to inform decision making nationally in 2019/20.

[75] It is also possible that those countries may be underestimating their surveillance capacity and/or that that capacity improved since they last reported to TrACSS. There are three countries enrolled in GLASS that did not report to any of the four rounds of TrACSS.
[76] It is possible that some of these countries are overestimating their surveillance capacity but this seems unlikely to be so in all cases.
[77] In 2018/19, the question (7.6) related to whether a multi-sectoral working group of coordination committee in charge of national AMR strategy reviews data on antimicrobial consumption and resistance in human and animal sectors at least annually, considers implications for and amends national strategy accordingly. It was possible to answer this question yes or no for each of human and animal health. In 2019/20, the question (7.6) was modified to read "*is the country using relevant antimicrobial consumption/use and/or antimicrobial resistance data to amend national strategy and/or to inform decision making, at least annually?*" If the response was yes, the respondent was asked to identify for which sector from the following – human health including WASH, animal health (terrestrial and aquatic), plant health, food production, food safety and environment.
[78] Although the questions changed between the two years.
[79] As compared to those reporting having a national AMR surveillance system for humans to TrACSS.

Figure 22: Percentage of Member States responding to a particular question on TrACSS that reported that AMC/AMU/AMR surveillance data is used at national level by sector: 2018/19 and 2019/20



65 By way of example, Figure 23 shows data (using the GS method) for national monitoring system for consumption and rational use of antimicrobials in human health. This shows that average score varies by country income group and by region, with performance levels highest in EUR and lowest in AFR. Improvements have occurred in all country income groups and across all regions, particularly EMR and SEAR.

66 The WHO Secretariat has contributed to this objective particularly through establishing and expanding GLASS which has supported many countries to strengthen their national AMR surveillance systems for human health. Box 5 briefly summarizes the WHO Secretariat's contributions to this objective.

Figure 23: Implementation scores (using GS method) for national monitoring system for consumption and rational use of antimicrobials in human health

Box 5: WHO Secretariat contributions to the GAP AMR Objective 2 - Strengthen the knowledge and evidence base through surveillance and research

Through collaborative efforts, the WHO Secretariat successfully launched GLASS in 2015. The number of countries enrolled in and reporting to the system has increased annually (see Table 7). The system has been a key incentive for countries to strengthen their national surveillance system, increase their laboratory capacity and build staff capacity to collect and report data.

The WHO Secretariat has developed a standardized approach for the collection, reporting and publication of GLASS data. The WHO Secretariat has also progressively included new modules. The WHO Secretariat is also promoting whole genome sequencing and providing guidance notes for molecular diagnostic methods.

The WHO Secretariat has published several guidance documents to guide countries in surveillance methods, data collection and monitoring the use of antimicrobials. Some examples of guidance documents include the GLASS guidance for national reference laboratories, a technical note on whole-genome sequencing for AMR surveillance, the GLASS methodology for surveillance of national antimicrobial consumption, a guide for national surveillance systems for monitoring antimicrobial consumption in hospitals, and a methodology to estimate attributable mortality of antimicrobial resistant bloodstream infections.

The WHO Secretariat has provided technical support to help countries strengthening their national surveillance systems and report to GLASS. For instance, the WHO Secretariat provides guidance for national focal points and/or ministries of health to complete the GLASS implementation questionnaire including a guide for countries to detect and report colistin resistance, a guide to uploading aggregated antimicrobial resistance data and a guide to the enrolment for antimicrobial resistance national focal points. The Secretariat provided on-site and remote workshops, trainings, webinars and protocols on surveillance, data collection and reporting at the regional and national levels.

The WHO AMR Surveillance and Quality Assessment Collaborating Centres Network (WHO AMR CC Network) and technical partners have also provided training for national AMR surveillance.

WHO Regional Offices have played an essential role in providing technical support to countries and ensuring they can report to GLASS. Examples of this include but are not limited to: training of national focal points in all regions; technical assessments; mapping of national laboratory capacity; the integration of antifungal and antibacterial resistance data into the Health Information Platform for the Americas (PLISA) by AMRO/PAHO; participation in the Central Asian and European Surveillance of Antimicrobial Resistance network (CAESAR) by EURO; the Tricycle Project in selected countries supported by AFRO, EMRO SEARO and WPRO.

Since 2018, WHO has been working with FAO and OIE to establish a Tripartite Integrated Surveillance System for AMR (TISSA) and integrate AMR data from the human, animal, food, plant and environment sectors. TISSA was approved as a global project by the MPTF in 2020, with WHO as the lead agency and a proposed budget of US$660,702.

3.4 Objective 3: Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures

67 This objective appears to have one desired outcome (reduced incidence of infection) and three means for achieving that (sanitation, hygiene and infection prevention). The GAP emphasizes the importance of preventing infections in health care settings and also through sex and drug injection. It also emphasizes that better sanitation, hand washing, food and water safety, and vaccination are also core components of infectious disease prevention. Vaccination of animals is also promoted as a way of preventing infection and the need for antibiotics to prevent infection.

68 One issue under this objective is that measures for infection prevention and control are much broader than AMR only as they address all aspects of pathogen transmission in community and healthcare settings. This presents an opportunity because initiatives taken to prevent a particular infection may have benefits on preventing or reducing AMR. An example of this has been steps taken to prevent and control COVID-19 and those are discussed later in this report.

69 However, this same issue may bring its own challenges. Infection prevention and control may be seen as not being specific to AMR so this objective may receive less emphasis than other objectives of the GAP AMR. There is a risk that infection prevention and control may be seen as everyone's responsibility so that it ends up not being owned by programmes focused on specific diseases or issues, such as AMR. There is also a risk that some of the issues, such as sanitation and hygiene, may be seen as being so huge that they may consume entire AMR programmes and budgets. According to respondents, many countries address IPC as part of the International Health Regulations (IHR) Preparedness agenda[80] and do not fully associate infection prevention and control with AMR. The breadth and cross-cutting nature of both AMR and IPC are challenging for countries to implement and integrate as they both include a wide variety of workstreams and sectors.

70 In addition, IPC remains affected by a lack of infrastructure and limited resources, both human and financial, to implement and monitor infection prevention and control measures in some low-income settings. The O'Neill report[81] states that improving unsanitary living environments would slow down the spread of antibiotic resistance. For example, the report estimates that universal access to improved water and sanitation would decrease prescription for antibiotics to treat diarrhoeal illness by 60%. Some respondents pointed to the lack of water as a barrier to hand hygiene in health care facilities, as well as overall weak sanitation services. In 2019, WHO reported that, out of 115 participating countries in the UN-WATER Global Analysis and Assessment of Sanitation and Drinking-Water, 75% reported the existence of financing plans for WASH but more than half of these plans were insufficiently implemented.[82]

71 Overall, there is concern about limited progress being made on water and sanitation globally. In 2021, the United Nations reported that the world is not on track to achieve SDG 6: Water and sanitation for all.[83] While some indicators, including access to safely managed drinking water services and handwashing facilities with soap and water at home, showed some progress compared to the 2015 baseline data, the report highlights stark regional differences in water stress levels, safe treatment of household wastewater and unsustainable usage practices. These differences in access to water and sanitation levels are underlined by weak political will, insufficient financial resources and limited cross-sectoral cooperation.

[80] World Health Organization (2019) *WHO Benchmarks for International Health Regulations (IHR) Capacities* available on https://apps.who.int/iris/bitstream/handle/10665/311158/9789241515429-eng.pdf?sequence=1 (accessed 23 July 2021).
[81] O'Neill J. (chair) (2016) *Tackling Drug-Resistant Infections Globally: Final Report and Recommendations* available on https://amr-review.org/sites/default/files/160525_Final%20paper_with%20cover.pdf (accessed 13 July 2021).
[82] World Health Organization (2019) *National Systems to Support Drinking-Water, Sanitation and Hygiene: Global Status Report 2019. UN-Water Global Analysis and Assessment of Sanitation and Drinking-Water (GLAAS) 2019 Report, p. 25* available on https://www.who.int/teams/environment-climate-change-and-health/water-sanitation-and-health/monitoring-and-evidence/wash-systems-monitoring/un-water-global-analysis-and-assessment-of-sanitation-and-drinking-water/2018-2019-cycle (accessed 14 July 2021).
[83] See https://www.unwater.org/publications/summary-progress-update-2021-sdg-6-water-and-sanitation-for-all/ (accessed 13 July 2021).

72 The M&E framework identifies five numbered outcome indicators for this objective but, when compound elements are considered, there are a total of nine or more outcome indicators for this objective. However, it does not appear that any of these are being actively tracked or used by the AMR Division.

73 The first outcome indicator relates to the incidence of surgical site infections following inpatient surgical procedures. This is one particular type of healthcare-acquired infections and focusing on this may overlook others, such as respiratory, urinary tract and gastrointestinal infections. While the indicator metadata provides access to guidance and protocols on surgical site infections, how to prevent healthcare associated infections,[84] including surgical site infections[85] [86] and how to conduct surveillance of surgical site infections,[87] [88] [89] it does not provide access to any data sets with the exception of some data from European countries on surgical site infections.[90]

74 The second indicator relates to immunization coverage with four vaccines.[91] Some of the links provided as references are no longer active,[92] potentially provide contradictory information[93] or are very generic.[94]

75 The third and fourth indicators relate to the proportion of the population using safely managed drinking-water services and sanitation services respectively. The M&E framework does provide a link to data on these[95] and data is also available from the SDG indicator website.[96]

76 The fifth indicator relates to environmental standards and is in two parts. The first part is the number of state parties to international multilateral environmental agreements on hazardous waste and other chemicals that meet their commitments and obligations in transmitting information as required by each relevant agreement. While the metadata for this indicator in the M&E framework links to relevant SDG metadata,[97] it does not link to data even though this is available.[98] The second part of this indicator is hazardous waste generated per capita and proportion of hazardous waste treated, by type of treatment. The metadata in the M&E framework for this indicator is largely blank. Although this is an SDG indicator (12.4.2), it is broken down into many different sub-types. More detail may be needed as to which is relevant.

77 In summary, it is difficult to see how the outcome indicators for this objective, are being or could be used to assess outcomes achieved under this objective. Relevant data is available in some areas (e.g. water, sanitation, environment and immunization) but how would this be used? Some stakeholders indicate that healthcare associated infections are particularly important in the context of AMR but it is unclear if data on the level of these is available, beyond possibly a few high-income countries in Europe.

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[84] See http://apps.who.int/iris/bitstream/handle/10665/251730/9789241549929-eng.pdf?sequence=1 (accessed 26 July 2021)
[85] See http://apps.who.int/iris/bitstream/handle/10665/250680/9789241549882-eng.pdf?sequence=8 (accessed 26 July 2021)
[86] See https://www.ecdc.europa.eu/en/publications-data/directory-guidance-prevention-and-control/healthcare-associated-infections-0 (accessed 26 July 2021)
[87] However, the first link provided entitled "*Protocol for surgical site infection surveillance with a focus on settings with limited resources*" does not work since the WHO site was revamped.
[88] See https://www.cdc.gov/nhsn/pdfs/pscmanual/9pscssicurrent.pdf (accessed 26 July 2021).
[89] See https://www.ecdc.europa.eu/en/publications-data/surveillance-surgical-site-infections-and-prevention-indicators-european (accessed 26 July 2021)
[90] See https://www.ecdc.europa.eu/en/all-topics-z/surgical-site-infections/surveillance-and-disease-data/disease-data-ecdc-surveillance (accessed 26 July 2021). Data is available for 14 European countries up to 2017. An epidemiological report for 2017 is available – see https://www.ecdc.europa.eu/sites/default/files/documents/AER_for_2017-SSI.pdf (accessed 26 July 2021).
[91] For pneumococcus, rotavirus, measles (including in combination with mumps and rubella) and Haemophilus Influenzae type B.
[92] For example, the Global Reference List of 100 Core Health Indicators 2018 and the WHO/UNICEF coverage estimates (methods and data).
[93] For example, the immunization indicator recommended in the publication *Monitoring Maternal Newborn and Child Health: Understanding Key Progress Indicators* – see http://apps.who.int/iris/bitstream/handle/10665/44770/9789241502818_eng.pdf?sequence=1 (accessed 26 July 2021) is for diphtheria, tetanus and pertussis and this is not mentioned in the M&E framework for GAP AMR. Similarly, the World Health Statistics report for 2017 – see http://apps.who.int/iris/bitstream/handle/10665/255336/9789241565486-eng.pdf?sequence=1 (accessed 26 July 2021) contains data for diphtheria, tetanus and pertussis and hepatitis B immunizations, not those mentioned in the GAP AMR M&E framework.
[94] For example, links to the SDG indicator website – see https://unstats.un.org/sdgs (accessed 26 July 2021) and the UNICEF data hub which seems to be mainly focused on COVID-19 – see https://data.unicef.org/ (accessed 26 July 2021).
[95] See https://washdata.org/ (accessed 26 July 2021).
[96] For indicators 6.1.1 and 6.2.1 (a) from https://unstats.un.org/sdgs/indicators/database/ (accessed 26 July 2021).
[97] See https://unstats.un.org/sdgs/metadata/?Text=&Goal=12&Target=12.4#foreword (accessed 26 July 2021).
[98] For indicator 12.4.1 – see https://unstats.un.org/sdgs/indicators/database/ (accessed 26 July 2021).

78 The M&E framework identifies seven output indicators for this objective and one of these[99] identifies TrACSS as a secondary data source.[100] However, the data provided from TrACSS seems to differ from what is specified in the M&E framework. Questions in TrACSS ask about infection prevention and control in human health care and good management and hygiene practices to reduce the development and transmission of AMR in animal production and food processing.[101]

79 The WHO Secretariat has carried out some analysis of TrACSS responses on the first of these questions[102] although this analysis has not yet been formally published. This shows that:

- There was a significant positive association between income level and the IPC implementation status.
- There was no significant improvement of IPC across the years except in some high-income countries.

80 Analysis carried out for this review confirms these findings and is briefly summarized here. Table 8 summarizes the implementation scores for three output indicators[103] under objective 3. The strongest performance is seen in relation to infection prevention control in human health but there has been little, if any, improvement in this indicator, or other indicators under this objective, since the GAP AMR was adopted.

Table 8: Implementation scores for output indicators within objective 3
Colour coding for scores – amber 0-40; yellow 41-60; light green 61-80; dark green >80; for change – amber 0-10; yellow 11-20; light green >21

Indicator	Baseline		Performance		Change	
	GS	C+	GS	C+	GS	C+
Infection prevention control in human health care	47	61	49	61	2	0
Good health, management and hygiene practices to reduce the use of antimicrobials and minimize development and transmission of AMR in animal production	29	31	35	33	6	2
Good management and hygiene practices to reduce the development and transmission of AMR in food processing	32	38	36	44	5	6

81 By way of example, Figure 24 shows data (using the GS method) for infection prevention control in human health care. This shows that average score varies by country income group and by region, with performance levels highest in high-income countries and in EUR. Change has been mixed with marked improvement reported in WPR and setbacks in some country income groups and regions, such as AMR, EMR and particularly SEAR.

82 The WHO Secretariat has contributed to this objective by developing normative guidance[104] on IPC, conducting global campaigns[105] and establishing an infection prevention and control global unit within the Secretariat. WHO has worked with FAO and OIE to establish linkages between IPC, WASH, AMR and related environmental components.[106] Box 6 briefly summarizes the WHO Secretariat's contributions to this objective.

[99] Indicator 3a – regulation for AM waste. However, the main data source for this is identified as FAOLEX.
[100] The other output indicators are as follows – 3b access to strengthened veterinary services (with data from OIE PVS pathway); 3c food safety standards (metadata not yet developed); 3d infection prevention at national level (in animal health with data from OIE PVS pathway); 3e hand hygiene in health care (with data from the WHO Hand Hygiene Self-Assessment Framework, and the WHO Infection Prevention and Control Assessment Framework); 3f basic water services in health care facilities; and 3g basic sanitation services in health care facilities (with data from WHO/UNICEF Joint Monitoring Programme for Water Supply, Sanitation and Hygiene).
[101] In the first two rounds of TrACSS, these two elements were combined but in rounds three and four they were separated out.
[102] In relation to human health care.
[103] Based on TrACSS questions.
[104] See World Health Organization (2016) *Guidelines on Core Components of Infection Prevention and Control Programmes at the National and Acute Health Care Facility Level* available on https://www.who.int/gpsc/core-components.pdf (accessed 15 July 2021), World Health Organization (2019) *Minimum Requirements for Infection Prevention and Control Programmes* available on https://www.who.int/publications/i/item/9789241516945 (accessed 15 July 2021) and World Health Organization (2018) *Global Guidelines for the Prevention of Surgical Site Infection* available on https://apps.who.int/iris/handle/10665/277399 (accessed 15 July 2021).
[105] See World Health Organization (2020) *Hand Hygiene for All Initiative: Improving Access and Behaviour in Health Care Facilities* available on https://www.who.int/publications/i/item/9789240011618 (accessed 13 July 2021) and World Health Organization Undated) *Save Lives: Clean Your Hands WHO's Global Annual Campaign Advocacy Toolkit* available on https://www.who.int/docs/default-source/save-lives---clean-your-hands/5may-advocacy-toolkit.pdf?sfvrsn=8301e563_2 (accessed 13 July 2021).
[106] See World Health Organization, Food and Agriculture Organization and World Organisation for Animal Health (2020) *Technical Brief on Water, Sanitation, Hygiene (WASH) and Wastewater Management to Prevent Infections and Reduce the Spread of Antimicrobial Resistance (AMR)* available on https://www.who.int/publications/i/item/9789240006416 (accessed 17 July 2021).

Figure 24: Implementation scores (using GS method) for infection prevention control in human health care

Box 6: WHO Secretariat contributions to the GAP AMR Objective 3 - Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures

WHO has published guidance documents and tools directly aimed at reducing AMR spread through strengthened IPC measures and practices, including guidelines for the prevention and control of carbapenem-resistant Enterobacteriaceae, *Acinetobacter baumannii* and *Pseudomonas aeruginosa* in healthcare facilities and the implementation manual of the WHO recommendations on prevention and control of carbapenem-resistant organisms.

The IPC and AMR divisions also collaborated to publish a list of core competencies for infection prevention and control professionals in 2020. The WHO Secretariat also developed an IPC training package focused on reducing the spread of infections resistant to antimicrobials, a student handbook, a protocol for surgical site infection surveillance with a focus on settings with limited resources and several surgical site infection prevention tools.

In partnership with UNICEF, WHO has conducted the "*Save Lives: Clean your Hands*" campaign to reduce health care-associated infections (HCAIs) since 2010 and disseminated posters, toolkits and other communication materials to raise awareness on hand hygiene. The WHO Secretariat published several resources to guide the implementation of hand washing measures including the hand hygiene for all initiative: improving access and behaviour in health care facilities, an education session for trainers, observers and health workers on hand hygiene and brochures.

In 2017-2018, WHO launched a global survey to assess the progress made and remaining gaps in IPC programmes in 88 countries. The results collected from this survey have helped inform decision-making on IPC guidelines and implementation and helped address the lack of monitoring of IPC measures worldwide. WHO continues to contribute to the Joint Monitoring Programme with UNICEF to provide global data on WASH practices and coverage.

WHO has worked with other agencies and countries to integrate IPC elements with AMR, WASH, and environment components. Across the three levels, the WHO Secretariat provides technical support to national governments to strengthen these components in national action plans as part of a broader One Health approach.

The WHO Secretariat has drawn further attention to the linkages between WASH and AMR in its Water, Sanitation and Hygiene Strategy 2018-2025.

As part of its Immunization Agenda 2030, the WHO Secretariat outlined the role of vaccines in reducing the spread of AMR through the development of new vaccines that contribute to the prevention and control of infections.

The WHO Secretariat has worked with partners, including UNICEF, to emphasize the linkages between weak WASH and IPC measures in health care facilities with the spread of AMR by integrating antimicrobial resistance in WASH technical documents[107]**Error! Bookmark not defined.** and activities[108].

The AMR Division has also worked towards more formal links with the IPC and WASH departments by establishing cross-cutting workstreams and regular meetings. The teams also work on developing common methodological approaches and objectives.

[107] See World Health Organization (2019) *Water, Sanitation and Hygiene in Health Care Facilities: Practical Steps to Achieve Universal Access* available on https://www.who.int/publications/i/item/9789241515511 (accessed 16 June 2021) and World Health Organization (2021) Guidelines on Recreational Water Quality: Volume 1: Coastal and Fresh Waters available on https://www.who.int/publications/i/item/9789240031302 (accessed 12 July 2021).
[108] See https://www.who.int/initiatives/hand-hygiene-for-all-global-initiative (accessed 6 July 2021).

3.5 Objective 4: Optimize the use of antimicrobial medicines in human and animal health

83 This objective appears to have two desired outcomes (optimized use of antimicrobial medicines in human health and optimized use of antimicrobial medicines in animal health). Unlike other objectives, the means of reaching these objectives is not specified in the statement of objective. The broader statement in the GAP briefly describes the ways in which antibiotics are over-used globally. Issues identified as needing emphasis include data on antibiotic use in humans; strengthened regulation of distribution, quality and use of antimicrobial medicines; patient and health care provider compliance; availability of substandard medicines (for both human and veterinary use); inappropriate or unregulated use of antimicrobial agents in agriculture; effective, rapid, low-cost diagnostic tools; and evidence-based prescribing and dispensing.

84 Respondents expressed concern that while there had been a great deal of focus on appropriate antimicrobial use in humans and animals there had been a lesser degree of focus on food, plants and the environment. Some noted that this potentially reflected how the objective was worded with only human and animal health specified. The IACG report[109] pointed to limited understanding of the links between food production and AMR, sub-optimal access to preventive measures, and overuse and availability of antimicrobial agents to treat bacteria and fungi as leading drivers for the use of antibiotics in animals and plants. Despite the guidance and tools developed by WHO[110], FAO[111] and OIE,[112] some respondents noted the need for increased Tripartite collaboration to address the underlying barriers to the optimal use of antibiotics in humans, animals, plants and the environment through a holistic approach.[113]

85 Although there have been considerable efforts, including by WHO, to guide the prescription of antibiotics and to support national regulatory authorities, respondents noted that the implementation of recommended guidance to optimize the use of antibiotics is challenged by structural barriers, particularly in low- and middle-income countries. Such barriers include weak national regulatory authorities, which may be underfunded or understaffed and may lack mechanisms to ensure independence.[114] In such cases, there may be regulations or policies in place requiring a prescription for antibiotics but there may be limited enforcement of regulations, availability of over-the-counter antibiotics and continued circulation of falsified or substandard medical products. There may also be other capacity-related barriers. For example, some respondents noted that capacity for laboratory testing and diagnostics is needed to deliver accurate diagnosis and to guide prescription for treatment (see paragraph 136). Some respondents also said that understanding drivers of behaviours, including of prescribers, can lead to more targeted guidelines and communications.

86 Limited availability of data on antimicrobial consumption and use may also be a barrier to optimizing the use of antimicrobials. It is difficult to optimize something when information on what is currently happening is

[109] Interagency Coordination Group on Antimicrobial Resistance (2018) Reduce Unintentional Exposure and the Need for Antimicrobials, and Optimize their Use p.5 available on https://www.who.int/antimicrobial-resistance/interagency-coordination-group/IACG_Optimize_use_of_antimicrobials_120718.pdf (accessed 11 June 2021).

[110] For example, World Health Organization Regional Office for Europe (2020) *Food Safety and the Fight against Antimicrobial Resistance* available on https://apps.who.int/iris/bitstream/handle/10665/337525/WHO-EURO-2020-1631-41382-56388-eng.pdf (accessed 12 July 2021) and World Health Organization (2017) *WHO Guidelines on Use of Medically Important Antimicrobials in Food-Producing Animals* available on https://apps.who.int/iris/handle/10665/258970 (accessed 16 June 2021).

[111] For example, Food and Agriculture Organization of the United Nations (2005) *Code of Practice to Minimize and Contain Antimicrobial Resistance* available on http://www.fao.org/fao-who-codexalimentarius/thematic-areas/antimicrobial-resistance/en/ (accessed 16 June 2021), Food and Agriculture Organization of the United Nations (2011) *Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance* available on http://www.fao.org/input/download/standards/11776/CXG_077e.pdf (accessed 27 July 2021) and Food and Agriculture Organization of the United Nations (2005) *FAO Responsible Use of Antibiotics in Aquaculture* available on http://www.fao.org/3/a-a0282e.pdf (accessed 16 June 2021).

[112] For example, World Organisation for Animal Health (2019) *OIE List of Antimicrobial Agents of Veterinary Importance* available on https://www.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/AMR/A_OIE_List_antimicrobials_July2019.pdf (accessed 22 June 2021) and World Organisation for Animal Health (2016) *The OIE Strategy on Antimicrobial Resistance and the Prudent Use of Antimicrobials* available on https://www.oie.int/fileadmin/Home/eng/Media_Center/docs/pdf/PortailAMR/EN_OIE-AMRstrategy.pdf (accessed 22 June 2021).

[113] As of April 2021, the Ad hoc Codex Intergovernmental Task Force on Antimicrobial Resistance, comprising FAO and WHO, is revising the *Code of Practice to Minimize and Contain Foodborne Antimicrobial Resistance* and is developing guidelines on integrated monitoring and surveillance of antimicrobial resistance.

[114] World Bank (2019) *Pulling Together to Beat Superbugs: Knowledge and Implementation Gaps in Addressing Antimicrobial Resistance* available on https://documents1.worldbank.org/curated/en/430051570735014540/pdf/Pulling-Together-to-Beat-Superbugs-Knowledge-and-Implementation-Gaps-in-Addressing-Antimicrobial-Resistance.pdf (accessed 12 July 2021).

absent or patchy. Respondents commented that while efforts are being made to monitor antibiotic consumption and use, these efforts are still in their early stages. The IACG noted[115] that "*data on antimicrobial consumption in low- and middle-income countries are sparse, patchy and usually aggregated at national level with little or no information on the place of use (for example, public or private sector; hospital or community level facilities).*" However, the review team have not found data on antimicrobial consumption and use to be particularly available at national level either. The issue of non-availability of antimicrobial consumption and use data at all levels emphasizes the interlinked nature of objectives 2 and 4 of the GAP AMR. Improving the availability of data on antimicrobial consumption and use is likely to require close collaboration between those working on these two objectives. Within the WHO Secretariat at global level, this may create some challenges as the two objectives are managed by different departments within the AMR Division.

87 Respondents recognized that, in developing the GAP AMR, there had been a tension between the need to recognize that, in some contexts, antimicrobial medicines were being used excessively while, in others, there might be difficulties in accessing antimicrobial medicines when their use was justified. Such access difficulties might include when someone could not access formal health services because of non-availability, distance or cost or the antimicrobial medicines needed were out-of-stock at the time needed. Civil society respondents explained that there had also been supply problems for the 40 million people requiring benzathine penicillin for rheumatic heart disease prophylaxis and that price issues had restricted access to liposomal amphotericin B for mucomycosis. There is recognition that appropriate or optimal use of antimicrobial medicines needs to tackle both these extremes of "*excess*" and "*access*". However, some respondents were concerned that the GAP AMR seems to place more emphasis on the issue of inappropriate overuse than on that of access to antibiotics when needed. They are concerned that this might hinder the ability to reduce the spread of AMR as they consider that expanding and regulating access to antibiotics by licensed individuals and understanding the reasons behind low access would help reduce AMR, notably by limiting treatment failure and the increase of resistance in patients.

88 A key concern raised by many respondents was the use of antibiotics, particularly those of critical importance for human health, in animal growth promotion and crop protection. Respondents recognized that restricting these could have commercial implications for those involved and, as a result, measures to restrict these practices were often strongly resisted. They expressed concern that the wording of the GAP AMR means that, while there is a commitment to phasing out the use of antibiotics for animal growth promotion and crop protection, the caveat of "*in the absence of risk analysis*" provides a significant loophole.

89 The GAP AMR referred[116] to the need to ensure that use of new products is governed by a public health framework of stewardship that conserves the effectiveness and longevity of such products and this was reflected in the resolution adopting the GAP AMR.[117] In 2016, options for a framework were submitted to the World Health Assembly.[118] Also, in 2016, the political declaration of the UN General Assembly high-level meeting on AMR[119] called for WHO, FAO and OIE to finalize a global development and stewardship framework on antimicrobial medicines and resistance. In their report to the World Health Assembly in 2017,[120] the WHO Secretariat noted that they continued to work on this by consulting Member States, FAO and OIE. They

[115] Interagency Coordination Group on Antimicrobial Resistance (2018) Reduce Unintentional Exposure and the Need for Antimicrobials, and Optimize their Use p.10 available on https://www.who.int/antimicrobial-resistance/interagency-coordination-group/IACG_Optimize_use_of_antimicrobials_120718.pdf (accessed 11 June 2021).

[116] Under objective 5

[117] Resolution 68.7 stated that the World Health Assembly requested the Director-General "*to develop, in consultation with Member States1 and relevant partners, options for establishing a global development and stewardship framework to support the development, control, distribution and appropriate use of new antimicrobial medicines, diagnostic tools, vaccines and other interventions, while preserving existing antimicrobial medicines, and promoting affordable access to existing and new antimicrobial medicines and diagnostic tools, taking into account the needs of all countries, and in line with the global action plan on antimicrobial resistance, and to report to the Sixty-ninth World Health Assembly*" – see https://apps.who.int/gb/ebwha/pdf_files/WHA68-REC1/A68_R1_REC1-en.pdf#page=27 (accessed 27 July 2021).

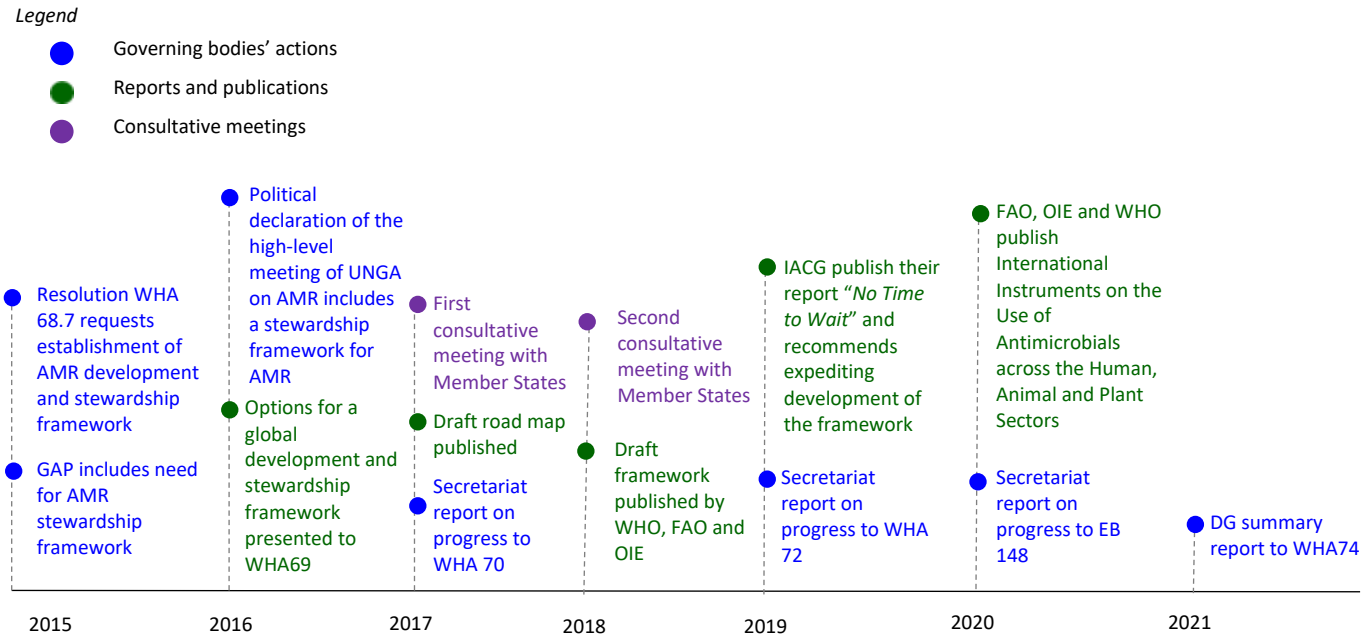
[118] See https://apps.who.int/gb/ebwha/pdf_files/WHA69/A69_24Add1-en.pdf (accessed 27 July 2021).

[119] See https://digitallibrary.un.org/record/842813?ln=en (accessed 29 July 2021).

[120] See https://apps.who.int/gb/ebwha/pdf_files/WHA70/A70_12-en.pdf (accessed 27 July 2021).

produced a draft road map[121] and then consulted Member States about this in Geneva in November 2017.[122] In October 2018, a draft framework was produced[123] and a second consultative meeting was held in Geneva in October 2018.[124] At that meeting, Member States noted the need for additional consultations to adjust the process and scope of the framework, including consideration of the work of the ad hoc Interagency Coordination Group on Antimicrobial Resistance and this was reported to the World Health Assembly in 2019.[125] The IACG's report[126] contained a recommendation on this framework (E4), namely that the Tripartite organizations and UNEP should expedite its development and Member States should also consider the need for new international instruments. Based on this, the Tripartite organizations published a review of International Instruments on the Use of Antimicrobials across the Human, Animal and Plant Sectors in 2020[127] and this process was reported to WHO's Executive Board in December 2020.[128] The main elements of this timeline are shown diagrammatically in Figure 25. It was not completely clear from the last reports to the WHO Executive Board and World Health Assembly whether there are still plans to develop a stewardship framework for AMR or whether it is considered that the instruments identified suffice. The WHO Secretariat report that following consultations with Member States, there are no longer plans to negotiate a specific AMR stewardship framework but it is expected that AMR would be reflected in the proposed pandemic treaty.

Figure 25: Activities conducted to develop an AMR stewardship framework



90 There have been some specific initiatives to support antimicrobial stewardship in particular countries and, in at least one case, such initiatives have been evaluated (see Box 7).

[121] FAO, OIE and WHO (2017) *Global Framework for Development & Stewardship to Combat Antimicrobial Resistance: Draft Roadmap* available on https://www.who.int/docs/default-source/antimicrobial-resistance/stewardship-and-development-framework-2018.pdf?sfvrsn=5f08c9c1_1&download=true (accessed 27 July 2021).
[122] See https://www.who.int/news-room/events/detail/2017/11/09/default-calendar/first-member-states-consultation-on-the-global-framework-for-development-and-stewardship-to-combat-antimicrobial-resistance (accessed 27 July 2021).
[123] FAO, OIE and WHO (2018) *Global Framework for Development & Stewardship to Combat Antimicrobial Resistance: Draft* available on https://www.who.int/docs/default-source/antimicrobial-resistance/stewardship-and-development-framework-2018.pdf?sfvrsn=5f08c9c1_1&download=true (accessed 27 July 2021).
[124] See https://www.who.int/news-room/events/detail/2018/10/01/default-calendar/second-member-states-consultation-on-the-global-framework-for-development-and-stewardship-to-combat-antimicrobial-resistance (accessed 27 July 2021).
[125] See https://apps.who.int/gb/ebwha/pdf_files/WHA72/A72_18-en.pdf (accessed 27 July 2021).
[126] See https://www.who.int/docs/default-source/documents/no-time-to-wait-securing-the-future-from-drug-resistant-infections-en.pdf?sfvrsn=5b424d7_6 (accessed 27 July 2021).
[127] See https://apps.who.int/iris/rest/bitstreams/1314292/retrieve (accessed 27 July 2021).
[128] See https://apps.who.int/gb/ebwha/pdf_files/EB148/B148_11-en.pdf (accessed 27 July 2021).

Box 7: Evaluation of health partnership approach to support antimicrobial stewardship in four countries

The Fleming Fund provided financial support to the Commonwealth Partnerships for Antimicrobial Stewardship (CwPAMS) Programme, a grant-making programme operated by the Tropical Health and Education Trust (THET) and the Commonwealth Pharmacist Association (CPA). The programme aimed to see an increase in the rational use of antibiotics and subsequent reduction in morbidity and mortality associated with AMR. It provided grants[129] to 12 health partnerships between UK institutions and their counterparts in four Commonwealth countries, Ghana, Tanzania, Uganda and Zambia. Support was provided in areas not being covered by other Fleming Fund financing. Required areas included antimicrobial stewardship, including building surveillance, and antimicrobial pharmacy expertise and capacity. Support could also be provided to infection prevention and control if contextually appropriate. Projects were expected to last from February 2019 to April 2020 but no-cost extensions were granted to January 2021. The programme was evaluated in August 2020 using an objective numerical scorecard which was structured around the OECD-DAC evaluation criteria of relevance, impact, effectiveness, efficiency and sustainability.[130] The evaluation considered that the health partnership approach had been effective in improving practice related to antimicrobial stewardship and prescribing practice in the countries supported. It also concluded that all the health partnerships had developed and implemented antimicrobial stewardship strategies, guidelines and tools within their hospitals which were considered important in ensuring the sustainability of CwPAMS' interventions and were also considered to have played a key role in tackling COVID- 19. Finally, it also found that UK NHS staff were able to translate the knowledge and skills they had received early on in the programme into clinical practice in response to COVID-19 challenges. They felt their participation in CwPAMS made them better equipped to deal with the limited resources and additional stresses brought on by COVID-19.

91 The M&E framework identifies seven numbered outcome indicators for this objective but, when compound elements are considered, there are a total of 11 outcome indicators for this objective. However, it does not appear that any of these are being actively tracked or used by the AMR Division. The first one relates to antimicrobial use in humans and is divided into four parts. The first two of these[131] have been discussed earlier (p7). The other two relate to the relative proportions of AWaRe antibiotics in paediatric formulations and among antibiotics prescribed in hospital. It appears that collecting such data will require prevalence surveys and no data from such surveys appears to be yet available.

92 The second outcome indicator relates to access to antibiotics and specifically the percentage of health facilities that have a core set of relevant antibiotics available and affordable on a sustainable basis. This is said to be a sub-set of an SDG indicator but it is unclear what data is currently available. The indicator metadata links to a 2008 document on measuring medicine prices, availability, affordability and price components[132] and a definition of defined daily dose.[133] [134]

93 The third outcome indicator relates to the appropriate use of antimicrobials in surgical prophylaxis. While reference is made in the indicator metadata to point prevalence surveys, no data is presented. The only reference is a link to guidelines on preventing surgical site infection.[135]

94 The fourth outcome indicator relates to use of antimicrobials in growth promotion. However, the indicator definition/metadata is largely blank and in places is contradictory.[136] Reference is made to data for this coming from TrACSS or the OIE AMU database. Availability of TrACSS data for this indicator is considered later in this section.

95 The fifth outcome indicator relates to levels and trends in sales/imports/use of antimicrobials in food producing animals. It is divided into two parts. The first is the total volume of sales/imports (or use), in mg/kg biomass, in food producing animals and the second is the percentage of total sales/imports (or use) classified as WHO Highest Priority Critically Important Antimicrobial agents. The source for data for both sub-indicators is said to be the OIE AMU database.

[129] Of between £20-75,000

[130] See https://commonwealthpharmacy.org/what-we-do/amr/ (accessed 26 July 2021). There was a "*final*" evaluation which covered the first three quarters of the programme from February to October 2019. There was then an addendum which covered the contract extension period from November 2019 to January 2021.

[131] Total human consumption of antibiotics for systemic use and the proportion of these that are ACCESS antibiotics.

[132] See https://www.who.int/medicines/areas/access/OMS_Medicine_prices.pdf (accessed 26 July 2021).

[133] See https://www.whocc.no/ddd/definition_and_general_considera/ (accessed 26 July 2021).

[134] Other links no longer work as the WHO site has been revamped.

[135] See http://apps.who.int/iris/bitstream/handle/10665/250680/9789241549882-eng.pdf?sequence=8 (accessed 26 July 2021).

[136] For example, is the indicator measuring the number of veterinary antimicrobials authorized or used for non-veterinary use, such as growth promotion, or the number of countries authorizing or using antimicrobial agents for growth promotion?

96 The sixth outcome indicator relates to levels and trends in sales/use of pesticides for the purpose of controlling bacterial or fungal disease in plant production. It is divided into two parts. The first is the total amount of pesticide (active substance) intended to repel, destroy or control bacterial or fungal disease and the second is the proportion of this that is aminoglycosides. The source of data is said to be FAOSTAT but this was to be confirmed.

97 The seventh outcome indicator relates to optimized antimicrobial use and regulation and specifically legislation or regulation that requires antimicrobials for human use to be dispensed only with a prescription from an authorized health worker. The source of data for this is said to be TrACSS.

98 So, two of the seven outcome indicators under this objective (4.4 and 4.7) are said to have data available from TrACSS. This is perhaps surprising as these are indicators of outcomes and TrACSS is mostly about reporting on progress on processes. It is also potentially confusing because the two outcomes are qualitatively similar to the three outputs under this objective.[137]

99 In the first TrACSS survey for 2016-17, there were two questions on this topic (9.1 and 9.2). The first covered antimicrobial stewardship and regulation in human health and the second covered antimicrobial stewardship and regulation in animal and crop production. There was also a third question (9.3) on legislation and/or regulations to prevent contamination of the environment with antimicrobials.[138] In 2017/18, the language was changed to move away from antimicrobial stewardship to optimizing/appropriate use. The first question (9.1) remained focused on human health[139] while the second question (9.2) was divided into two[140] parts, one related to animal health (terrestrial and aquatic) and the second related to plant health. Two yes/no questions (9.4) were also added in 2017/18, as to whether a country has regulations on prescription and sale of antimicrobials, including requiring prescription for human use and whether a country does not authorize the use of human and animal critically important antimicrobials for growth promotion. In 2018/19, question 9.2 was modified to no longer cover plant health. Question 9.4 was renumbered 5.4 and adjusted to cover three areas of policy/regulation. The first and third of these remained focused on laws and regulations on prescription and sale of antimicrobials for human use and on prohibiting the use of antibiotics for growth promotion.[141] A new area was added which related to laws and regulations on prescription and sale of antimicrobials for animal use. In 2019/20, additional questions were added related to antimicrobial use in human health (9.1.1 and 9.1.1a).[142] In addition, a new question 9.3 was added related to optimizing antimicrobial pesticide such as bactericides and fungicides use in plant production.[143] As in 2018/19, the question on legislation/policy/regulations remained as question 5.4 but a fourth element was added which

[137] The two outcomes are the percentage of antimicrobials (or the percentage of countries that use antimicrobials) for non-veterinary medical use (such as growth promotion) and the number of countries that have legislation or regulation that requires antimicrobials for human use to be dispensed only with a prescription from an authorized health worker. But, the three outcomes also relate to regulatory environment, namely:

- Percentage of countries that have a regulatory framework for veterinary medicinal products (including medicated feed) that covers all stages of the cycle (manufacture, supply, sale, use, disposal) and meets other requirements in the OIE and Codex standards.
- Percentage of countries that have a regulatory framework for pesticides that considers all stages of the antimicrobial life cycle (production, supply, sale, use, disposal) and meets other requirements in the reference international standards.
- Percentage of countries that have laws or regulations that prohibit the use of antibiotics for growth promotion in the absence of risk analysis.

It is very unclear why legislation or regulation on needing a prescription for human use of an antibiotic is considered an outcome but laws or regulations prohibiting the use of antibiotics for growth promotion is an output. It might be more consistent if the presence or absence of laws/regulations was considered an output and the extent to which they were observed was considered the outcome.

[138] This question was also included in 2017/18 but this was dropped in 2018/19.

[139] As it did in 2018/19 and 2019/20.

[140] Unnumbered

[141] However, the wording was modified in both cases. In relation to human use, the explicit requirement of a prescription for human use was dropped and, in relation to antimicrobials for growth promotion, the caveat of a risk analysis was added and reference to human and animal critically important antimicrobials was changed to antibiotics.

[142] The first of these related to whether a country had adopted the AWaRe classification of antibiotics in the National Essential Medicines List and the second related to the level at which the country's stewardship strategies operated (national, community, facility). Countries were also invited to submit a copy of, or a link to, their National Essential Medicines List.

[143] In some ways, this was reinstating the question on antimicrobial stewardship/appropriate use which was included in 2017/18 but which was dropped in 2018/19.

was whether the country had legislation on marketing of pesticides including antimicrobial pesticides, such as bactericides and fungicides used in plant production. There was also opportunity to share copies of, or links to, relevant legislation.

100 For the purpose of assessing progress on this objective, the review took five TrACSS elements.[144] Table 9 summarizes the implementation scores for these five elements/output indicators under objective 4.[145] In general, the indicators under this outcome score relatively strongly (see Figure 6, p11). However, there has been relatively little progress between baseline and performance data with the exception of optimizing antimicrobial use in human health.

Table 9: Implementation scores for output indicators within outcome 4
Colour coding for scores – amber 0-40; yellow 41-60; light green 61-80; dark green >80; for change – amber 0-10; yellow 11-20; light green >21

Indicator	Baseline		Performance		Change	
	GS	C+	GS	C+	GS	C+
Optimizing antimicrobial use in human health	34	44	45	67	11	24
Optimizing antimicrobial use in animal health (terrestrial and aquatic)	37	44	37	44	1	0
Laws or regulations on prescription and sale of antimicrobials for human use	77	77	86	86	9	9
Laws or regulations on prescription and sale of antimicrobials for animal use	61	61	65	65	4	4
Laws or regulations that prohibit the use of antibiotics for growth promotion	41	41	50	50	9	9

101 By way of example, Figure 26 shows data (using the GS method) for optimizing antimicrobial use in animal health (terrestrial and aquatic). This shows that average score varies by country income group and by region, with performance levels highest in high-income countries and in EUR. Change has however been very mixed with setbacks in UMIC and HIC and in EUR.

[144] These were optimizing antimicrobial use in human health (Q9.1 in all four rounds); optimizing antimicrobial use in animal health (terrestrial and aquatic) (Q9.2 in all four rounds but, in round 1, this also included crop production); laws or regulations on prescription or sale of antimicrobials for human use (Q9.4 in round 2 and Q5.4 in rounds 3 and 4); laws or regulations on prescription and sale of antimicrobials for animal use (Q5.4 in rounds 3 and 4); laws or regulations that prohibit the use of antibiotics for growth promotion (Q9.4 in round 2 and Q5.4 in rounds 3 and 4).
[145] It should be noted that the last three indicators under this output are measured on a different basis from the others in that they are based on Y/N responses rather than grading from A to E.

Figure 26: Implementation scores (using GS method) for optimizing antimicrobial use in animal health (terrestrial and aquatic)

102 The WHO Secretariat has contributed to this objective by supporting the rational use of antimicrobials through the development of key normative products to help ensure the responsible use of safe antimicrobials, including the Essential Medicines List,[146] the AWaRe Classification Database of Antibiotics for evaluation and monitoring of use,[147] the Priority Pathogens List,[148] List of Critically Important Antimicrobials for Human Medicine,[149] guidance on controlling effluents from manufacturing processes[150] and guidance on integrated antimicrobial stewardship activities.[151] Box 8 briefly summarizes the WHO Secretariat's contributions to this objective.

[146] See World Health Organization (2019) *World Health Organization Model List of Essential Medicines: 21st List* available on https://apps.who.int/iris/bitstream/handle/10665/325771/WHO-MVP-EMP-IAU-2019.06-eng.pdf (accessed 27 May 2021) and World Health Organization (2019) *World Health Organization Model List of Essential Medicines for Children: 7th List* available on https://apps.who.int/iris/handle/10665/325772 (accessed 27 May 2021).

[147] World Health Organization (2019) *2019 WHO AWaRe Classification Database of Antibiotics for Evaluation and Monitoring of Use* available on https://www.who.int/publications/i/item/WHOEMPIAU2019.11 (accessed 24 May 2021).

[148] World Health Organization Media Centre (2017) *WHO Publishes List of Bacteria for which New Antibiotics are Urgently Needed* available on https://www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed (accessed 17 May 2021).

[149] World Health Organization (2018) *Critically Important Antimicrobials for Human Medicine* available on https://apps.who.int/iris/bitstream/handle/10665/312266/9789241515528-eng.pdf (accessed 17 May 2021).

[150] See Annex 6 of https://www.who.int/publications/i/item/978-92-4-000182-4 and http://www.fao.org/3/ca9120en/CA9120EN.pdf (both accessed 31 August 2021).

[151] See https://www.who.int/publications/i/item/9789240025530 (accessed 31 August 2021).

Box 8: WHO Secretariat contributions to the GAP AMR Objective 4 - Optimize the use of antimicrobial medicines in human and animal health

In addition to developing normative guidance for antimicrobial use, the WHO Secretariat has worked on developing guidance and tools for implementing stewardship programmes, particularly in low- and middle-income countries. The Secretariat published a toolkit to help hospitals in low resource settings to implement antimicrobial stewardship. The Secretariat also supports countries in updating their essential medicines list, notably with the Global Essential Medicines Dashboard, and a practical guide for stewardship interventions.

At the global level, WHO has worked with FAO and OIE on the development of the Global Framework for Development & Stewardship to Combat Antimicrobial Resistance. A draft version of the framework was submitted to Member States for consideration in 2018. In 2020, the WHO Secretariat reported that the Tripartite Organizations are reviewing existing instruments related to development and stewardship to identify critical gaps. In 2021, WHO published policy guidance on integrated antimicrobial stewardship activities.

Across the three levels, the WHO Secretariat provides technical support to national governments to strengthen regulatory systems with a three-pronged approach: use of the WHO Global Benchmarking Tool by national authorities to assess the strengths of their regulatory systems, identify gaps and monitor overall progress; reporting in the Global Surveillance and Monitoring System for substandard and falsified medical products to improve regulatory authorities' ability to detect and counter them; facilitating the access and registration of quality-assured antimicrobial products to treat diseases.

The WHO Secretariat works to improve the monitoring of use and consumption of antimicrobials by developing methodologies to monitor both components and by collecting and publishing reports on the surveillance of global antibiotic consumption.

The WHO Secretariat works with partners towards joint initiatives to strengthen antimicrobial stewardship. The Secretariat is working with different partners to expand access to essential antibiotics through the SECURE initiative, as well as to accelerate antibiotic development through the establishment of the AMR Action Fund. WHO has also partnered with national governments and international organizations to create the Global AMR R&D Hub, and provides data to monitor antibacterial products in pre-clinical and clinical development.

The WHO Secretariat has produced guidelines for controlling effluents from manufacturing processes. In addition, the Tripartite organisations produced a technical brief on water, sanitation, hygiene and waste water management.

3.6 Objective 5: Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions

103 This objective has two distinct elements. The first is developing the economic case for sustainable investment that takes accounts of the needs of all countries and the second is increasing investment in four things – medicines, diagnostic tools, vaccines and other interventions. On the first, the GAP emphasized the need for the economic case to reflect the need for capacity development, including training in low-resource settings. The GAP argued for economic impact assessments on the health and broader socioeconomic burden of AMR comparing the cost of doing nothing with the cost and benefit of action. On the second element, the GAP emphasized that use of interventions, such as medicines, diagnostic tools and vaccines, should be evidence-based. It particularly emphasized the need for investment in the development of new antimicrobial medicines and explained the barriers to such investment.[153] It also noted that the cost of R&D may need to be de-linked from price and volume of sales. The GAP also emphasized the need for affordable, point-of-care diagnostic tools.

[152] SECURE is a new initiative to develop proposals for a new international antibiotic pooled procurement scheme. It was referenced in a recent G7 health ministers' communique – see https://www.g7uk.org/g7-health-ministers-meeting-communique-oxford-4-june-2021/ (accessed 27 July 2021). WHO describe SECURE as a novel access initiative which is intended to support countries to access and sustainably manage new and existing antibiotics that are needed to cope with AMR.

[153] Fear of resistance emerging, limits on use etc.

104 Overall, there appears to have been much more focus on the second element than the first and this is evident in the indicators selected for this objective in the M& E framework[154] and also in WHO Secretariat progress reports (see Box 9). This is highly problematic as the initial enthusiasm for AMR both globally, as a result of the launch of the Global Action Plan and the UN General Assembly high-level meeting, and nationally, as evidenced by the development of national action plans, has often not translated into provision of resources needed to implement planned actions. One problem with the GAP AMR is that there is little, if anything, purposive in the plan to go beyond raised awareness of AMR to sustained political commitment with allocation and/or raising of funding although these issues are addressed in the recently-published priorities of the Global Leaders Group.[155] It is almost as if the GAP assumes that sustained political commitment and allocation of resources will follow naturally if senior decisionmakers are aware of AMR rather than deliberately planning for how these things might be achieved both globally and in particular countries. There is also little clarity about what funding is needed globally or in different national settings or how this might be calculated. There is also little guidance about what to prioritize when funding is limited. There is however, a high degree of consensus that funds raised, e.g. for the Multi-Partner Trust Fund (MPTF) currently fall far short of what is needed (see Box 11).[156]

Box 9: The AMR Multi-Partner Trust Fund (AMR MPTF)

In 2019, WHO, FAO and OIE launched the AMR Multi-Partner Trust Fund (AMR MPTF), a joint funding mechanism to drive the financing and support the implementation of NAPs. Established for a five-year period (2019-2024), the MPTF had an initial funding request/budget of US$70m. However, to date, just under US$15m has been provided by three funders, the Netherlands, Sweden and the UK. The funds are intended to support the implementation of the Tripartite Workplan on AMR and to support country operations. To date, seven countries (Cambodia, Ethiopia, Ghana, Indonesia, Kenya, Morocco, Zimbabwe) have each been allocated around US$1m to implement the activities outlined in their respective NAPs.

105 Respondents commented that it is difficult to develop an economic case in the absence of knowledge of what the AMR disease burden is or how this might be calculated.[157] However, there have been some attempts to do this. As early as 2016, the UK's Review on Antimicrobial Resistance estimated that an investment of US$3-4 billion per year over ten years was needed to address AMR.[158] In 2017, the World Bank produced a report which looked at the potential economic impact of drug-resistant infections.[159] It used World Bank Group economic simulation tools and estimated that between 1.1% and 3.8% of global GDP could be lost by 2050 if adequate measures aren't taken. Negative effects would be most severe in the poorest countries with a serious negative impact on poverty. The report focused on low- and middle-income countries including identifying actions that can be taken emphasizing that these need to be part of an overall response to infectious diseases based on building durable health systems. The report distinguished AMR-specific[160] and AMR-sensitive[161] policy measures and identified three main entry points to drive AMR progress – promoting universal health coverage, harnessing the international health regulations and strengthening laboratory-based surveillance. It also highlighted the importance of interventions on agriculture and WASH. In 2018, OECD drew on experience in high-income countries to identify a set of "*best buys*" to tackle AMR in an affordable and cost-effective way.[162] It advocated an investment of US$2 per person per year to promote effective responses based on five prongs – promoting better hygiene, ending over-prescription of antibiotics, rapid testing for viral and bacterial infections, delays in prescribing antibiotics and mass media campaigns. Interventions are

[154] See paragraphs 111-113, p46.
[155] See paragraph 123, p52.
[156] Financial details provided in Box 11 are available on http://mptf.undp.org/factsheet/fund/AMR00 (accessed 28 July 2021). According to the 2020 progress report – see http://mptf.undp.org/document/download/27752 (accessed 28 July 2021) – six country proposals had been approved. Ethiopia was not mentioned in the 2020 report.
[157] See paragraph 21, p7.
[158] O'Neill J. (chair) (2016) *Tackling Drug-Resistant Infections Globally: Final Report and Recommendations* available on https://amr-review.org/sites/default/files/160525_Final%20paper_with%20cover.pdf (accessed 13 July 2021).
[159] Jonas et al (2017) *Drug-Resistant Infections: A Threat to our Economic Future (Vol. 2): Final Report* available on http://documents.worldbank.org/curated/en/323311493396993758/final-report (accessed 12 July 2021)
[160] For example, tightening legislation and enforcement on the sale of antimicrobials without a prescription.
[161] For example, expanding access to clean water and sanitation.
[162] OECD (2018) *Stemming the Superbug Tide: Just a Few Dollars More* available on https://www.oecd.org/health/stemming-the-superbug-tide-9789264307599-en.htm (accessed 27 July 2021)

grouped together into three packages – for hospitals, community action and a mixed package.[163] They estimate that this would save 1.6m lives across 33 countries by 2050 and end up saving US$4.8 billion per year. While advocating a "*One Health*" framework, all the best buys identified are in the human health sector.

106 However, it does not appear that analyses such as these have yet been used to develop global fundraising targets for AMR responses or to identify how AMR funding might be identified and tracked. Similarly, there does not yet appear to have been clear guidance for countries on either the importance of attracting funding for national AMR action plans and how they might do this or what AMR priorities (or best buys) might be in different contexts.

107 Rather the focus of this objective has very much been on the second element namely increasing investment in four things – medicines, diagnostic tools, vaccines and other interventions. While there has been some focus on diagnostic tools and vaccines, the main focus has been on increasing investment in medicines, particularly new antimicrobials. In 2016, the UK's Review on Antimicrobial Resistance argued for an increase in the number of effective antimicrobial drugs and specifically advocated establishing a Global Innovation Fund for early stage and non-commercial research and better incentives to promote investment for new drugs and improving existing ones.[164] In 2018, a report on revitalizing the antibiotic pipeline distinguished between "*push*" and "*pull*" incentives and identified the four most effective incentives – grants, pipeline coordinators, market entry rewards and a long-term supply continuity model.[165] The report identified that while there had been an increase in "*push*" incentives through new initiatives such as CARB-X and GARDP, current levels of investment (approx. US$550m per year) were still inadequate for what is needed (approx. US$800m per year). It argued that market-entry rewards needed to be set at around US$1 billion per antibiotic and should be a partially de-linked model.[166] Some have described this approach using fire extinguishers as a metaphor.[167] The UK has started an antibiotic subscription pilot which would provide £10m for use of a new antibiotic.[168] Box 10 summarizes progress reports made by the WHO Secretariat under this objective of the GAP AMR.

[163] The hospital package includes improved hand hygiene, stewardship programmes and enhanced environmental hygiene in health care settings. The community actions include delayed prescriptions, mass media campaigns and use of rapid diagnostic tests. The mixed intervention package includes stewardship programmes, enhanced environmental hygiene, mass media campaigns, and use of rapid diagnostic tests.

[164] O'Neill J. (chair) (2016) *Tackling Drug-Resistant Infections Globally: Final Report and Recommendations* available on https://amr-review.org/sites/default/files/160525_Final%20paper_with%20cover.pdf (accessed 13 July 2021).

[165] Årdal et al (2018) *Revitalizing the Antibiotic Pipeline: Stimulating Innovation while Driving Sustainable Use and Global Access* available on http://drive-ab.eu/wp-content/uploads/2018/01/DRIVE-AB-Final-Report-Jan2018.pdf (accessed 27 July 2021). "*Push*" incentives support R&D directly while "*pull*" incentives reward successful R&D outcomes. Broadly, the report assumes that "*push*" incentives might be provided as public or philanthropic funding while "*pull*" funding would be required to attract private-sector investment. Of the effective incentives identified, grants and pipeline coordinators are "*push*" incentives while market entry rewards and a long-term supply continuity model are both "*pull*" incentives.

[166] That is the incentive would be given in addition to sales revenue. However, concerns were noted that maintaining income from sales revenue could create an incentive to oversell the medicine.

[167] See https://amr.solutions/ (accessed 28 July 2021).

[168] See https://www.gov.uk/government/news/development-of-new-antibiotics-encouraged-with-new-pharmaceutical-payment-system (accessed 28 July 2021) and https://www.gov.uk/government/news/world-first-scheme-underway-to-tackle-amr-and-protect-uk-patients (accessed 28 July 2021).

Box 10: Progress reported by the WHO Secretariat on GAP AMR Objective 5 – Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions

The Global Antibiotic Research and Development Facility (now Partnership) (GARDP) was incubated by the Drugs for Neglected Diseases Initiative (DNDi) in partnership with WHO. Its initial aim was to make products that no-one else is developing. It initially focused on new products for gonorrhoea, neonatal sepsis, maternal sepsis and drug combinations. Other programmes have included recovering knowledge, data and assets of forgotten or abandoned antibiotics and identifying new treatments.

WHO worked with European Investment Bank to develop a concept for an impact investment fund. This led to the establishment of the AMR Action Fund which is expected to inject around US$1 billion in the development of novel antibacterial treatments. The Fund is a partnership of international organizations, development banks and the private sector aiming to advance the development of new antibiotics by investing in biopharmaceutical companies working towards innovative antibiotics. The Fund specifically intends to deliver 2 to 4 new antibiotics to patients by 2030.

The WHO Secretariat provides reports on the antibiotic pipeline and makes these available through the Global Health R&D Observatory. These reports cover antibacterial treatments, including for tuberculosis. Initially, these analyses covered the clinical pipeline but they now cover the pre-clinical pipeline too. As part of this process, the WHO Secretariat has established an open access database. In 2020, the WHO Secretariat announced that it would be publishing a priority list of fungal pathogens of public health importance and a review of the clinical antifungal pipeline in 2021. An expert group established for this purpose met in April 2020.

In addition, the WHO Secretariat published in 2017 a priority list of bacterial pathogens for new drug development and has also produced target product profiles to guide the development of antibacterial agents for four diseases of public health importance – enteric fever, gonorrhoea, neonatal sepsis and urinary tract infections. The Secretariat also published two target product profiles for antibacterial resistance diagnostic tools, following a landscape analysis of relevant gaps and priorities The WHO Secretariat has also worked on developing a global development and stewardship framework (see paragraph 89, p36).

WHO has worked with partners to develop multipurpose, open point of care diagnostic platforms and on specific assays. The WHO Secretariat also conducted a landscape analysis of available diagnostic technologies and promising products for low- and middle-income countries. WHO has also sought to incorporate AMR into new vaccine prioritization and has developed an action framework to leverage vaccines to reduce antibiotic use.

Several respondents commented very positively on the role the WHO Secretariat has played on R&D for new products. Certain actions, such as developing the priority list of bacterial pathogens were of particular importance and carried weight because they were done by WHO. WHO reports on pipeline development are considered good, well-balanced, effective and influential. While others, e.g. the Pew Trust, have also conducted pipeline analysis, one respondent commented that they had decided to merge their reports with those of WHO.

108 While there is recognition of the progress being made on developing new antimicrobial products, some respondents were concerned that any new antimicrobials may only be available for high-income countries. Civil society respondents are particularly concerned that a focus on industry concerns about insufficient reimbursement would result in higher-priced antibiotics that would be beyond the reach of low- and middle-income countries. Respondents also expressed concern that other areas of research and innovation might be overlooked under this objective and may not be adequately covered under objective 2. Such areas include operational and implementation research and research and development in sectors beyond human health, e.g. in animal, plant and environmental sectors. Some respondents identified specific areas needing more research, for example what can be done to reduce resistance and research on identifying the main mechanisms involved in spreading AMR in different contexts. The IACG report noted that it is important to look at innovation beyond antimicrobials, diagnostics, and vaccines—for example, considering alternatives for growth promotion and disease prevention and also innovation in stewardship practices such as animal husbandry.

109 In many ways, objective 5 is qualitatively different from the other four objectives of the GAP AMR, particularly the part that has been mostly emphasized, i.e. product research and development. Many countries find it difficult to see how they would apply this objective in their national action plan. One piece of evidence for this is that TrACSS reports on progress at national level, while they cover objectives 1-4, do not cover objective 5. The GAP itself does identify possible Member State actions under this objective. These include:

- Assessing investment needs for implementation of their national action plans on antimicrobial resistance and developing plans to secure and apply the required financing.[169]

[169] Overall, this element has not been prioritized within this objective including in national action plans. For example, there are no specific questions about this in TrACSS (beyond inclusion as one part of the criteria for assessing national action plans). It is unclear if the WHO Secretariat or others have provided

- Encouraging participation in international collaborative research to support the development of new medicines, diagnostic tools and vaccines.

110 There has been a tendency for countries to consider that objective 5 is about product R&D and that many low- and middle-income countries have little, if any, role to play in such developments. In some cases, countries have omitted objective 5 from their national action plan covering any elements of research and innovation under objective 2. In others, objective 5 has been used to address research, innovation and other issues more broadly including setting a research agenda into AMR in affected sectors; improving the manufacturing, supply and distribution of antimicrobial agents including research and development; strengthening the regulatory and enforcement regime for antimicrobials;[170] and strengthening governance and stakeholder collaboration for implementation of AMR interventions.

111 According to the M&E framework, there is one outcome indicator for this objective, that is the global R&D pipeline. However, this is broken down into three elements – medicines, diagnostics and vaccines.[171] Various data sources are identified for the first two elements including the WHO vaccine pipeline tracker,[172] the WHO observatory on health R&D[173] and the Global AMR R&D Hub.[174] The links provided give access to the WHO priority list of bacteria,[175] a model list of in vitro diagnostics[176] and a report on revitalizing the antibiotic pipeline.[177] [178]

112 Similarly, the M&E framework has one output indicator for this objective and that is mechanisms and investments for R&D. It is broken down into two parts – funding and partnerships.[179] Various data sources are identified including the Global AMR R&D Hub for both parts and the WHO Observatory on Health R&D for the second part.[180] A link is provided to the GARDP website.[181] [182] There are potentially other sources of data on funding on AMR research and development. For example, the Joint Programming Initiative on Antimicrobial Research (JPIAMR) conducted systematic analysis of funding on research on AMR in 2014 and 2017. In 2014, the analysis focused on research on antibacterial resistance while, in 2017, the exercise was expanded to also include anti-fungal and anti-parasitic research. Reports and core data (in Excel) are available.[183]

113 One observation about these indicators is that they focus exclusively on the second part of this objective, product research and development – levels of funding for product R&D and the pipeline for R&D products. There are no indicators for the first part, such as, at the outcome levels, global levels of funding for work on AMR, and perhaps, at the output level, the proportion of national action plans that are funded.[184]

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guidance or technical support to countries in this area. It is perhaps assumed that, if countries have sufficient political commitment to AMR, they will provide the resources needed to implement the AMR national action plan. There seems to be little appreciation that this might need to be purposefully planned for and supported.

[170] Which in many countries is covered under objective 4.

[171] This specifically relates to vaccines to prevent prioritized diseases in animals (pigs, poultry, fish, cattle, sheep and goats). The data source is considered to be "*Health for Animals*" and this is not considered further here.

[172] It is unclear why a vaccine pipeline tracker is mentioned here in relation to indicators for medicines and diagnostics.

[173] See https://www.who.int/observatories/global-observatory-on-health-research-and-development (accessed 26 July 2021).

[174] See https://globalamrhub.org/ (accessed 28 July 2021).

[175] See https://www.who.int/medicines/publications/WHO-PPL-Short_Summary_25Feb-ET_NM_WHO.pdf (accessed 27 July 2021).

[176] See https://www.who.int/medical_devices/diagnostics/WHO_EDL_2018.pdf (accessed 27 July 2021).

[177] Årdal et al (2018) *Revitalizing the Antibiotic Pipeline: Stimulating Innovation while Driving Sustainable Use and Global Access* available on http://drive-ab.eu/wp-content/uploads/2018/01/DRIVE-AB-Final-Report-Jan2018.pdf (accessed 27 July 2021).

[178] The other links provided no longer work either because of a "*maintenance break*" (1) or since WHO revamped its website (3).

[179] The first is called list of mechanisms and funding for R&D to prevent, diagnose and treat priority pathogens (new medicines, diagnostics, vaccines, etc.) and the second is called list of mechanisms, commitments and expenditures for R&D targeting priority pathogens (new medicines, diagnostics, vaccines, etc.). The distinction between these two is not very clear based on these statements and the indicator descriptions/metadata in the M&E framework lack detail.

[180] The STAR-IDAZ International Consortium on Animal Health is also considered a data source for the second part but this is not considered further in this report.

[181] See https://www.gardp.org/ (accessed 27 July 2021).

[182] Another link is provided to the WHO website but this is not working following the revamp of the WHO website.

[183] See https://www.jpiamr.eu/resources/amr-knowledge-hub/research-funding-datahub/ (accessed 4 May 2021)

[184] Some of this information would be available from TrACSS including on whether a NAP has a budget and has identified funding sources. However, as these are only some of the elements to achieve certain grades on TrACSS, there is a risk of misinterpretation and potentially undercounting country NAPs with

3.7 International and National Partners

114 The framework for action in the GAP AMR identifies three main groups of actors – Member States, the [WHO] Secretariat[185] and international and national partners. Because of the nature of this review, this report focuses mainly on the first two groups (Member States and the WHO Secretariat). But, the contributions of others in addressing AMR are huge and these are acknowledged both in the GAP AMR and in this review. This section briefly documents who these partners are and some of the contributions they have made.[186] Issues of coordination between Member States, the WHO Secretariat and other partners are considered later in this report.

115 The following international and national partners are specifically mentioned in the GAP AMR framework for action:

- Professional bodies, organizations and societies – including industry associations and accreditation bodies
- Intergovernmental organizations including FAO, OIE, the World Bank
- Civil society organizations
- Trade and industry bodies
- Employee organizations
- Foundations with an interest in science education
- Media
- International research community
- Research community in the public and private sectors including the pharmaceutical industry
- Global health donors
- International development bodies
- Aid and technical agencies
- Research funding organizations
- Philanthropic organizations
- Non-governmental organizations
- Health insurance providers and other payers
- Partners in finance and economic sectors

116 Box 11 briefly documents reported contributions of international and national partners under particular GAP AMR objectives. Both FAO and OIE are mentioned extensively in the GAP AMR and also in WHO progress reports. In 2021, FAO published an evaluation of their work on AMR[187] and this is briefly summarized in Box 12. OIE is a smaller organization than either FAO or WHO and does not have a separate evaluation function. It has not yet systematically evaluated its work on AMR. UNEP is not mentioned explicitly in the GAP AMR framework for action but, since the GAP was adopted, the potential importance of the environment in relation to AMR has been increasingly recognised. The need for greater understanding of environmental pathways to the development and transmission of AMR has been recognised as one of six priorities by the Global Leaders Group. Many stakeholders argued for greater consideration of environmental matters and greater inclusion of UNEP. WHO Secretariat progress reports do mention UNEP in places but not to the same extent that they mention FAO and OIE.

budgets and funding sources identified. It should also be noted that identifying sources of funding does not necessarily mean that that funding has been secured let alone that the NAP overall is fully funded – see paragraph 31, p14.

[185] For discussion of what the GAP AMR means by Secretariat see footnote 2, p1. It should be noted that the GAP AMR framework for action sometimes describes WHO as an international and national partner. However, this review has treated the Secretariat as the WHO Secretariat so any actions by WHO are considered there and not here.

[186] But, it should be noted that this is not a review of the performance of other partners, international or national.

[187] FAO (2021) *Evaluation of FAO's Role and Work on AMR* available on http://www.fao.org/3/cb3680en/cb3680en.pdf (accessed 28 July 2021).

117 There is little, if any mention of other UN agencies and multilaterals in the Global Action Plan and in WHO Secretariat progress reports with the possible exception of the World Bank. Similarly, there is little reporting of contributions from other sectors, such as civil society or the private sector. WHO Collaborating Centres are mentioned briefly in some reports but their role in the GAP AMR is not particularly clearly explained or consistently reported on. One issue that perhaps arises is that some of the most significant donors for work on AMR are themselves WHO Member States. Perhaps there needs to be differentiation between when these

Member States are acting on their own domestic issues and when they are acting as development partners or donors.[188]

Box 11: Contributions of international and national partners across GAP AMR objectives as reported by the WHO Secretariat

Objective 1 – Multiple partners have participated in World Antibiotic Awareness Week including FAO, OIE, ECDC, CDC and the African Union Commission. This included developing materials for agriculture audiences jointly with FAO and OIE. In 2020, WHO, FAO and OIE organized a global consultation to discuss shifting the focus of this week from antibiotics to antimicrobials more broadly. The UN General Assembly high-level meeting was recognized as a useful way of engaging with multiple partners, particularly in the media. Other areas in which WHO has collaborated with FAO and OIE include technical consultations with behaviour change experts and developing, adapting and disseminating cross-sectoral educational materials. Specifically, OIE developed the "*We Need You*" communication campaign which was reported to be the first global campaign dedicated to raising awareness of AMR in the animal health sector. In 2018, OIE brought together 530 participants from 95 countries at the second global conference on AMR and the prudent use of antimicrobials in Marrakech, Morocco. WHO and FAO initiated a programme known as "*Smartphone for Change*" which aimed to enable health, pharmacy and veterinary students to take an active role in promoting the responsible use of antibiotics (see Box 6). In addition, FAO launched an AMR case study series, developed a global expert network and a repository of resources and is piloting a holistic approach to addressing AMR through behaviour change projects in Africa and Asia. OIE, with FAO and WHO, has conducted training for AMR national focal points on risk communication, behaviour change and OIE standards.

Objective 2 – Other organizations including OIE were involved in consultation over surveillance of antimicrobial consumption. WHO Collaborating centres have been identified who can support AMR surveillance in different countries. WHO, FAO and OIE have been involved in developing TISSA (see Box 5). WHO and FAO have also cooperated in revision of the Codex Alimentarius. WHO has also collaborated with other UN agencies in improving the understanding of the role of inadequate water, sanitation and hygiene (WASH) facilities and environmental contamination with residues and resistant bacteria as drivers of AMR. WHO, FAO and OIE have collaborated on the ESBL Ec Tricycle Project. On surveillance, the WHO Secretariat cooperates with regional networks, such as CAESAR and PLISA.

Objective 3 – WHO and UNICEF have collaborated on some areas of WASH including production of joint programme reports. In 2018, the WHO Secretariat acknowledged the need to collaborate more with UNEP and other UN agencies on these issues. OIE have convened ad hoc groups to develop prioritized lists of diseases in animals for which the availability of vaccines could reduce antimicrobial use. The InnoVet-AMR partnership is funding research on innovative veterinary solutions for AMR. FAO have promoted disease prevention at farm level. FAO and the International Atomic Energy Agency have collaborated to develop an isotopic analytical toolbox that provides information of the movement of antibiotics through soil and water. The International Plant Protection Convention are considered to play an important role in preventing the spread of pests in plants which may reduce the need for pesticides. In 2017, UNEP highlighted the issue of AMR in its report entitled *Frontiers 2017: Emerging Issues of Environmental Concern*. In June 2020, WHO, FAO and OIE published a technical brief on water, sanitation, hygiene and wastewater management to prevent infections and reduce the spread of AMR.

Objective 4 – Efforts to develop a global development and stewardship framework have involved FAO, OIE and UNEP (see paragraph 89, p36). WHO collaborated with FAO to update relevant Codex Alimentarius standards relating to AMR. FAO has worked in low- and middle-income countries to analyse stakeholder practice and implement interventions that promote the responsible use of antimicrobials. Other areas of FAO work under this objective have included:

- Preparing a technical paper on animal nutrition strategies to reduce the use of antibiotics in animal husbandry
- Development of guidelines on the prudent use of antimicrobials in the treatment of poultry and swine
- Development of community-level guidelines related to antimicrobial resistance in line with OIE standards for aquaculture and fisheries
- Preparation of a publication on the responsible management of bacterial diseases in aquaculture, along with brochures on biosecurity for aquaculture species that are important for food security especially in low- and middle-income countries, such as carp, tilapia and shrimp
- A partnership with the Istituto Zooprofilattico Sperimentale delle Venezie to conduct a project on bee health and antimicrobial use.
- The Development Law Service of FAO designing a method for assessing national legislation relevant to antimicrobial resistance, including regulatory frameworks for antimicrobials, legislation aimed at preventing the contamination of food and the environment with antimicrobials and legislation on improving animal and plant health to minimize the need for antimicrobials. OIE also collaborated on the initiative
- Work to identify relevant antimicrobial resistance legislation and policies across countries through its comprehensive database of national laws, regulations and policies on food, agriculture and natural resource management (FAOLEX), so as to facilitate the identification of existing legislation and good practices.

In addition, the OIE veterinary legislation support programme and the Development Law Service of FAO have collaborated to strengthen the regulatory framework on antimicrobial resistance. OIE has explored the possibility of using a similar approach to WHO to understand the impact of substandard and falsified products. The Tripartite Joint Secretariat has produced a compilation of existing international instruments, including relevant environmental instruments, on the appropriate and prudent use of antimicrobials across the human, animal and plant sectors.

Objective 5 – WHO has supported the formation and establishment of GARDP and the AMR Action Fund. In their progress report to the World Health Assembly in 2019, the WHO Secretariat acknowledged the economic case analysis conducted by the World Bank and OECD. The same report also acknowledged investments made by regional banks, such as the European Investment Bank and the Asian Development Bank and other successful investment initiatives, such as the Coalition for Epidemic Preparedness Innovations.

[188] The approach taken by this review is to consider them under Member State actions when acting domestically and to consider them under international partners when they act as a donor or development partner.

Box 12: Brief summary of FAO evaluation of its role and work on AMR

This evaluation focused on FAO's work on AMR and results achieved. It is structured around a number of evaluation criteria including relevance, internal and external coherence, effectiveness, efficiency, sustainability and a number of crosscutting issues. The evaluation was carried out across two phases. The first focused on work at the global level while the second focused on work at regional and country level and included five country case studies, in Armenia, Peru, Ukraine, Viet Nam and Zimbabwe. Because of the technical nature of the subject, the evaluation team also convened a panel of AMR experts. The evaluation made eight conclusions and four recommendations. In brief, the conclusions cover the importance of AMR, the lack of an FAO AMR strategy, the lack of an FAO AMR management team or structure, the alignment of FAO's work on AMR with the Tripartite and the GAP AMR, the strong coordination and collaboration role played by FAO on AMR, the technical expertise offered by FAO, the importance of a One Health approach and the results of the FAO Action Plan. Areas covered by the recommendations included the need for a long-term AMR strategy, the need for a central coordination and management structure, the need to sustain and strengthen its scientific approach and the need for innovative approaches.

3.8 Crosscutting Issues

Coordination

118 The need for effective coordination is a key point emphasized in the GAP AMR. The GAP refers to a One Health approach as the basis for this and emphasizes that coordination involves numerous international sectors and actors, including human and veterinary medicine, agriculture, finance, environment, and well-informed consumers. The (WHO) Secretariat[189] is identified as having a role in leading and coordinating support to countries for assessment and implementation of investment needs and, under objective 5, in exploring option for a new partnership or partnerships to coordinate the work of many unlinked initiatives aiming to renew investment in research and development of antibiotics.[190] The resolution adopting the GAP AMR[191] included the provision for this comprehensive review and part of the focus of that was to ensure that activities are well-coordinated, including with relevant UN agencies and other relevant stakeholders. This requirement was included as the review's third objective (see paragraph 5, p2).

119 Although the GAP AMR refers to coordination among agencies using a One Health approach, the concept is not specifically defined in the GAP.[192] In general, there does not appear to be a universally-accepted definition of One Health.[193] Various definitions are summarized in Box 13.[194]

[189] See footnote 2.
[190] See paragraph 131, p55.
[191] WHA72.5, Resolution on Antimicrobial resistance, https://apps.who.int/gb/ebwha/pdf_files/WHA72-REC1/A72_2019_REC1-en.pdf#page=1 (accessed 16 July 2021).
[192] Respondents did comment that the GAP AMR could emphasize the One Health concept more. Many were of the view that any revised or updated GAP would ned to be a multi-agency document.
[193] Mackenzie and Jegge (2019) *The One Health Approach: Why is it so Important?* available on https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6630404/ (accessed 29 July 2021).
[194] Based on https://www.who.int/news-room/q-a-detail/one-health, http://www.fao.org/one-health/en/ and https://www.oie.int/en/what-we-do/global-initiatives/one-health/, https://www.unep.org/news-and-stories/story/unep-joins-three-international-organizations-expert-panel-improve-one-health and https://www.who.int/zoonoses/tripartite_oct2017.pdf.

Box 13: How is One Health defined?

The concept of what is now termed One Health was recognized more than 200 years ago, initially as One Medicine and then as One World, One Health.

CDC and the One Health Commission define One Health as a collaborative, multisectoral, and transdisciplinary approach—working at the local, regional, national, and global levels—with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment.

One Health Global Network define One Health as recognizing that the health of humans, animals and ecosystems are interconnected. It involves applying a coordinated, collaborative, multidisciplinary and cross-sectoral approach to address potential or existing risks that originate at the animal-human-ecosystems interface.

The One Health Institute simply defines One Health as an approach to ensure the well-being of people, animals and the environment through collaborative problem solving—locally, nationally, and globally.

WHO refers to One Health as an approach to designing and implementing programmes, policies, legislation and research in which multiple sectors communicate and work together to achieve better public health outcomes recognizing that the approach is particularly relevant in areas of food safety, the control of zoonoses, and addressing AMR.

FAO refers to One Health as an integrated approach that recognizes that the health of animals, people, plants and the environment is interconnected and ensures that specialists in multiple sectors work together to tackle health threats to animals, humans, plants and the environment.

OIE recognizes that the One Health concept summarised an idea that had been known for more than a century; that human health and animal health are interdependent and bound to the health of the ecosystems in which they exist. OIE envisaged and implemented it as a collaborative global approach to understanding risks for human and animal health and ecosystem health as a whole.

The Tripartite notes that the One Health approach recognizes that the health of people is connected to the health of animals and the environment.

UNEP defines One Health as a cross-cutting and systemic approach to health based on the fact that human health and animal health are interdependent and linked to the health of the ecosystems in which they co-exist.

120 Whichever definition is followed, the approach focuses on consequences, responses and actions at the animal-human-ecosystem interface and has interdisciplinary collaboration at its heart. Respondents recognized a growing acceptance of the One Health approach, as evidence by the Tripartite collaboration towards addressing AMR. This Tripartite collaboration, between FAO, OIE and WHO, was recognized in the GAP AMR.[195] A Tripartite Joint Secretariat has been established, hosted by WHO, based on terms of reference developed in 2019.[196] According to the terms of reference and information provided by the WHO Secretariat, the Tripartite Joint Secretariat consists of:

- An Executive Committee made up of the Directors-General of the Tripartite organizations. It meets annually.
- A Senior Management Group made up of Assistant and Deputy Directors-General and relevant department Directors. It meets more frequently than envisaged in the terms of reference, every two months or as needed.
- Secretariat staff and liaison officers for OIE and FAO. The size of the Secretariat staff team has grown to reflect the workload associated with establishing governance structures and managing the MPTF. There are currently staff, a technical officer, a liaison officer, two governance officers,[197] MPTF programme manager, a team assistant (80%), a junior professional officer and two consultants providing communications support to the Global Leaders Group. Partnership work is taken forward by the acting head of the Advocacy and Stewardship team.

121 Overall, the Tripartite collaboration is functioning well. A Tripartite Strategic Framework, developed in conjunction with UNEP, is due to be published in September 2021. However, some respondents commented

[195] Based on a concept note developed in 2010 – see https://www.who.int/influenza/resources/documents/tripartite_concept_note_hanoi_042011_en.pdf (accessed 29 July 2021).
[196] See https://www.who.int/docs/default-source/antimicrobial-resistance/amr-gcp-tjs/tjs-tor-final-october-2019.pdf?sfvrsn=bbd8a3fe_0 (accessed 29 July 2021).
[197] One is under recruitment. The other works with the Global Leaders Group and was, until recently, employed as a consultant.

that initial progress had been slow.[198] The challenges that there are have been discussed under the One Health approach. However, there are some stakeholders who are concerned that an excessive focus on the Tripartite globally risks distracting from the crucial aspect of supporting in-country plan implementation. There are also concerns from multilateral agencies outside the Tripartite that it does not represent fully the multisectoral nature of AMR and there is a need for a more diverse and representative global body that brings together different sectors of AMR. Many respondents recognized the need for the GAP to have greater focus on the environment and this likely means a greater role for UNEP, e.g. expanding the Tripartite to a Quadripartite. If this expansion goes ahead, the need to clarify some of the things identified earlier, e.g. respective roles and responsibilities becomes more pressing.

122 One area of particular focus of the review is the extent of coordination with other multilateral agencies, including UN agencies. The political declaration[199] of the UN General Assembly high-level meeting requested the UN Secretary General to establish, in consultation with WHO, FAO and OIE, an ad hoc inter agency coordination group, co-chaired by the Executive Office of the Secretary General and the World Health Organization. The purpose of this group was to provide practical guidance for approaches needed to ensure sustained effective global action to address antimicrobial resistance. The Secretary General was also asked to submit a report to the seventy third session of the General Assembly on the implementation of the present declaration and on further developments and recommendations emanating from the ad hoc inter agency group, including on options to improve coordination, taking into account the global action plan on antimicrobial resistance. The way this inter-agency coordination group (IACG) was understood was quite different from other IACGs and similar structures across the UN system.[200] Rather than focusing on ongoing coordination between agencies, the IACG's remit was seen as time-limited, focused on producing a report for the UN Secretary General, including recommendations on future coordination/governance mechanisms.[201] The IACG recommended:[202]

- The urgent establishment of a One Health Global Leadership Group on Antimicrobial Resistance, supported by a Joint Secretariat managed by the Tripartite agencies (FAO, OIE and WHO).[203]
- Convening an Independent Panel on Evidence for Action against Antimicrobial Resistance in a One Health context to monitor and provide Member States with regular reports on the science and evidence related to antimicrobial resistance, its impacts and future risks, and recommend options for adaptation and mitigation.[204]
- The establishment of a constituency-based partnership platform facilitated and managed by the Tripartite agencies with diverse representation (e.g. governments, private sector and civil society representing human, animal, plant and environment health, as well as agriculture and food and feed production) to develop and implement a shared global vision, narrative and targets.[205]

123 Two years after the production of the IACG's report, progress on establishing these structures has been limited despite the fact that senior management meetings of the Tripartite organisations have been held every two

[198] Not least because of the time and energy needed to support the IACG process.
[199] See https://digitallibrary.un.org/record/842813?ln=en (accessed 29 July 2021).
[200] These tend to be ongoing collaborative mechanisms across UN agencies and others. They cover a wide range of topics, such as mine action (see https://www.mineaction.org/en/un-inter-agency-coordination-group-mine-action-iacg-ma - accessed 29 July 2021), small island developing states (see https://sustainabledevelopment.un.org/topics/sids/iacg - accessed 29 July 2021) and landlocked developing countries (see https://www.un.org/ohrlls/content/inter-agency-consultative-group-iacg-ldcs - accessed 29 July 2021). There are also similar structures with slightly different names, such as the Inter-Agency Task Force on noncommunicable diseases, see https://www.who.int/fctc/implementation/cooperation/un-task-force/en/ (accessed 29 July 2021).
[201] See https://www.who.int/docs/default-source/documents/no-time-to-wait-securing-the-future-from-drug-resistant-infections-en.pdf?sfvrsn=5b424d7_6 (accessed 29 July 2021). Respondents commented that the IACG process was difficult, slow and time consuming. Nevertheless, the group produced a valuable report although progress on implementing its recommendations has been limited.
[202] These structures are summarized in an information note – see https://www.who.int/docs/default-source/antimicrobial-resistance/information-note-governance-structures-amr.pdf?sfvrsn=228d858a_13 (accessed 29 July 2021).
[203] Recommendation E2.
[204] Recommendation E3.
[205] This was a sub-point within recommendation E2.

months since January 2020 to seek to expedite the implementation of the recommendations of the IACG including the governance structures. Terms of reference for the Global Leaders Group were developed in 2019/20 and approved by the UN Secretary General in June 2020.[206] The group is led by the Prime Ministers of Bangladesh and Barbados. An inaugural meeting was held in January 2021 with a formal first meeting in May 2021. The group has produced a number of information notes including an overview of the group,[207] a note on financing to address AMR[208] and a note on surveillance of antimicrobial resistance and use.[209] In July 2021, the group published its priorities in the form of a rolling action plan.[210] While these six priorities do reflect some of the objectives of the Global Action Plan,[211] there are some areas which are emphasised less[212] and some which are emphasised more.[213] The brief priorities document is not clear on a number of issues including how the priorities and plans to monitor progress towards them fits with the GAP AMR and its M&E framework. Indeed, the priorities document simply gives titles of key performance indicators without defining them in detail or explaining how data on them will be collected and reported or whether baseline data exists or not. While the identification of deliverables for 2021 is good, presumably there will need to be a more detailed workplan with expected dates for the various deliverables. Given that the priorities document was only published in July 2021, this effectively means that there were only five months remaining in which 2021 deliverables could be produced. The priorities document is not very clear as to whether all that is contained in it is feasible or what resources are available or needed. While respondents, in general, welcomed the establishment of the Global Leaders Group, some respondents had expected more, e.g. in terms of helping identify funding sources for responses to AMR. There were also concerns that the group was at a very high political level and might lack the kind of high-level technical expertise that had been available to the IACG. Civil society representatives raised concerns that , while the priorities document had been published, there had been no public input or transparency and there was no connection to the Tripartite's M&E Framework.

124 While there has been a consultation on the draft terms of reference for the proposed Independent Panel on Evidence for Action against Antimicrobial Resistance[214] and this generated extensive feedback,[215] it is not clear to external stakeholders what the current status of this panel is. A report was submitted by the Tripartite organizations to the UN Secretary General in February 2021 outlining the final terms of reference and proposed next steps. However, a response is awaited from the Secretary General and that report has not been made public nor shared with the review team. Points commented on in the feedback included how the panel

[206] See https://www.who.int/groups/one-health-global-leaders-group-on-antimicrobial-resistance (accessed 29 July 2021).
[207] See https://cdn.who.int/media/docs/default-source/antimicrobial-resistance/amr-gcp-tjs/glg-information-note.pdf?sfvrsn=1989ea9_8 (accessed 29 July 2021).
[208] See https://cdn.who.int/media/docs/default-source/antimicrobial-resistance/amr-gcp-tjs/financing-to-address-amr.pdf?sfvrsn=c982548e_5 (accessed 29 July 2021).
[209] See https://cdn.who.int/media/docs/default-source/antimicrobial-resistance/amr-gcp-tjs/surveillance-of-antimicrobial-resistance-and-use-.pdf?sfvrsn=caa5a9a7_9 (accessed 29 July 2021).
[210] See https://cdn.who.int/media/docs/default-source/antimicrobial-resistance/glg-action-plan-july-2021_final.pdf?sfvrsn=daa1bd02_5&download=true (accessed 30 August 2021). These identify six advocacy priorities and for each of these one or more outcomes (9 in total), some key performance indicators (25 in total), some key activities (46 in total) and some key deliverables for 2021 (18 in total). The six advocacy priorities include (1) for sustained political action on antimicrobial resistance by seizing critical opportunities including the COVID-19 pandemic response and recovery, embedding it in the implementation of the Sustainable Development Goals and promoting a One Health approach; (2) for transforming the human health, animal health, food, plant and environment eco-systems focusing on infection prevention and control and the responsible and sustainable use of antimicrobials; (3) for improved surveillance and monitoring of antimicrobial use and resistance across all sectors to inform ambitious, science and risk-based, global and national targets and interventions to address gaps in the response to AMR; (4) for increased mobilization of internal and external financial resources, with a focus on low- and middle-income countries, to support the development and implementation of ambitious, multisectoral national action plans in all countries; (5) for increased, effective and affordable innovations across all sectors and stakeholders to secure a sustainable pipeline for new antimicrobials (particularly antibiotics), vaccines, diagnostics, waste management tools ,and safe and effective alternatives to antimicrobials, and to ensure equitable access to them; and (6) for better understanding of environmental pathways to the development and transmission of antimicrobial resistance.
[211] For example, there is a degree of read across from priority 2 to GAP objectives 3 and 4, from priority 3 to GAP objective 2 and from priority 5 to GAP objective 5.
[212] Particularly objective 1 of the GAP which is focused on "*awareness*" raising.
[213] In particular, priorities 1 and 4 reflect the kind of purposive focus on political actions and funding which will be needed to turn increased high-level awareness of AMR into practical and sustained actions at global, regional and country levels. In addition, priority 6 reflects a specific focus on better understanding environmental pathways to the development and transmission of AMR.
[214] See https://www.who.int/publications/m/item/public-discussion-draft-terms-of-reference-independent-panel-on-evidence-amr (accessed 29 July 2021).
[215] See https://www.who.int/docs/default-source/antimicrobial-resistance/evidence-panel-public-discussion-feedback-compiled-08-07-20.pdf?sfvrsn=3d0d9b66_2 (accessed 29 July 2021).

would interact with scientific panels, such as the STAG-AMR[216] and how duplication and overlap could be avoided, and how the independence of the panel could be assured if the secretariat for it was the Tripartite Joint Secretariat.

125 Based on publicly-available documentation, there appears to have been least progress on establishing the partnership platform. However, the Joint Tripartite Secretariat is organising a meeting of Member States to discuss the draft terms of reference for the platform. This meeting is being hosted by WHO and is scheduled for 30 September 2021. According to the draft terms of reference, there will be five representative clusters[217] with other technical action groups.

126 It is difficult to see how the proposed structures, even if operationalized, are going to meet the need for technical coordination across multilateral agencies including UN agencies beyond the agencies that are part of the tripartite/quadripartite. Multilateral agencies were not explicitly identified as part of the stakeholder platform proposed by the IACG and they do not appear to be among the five representative clusters that FAO is planning. In response to questioning, it does appear that the intention is that the stakeholder platform will allow the inclusion of multilateral agencies, including from the UN. However, it is not clear when that will be established or how it will function, particularly in comparison to the more ongoing IACGs or task forces referenced above. This is problematic now and respondents expressed concern that there seems little focus from the Tripartite organizations on including other multilaterals, such as the Global Fund to Fight AIDS, Tuberculosis and Malaria, Gavi, the World Bank and other UN agencies, particularly UNDP and UNICEF. One respondent considered that it had been a missed opportunity not to include AMR as one of the accelerators in the SDG GAP.[218] It is potentially a problem that that initiative seeks greater coordination of work towards the SDGs of WHO and 12 other organizations (but not FAO, OIE or UNEP) and the planned coordination structures for AMR include WHO, FAO, OIE and (potentially) UNEP but do not seem to have meaningful ways of engaging other agencies involved in the SDG GAP.

127 While the proposed stakeholder platform does seem to include civil society, e.g. within one of the representative clusters, the long delay between the IACG report and establishment of this platform means that there has been a hiatus in relationships between WHO and other Tripartite organizations and civil society, meaning that gains that were previously made in this have been or risk being lost. Civil Society representatives explained that there had been a shift from an annual WHO-NGO Dialogue with senior officials involved in AMR to more targeted discussions on specific issues.[219] While civil society representatives were often actively involved in World Antimicrobial Awareness Week, they expressed the view that there was scope for more year-round involvement as is seen in other areas, for example, handwashing, immunization and tobacco control. Civil society representatives identified a number of ways in which WHO could better engage civil society including:

- Holding dialogues between WHO experts and civil society organizations on priority issues in AMR. While recognizing the need for an inclusive approach to all stakeholders, civil society representatives expressed the need for safe spaces where voices from civil society and from low- and middle-oncome countries can be heard.
- Involving civil society in processes to set indicators for monitoring and benchmarks for accountability.
- Promoting bottom-up innovation as in antimicrobial stewardship and access initiatives at the community level and in the healthcare delivery system.

[216] And potentially the Advisory Group on Integrated Surveillance of AMR (see http://www.agisar.org/ - accessed 29 July 2021) if that is still operational.
[217] Covering academia, civil society, resource partners, private sector and governance (or governments?). This is based on a verbal briefing only and the review team has not seen the draft terms of reference.
[218] See https://www.who.int/initiatives/sdg3-global-action-plan/about (accessed 29 July 2021).
[219] Examples include a civil society consultation on the vision and plans for SECURE, convened by GARDP, WHO, UNICEF and the Clinton Health Access Initiative and an Antimicrobial Resistance Collaborative (ARC) dialogue on innovative financing for novel antibiotics and the AMR Action Fund, with WHO and the European Investment Bank.

- Enlisting civil society in mobilizing for campaign action, behaviour change and greater financing of AMR efforts. We recognize the need for WHO to conduct this in a way that involves all stakeholders, but as in other areas where significant financial conflict of interest exists, we hope that WHO can go the extra mile in creating separate, safe space for the voices from LMICs and civil society to share their inputs.

128 Some stakeholders were concerned that there needs to be space for Member States to engage with Tripartite/Quadripartite organizations in relation to the GAP AMR in a dedicated space, i.e. separate from other stakeholders. While this may be the intention of the governance (or government) representative cluster, it appears that the IACG's original idea was to have one platform which included a diverse range of different stakeholders. While it may be useful to have this, respondents also wanted opportunity to engage with similar stakeholders and the FAO representative clusters may provide that opportunity. Some respondents have existing concerns about the level of private sector influence regarding AMR. These respondents cite concerns about the profits of pharmaceutical companies and the practices of some agricultural companies. They are therefore concerned about involving private sector in the stakeholder platform (even though this was part of the IACG proposal) and would want stringent safeguards, in terms of avoiding conflicts of interest, if that part does proceed.

129 While it is difficult to assess in the absence of detailed terms of reference for all the proposed structures, details of how they interact among themselves and with other mechanisms,[220] and the anticipated cost, it does seem that there could be a risk of the global governance and coordination mechanisms being too cumbersome, bureaucratic and costly. Would there be similar structures regionally. While it is difficult to comment on coordination mechanisms at country level, presumably it is this level which will be the most important? Where countries have functioning multisectoral coordination mechanisms, it may be that these incorporate the need for coordination among Tripartite/Quadripartite organizations and other multilaterals. If not, how is coordination happening? Would it be through existing UN country teams? How would they include OIE given that they are not a UN agency and may lack in-country presence? If there are separate in-country Tripartite/Quadripartite structures, how do they involve other multilateral/UN agencies? Is there any role for the UN Resident Coordinator?

<u>Equity and inclusion</u>

130 The GAP AMR recognized that actions to optimize use of antimicrobial medicines and to renew investment in research and development of new products need to be accompanied by actions which ensure affordable and equitable access by those who need those products. In particular, it noted that the cost of investment in research and development of new medicines, diagnostic tools and vaccines needs to be delinked from price and the volume of sales to facilitate equitable and affordable access. It also highlighted the role of public sector partnerships with the private sector to ensure equitable access through fair pricing and donations for the poorest populations and the need for collaboration on research to be based on fair and equitable benefit sharing. The GAP also pointed out that many of the actions that can support affordable and equitable access to medicines had been set out previously by WHO.[221] Specifically, one of the Secretariat actions under objective 5 was to explore with Member States, intergovernmental organizations, industry associations and other stakeholders, options for the establishment of a new partnership or partnerships to facilitate affordable and equitable access to existing and new medicines and other products while ensuring their proper and

[220] For example, is there overlap with the One Health High-Level Expert Panel that is currently being established – see https://www.who.int/news/item/20-05-2021-new-international-expert-panel-to-address-the-emergence-and-spread-of-zoonotic-diseases (accessed 29 July 2021)

[221] WHO (2011) *Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property* available on https://www.who.int/phi/publications/Global_Strategy_Plan_Action.pdf (accessed 29 July 2021). For example, element 6 on improving delivery and access identifies three key actions - encouraging increased investment in the health delivery infrastructure and financing of health products in order to strengthen the health system; establishing and strengthening mechanisms to improve ethical review and regulate the quality, safety and efficacy of health products and medical devices; and promoting competition to improve availability and affordability of health products consistent with public health policies and needs:

optimal use (see Annex 5).[222] Issues relating to gender or human rights were not explicitly explored in the GAP AMR.

131 The 2016 political declaration on AMR[223] underlined that "*all research and development efforts should be needs-driven, evidence-based and guided by the principles of affordability, effectiveness and efficiency and equity, and should be considered as a shared responsibility.*" It also acknowledged the importance of delinking the cost of investment in research and development on antimicrobial resistance from the price and volume of sales so as to facilitate equitable and affordable access to new medicines, diagnostic tools, vaccines and other results to be gained through research and development.

132 The IACG highlighted issues of equity. For example, in its recommendation (E1) on identifying new antimicrobials, the IACG's report stressed the principles on equity outlined in the political declaration. Also, a report by the IACG's subgroup on innovation, research and development, and access recommended that any attempts to identify "*best buys*" should include equity considerations.[224]

133 The WHO Secretariat has taken some actions to promote equity and inclusion when responding to AMR. Specifically, in 2018, the Secretariat published guidance on enhancing the focus on gender and equity in national efforts to respond to AMR.[225] WHO was actively involved in establishing the Global Antibiotic Research and Development Partnership (GARDP) and part of GARDP's role is to ensure sustainable access to treatments and affordability to all in need.[226] However, respondents expressed some concern that while there had been major development in terms of ensuring proper and optimal use of antimicrobials, e.g. development of the AWaRe system, there had been less definitive progress in terms of ensuring equitable access to appropriate antibiotics when needed. One respondent commented that the GAP could give more detail on promoting equity, e.g. stratifying by gender and vulnerable groups. Although, as early as 2005, the World Health Assembly noted that countries should use valid indicators to monitor the long-term impact on equity of access to medicines, quality of care, affordability and cost, such metrics do not currently seem to be included in the GAP AMR monitoring framework or major tools, such as TrACSS. While some Member States[227] have used the Health Equities Assessment Tool[228] to assess their public-facing AMR activities, this appears to be the exception rather than the rule. Similarly, while some agencies are using tools to think and work politically,[229] this is again the exception rather than the rule. An internal audit found that there had been insufficient analysis and attention to mainstreaming gender, equity and human rights.[230] This is of concern particularly given that some consider that antibiotic resistance may be the next epidemic of inequality.[231]

[222] This was one of five aims under this action. The others were to coordinate the work of many unlinked initiatives aiming to renew investment in research and development of antibiotics (including follow up initiatives from the Consultative Expert Working Group on Research and Development24); to identify priorities for new treatments, diagnostics and vaccines on the basis of emergence and prevalence of serious or life-threatening infections caused by resistant pathogens; to act as the vehicle(s) for securing and managing investment in new medicines, diagnostics, vaccines and other interventions; to establish open collaborative models of research and development in a manner that will support access to the knowledge and products from such research, and provide incentives for investment.

[223] See https://digitallibrary.un.org/record/842813?ln=en (accessed 29 July 2021).

[224] IACG (2018) *Seventh Meeting of the Ad-hoc Interagency Coordination Group on AMR* available on https://www.who.int/antimicrobial-resistance/interagency-coordination-group/IACG-AMR_SeventhMtgReport.pdf (accessed 29 July 2021).

[225] WHO (2018) *Tackling Antimicrobial Resistance Together: Working Paper 5.0: Enhancing the Focus on Gender and Equity* available on https://www.who.int/antimicrobial-resistance/national-action-plans/AMRGenderEquityGuidance-Sept2018.pdf (accessed 29 July 2021).

[226] See https://www.gardp.org/who-we-are/about-gardp/ (accessed 29 July 2021).

[227] Public Health England (2018) *Assessing Public Facing AMR Activities Using the Health Equities Assessment Tool* available on http://antibioticguardian.com/assets/AntibioticGuardianConference2018-11-DianeAshiruOredopeGrahamHood.pdf (accessed 29 July 2021) and Public Health England (2020) *Health Equity Assessment Tool (HEAT): Practice Example: Antimicrobial Resistance (AMR)* available on https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/920027/AMR_HEAT-case_study.pdf (accessed 29 July 2021).

[228] See https://www.who.int/data/gho/health-equity/assessment_toolkit (accessed 29 July 2021).

[229] The Fleming Fund (2021) *Thinking and Working Politically in AMR Surveillance* available on https://www.flemingfund.org/publications/thinking-and-working-politically-in-amr-surveillance/ (accessed 29 July 2021).

[230] And that this constituted a moderate level of risk.

[231] Nadimpali et al (2021) *Antibiotic Resistance: A Call to Action to Prevent the Next Epidemic of Inequality* available on https://doi.org/10.1038/s41591-020-01201-9 (accessed 29 July 2021).

134 Respondents raised a number of issues which relate to how equitable and inclusive responses to AMR are and these are briefly summarized here:

- There are concerns that narratives on appropriate and optimal use of antimicrobials are framed more in terms of curbing excessive and inappropriate use of antimicrobials rather than on ensuring access to appropriate antibiotics when needed. This framing may assume that an appropriate prescriber and any prescribed medicines are available, accessible and affordable to people when sick and this is not the case in many resource-constrained settings. For example, in 2021, more people in low- and middle-income countries are reported to have died from lack of access to antimicrobials than from resistant infections.[232]

- Discussions on and approaches to prioritization should consider issues of equity and inclusion. Many respondents are concerned that there is currently excessive focus on developing new antimicrobials, particularly as the financial sums needed for these are huge. They argue that these monies could benefit more people if invested in different ways. However, these arguments may assume that funds available for one purpose could be easily transferred to another which may not be the case in practice. Proponents of increased investment in new antimicrobials argue that the costs of not doing this are potentially much greater, for example, if a resistant infection spread widely and there was no medicine available to treat it.

- When new medicines are developed, these should be available in an equitable and inclusive manner. There are concerns that any new antibiotic may only be available in high-income countries. A key issue identified here is delinking costs of research and development from issues of price and volume of sales. While there has been some progress on such matters, e.g. in relation to pull incentives, there will be need to take steps to ensure equitable access to any such new medicines and to monitor actively the extent to which this is happening. If these pull incentives are provided on a country-by-country basis, it may be easier to ensure equity within countries than across different countries. There are particular concerns from civil society respondents that following initially publicly-funded research, private companies may select the most-promising candidates to bring to market without making commitments on access and stewardship conditions. They considered this to be a particular issue within the AMR Action Fund. They are also concerned that apparently positive efforts by private sector groups to enhance equitable access[233] might result in WHO losing the normative lead to an industry-funded roadmap.

- There are concerns that communications on AMR, e.g. to raise awareness may not be done in ways which are equitable and inclusive. For example, special events, such as World Antimicrobial Awareness Week may be celebrated in some geographical areas only, e.g. in a country's capital city.

- There are concerns among some respondents that there may be conflict and tension, in some settings, between commercial interests and principles of equity and inclusion. Areas identified where this is an issue is the R&D of new products and some agricultural practices, particularly the use of antimicrobials for growth promotion.[234]

[232] The Center for Disease Dynamics, Economics and Policy (2021) *The State of the World's Antibiotics 2021: A Global Analysis of Antimicrobial Resistance and its Drivers* available on https://cddep.org/wp-content/uploads/2021/02/The-State-of-the-Worlds-Antibiotics-in-2021.pdf (accessed 29 July 2021)
[233] See https://www.amrindustryalliance.org/wp-content/uploads/2021/06/AMR-Industry-Alliance-Scaling-Access-RFP.pdf (accessed 4 August 2021).
[234] See for example ODI (2017) *Beating the Superbugs: The Role of Politics in Antibiotic Resistance* available on https://odi.org/en/insights/beating-the-superbugs-the-role-of-politics-in-antibiotic-resistance/ (accessed 29 July 2021) and Kahn (2016) *One Health and the Politics of Antimicrobial Resistance* available on https://academic.oup.com/ije/article/46/5/1723/4031393 (accessed 29 July 2021).

Health Systems

135 The GAP AMR recognizes that countering AMR needs long-term investment in strengthening health systems in developing countries, and that this applies to animal as well as human health systems. A World Bank report on the economic threat of AMR stated that "*competencies for the AMR fight can't be built independently of the health system's durable core capacities. Effective AMR action depends, for example, on reliable health information systems, rational procurement and management of drugs, and the presence of a trained and motivated health workforce.*"[235] This section reviews the review's findings on issues related to health systems structured around WHO's six health system building blocks[236] (see Figure 27). Much of the information is drawn from countries' joint external evaluations and country cooperation strategies.

Figure 27: WHO's six health system building blocks

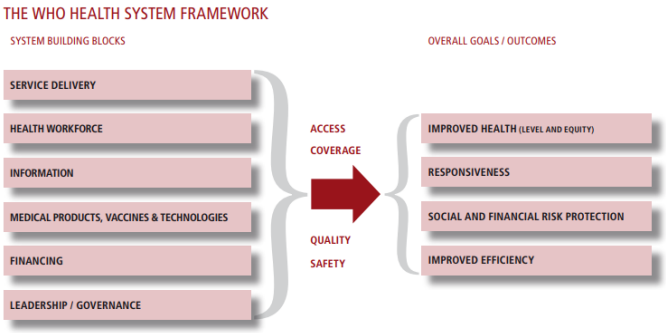


Image Source: [*Everybody's Business: Strengthening Health Systems to Improve Health Outcomes : WHO's Framework for Action*]

Service Delivery

136 Laboratory services play an essential role in detecting, reporting, notifying and monitoring infections, efficacy of antibiotic treatments and resistant pathogens. Well-functioning laboratory and diagnostic services are key to informed patient care decisions and rational use of antibiotics[237] by providing definitive evidence of resistance. As a result, laboratory systems are a key part of service delivery in relation to AMR. Laboratory systems also provide data to surveillance systems on the nature, scope and extent of antimicrobial resistance.[238] Respondents expressed concerns that while the GAP AMR focused on the importance of AMR surveillance, the need to strengthen laboratory capacity to achieve this and particularly to improve clinical management was not particularly emphasized. As key drivers of quality care and surveillance of AMR, laboratories must adhere to standards and ensure the quality and validity of data. However, joint external evaluations show that many countries have experienced challenges related to laboratory capacity, resources and structure which hinder their ability to provide clinical services, monitor resistance and strengthen national surveillance. These challenges include:

- *Limited capacity of laboratory staff* – in many countries laboratory staff have limited capacity and skills needed to test, analyse and diagnose resistant pathogens. Specifically, there are gaps regarding laboratory personnel's ability to conduct antimicrobial susceptibility testing (AST) and detection of AMR pathogens in animals. Some countries lack effective laboratory networks with a national reference laboratory to set and ensure the maintenance of protocols and testing standards. In addition, some countries experience disparities in technical skills of personnel between national and sub-national levels related to different opportunities to access training materials and participate in training events.

[235] World Bank (2017) *Drug-Resistant Infections: A Threat to Our Economic Future* available on https://openknowledge.worldbank.org/handle/10986/26707 (accessed 12 July 2021)
[236] World Health Organization (2007) *Everybody's Business: Strengthening Health Systems to Improve Health Outcomes: WHO's Framework for Action* available on https://www.who.int/healthsystems/strategy/everybodys_business.pdf (accessed 4 June 2021)
[237] Okeke et al (2011) *Diagnostics as Essential Tools for Containing Antibacterial Resistance* available on https://doi.org/10.1016/j.drup.2011.02.002 (accessed 7 June 2021).
[238] Petti et al (2006) *Laboratory Medicine in Africa: A Barrier to Effective Health Care* available on http://dx.doi.org/10.1086/499363 (accessed 7 June 2021)

- *Procurement and supply of laboratory reagents and equipment* – some JEEs identified issues related to the procurement and supply of laboratory reagents and equipment. Essential reagents, including from the American Type Culture Collection (ATCC) used to monitor the quality of AST, are not supplied to some laboratories, resulting in increasingly limited availability of testing. Some countries referred to shortages and difficulties in accessing reagents due to insufficient financial resources. Some laboratories use expired reagents, which can in turn compromise clinical testing. There are also shortages and limited availability of key laboratory equipment, including isolation rooms and automated equipment. Limited resources also translate to poor maintenance of laboratory equipment and repair services. Weak supply chain and maintenance processes contribute substantially to delays in testing and diagnosis of resistant pathogens.

- *Funding* – limited funding for laboratories contributes to weak laboratory services. Some national governments have not been able to allocate adequate funds to purchase equipment and reagents, support maintenance and repair services, and support the hiring of skilled staff. These elements are essential to ensure the continuity and sustainability of quality-assured, public laboratory services. In addition, AMR is not included in some national health laboratory strategic plans or policies and is therefore not considered in strategic financial planning for laboratory services.

- *Regulatory framework* – some countries have experienced challenges related to the accreditation of laboratories. Some national accreditation standards are not aligned with international standards and are insufficient to ensure the quality of laboratories. Lack of adequately skilled staff, inadequate equipment or maintenance and adequate budget to support the accreditation process are common barriers for LMICs.[239]

137 Box 14 briefly summarizes ways in which the WHO Secretariat has supported Member States to strengthen their laboratory services.

Box 14: WHO Secretariat support to strengthening laboratory services in Member States

The WHO Secretariat has published guidance for national reference laboratories and provides technical assistance for laboratories to countries through its WHO Collaborating Centres Network. The AMR Surveillance Collaborating Centre Network also supports External Quality Assessments in the six WHO regions.

The WHO Regional Office for Europe launched the "*Better Labs for Better Health*" initiative in the context of International Health Regulations (IHR) core capacities. The initiative provides support in four areas: development of national laboratory policies and strategic plans in countries lacking a legal and regulatory framework for laboratories; improvement of national training programmes and implementation of laboratory quality management systems; establishing networks for emergency preparedness and response; and advocacy, partnership and leadership.

At the country level, WHO Country Offices support the strengthening of laboratory services by including it as a strategic priority in Country Cooperation Strategies, often as part of the IHR core capacities. Core activities include support for the establishment of quality control laboratories, quality improvement of diagnostic laboratories, support to laboratory surveillance, capacity building for laboratory-based surveillance, strengthening of national supply chain management, strengthening of diagnostic capacities, support towards the certification and accreditation of laboratories, and support for the coordination of national laboratories networks.

Health Workforce

138 The health workforce are a key element in the sustained and quality delivery of health services. To have a competent and available workforce, WHO considers that the following actions are necessary: planning and monitoring of workforce availability, distribution and performance; design and availability of training programmes; adequate funding for the scaling-up of education programmes; distribution of the workforce at

[239] Dacombe et al (2016) Fleming Fund: Supporting Surveillance Capacity for Antimicrobial Resistance An Analysis of Approaches to Laboratory Capacity Strengthening for Drug Resistant Infections in Low and Middle Income Countries available on https://www.flemingfund.org/wp-content/uploads/a542c98413458b331934650ff46c4214.pdf (accessed 8 July 2021).

the different levels of the health system for effective service delivery and strategies to retain an effective workforce.[240] However, joint external evaluations identify that many countries are experiencing problems in this area including:

- *Human resources policies and mechanisms* – some countries have insufficient policies in place to identify gaps in technical skills and training for the health workforce. Without assessments being conducted to review the distribution and competency of staff, needs of the health system risk not being reviewed adequately. In turn, there can be poor matching of staff to health system needs and inadequate availability of training.

- *Training for capacity building* – staff may have limited capacity in the areas of AMR detection, diagnosis, data collection, analysis and reporting, and AMR surveillance in animals and aquaculture. Specifically, countries experience limited technical skills to perform antimicrobial sensitivity testing, inadequate qualification in laboratory microbiology, limited capacity to conduct antimicrobial risk assessments and to set up warning systems at the national level. This can be due to inadequate education programmes and in-service trainings to establish a qualified workforce by developing the necessary technical skills. In addition, in some countries, AMR is poorly covered in education programmes, resulting in low awareness and understanding of resistant pathogens. There are also challenges in providing updated training to health workers to work with, for example, new equipment or diagnostic tests. These limitations pose a challenge to AMR surveillance in the human, animal and plant sectors and to the rational use of antibiotics, partly dependent on correct diagnoses. There are disparities in the availability and access to training of technical skills between the national and sub-national levels. Health workers residing in capitals can access relevant training materials, short-term courses and events to upgrade technical skills compared to personnel outside the capital. This can result in a skewed distribution of the workforce and disparate reporting and surveillance of AMR.

- *Attraction and retention of health workers* – some countries have difficulties in attracting and retaining qualified staff, particularly at the sub-national level. Some examples include lack of qualified microbiologists in provincial hospitals, staff not trained in clinical case definition for diagnostics or in the characterization of antimicrobial resistant organisms. This can in turn lead to underserved remote communities and biases in data reporting, focused on hospitals in larger cities. WHO recommends a multisectoral approach to develop tailored national guidelines to attract and retain qualified staff,[241] including for ministries of education to increase focus on geographic distribution of staff at the sub-national level by developing education on rural health topics, promoting engagement in remote communities and promoting the enrolment of students coming from rural areas.

- *Barriers to an AMR- competent health workforce* – perhaps the most substantive barrier to a competent, well-trained and evenly-distributed workforce in relation to AMR is the lack of financial resources to provide pre- and in-service training on AMR. There are limited budgets to match the needs of health workers and poor sustainable financing plans to develop the skills and competences of staff. In addition, limited multisectoral governmental coordination between relevant ministries results in inadequate education programmes. As a result, there can be a lack of qualified personnel with the necessary knowledge and technical skills, and limited incentives to promote the even geographical distribution of health workers. Coordination between health, finance and education ministries, as well as public health institutes and universities, is key to a competent workforce.[242]

[240] World Health Organization (2007) *Everybody's Business: Strengthening Health Systems to Improve Health Outcomes: WHO's Framework for Action* available on https://www.who.int/healthsystems/strategy/everybodys_business.pdf (accessed 4 June 2021)
[241] World Health Organization (2021) *WHO Guideline on Health Workforce Development, Attraction, Recruitment and Retention in Rural and Remote Areas* available on https://apps.who.int/iris/rest/bitstreams/1344850/retrieve (accessed 9 July 2021).
[242] WHO Regional Office for Europe (2011) *Attracting and Retaining Health Workers in the Member States of the South-Eastern Europe Health Network* available on https://www.euro.who.int/__data/assets/pdf_file/0013/152203/e95774.pdf (accessed 9 July 2021).

139 Box 15 briefly summarizes ways in which the WHO Secretariat has supported Member States to strengthen their health workforce.

Box 15: WHO Secretariat support to strengthening health workforce in Member States

The WHO Secretariat has supported professional education and training as key components of the GAP AMR's first objective. The WHO Secretariat has supported the strengthening of health workers' competences and skills by publishing guidance documents, including a competence framework for training and education on AMR, curricula and training guide to build capacity or update staff on key skills for AMR. The Secretariat has also published guidance documents, evidence-based guidelines and training materials for IPC and antimicrobial stewardship.

At the country level, a review of Country Cooperation Strategies shows that building capacities of health personnel is often a key strategic priority. Activities supported by WHO Country Offices include the development of national human resources for health plans, advocacy for strategies to retain health workers, strengthening of IPC standards in health facilities, building of technical skills for laboratory capacity, upgrading pre- and in-service curricula, support to diagnostics capacity building, support for health education and integrated human resources development.

Information

140 Information systems are essential for decision-making by providing and disseminating quality-assured, timely and reliable health data. WHO considers the following conditions needed for a well-functioning health information system: generate population and facility-based data; have the capacity to detect, investigate, communicate and contain events that threaten public health security at the place they occur, and as soon as they occur; have the capacity to synthesize information and promote the availability and application of this knowledge.[243] Challenges identified through joint external evaluations include:

- *Lack of monitoring and evaluation systems for national AMR action plans* – many countries' national action plans lack clear monitoring and evaluation systems. Few countries are systematically tracking and reporting progress of implementation of their national AMR action plans.

- *Lack of national strategic plans for AMR surveillance* – some countries, particularly LICs and LMICs, do not have a national strategic plan for the surveillance of AMR. While this does not necessarily equate with not conducting AMR surveillance, countries without an explicit plan and budget may lack several key components for AMR surveillance and adequate human and financial resources included. This may result in the lack of designated national reference laboratories, coordinating bodies with appointed focal points and designated sentinel sites to collect information on drug-resistant pathogens in humans and animals.

- *Data management systems for AMR surveillance* – some countries lack a designated, centralized database or integrated surveillance system to report AMR-related events. Many health facilities use their own software to collect AMR data, posing challenges for harmonized data. There are also challenges in staff capacity to collect, analyse and report data in the relevant information systems, leading to weak analysis of AMR resistance, inadequate mapping of infections and insufficient notification of AMR events. In addition, reporting of data in information systems can be limited to large national or regional hospitals in some countries, thus underrepresenting some populations in rural or community hospitals.[244] Weak management of data can lead to diminished trust in results and reporting, and unrepresentative capturing of national AMR resistance. Some barriers to capturing quality data at country-level include the absence of data standards for collection, reporting and analysis; limited information technology skills of staff, particularly in remote areas; poor laboratory infrastructure; low interoperability between information systems (laboratory, hospital and health information systems) due to limited coordination across sectors (animal, health, plant) and health facilities (laboratories and clinics).[245] Inadequate coordination between facilities can limit the validation of data by laboratories. In addition, some LMICs report data using paper-based systems which may

[243] World Health Organization (2007) *Everybody's Business: Strengthening Health Systems to Improve Health Outcomes: WHO's Framework for Action* available on https://www.who.int/healthsystems/strategy/everybodys_business.pdf (accessed 4 June 2021).
[244] Temkin et al (2018) *Estimating the Number of Infections Caused by Antibiotic-Resistant Escherichia Coli and Klebsiella Pneumoniae in 2014: A Modelling Study* available on https://doi.org/10.1016/S2214-109X(18)30278-X (accessed 9 July 2021).
[245] Vong et al (2017) *Using Information Technology to Improve Surveillance of Antimicrobial Resistance in South East Asia* available on https://doi.org/10.1136/bmj.j3781 (accessed 7 July 2021).

leading to fragmented and inaccurate reporting of AMR data.[246] Additional barriers to adequate data management include limited financial support to develop or sustain information systems. Some countries do not have a budget allocated for this component as part of a national AMR surveillance strategy; some are dependent on external funding for surveillance, leading to question the sustainability of these investments.[247]

- *Limited coordination and integration with overall health management information systems* – focusing only on AMR-related data, particularly AMR surveillance data risks promoting this as another vertical information system rather than as part of overall health management information systems. There are particular challenges here, not least because of the need to coordinate data across many sectors, including human health, animal health, plant health, food production, food safety and the environment. Currently, in some countries, there is poor communication between Laboratory Information Management System (LIMS), hospital information systems and national health information systems.

141 Box 16 briefly summarizes ways in which the WHO Secretariat has supported Member States to strengthen health information systems and data management.

Box 16: WHO Secretariat support towards strengthened health information systems and data management in Member States

The WHO GLASS team has disseminated several guidance and technical documents to help countries assess the strengths of national surveillance systems; establish mechanisms for data management and coordinated surveillance activities; hire skilled IT personnel; and strengthen data collection for AMR surveillance, data analysis and submission. The WHO Secretariat has also conducted webinars and training sessions on AMR surveillance and data collection, analysis and reporting at the global and regional levels.

At the country level, WHO country offices provide technical assistance and support to national government efforts towards strengthening the reporting of AMR data using the WHONET software, improving the regular sharing of health information between countries and GLASS, providing training to report in national surveillance systems and in GLASS, and activities aimed at ensuring the completeness, quality and timeliness of data.

Medical Products, Vaccines and Technologies

142 WHO defines a well-functioning health system as one which provides affordable and equitable access to medical products, vaccines and technologies, and ensures their cost-effectiveness, safety and quality.[248] The adequate prescription of appropriate antibiotics is essential for the rational use of antimicrobial agents and to reducing the spread of AMR. However, joint external evaluations show that countries have experienced a number of issues in this area:

- *Regulations on access to antimicrobial agents* – many countries, particularly low- and middle-income countries, lack regulatory frameworks to guide the prescription of antibiotics. As a result, antibiotic treatments can be accessed over-the-counter, often resulting in ineffective treatment due to self-medication and incorrect diagnoses. In others, the ongoing over-the-counter sales of antibiotics persists despite the existence of regulations prohibiting this often because of lack of capacity to enforce the regulations. Additionally, there are structural and socio-economic barriers in some low- and middle-income countries that contribute to this system, while few incentives are created to ensure the enforcement of the regulations. Lack of regulations for antimicrobials, both in the human and animal sectors, can lead to overuse and emergence of drug-resistant pathogens.[249] Inappropriate use and prescription of antibiotics can result from many factors, including limited awareness and understanding of resistance among prescribers; low incentives to promote the rational use of antibiotics; lack of

[246] Gandra et al (2020) *Antimicrobial Resistance Surveillance in Low- and Middle-Income Countries: Progress and Challenges in Eight South Asian and Southeast Asian Countries* available on https://doi.org/10.1128/cmr.00048-19 (accessed 7 July 2021).
[247] Wellcome Trust (2020) *The Global Response to AMR Momentum, Success, and Critical Gaps* available on https://wellcome.org/sites/default/files/wellcome-global-response-amr-report.pdf (accessed 14 July 2021).
[248] World Health Organization (2021) *WHO Guideline on Health Workforce Development, Attraction, Recruitment and Retention in Rural and Remote Areas* available on https://apps.who.int/iris/rest/bitstreams/1344850/retrieve (accessed 9 July 2021).
[249] World Health Organization (2018) *WHO Report on Surveillance of Antibiotic Consumption: 2016-2018 Early Implementation* available on https://www.who.int/medicines/areas/rational_use/who-amr-amc-report-20181109.pdf (accessed 21 June 2021).

diagnostic capacity; high poverty rates leading to self-medication and ineffective use of antibiotics; and cultural beliefs and background.[250] [251] [252]

- *Lack of access to medicines* – the UN defined access to medicines as "*as having medicines continuously available and affordable at public or private health facilities or medicine outlets that are within one hour's walk from the homes of the population*".[253] Lack of access to antibiotics is estimated to cause over five million deaths annually.[254] Lack or delayed access to antibiotics, when they are needed, can cause ineffective treatment and avoidable use of higher groups of antibiotics, for example overuse of Watch compared to Access antibiotics[255] which can create higher levels of resistance. As a result, access to first-line antibiotics is key to reducing AMR by ensuring proper supply and prescription of appropriate medicines.[256]

- *Other barriers to the rational use of antibiotics* – including high poverty rates, which can result in patients not completing their antibiotic treatment to reserve the medicine for future use; weak knowledge and understanding of prescribers; poor supply of appropriate antibiotics; and low financial incentives for prescribers to engage in rational use.[257]

143 Box 17 briefly summarizes ways in which the WHO Secretariat has supported Member States to improve regulations and access to medical products, vaccines and technologies.

Box 17: WHO Secretariat support to Member States to improve regulations and access to medical products, vaccines and technologies

The WHO Secretariat published the 2019 WHO AWaRe Classification Database, which includes the List of Essential Medicines and antibiotics classified between the Access, Watch and Reserve groups. The classification helps optimize the use of antibiotics by providing the most effective treatment. WHO, in collaboration with FAO and OIE, also developed the Draft Framework for Development and Stewardship, which provides standards, regulations and targets to improve access to essential antibiotics. In 2020, the WHO Secretariat published an Action Framework to leverage vaccines to reduce antibiotic use and prevent antimicrobial resistance.

At the country level, WHO Country Offices provide support to national authorities to develop regulations on prescription of antibiotics; advocate for optimal and rational use of medicines; implement stewardship programmes in national and referral hospitals; strengthen mechanisms to monitor and regulate the quality and safety of drugs; develop pharmacovigilance activities; ensure that populations have access to affordable medicines; and strengthen supply chain management to facilitate access to essential medicines and first-line antibiotics.

Financing

144 WHO identifies a strong health system as one which "*raises adequate funds for health, in ways that ensure people can use needed services, and are protected from financial catastrophe or impoverishment associated with having to pay for them*".[258] However, respondents report that one of the main obstacles facing national AMR responses is the lack of financing needed to implement planned activities. Some of the challenges in this area identified through joint external evaluations include:

[250] Sharaf et al (2021) *Barriers of Appropriate Antibiotic Prescription at PHCC in Qatar: Perspective of Physicians and Pharmacists* available on https://doi.org/10.3390/antibiotics10030317 (accessed 14 July 2021).
[251] Lin et al (2020) *Factors Influencing Inappropriate Use of Antibiotics in Outpatient and Community Settings in China: A Mixed-Methods Systematic Review* available on https://gh.bmj.com/content/5/11/e003599 (accessed 14 July 2021).
[252] Nahar et al (2020) *What Contributes to Inappropriate Antibiotic Dispensing among Qualified and Unqualified Healthcare Providers in Bangladesh? A Qualitative Study* available on https://doi.org/10.1186/s12913-020-05512-y (accessed 14 July 2021).
[253] United Nations (2003) *Indicators for Monitoring the Millennium Development Goals* available on http://mdgs.un.org/unsd/mdg/Host.aspx?Content=Indicators/OfficialList.htm (accessed 14 July 2021).
[254] Daulaire et al (2015) *Universal Access to Effective Antibiotics is Essential for Tackling Antibiotic Resistance* available on https://doi.org/10.1111/jlme.12269 (accessed 16 July 2021).
[255] Gandra and Kotwani (2019) *Need to Improve Availability of "Access" Group Antibiotics and Reduce the Use of "Watch" Group Antibiotics in India for Optimum Use of Antibiotics to Contain Antimicrobial Resistance* available on https://doi.org/10.1186/s40545-019-0182-1 (accessed 6 July 2021).
[256] Faizi (2020) *Antimicrobial Resistance: The Need to Tackle Access-Excess Problem* available on https://www.downtoearth.org.in/blog/health/antimicrobial-resistance-the-need-to-tackle-access-excess-problem-74271 (accessed 7 July 2021).
[257] Heyman et al (2014) *Access, Excess, and Ethics – Towards a Sustainable Distribution Model for Antibiotics* available on https://doi.org/10.3109/03009734.2014.904958 (accessed 26 July 2021).
[258] World Health Organization (2021) *WHO Guideline on Health Workforce Development, Attraction, Recruitment and Retention in Rural and Remote Areas* available on https://apps.who.int/iris/rest/bitstreams/1344850/retrieve (accessed 9 July 2021).

- *National financial resources for AMR are inadequate in many countries* – joint external evaluations for many countries show that there is no or insufficient funding to implement and sustain AMR-related, including from the national government budget. While this may be partly due to the fact that some NAPs are not costed or do not have an allocated budget, or that AMR is not included in budget planning processes, the main issue in many low- and middle-income countries is inadequate funding available to allocate to health. There are many reasons why AMR may not be prioritized financially and these are likely to vary from context to context. These reasons may include lack of compelling data on the health burden posed by AMR particularly in countries facing other health burdens and socio-economic challenges. Additionally, some countries do not have adequate channels to mobilize sustainable and predictable financial resources.

- *Dependency on donor funding* – while ideally, AMR responses would be funded from budgets to different sectors, such as human health, animal health, plant health, food production, food safety and the environment. Financial realities mean that in many low- and middle-income countries AMR responses, and many other areas of health, are dependent on donor funding, often provided as earmarked project funding.[259] Because of low resources to finance AMR activities, many countries are heavily reliant on donor funding. This reliance may have negative implications for prioritization and sustainability of financing. For example, availability of funding for surveillance activities may mean that they are implemented more than other areas but this does not necessarily reflect national priorities.

145 Box 18 briefly summarizes ways in which the WHO Secretariat has supported Member States to access sustainable financing for their AMR responses. However, this is an area of the GAP that has received relatively little emphasis (see Section 3.6, from p42).

Box 18: WHO support to Member States on sustainable financing

Financial support available through the MPTF is likely to assist implementation of national action plans. However, the amount is very limited currently and seems to be being largely used to support in-country activities of Tripartite organizations.

At the country-level, some WHO Country Offices have supported the development and implementation of costed national action plans and coordination with development partners able to provide financial support.

Leadership and Governance

146 The effective leadership and governance of a health system is essential to ensuring adequate intersectoral coordination and the design, financing and implementation of national health policies. WHO defines this building block as "*the role of the government in health and its relation to other actors whose activities impact on health.*"[260] Challenges include:

- *Difficulties establishing and operating multisectoral AMR coordination mechanisms* – some countries have found it difficult to establish multisectoral AMR coordination mechanisms and respondents report that, even where they have been established, they may not have been formally approved and often function suboptimally, for example, meeting very infrequently. Some mechanisms omit some important sectors, such as plant health, agriculture or the environment resulting in limited data and information sharing and poor dissemination of key protocols and national plans. This further contributes to a fragmented AMR response with insufficient intersectoral coordination.

- *Difficulties operationalizing a One Health approach* - effective national governance of AMR through a One Health approach requires the involvement of all key sectors, including human and animal health, plant, agriculture, food production and environment sectors. It also necessitates the inclusion of different state and non-state actors, such as education and finance ministries, national public health institutes, health facilities at different levels and academia, to enable the implementation of activities

[259] Gandra et al (2020) *Antimicrobial Resistance Surveillance in Low- and Middle-Income Countries: Progress and Challenges in Eight South Asian and Southeast Asian Countries* available on https://doi.org/10.1128/cmr.00048-19 (accessed 7 July 2021).
[260] World Health Organization (2021) *WHO Guideline on Health Workforce Development, Attraction, Recruitment and Retention in Rural and Remote Areas* available on https://apps.who.int/iris/rest/bitstreams/1344850/retrieve (accessed 9 July 2021).

related to AMR awareness, education, infection prevention and control, regulation of antimicrobial agents, laboratory functions and AMR surveillance. To ensure that remote areas and communities are appropriately targeted, committees should also include non-governmental organizations, civil society and community health workers.

- *The risks of setting up another parallel coordination mechanism* – while there is little doubt that effective programmes to address AMR require effective intersectoral coordination, it is more questionable whether this needs another parallel coordination mechanism. A health systems approach might argue for one coordination mechanism across and between health systems rather than having individual separate coordination mechanisms for particular issues, diseases and funding sources.[261] [262] While earmarked funding has helped the control of some diseases and contributed to disease management, service specialization and increased momentum,[263] it has also created vertical national health workforces, information systems and management mechanisms. Development assistance funding can lead to a plurality of technical working groups, committees and sub-committees.[264] Many of these groups require the presence of the same government representatives, leading to time and workload constraints.

- *The tendency to promote inappropriate one-size fits all approaches* – all country contexts are unique and, in some, there are particular challenges for effective coordination. For example, there may be particular difficulties in countries with unstable, fragmented or absent governance structures.[265]

147 Box 19 briefly summarizes ways in which the WHO Secretariat has supported Member States to strengthen AMR leadership and governance.

Box 19: WHO Secretariat support to Member States to strengthen AMR leadership and governance

The WHO Secretariat conducted a worldwide country situation analysis on the response to antimicrobial resistance in 2015, which documented whether countries had an existing coordinating mechanism in place. The Secretariat also published a working paper on multisectoral coordination to assist countries set up structures tailored to fit countries' needs. WHO has also operated a shift by using a Universal Health Coverage (UHC) and health system approach to country support.

At the country level, WHO Country Offices support leadership and governance by working with national ministries to extend coordination to other sectors by collaborating with other ministries, non-state actors, UN agencies and development partners. COs also support the strengthening of health systems' capacities with a focus on health leadership, and technical assistance to implement national plans.

WHO internal structures and systems

148 This section focuses on a number of issues which are largely internal to WHO and, indeed, are largely internal to the WHO Secretariat. They include leadership, strategy and vision; structures; and staffing. There is a final section which seeks to link AMR to broader WHO priorities, including the SDGs.

[261] Joint Inspection Unit (2017) Review of Donor Reporting Requirements across the United Nations System available on https://www.unjiu.org/sites/www.unjiu.org/files/jiu_rep_2017_7_english.pdf (accessed 23 July 2021).
[262] Mussa et al (2013) *Vertical Funding, Non-Governmental Organizations, and Health System Strengthening: Perspectives of Public Sector Health Workers in Mozambique* available on https://doi.org/10.1186/1478-4491-11-26 (accessed 30 July 2021).
[263] World Health Organization (2008) *When do Vertical (Stand-Alone) Programmes Have a Place in Health Systems?* available on https://www.who.int/management/district/services/WhenDoVerticalProgrammesPlaceHealthSystems.pdf (accessed 19 July 2021).
[264] German Development Institute (2011) *Multi-Donor Budget Support: Only Halfway to Effective Coordination* available on https://www.oecd.org/dac/evaluation/dcdndep/50036948.pdf (accessed 19 July 2021).
[265] Interagency Coordination Group on AMR (2018) *Antimicrobial Resistance: National Action Plans IACG Discussion Paper* available on https://www.who.int/antimicrobial-resistance/interagency-coordination-group/IACG_AMR_National_Action_Plans_110618.pdf (accessed 19 May 2021).

Leadership, Strategy and Vision on AMR in the WHO Secretariat

149 Overall leadership within the WHO Secretariat on AMR is provided by an Assistant Director-General (ADG) on AMR and many stakeholders commented positively on this and that it signalled the priority and importance given to AMR within WHO. However, respondents commented that, since the adoption of the GAP, there had been four different ADGs leading work on AMR. Some respondents expressed fatigue over the ADG turnover, as they had found that it had resulted in variations in visions, scope of work and priorities and a tendency to reinvent the programme with each new ADG. These respondents considered that continuity in leadership and vision for the division is essential to sustain progress against the GAP AMR objectives.

150 Some respondents expressed concern over the lack of a clear overall AMR strategy for and within the WHO Secretariat. While the GAP AMR and its M&E framework are considered useful documents, respondents within the Secretariat saw them largely as advocacy documents, that is to be used with others to emphasize the importance of AMR and responses to it. But, these documents are less clear in terms of what the WHO Secretariat should be doing it and how. The M&E framework, in particular, is almost completely focused on monitoring Member State actions and related outcomes. Respondents are concerned that there is no clear strategy or guide for how they should engage with other divisions and coordinating workstreams. The review notes that WHO lacks a clear theory of change for the GAP AMR or for its constituent parts, e.g. on awareness raising. Such a theory of change could be a useful component of any AMR strategy for the WHO Secretariat. A particular lack is a short-term or long-term roadmap or workplan for the WHO Secretariat focused on what the Secretariat will do to contribute to progress towards the GAP AMR objectives, when that will be done and how that would be monitored. Criticisms of national action plans for not being budgeted and funded would be more credible if the WHO Secretariat had a budgeted and funded workplan for its own contribution to the GAP AMR. It is of note that other Tripartite organizations do have such workplans and FAO used theirs as the basis for their recent evaluation. They see the GAP AMR as the overall guiding document but their own workplan as a mor specific guide as to what they will do as an organization to contribute overall to AMR responses. The WHO secretariat could usefully follow this approach and it will be even more important to do so for any subsequent GAP AMR assuming that that might be developed as a Tripartite or Quadripartite document. While the Secretariat actions in the GAP AMR could be a useful starting point for developing a more specific roadmap or workplan, these are not sufficient on their own. Many are very generic (see Annex 5). They lack any timeframe or indicators of success. In addition, given the nature of AMR, it is likely that some of the actions that were needed in 2015 are less relevant now and things which are very relevant now, for example work around the AWaRe criteria, was not included (as those criteria had not been developed) when the GAP AMR was adopted. It is unrealistic to develop a detailed roadmap or workplan of this nature and expect it to remain fixed and relevant for multiple years in the future.

Structures

151 An AMR Division was created within the Secretariat in 2019 to support the implementation of the GAP AMR. This division is divided into two departments – Global Coordination and Partnership (GCP) and Surveillance, Prevention and Control (SPC). Prior to the establishment of this division, there had been an AMR Secretariat within the Director-General's Office and, in the initial stages of the Transformation, AMR was placed under an ADG for special initiatives.

152 The GCP Department has a team for antimicrobial stewardship and awareness with a group responsible for antimicrobial stewardship and behaviour change, and another responsible for awareness and campaign. There is another team for impact initiatives and research coordination with groups responsible for (i) One Health research priority setting and synergy and (ii) global initiatives and instruments respectively. This department also houses the Tripartite Joint Secretariat and a group responsible for coordination for country impact and governance and partnership. Broadly, this department is responsible for headquarters' activities on objectives 1, 4 and 5 of the GAP AMR. The SPC Department has teams for (i) control and response strategies, (ii) national action plans and monitoring and evaluation, and (iii) surveillance and evidence lab strengthening. The latter team has three groups working on (i) antimicrobial consumption and use surveillance, (ii) laboratory strengthening and integrated surveillance, and (iii) evidence and emerging AMR. Broadly, this department is responsible for objective 2 of the GAP AMR. Responsibility for infection, prevention and control seems to rest outside of the AMR Division.

153 Within any structure, there will be a need to coordinate with others beyond a particular team, department, division or organization and that is particularly the case with AMR. Respondents raised a number of areas where they may be or have been challenges:

- With other organizations outside WHO. This is particularly focused on the Tripartite or Quadripartite organizations and is managed by the Tripartite Joint Secretariat located within the GCP department.

- Elements of AMR require coordination with groups, teams, departments and divisions in other parts of WHO. This is particularly the case for infection prevention and control, that is objective 3 of the GAP AMR. In many ways, this makes sense as IPC is relevant to many areas other than AMR but it is likely to require different ways of working than for topics directly managed by the AMR Division.

- There may be elements of AMR which require coordination between the two departments of the AMR Division. One identified by respondents relates to antimicrobial consumption with the topic falling under one department while surveillance of AMC falls under the other. While some respondents identified the problem as lying with the way responsibilities had been allocated, there will always be issues of this nature requiring staff to find ways of working together across departments. There may be other similar issues.

- There may be elements of AMR which require coordination between teams within the same department. For example, monitoring, evaluation, surveillance and research are often seen as interlinked and they may often be handled by the same team or linked teams. In this case, responsibilities for monitoring and evaluation and surveillance sit with different teams albeit within the same department. Responsibility for research[266] appears to be with different teams in a different department.

154 In general, respondents were of the view that the creation of the AMR Division was a positive step to leverage resources and political will towards AMR. It also marked the recognition of the threat posed by antimicrobial resistance. The subsequent appointment of an ADG for AMR has helped bring relevant issues to the WHO senior leadership and raise awareness on some of challenges faced by the teams. The Transformation agenda[267] has also contributed to less siloed programmes within WHO. As AMR is an interdisciplinary and crosscutting issue, some respondents said it had benefited from new planning and budget processes aimed at delivering country-level impact and improved coordination between divisions and departments. However, some respondents expressed concerns related to the structural changes resulting from the implementation of the Transformation agenda within WHO. Reportedly, this caused disruption among some staff, as it entailed

[266] To the extent that this responsibility is allocated

[267] See https://cdn.who.int/media/docs/default-source/documents/about-us/who_transformation_plan_-_architecture_16feb2018.pdf?sfvrsn=b9f72218_7&download=true (accessed 5 March 2021)

some level of participation or training. Additionally, some staff had to learn and integrate new planning and budget processes across different outputs. One result of the Transformation has been the spread of AMR outputs across the three Triple Billion targets, as part of the GPW13. Through review of programme budget documents, the review team identified 17 outputs linked with AMR. Concerns were raised that this division between outputs and outcomes made budgeting and planning difficult and this means that it is not easy to track and monitor the AMR Division's budget across outputs.

155 In terms of interactions between the three levels of the Secretariat (headquarters, regional offices and country offices), respondents reported that overall communication and coordination has been good and effective. The AMR Division is reported to be very responsive to requests for data, information or training materials. HQ staff have provided training and technical assistance to their counterparts, including on the use of the global surveillance system and on new GLASS modules. Regional offices have also been essential in providing training and technical support to country offices and national stakeholders across the objectives of the GAP. Examples include the celebration of World Antimicrobial Awareness Week at the continental level,[268] support for proof-of-principle projects to advance country-level surveillance capacities, and the leveraging of existing regional infection prevention and control frameworks to strengthen clinical management. Nevertheless, there have sometimes been different emphases between some parts of headquarters and some regional offices, e.g. over aligning surveillance protocols and information sharing and these may have affected enrolment rates in GLASS in some regions, e.g. AMR and WPR. Some country offices also commented that sometimes there might appear to be a lack of coordination between different staff in a particular regional office, but this was thought to be down to the large number of countries a small number of staff needed to support.

156 Many internal respondents expressed concerns about the division of the AMR Division's work between two departments. These concerns included a lack of understanding of the rationale behind the creation of the departments and how the respective workstreams were assigned. There were concerns that there had been limited coordination between the two departments with one not always knowing what the other was doing even in areas that potentially affected them, for example discussions over GAP revision. This led to perceptions of an imbalance of power and feelings of the work being fragmented. Respondents commented that the culture of headquarters sometimes appeared not to favour collaboration between divisions or departments and, at times a more competitive work culture was encouraged, albeit involuntarily.

Staffing

157 Many respondents at headquarters level expressed concerns that the level of staffing, particularly within headquarters, was insufficient to deliver on the objectives of the GAP. It is not clear if this relates to staffing levels overall or is a more nuanced issue, for example relating to unfilled posts and/or shortages in particular areas. Table 10 seeks to analyse different staffing levels available to different teams within the AMR Division.[269] It does appear that some teams, e.g. surveillance and evidence lab strengthening are relatively well-staffed and this may reflect historical priorities and available funding. There is also need to note that the WHO Secretariat is relatively well-staffed on AMR when compared to other Tripartite or Quadripartite organizations, particularly OIE and UNEP.

[268] See https://apps.who.int/gb/ebwha/pdf_files/EB148/B148_11-en.pdf, (accessed 27 July 2021)
[269] Figures are based on a document obtained from the WHO intranet which appears to be dated December 2019.

Table 10: Reported staffing levels of different teams within the AMR Division[269]

Team	Mapped	Matched	Vacant budgeted	Vacant unbudgeted
ADG's Office[270]	5		2	
GCP Director[271]	1		1	2
Impact Initiatives and Research Coordination	2	1	2	5
Tripartite Joint Secretariat[272]	2		4	1
Antimicrobial Stewardship and Awareness	2		3	6
SPC Director[273]	2			2
Control and Response Strategies		1	2	1
National Action Plans and Monitoring and Evaluation	5		2	
Surveillance and Evidence Lab Strengthening	13		4	

158 Other respondents identified that the biggest capacity gaps within the WHO Secretariat were at country level and these gaps were often mirrored, and indeed amplified, within national governments, particularly in low- and middle-income countries. The review team was not able to identify precisely what human resources are available on AMR in different country offices. While some do have a staff member assigned to AMR, this may only be part of their role and the precise proportion may not be clearly defined even notionally. This may mean that when there are peaks of work, e.g. as there was in relation to COVID, other areas of work may expand to effectively crowd out any work on AMR (see paragraphs 162-174). While ROs did not report the same understaffing issues as COs, there was concern that staffing levels were not sufficient to match the breadth of AMR activities and training needed to support countries.

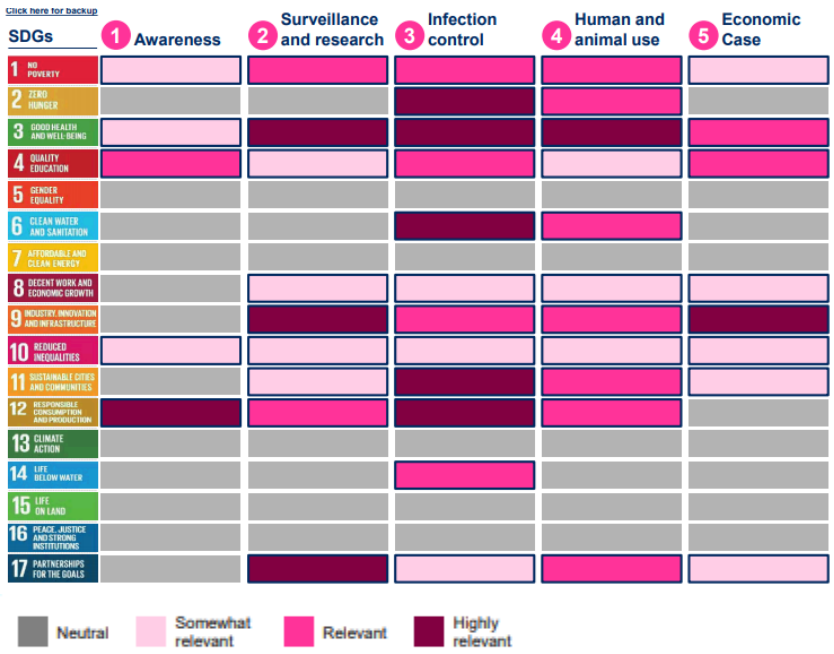
159 Respondents explained that inadequate human resources often reflect a lack of funding and it was this lack of funding that was the main constraint hindering the ability of country offices to support and contribute to work on AMR. Respondents commented that it was not unusual for WHO to be in a place where resources available did not match the aspirations of a particular strategy. This meant that WHO country offices had to work in areas where they could get funding, not necessarily areas of the most strategic importance. This explained why much of the support provided on AMR had been related to surveillance.

[270] Excluding ADG
[271] Excluding Director
[272] Including group on coordination for country impact and governance and partnership
[273] Excluding Director

Linking AMR to broader WHO priorities including the SDGs

160 WHO has a strong focus on contributing to the SDGs, particularly those on health. The Secretariat advocated for an AMR indicator to be included as one of the indicators on health and this was agreed.[274] The IACG found that AMR is also relevant to several other indicators in the 2030 Agenda for Sustainable Development (see Figure 28).[275] An analysis of the relevance between the GAP AMR strategic objectives and relevant SDG indicators shows that AMR has the capacity to threaten the achievement of some SDG goals. While the spread of AMR is most closely linked to SDG3, other goals are at risk. The World Bank's report[276] on the potential economic consequences of AMR estimates that up to 24 million people could be pushed into extreme poverty by 2030, thus compromising the ability to reach SDG1: End poverty in all its forms everywhere and SDG8: Promote sustained, inclusive and sustainable economic growth, full and productive employment and decent work for all. Failure to reduce AMR would have an indirect impact on several other goals of the 2030 Agenda.

Figure 28: Analysis of IACG of GAP AMR objectives and their relevance to SDG indicators



Note: this graphic is from an IACG presentation

161 Despite progress made on linking AMR to the SDGs, AMR is still insufficiently framed within the 2030 Agenda and this hinders a clearer, more visual understanding of the socio-economic, health and environmental impacts of AMR, which could further strengthen support for a One Health approach which in turn might contribute to greater willingness to coordinate across sectors and address some of the underlying causes of antimicrobial resistance.

COVID-19

162 While this is not a review of COVID-19 responses, the review did take place at a time when the world was experiencing a COVID-19 pandemic. It affected the review, for example, meaning that all interviews were conducted remotely. More significantly, COVID affected actions on GAP AMR in a number of ways. It displaced focus away from AMR to the pandemic.[277] It disrupted some planned activities, e.g. STAG AMR meetings, technical support missions to countries, joint external evaluations, updating of country cooperation strategies and a variety of AMR-specific interventions and there was displacement of activity away from actions on AMR

[274] Indicator 3.d.2: Percentage of bloodstream infections due to selected antimicrobial resistant organisms

[275] Inter-Agency Coordination Group (IACG) on Antimicrobial Resistance (2018) *AMR Indicators and their Relevance to the Global Indicator Framework for the SDGs and Targets for the 2030 Agenda for Sustainable Development* available on https://www.who.int/antimicrobial-resistance/interagency-coordination-group/AMR_SDG_indicators_analysis_slides.pdf (accessed 6 July 2021).

[276] See https://documents1.worldbank.org/curated/en/323311493396993758/pdf/final-report.pdf (accessed 12 July 2021)

[277] Lynch et al (2020) *Antimicrobial Stewardship: A COVID Casualty?* available on https://www.journalofhospitalinfection.com/article/S0195-6701(20)30462-X/fulltext (accessed 30 July 2021) and Pelfrene et al (2021) *Antimicrobial Multidrug Resistance in the Era of COVID-19: A Forgotten Plight?* available on https://aricjournal.biomedcentral.com/articles/10.1186/s13756-021-00893-z (accessed 30 July 2021).

to COVID-19 responses. This particularly affected WHO Country Offices where staff are often covering multiple issues. Given the nature of the pandemic, staff were often pulled into supporting COVID responses reducing the amount of time they had available for other things, including GAP AMR interventions. It also affected WHO Regional Offices and had a particularly severe effect on many government partners. However, some stakeholders raised concerns that some negative changes which may be being attributed to COVID, e.g. reduced TrACSS reporting for 2019/20, may be due to other factors.[278]

163 Respondents noted that, because of COVID, many activities which might have been conducted face-to-face were carried out virtually. This affected awareness raising activities, in particular, and led to greater reliance on social media.

164 One lesson learned from COVID-19 responses has been the importance of talking to end-users, such as practitioners, patients and pharmacists particularly when seeking to design behaviour change messages. Historically, WHO has tended to see Ministries or Ministers of Health as the end-users of information they produce and this has meant that WHO has tended to communicate in a similar way on all things. This changed to some extent in the response to COVID and lessons can be learned for AMR programmes and interventions.

165 The COVID-19 pandemic emphasized the importance of diagnostic testing and of laboratories to allow testing to take place. Again, this provided an opportunity to emphasize the importance of laboratory strengthening with potential benefits to AMR responses, e.g. patient management and surveillance. However, some laboratories found that they were repurposed to focus exclusively on COVID-19.

166 The occurrence of the COVID-19 pandemic has brought issues of infection, prevention and control into sharp focus and there has been emphasis on reducing transmission of infection through measures, such as handwashing, social distancing and use of appropriate personal protective equipment. It is possible that such measures could have had a general positive benefit on infection prevention but there are some concerns that the measures are quite focused on respiratory viruses and it is unclear how sustainable the different measures are.[279] Respondents were also concerned that the WHO Secretariat and others had failed to capitalize on the opportunity provided by COVID-19 to emphasize the wider benefits of better infection prevention and control. Some respondents also raised concerns that some practices might have undermined IPC measures. For example, staff may have been too busy to observe proper procedures and, in some cases, staff with limited experience were deployed to unfamiliar areas.

167 Another issue highlighted by the COVID-19 pandemic is the role played by health-care settings in transmitting infection and, in some cases, acting as epidemic amplifiers. Again, this was an opportunity to raise wider issues about healthcare acquired infections which respondents felt had been largely missed.

168 COVID-19 has had a mixed effect on levels of human antibiotic use with possible mixed effects on levels of AMR.[280] In many hospital settings, particularly in low- and middle-income countries, but also in some critical care settings in high-income countries, there has been an increase in the use of antibiotics, even in the absence of evidence of their value.[281] This has been very substantial in some settings and is considered likely to have

[278] See https://www.ignitetheidea.org/whoeb-amrbriefing (accessed 30 July 2021).
[279] The Center for Disease Dynamics, Economics and Policy (2021) *The State of the World's Antibiotics 2021: A Global Analysis of Antimicrobial Resistance and its Drivers* available on https://cddep.org/wp-content/uploads/2021/02/The-State-of-the-Worlds-Antibiotics-in-2021.pdf (accessed 29 July 2021).
[280] Knight et al (2021) *Antimicrobial Resistance and COVID-19: Intersections and Implications* available on https://elifesciences.org/articles/64139 (accessed 30 July 2021) and Ansari et al (2021) *The Potential Impact of the COVID-19 Pandemic on Global Antimicrobial and Biocide Resistance: An AMR Insights Global Perspective* available on https://academic.oup.com/jacamr/article/3/2/dlab038/6217452 (accessed 30 July 2021).
[281] For example, Hsu (2020) *How COVID-19 is Accelerating the Threat of Antimicrobial Resistance* available on https://www.bmj.com/content/369/bmj.m1983 (accessed 30 July 2021), Beovic et al (2020) *Antibiotic Use in Patients with COVID-19: A 'Snapshot' Infectious Diseases International Research Initiative (ID-IRI) Survey* available on https://www.semanticscholar.org/paper/Antibiotic-use-in-patients-with-COVID-19%3A-a-survey-Beovic-Dou%C5%A1ak/c20bba237acbb8394f6014c1aba8b630d1fa5d7c (accessed 30 July 2021), Vaughan et al (2020) *Empiric Antibacterial Therapy and Community-onset Bacterial Coinfection in Patients Hospitalized With Coronavirus Disease 2019 (COVID-19): A Multi-hospital Cohort Study* available on https://pubmed.ncbi.nlm.nih.gov/32820807/ (accessed 30 July 2021), Huttner et al (2020) COVID-19: *Don't Neglect Antimicrobial Stewardship Principles!* available on https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30232-9/fulltext (accessed 30 July 2021) and The Center for Disease

had a substantial negative effect on AMR rates. It may also have caused shortages of some antibiotics in some settings. There was also evidence of a surge in bacterial and fungal co-infections among patients with COVID infection.[282] WHO did issue interim evidence-based guidelines on the optimal use of antibiotics for COVID-19 patients.[283] Conversely, in many community settings, as COVID-19 infections rose and lockdown measures were imposed, the number of people attending health services for other conditions fell, in some cases dramatically. As a result of this, rates of antibiotic prescription and use fell in these contexts.

169 Another lesson from the COVID-19 response has been increased understanding of how quickly therapeutics and vaccines can be developed when there is an imperative to do so and financing is provided in a way that permits progress to be made on different stages of development often in parallel. While it might be difficult to galvanize such a response in relation to AMR given its "*silent*" nature, experience of COVID shows what is possible in the face of a dire emergency and with good data available. What seems clear is that if AMR is ever to galvanise the kind of support that was made available for COVID, it will need accurate and credible data on rates of AMR and the level of health burden they are creating. The AMR pandemic will only remain "*silent*" as long as such data remains largely unavailable.

170 Another lesson that emerges from COVID relates to deficiencies in the current mechanisms for reimbursing medicine development based solely on use. If a therapeutic had been developed for an earlier coronavirus infection, such as SARS or MERS that was hypothetically effective against COVID-19, it probably would not have been available as sales to combat MERS or SARS would not have been sufficient to sustain the company that had created it. If, by some chance, the medicine had been available and it could have been used to control the outbreaks in Wuhan and elsewhere, preventing the pandemic, the financial value paid based on the use of the medicines would not represent the true value to the world and to the world economy. Time will perhaps tell whether experience of the pandemic has changed attitudes towards financial mechanisms for rewarding R&D delinked from price and volume of sales. If they have, this could be beneficial for the development of new antibiotics.

171 The COVID pandemic has provided a stark object lesson on what a pandemic is and its potential consequences, particularly in the absence of effective medical countermeasures, especially therapeutics.[284] It has also emphasized the value of good pandemic preparedness. These issues were referred to by WHO's Director-General in a report to the Executive Board as having spotlighted the impact of infectious diseases on human health and economic development.[285]

172 The COVID pandemic has also illustrated the importance of having diagnostic tests that can be made available quickly, at the point-of-care and at sufficient scale. Indeed, COVID has shown the value of all types of medical countermeasures, e.g. diagnostics, therapeutics and vaccines.

173 Given that COVID-19 is considered to have spread to humans from animals, i.e. it is a zoonosis, it has increased public recognition and understanding of a key One Health concept, namely that the health of humans, animals, and the environment are intricately connected.

174 Given these and potentially other points, there is probably justification for some sort of lesson learning exercise from COVID-19 for the benefit of responses to AMR. This could take the form of some sort of review.

Dynamics, Economics and Policy (2021) *The State of the World's Antibiotics 2021: A Global Analysis of Antimicrobial Resistance and its Drivers* available on https://cddep.org/wp-content/uploads/2021/02/The-State-of-the-Worlds-Antibiotics-in-2021.pdf (accessed 29 July 2021).

[282] Nori et al (2020) *Bacterial and Fungal Coinfections in COVID-19 Patients Hospitalized During the New York City Pandemic Surge* available on https://pubmed.ncbi.nlm.nih.gov/32703320/ (accessed 30 July 2021).

[283] A second updated version was published in January 2021 – see https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-1 (accessed 30 July 2021).

[284] See, for example, The Center for Disease Dynamics, Economics and Policy (2021) *The State of the World's Antibiotics 2021: A Global Analysis of Antimicrobial Resistance and its Drivers* available on https://cddep.org/wp-content/uploads/2021/02/The-State-of-the-Worlds-Antibiotics-in-2021.pdf (accessed 29 July 2021).

[285] See https://apps.who.int/gb/ebwha/pdf_files/EB148/B148_11-en.pdf (accessed 27 July 2021)

Given that some respondents think that opportunities have already been missed, there is an argument for doing this sooner rather than later. It might have been better to have used some form of real-time methodology, such as has been commonly used in humanitarian settings, where lessons are learned while an emergency is ongoing rather than waiting until it is over to learn lessons. One concern raised by respondents was that lessons from COVID-19 responses may not be learned fully if different parts of WHO do not speak to each other.

4. Conclusions

175 The review has drawn a number of conclusions and these are summarized here and are the basis for recommendations in the section that follows. They follow the same structure as the findings, namely considering the GAP AMR overall, each of the five objectives and then a number of crosscutting issues.

GAP AMR Overall

C1. It is very difficult to assess overall progress towards outcomes as these are not clearly defined. While the M&E framework provides a menu of possible outcome indicators for the GAP AMR, a smaller number is needed that can be actively monitored and tracked. While performance in terms of GAP implementation by Member States is statistically-associated with country income level, there are countries that have managed to achieve higher levels of implementation than might be expected based on country income level. Identified success factors include using data as an "*eyeopener*"; being willing to recognize and respond to challenges and difficulties; high level political support and the role of AMR champions; financial and technical support; and effective coordination often based on existing mechanisms. There is some evidence that WHO support has contributed to levels of and improvements in country performance in terms of GAP AMR implementation. While the biggest areas of improvement have been in core areas, such as developing national action plans and multisectoral coordination, there is evidence that these elements are associated with improved performance overall. While performance on human health indicators is stronger than in other areas, there is a statistically-significant positive association between improvements in human health indicators and improvements in other areas.

C2. The review has highlighted a number of deficiencies in the GAP AMR which need to be addressed in the short-term through strengthening guidance and application of the current GAP and in the medium- to longer-term through revising and updating the GAP. These areas include:

- The current GAP was originally conceived as a WHO document which other partners, FAO and OIE, later adopted. The STAG has agreed that any future revised GAP would need to be a Tripartite (plus UNEP) document.
- Unlike other Tripartite organizations, such as FAO, the WHO Secretariat lacks a detailed workplan for its own contribution to the GAP AMR. Such a plan is needed and should contain clear milestones which could be monitored to assess progress.
- Developing a tool or tools which allow prioritization of responses, particularly in contexts where resources are limited.
- The need for a clearer focus on how raised political awareness is translated into practical political commitment and provision of resources globally, regionally and nationally, for example as reflected in the recently-published priorities of the Global Leaders Group.
- The need for a more practical M&E framework with clearer indicators and targets which are actively tracked and reported on.
- The need to reflect the importance of research and innovation beyond product research and development.
- The need within product research and development to emphasise the importance of diagnostics and vaccines.

- Greater emphasis on the importance of plant health, food production, food safety and the environment, for example in the area of optimizing antimicrobial use.

Objective 1: Improve awareness and understanding of antimicrobial resistance through effective communication, education and training

C3. Clearly, the GAP AMR has raised awareness of AMR globally and, in many countries. It has become the recognized reference document for responses to AMR. But, this has largely not been translated into increased financial resources available to the AMR response, not least because there is no clear purposive plan of action for how this should be achieved globally or in country although the recently-published priorities of the Global Leaders Group (particularly priorities 1 and 4) do focus on these issues. It is very difficult to assess progress towards objective 1 because of a lack of a clear and shared understanding of what awareness and understanding are to be promoted, among whom and for what purpose. The current outcome indicator is currently little more than a title. What efforts there have been to collect data at outcome level have been sporadic and fragmented.

Objective 2: Strengthen the knowledge and evidence base through surveillance and research

C4. Clearly, there has been a strong commitment to developing the Global Antimicrobial Resistance and Use Surveillance System (GLASS) and this has expanded the number of countries enrolled and the number of areas or modules covered. GLASS has provided support and incentives to many countries to develop or strengthen their AMR surveillance systems. However, there are still many countries, that report having national AMR surveillance systems that are not part of GLASS and this is particularly an issue in some countries. One of the main issues with GLASS is that it is not currently able to provide representative and comparable data on AMR across countries and it is unlikely that any system based on sentinel surveillance could do this in the foreseeable future because of differences in laboratory capacity and clinical testing practices. The recent review of GLASS concluded that there was a need to develop complementary approaches, such as prevalence surveys. Much of the focus on surveillance has been on human health. Integration of surveillance across sectors remains a challenge. Many countries reportedly lack a One Health approach to surveillance due to technical, financial and coordination constraints. There has been much less focus on research under this objective and, in practice, research activities under the GAP are mainly focused on product research and development.

Objective 3: Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures

C5. The main challenge with this objective is the breadth of infection prevention and control measures and that they benefit a wide range of other diseases and issues apart from AMR. As a result, the AMR Division does not have direct control and responsibility for this objective so needs to work with others to make progress. This has proved difficult. Analysis by the WHO Secretariat and for the review shows that there had been little progress in this area in many countries as of 2020.

Objective 4: Optimize the use of antimicrobial medicines in human and animal health

C6. There are concerns that this objective focuses only on human and animal health, so excludes important areas, such as plant health, food production, food safety and the environment. There are many barriers to optimal use of antimicrobials, not least limited data on how antimicrobials are currently being used. There are also concerns that the GAP AMR and its implementation may be focusing more on excessive use of antimicrobials rather than ensuring access to appropriate antibiotics when they are needed. There has been extensive work on a stewardship framework for AMR but the WHO Secretariat report that, following consultations with

Member States, there are no longer plans to negotiate a specific AMR stewardship framework but it is expected that AMR would be reflected in the proposed pandemic treaty. Some of the initiatives taken by the WHO Secretariat, for example, the development of the AWaRe classification, revision of Essential Medicines List, development of the priority pathogens list and development of the List of Critically Important Antimicrobials are considered to have been particularly influential.

Objective 5: Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions

C7. Relatively little has been done on the first part of this objective not least because of a lack of information on the disease burden caused by AMR globally, regionally and in particular countries. While some organizations have done work on the economic case globally, this has not been used to advocate for or track global resources available to respond to AMR or to provide guidance and support for countries in terms of identifying resources available to their national action plan. While the development of the MPTF is a welcome development, it is of concern that it is currently only very partially funded. There has been much more progress on the second element of the objective with the WHO Secretariat playing a key role in many important initiatives including establishing the Global Antibiotic Research and Development Partnership, establishing the AMR Action Fund, providing valued reports on the antibiotic pipeline, developing a priority list of bacterial pathogens for new product development and developing a number of target product profiles for antibacterial agents and diagnostics.

Coordination with international and national partners

C8. The importance of coordination is emphasized in the GAP AMR and a One Health approach is widely accepted as the way to achieve this. However, there is no clear shared understanding of what the definition of One Health is or what this means in practice, including at country level. The Tripartite collaboration is perhaps the clearest expression of this coordination/collaboration. In the Tripartite Strategic Framework, to be published in September 2021, One Health is described as a collaborative, multisectoral, and trans-disciplinary approach recognizing the interconnections between people, animals, plants and their shared environment. OIE and FAO are key international partners and the importance of their role is recognized both in the GAP AMR and in progress reports. Respondents would like to see more focus on environmental issues within the GAP AMR and more inclusion of UNEP, for example by expanding the Tripartite to be a Quadripartite. The IACG recommended the establishment of a number of global governance structures but, two years on, progress with implementation has been limited despite regular meetings of Tripartite organizations senior management since January 2020 to try to expedite progress. The Global Leaders Group has been established, has had two meetings and published its priorities in July 2021. However, although there was a consultation about the proposed Independent Evidence Panel and many comments were received, it is currently unclear to external stakeholders what the status of this panel is. A report was submitted by the Tripartite organizations to the UN Secretary General in February 2021 outlining the final terms of reference and proposed next steps. However, a response is awaited from the Secretary General and that report has not been made public nor shared with the review team. Finally, the partnership platform is being taken forward by the Tripartite organizations and the Tripartite Joint Secretariat is organising a meeting of Member States on 30 September 2021 to discuss the draft terms of reference and this meeting is being hosted by WHO. It is unclear how all these structures will fit together with each other and with existing structures. In the absence of costs, it is difficult to assess whether or not these are justified. What is clear is that the current proposals are unlikely to meet the coordination needs of other multilaterals, including UN agencies, working on AMR, whereas a simpler inter-agency coordination group or task force as conceived in other areas, such as non-communicable diseases might. The important roles of other multilaterals and UN agencies in responding to AMR are largely overlooked in the GAP AMR and in progress reports. Similarly, there is little systematic progress reporting of the contribution of other sectors including civil society and the private sector. In addition, presumably the main need for coordination is probably at country level and it is unclear how this

might operate in a way which brings in various development partners and maximizes use of existing structures, e.g. the UN country team.

Equity and inclusion

C9. While the importance of equity and inclusion are recognized in the GAP AMR, and in subsequent publications, there are concerns, not least in the recent audit, that GAP AMR implementation is not sufficiently focused on gender, inclusion and human rights. The WHO Secretariat has provided guidance to Member States as to how they might enhance the focus on gender and equity in national efforts to respond to AMR but more thought and analysis are probably needed to identify how a greater focus on equity and inclusion could be ensured in other areas of GAP AMR implementation.

Health Systems

C10. Weak laboratory services are a major barrier to effective programmes to respond to AMR but these are not explicitly recognized in the GAP AMR. Other elements of health systems building blocks are also extremely relevant to responses to GAP AMR. It is unclear how things envisaged in response to AMR fit into a wider systems view. For example, will AMR multisectoral coordination mechanisms and AMR surveillance data systems end up being yet another vertical or parallel system or are there ways of integrating them into existing governance systems and health management information systems. One particular complexity is that AMR is not limited to the human health sector but it also involves other sectors including animal health, plant health, food production, food safety and the environment.

WHO internal structures and systems

C11. Overall, WHO has signalled its commitment to AMR by establishing an AMR Division and providing some allocated funding and personnel. The appointment of an ADG for AMR has increased the visibility and profile of AMR both within and outside of the Organization. There are severe staffing shortages in a number of organizations in relation to AMR including WHO Country Offices, national government ministries, UNEP and some Tripartite organizations, particularly OIE. While links between AMR and broader WHO objectives, e.g. the health SDGs exist, these could be emphasized more.

COVID-19

C12. There are many lessons which can be learned from the COVID-19 pandemic and the response to it of relevance to AMR. Not only did COVID-19 cause many AMR responses and programmes to be disrupted or adapted but there were many issues of relevance to COVID-19 which were also of relevance to AMR and there were opportunities for enhanced action which may or may not have been taken. Such issues included the importance of diagnostic testing and laboratory capacity, the need for infection prevention and control and the important role of health-care settings as amplifiers of infectious diseases. In addition, COVID-19 responses may have had effects on levels of antibiotic use and, through that, on levels of AMR. These effects may have been mixed and may have differed in different contexts. COVID-19 has demonstrated very clear what a pandemic can be like particularly in the absence of effective medical countermeasures. It has also raised awareness and understanding of the connection between the health of humans, animals and the environment. COVID-19 also highlighted the deficiencies of some accepted approaches to research and development, e.g. relying on price and volume of sales to reimburse research and development costs of antimicrobials with the potential to prevent outbreaks becoming pandemics. It also showed what is possible, e.g. in terms of developing vaccines and therapeutics, when there is sufficient imperative for that.

5. Recommendations

176 The review has identified the following recommendations. They follow the same structure as the findings and conclusions, namely considering the GAP AMR overall, each of the five objectives and then a number of crosscutting issues.

GAP AMR Overall

R1. **WHO Secretariat and Member States to determine how best to strengthen the current GAP AMR both in the short-term and in the medium- and longer term.** Specifically:

In the short-term

- WHO Secretariat to provide guidance on how Member States might prioritize in low-resource settings, for example by identifying "*best buys*".
- WHO Secretariat to provide more support and guidance on how raised political awareness of AMR might be translated into practical political commitment and provision of resources globally, regionally and nationally.
- WHO Secretariat to develop a detailed workplan as to what it will do to implement the GAP AMR. This should include some form of M&E framework including, for example, tangible milestones.
- WHO Secretariat to identify a sub-set of clear indicators and targets which will be used to monitor progress of the GAP AMR overall and which the WHO Secretariat will actively track and report progress against.
- WHO Secretariat to provide guidance on how research and innovation will be promoted through the GAP AMR. This might include an overarching AMR global research agenda and guidance to countries on how they might reflect research and innovation in their national action plans.

In the medium- and longer term

- Member States and the WHO Secretariat to determine when the GAP AMR should be revised and updated to fully reflect a One Health approach covering aspects of human health, animal health, plant health, food production, food safety and the environment, jointly owned by Tripartite organizations and UNEP. One option would be to revise and update the GAP more in line with the recently-published priorities of the Global Leaders Group.

Objective 1: Improve awareness and understanding of antimicrobial resistance through effective communication, education and training

R2. **WHO Secretariat and Member States to clarify understanding and scope of this objective.** Specifically:

- WHO Secretariat to develop a theory of change covering awareness and understanding of what, by whom and for what purpose. This should be based on available evidence.
- WHO Secretariat to propose a clear indicator for the expected outcome of this objective including plans for how they will actively monitor this.

Objective 2: Strengthen the knowledge and evidence base through surveillance and research

R3. **WHO Secretariat and Member States to maintain support to GLASS and to supplement with methods to collect accurate, representative, comparable AMR data nationally, regionally and globally.** Specifically:

- WHO Secretariat and Member States to further expand enrolment in GLASS particularly among those Member States who have reported through TrACSS that they have a national AMR Surveillance system but are not yet enrolled in GLASS.
- WHO Secretariat to propose ways in which prevalence surveys can be conducted to supplement availability of representative, comparable AMR data nationally, regionally and globally.
- WHO Secretariat and Member States to identify ways in which use of surveillance data national can be increased and enhanced.
- WHO Secretariat to identify ways in which research and innovation, beyond product research and development, can be encouraged and promoted through the GAP, perhaps under this objective.

Objective 3: Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures

R4. **WHO Secretariat and Member States to identify ways in which effective sanitation, hygiene and infection prevention measures can be promoted in ways which reduce AMR.** Specifically:

- WHO Secretariat and Member States to explore ways in which effective infection prevention and control can be reflected in national AMR action plans.
- WHO Secretariat to review how parts of the Secretariat working on AMR and those working on IPC can work more effectively together.
- WHO Secretariat to review whether gains made on IPC related to COVID-19 responses are sustained and their effect on antimicrobial use and AMR.
- WHO Secretariat to develop plans to more effectively include AMR in any future plans to strengthen IPC in the light of a specific disease outbreak.

Objective 4: Optimize the use of antimicrobial medicines in human and animal health

R5. **WHO Secretariat and Member States to consider how progress under this objective can be expanded and monitored more effectively.** Specifically:

- WHO Secretariat to propose how this objective could include plant health, food production, food safety and the environment in the short-term.
- WHO Secretariat to continue with plans to track effectively antimicrobial consumption and use, particularly in the human health sector.
- WHO Secretariat to clarify the importance of appropriate clinical management of people with infections as a key part of optimal use of antimicrobials. This could take the form of guidance, including a focus on the importance of good laboratory services.

Objective 5: Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions

R6. **WHO Secretariat to explain how the economic case for investment in AMR responses will be made and used to advocate for the resources needed including globally, regionally and nationally.** Specifically:

- WHO Secretariat with others, including the Tripartite organizations, UNEP and others who have worked in this field, e.g. the World Bank and OECD to develop a clear economic case for investment in responses to AMR. This will include clear, credible data on the disease burden posed by AMR globally, regionally and in different countries.

- WHO Secretariat to develop clear plans and guidance as to how the economic case (above) can be used to advocate for sustained political commitment to and greater financial resources for AMR responses.

- WHO Member States to consider ways in which the increased financial resources needed to respond to AMR can be made available, not least through more Member States providing funds to the MPTF.

R7. **Member States and the WHO Secretariat to sustain and expand progress made on research and development for products.** Specifically:

- Member States to identify ways in which they can finance product research and development in ways which are delinked from cost and volume of sales.

- Member States, the WHO Secretariat and others to continue efforts to maximize the benefits of existing antimicrobial agents.

- WHO Secretariat to continue efforts to expand research and development efforts to also include diagnostics and vaccines.

Coordination with international and national partners

R8. **The WHO Secretariat and other Tripartite organizations to identify ways in which coordination can be enhanced and the contribution of other actors recognized and maximized.** Specifically:

- WHO Secretariat, FAO and OIE to identify organizations, such as UNEP and other multilateral agencies, and sectors, such as civil society and the private sector that are making important contributions to AMR and to identify ways in which their contributions can be maximized and recognized, e.g. in progress reports.

- WHO Secretariat to cooperate with FAO, OIE and UNEP to develop guidance on the One Health approach. While this could include a working definition of One Health, it needs to focus mostly on the practical implications of what the One Health approach does (and does not) mean for AMR approaches globally, regionally and nationally.

- WHO Secretariat, FAO and OIE to work with UNEP to expand the current Tripartite arrangement to a Quadripartite.

- The Tripartite Joint Secretariat and Global Leaders Group to develop a framework to monitor and report on progress towards the Global Leaders Group's six priorities, key performance indicators and 2021

deliverables. This might include more detailed descriptions of the key performance indicators and how these will be measured, when particular deliverables might be expected in 2021 and how these plans fit with other monitoring and reporting efforts, e.g. for the GAP AMR, SDGs and GPW13.

- The Tripartite organisations to follow up with the UN Secretary General to determine the response to the proposal submitted six months ago. The Tripartite Joint Secretariat to explain to stakeholders the nature of the platform once a response has been received and to explain how this panel will fit with other AMR structures.

- The Tripartite Joint Secretariat to update stakeholders on the status of the proposed partnership platform following the planned meeting with Member States on 30 September 2021 to discuss the draft terms of reference.

- The WHO Secretariat, OIE, FAO and UNEP to identify ways in which work with other multilaterals, including UN agencies, can be more effectively coordinated. This could involve the establishment of an inter-agency task force.

- The WHO Secretariat, OIE, FAO and UNEP to produce guidance as to how coordination on AMR between development partners at country level might work. This should include relationships with national AMR multisectoral coordination mechanisms and links to existing structures including the UN country team and Resident Coordinator.

Equity and inclusion

R9. **Member States and the WHO Secretariat to identify ways in which equity and inclusion can be better reflected in AMR programmes and responses.** Specifically:

- WHO Secretariat to produce guidance as to how equity and inclusion can be better reflected in AMR responses globally and regionally in a similar way to the guidance produced for national AMR action plans.

Health Systems

R10. **Member States and the WHO Secretariat to identify ways in which the importance of an approach based on understanding of health systems can be incorporated more effectively into AMR responses.** Specifically:

- WHO Secretariat to produce guidance on laboratory strengthening as part of responses to AMR recognizing the importance of laboratories in delivery of clinical services and surveillance.

- WHO Secretariat to produce guidance on how AMR responses might fit with a broader health systems approach, for example, using existing systems where possible.

- WHO Secretariat to work with OIE, FAO and UNEP to provide guidance on what a health systems approach looks like in a One Health context, i.e. how can a health systems approach consider not only human health but also animal health, plant health, food production, food safety and the environment.

WHO internal structures and systems

R11. **Member States and the WHO Secretariat to review WHO internal structures and systems to ensure they are able to support effectively AMR responses.** Specifically:

- WHO Secretariat to identify ways in which effective coordination can be achieved on AMR across organizations, WHO levels, divisions, departments, teams and groups.
- Member States and the WHO Secretariat to cooperate with OIE, FAO and UNEP to better understand the level of resourcing needed to ensure optimal staffing levels across responses to AMR.
- WHO Secretariat to identify ways in which AMR responses can be more effectively linked to overall organizational priorities, for example, the health SDGs.

COVID-19

R12. **The WHO Secretariat to conduct a review of lessons learned relating to AMR responses as a result of the COVID-19 pandemic.** Specifically, this should include:

- Understanding the disruptions and adaptations that took place in AMR responses because of COVID-19.
- The opportunities that were created for AMR responses by the COVID-19 pandemic and responses to it and the extent to which these were or were not maximized.
- Better understanding of the effects of COVID-19 on antibiotic use and levels of AMR.
- Understanding how AMR responses can use increased public understanding of pandemics, the need for effective medical countermeasures and the links between human health, animal health and the environment to promote better understanding of and commitment to AMR responses.
- Lessons learned for product research and development.