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Creating a framework to align antimicrobial resistance (AMR) research with the global guidance: a viewpoint

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Running titles (left and right): Viewpoint

We describe here an initial analysis of national and international guidance documents on antimicrobial resistance (AMR) to propose a framework to align AMR research activities with global guidance. The framework provides a summary roadmap for core activities in AMR research and highlights the need for interdisciplinary and One Health collaboration. This analysis also revealed limitations in the current guidance, including a lack of explicit mention of some research activities highly relevant to AMR and a dearth of concrete objectives; consequently, an over-reliance on global guidance could be funnelling research efforts down a generic trajectory without regard to contextual factors. We suggest this framework be used by academics and policymakers to align AMR research and guidance. However, we recommend that deeper exploration be undertaken to fully contextualize the development of meaningful questions based on current knowledge, methodologies and gap analyses.

Background

Between 2014 and 2017, several reports were published that stressed the humanitarian, economic and planetary costs of failing to tackle antimicrobial resistance (AMR) in the coming decades.[1–3] A plethora of global guidance has followed, including 96 (and counting) National AMR Action Plans (NAPs) based on WHO guidance,[2] plus more specialist reports on sector-specific AMR challenges such as agriculture and environmental health. The urgency of the AMR issue has been underscored by the recent Global Research on Antimicrobial Resistance (GRAM) study, which estimates that bacterial AMR accounted for a staggering 1.27 million human deaths in 2019;[4] this study has also made recommendations for addressing the problem. However, this growing body of AMR guidance is not necessarily straightforward to translate across policy, practice or research activity.[5] Here we describe an exploratory analysis of AMR guidance, with a view to providing a practical framework for the AMR community to map their research, policy and practice back to. This process identified eight key themes, which consolidate priority areas for AMR research and highlight interdisciplinary connections across the One Health landscape.

Process

The study presented here constituted an initial document analysis and thematic synthesis of existing key AMR guidance. The sample of 24 documents (Table 1) was purposively selected to include policy-level and policy-influencing AMR guidance from across the world. This included global documents such as WHO's 2015 Global Action Plan on AMR and the IACG recommendations of 2019, which were selected because they represent macro-level, global guidance and are often utilized to shape policy. We also included national documents to gain a more nuanced view of AMR guidance across countries. Using the WHO NAP reference database, we selected a minimum of two NAPs per continent. Where large economic disparities occur between countries within continents, additional NAPs were collated to represent this diversity and thereby better reflect differences in healthcare and governance structures. This approach was reflects that economic measures are a key predictor of the ability of countries to turn policy into practice,[6,7] and are therefore highly relevant to the expensive challenge posed by AMR.

Synthesizing themes for AMR policy, action and research was an iterative process. Initially, each document was reviewed to identify its key recommendations. Clear thematic areas emerged (Figure 1), such as *Optimizing antimicrobial use in humans and animals*; *Developing new drugs, diagnostics and vaccines*; *Preventing infection in humans and animals*; and *Increasing financial investment in AMR*. In most cases, themes predominantly referred to human health actions, with recommendations on animal health focused on food-producing animals. In the second stage, each document was reviewed in full to identify further cross-cutting themes and emerging subthemes. In this latter stage, we developed a more complete thematic framework and considered how themes related to the Sustainable Development Goals (SDGs) (Table 2).

Additional themes that emerged from the close reading of the documents on the broader One Health dynamics of AMR such as *Understanding AMR in the environment* and *Optimizing AMR surveillance* (Figure 1). These themes emerged across multiple NAPs and global documents and were not confined

to subject-specific reports. For example, environmental AMR is an area of growing interest in the UK and high-income settings due to the recent Wellcome Trust report on tackling AMR in the environment; however, closer inspection of the NAPs selected for this analysis revealed that even within low-resource settings, environmental AMR is a key theme across the global guidance. The theme of coordinated action and *Governance on AMR* also appeared across documents, although the wording did differ substantially, with lower-income countries calling for targeted support on AMR and higher-income countries pledging to develop and support international collaborations.

Discussion

Figure 1 outlines the eight key themes emerging from this mapping exercise. Whilst some of these (1, 2, 5 and 6) are familiar areas for action on AMR, and are explicitly highlighted as such by the recent GRAM paper,[4] others (e.g. 3, 7) may appear confined to specialist research groups. However, the inclusion of subthemes in this analysis stresses how interlinked the eight key themes are (Table 2). Following the identification of eight key themes (Figure 1), the authors presented the analysis to a UK-based group of 18 academics working on AMR across multiple disciplines and One Health perspectives. Although a small audience, this group identified potential gaps relating to the key themes, which were then considered in light of the thematic analysis. Based on this exercise, points of challenge and opportunity were identified within the source documents and are reflected on below.

Several documents contain calls to action, which cut across One Health areas and our key themes. For example, the need to expand the monitoring of antimicrobial waste speaks to themes 4, 6 and 8. Other themes highlight the interdisciplinary nature of AMR. Water, sanitation and hygiene (WaSH) measures are critical to reducing infections and preventing their spread.[8] In theme 5, many subobjectives refer to good standards of hygiene and cleanliness whilst similar objectives are discussed in terms of public health messaging in theme 3. Financial support for clean water appears in theme 7, whilst theme 6 discusses surveillance of water and sanitation provisions as a means of reducing and preventing infection. However, the WaSH acronym is rarely utilized in these guidance

documents, and many sanitation actions are discussed in relation to human healthcare facilities, with little acknowledgement of similar standards outside formal healthcare, or in animal health. WaSH specialists are very aware of the need for a One Health focus on water and sanitation,[9] yet poor signposting of WaSH and AMR interlinkages may prevent fruitful collaborations forming. Similarly, the term 'One Health' was also sparsely utilized in the documents analysed, particularly the NAPs. Again, this could impede the formation of effective research and policy collaborations if siloed sectors such as medicine, agriculture and environmental health are not supported to identify key interdisciplinary overlaps in AMR.

Potential barriers to collaboration and AMR action also appear in theme 3, which focuses on educational and awareness activities. A growing realization in the field of community engagement is that awareness-raising approaches in isolation are not sufficient to create meaningful behaviour change on issues such as antimicrobial misuse or non-prescription purchasing.[10] Rather, communities must be engaged with a challenge and encouraged to co-produce their own solutions.[11,12] This type of intervention requires social scientists and participatory researchers, yet these groups may not be able to engage with AMR effectively if they do not see space for their expertise in the existing global guidance.

Other areas appear to be missing from the analysed documents. Dentistry, for example, receives little attention despite dental treatment accounting for >10% of prescribed antibiotics in some countries, much of which may be unnecessary and driven by patient demand rather than diagnostic information.[13] Understanding the biology of AMR is an important and expansive research area, yet it is not discussed beyond understanding how AMR can develop and spread between environments (theme 6). There is also scant consideration of the need to better understand AMR in the context of other global challenges, such as climate change.[14,15]

A final challenge is the repetition of generic objectives across NAPs without consideration of local capacity or context. Within the sampled documents, some NAPs (UK, Canada, Iran) provide detail on how to monitor and manage infections, fund research and join up existing AMR surveillance systems. Others contain generic targets with little indication as to what success will look like or how it will be

measured (Fiji, Indonesia, Costa Rica). Extensive analysis by Murray *et al.*[4] of AMR-related deaths highlights the challenges of setting such context-specific AMR targets due to the serious data and surveillance gaps in many low- and middle-income countries (LMICs). Indeed, most NAPs conceptualize their overarching objectives in very similar, broad language, which makes it difficult to identify country-specific priorities. In combination with the previously described research omissions, these issues have the potential to hinder the uptake of research on AMR and slow the development of solutions. It is therefore suggested that, whilst the framework presented here can help to align AMR research to the broad objectives of global guidance, researchers will also need to draw on the interdisciplinary expertise of colleagues and wider literature to create meaningful and sustainable action on AMR. The authors consider that a more thorough gap analysis, involving global AMR stakeholders from across One Health fields, will ultimately be needed to fully evaluate the relationship between AMR guidance and action on the ground. However, this framework provides a first step to aligning AMR research and policy objectives, with the aim of supporting more cohesive, collaborative and interdisciplinary approaches to tackling AMR.

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Transparency declarations

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Table 1. Global and national AMR action plans utilized within this analysis

Global guidance	Specialist area guidance	Action plans for:		
		High-income countries	Upper-middle-income countries	Low- and lower-middle-income countries
WHO Global Action Plan on AMR (2016) https://www.who.int/publications/i/item/9789241509763	Wellcome initiatives for environmental AMR (2018) https://wellcome.ac.uk/sites/default/files/antimicrobial-resistance-environment-report.pdf	UK AMR nine ambitions for change	National Action Plan of the Islamic Republic of Iran for Combating Antimicrobial Resistance during 2016–2021	India: National Action Plan on Antimicrobial Resistance (2017)
IACG 'No time to wait' recommendation (2019) https://www.who.int/docs/default-source/documents/no-time-to-wait-securing-the-future-from-drug-resistant-infections-en.pdf	A European One Health Action Plan against Antimicrobial Resistance (AMR) (2017) https://ec.europa.eu/health/system/files/2020-01/amr_2017_action-plan_0.pdf	Australian National Antimicrobial Resistance (AMR) Strategy (2015–2019)	Costa Rica: National Action Plan to Combat Antimicrobial Resistance (2018–2025)	Cambodia: National Strategy to Combat Antimicrobial Resistance (2015–2017)
Fleming fund 2018–2022 research and development areas https://www.flemingfund.org/about-us/investment-areas/	Highlights from the UK AMR Strategy (2019) https://microbiologysociety.org/blog/highlights-from-the-uk-amr-strategy.html	Strategic Goals of Pan-Canadian Framework for Action on Antimicrobial Resistance and Antimicrobial Use (2017)	South African Antimicrobial Resistance National Strategy (2018–2024)	Morocco: National strategic plan for prevention and control of antimicrobial resistance (2019–2022)
The WHO policy package to combat antimicrobial resistance https://apps.who.int/iris/handle/10665/270914	CDDEP: Reducing Antimicrobial Use in Food Animals (2017) https://cddep.org/publications/reducing-antimicrobial-use-food-animals/	Denmark: One Health Strategy Against Antibiotic Resistance (2017)	Fiji National Antimicrobial Resistance Action Plan (2015)	Kenya: National Action Plan on Prevention and Containment of Antimicrobial Resistance (2017–2022)
GLASS surveillance objectives https://www.who.int/initiatives/glass		Spain: National Plan to Confront Antibiotic Resistance (2019–2021)		Indonesia: National Action Plan on Antimicrobial Resistance (2017–2019)
		USA: National Action Plan for Combating Antibiotic-Resistant Bacteria (2015)		

CDDEP, Center for Disease Dynamics, Economics & Policy. NAPs can be accessed via https://www.who.int/teams/surveillance-prevention-control-AMR/national-action-plan-monitoring-evaluation/library-of-national-action-plans and links to additional documents are provided in this table.

Table 2. Summary of the eight key themes and their subthemes generated from the synthesis of the 22 global AMR guidance documents displayed in Table 1

Key theme	Subtheme	SDGs relevant to this theme
1. Optimal use of antimicrobials in humans and animals	Ensure equitable, affordable and uninterrupted access to existing drugs	Goal 1. No poverty
	End or reduce the use of antimicrobials as growth promoters or pesticides	Goal 2. Zero hunger
	Promote the responsible use of antimicrobials (complete full course of drugs, source by prescription only, protect last-resort treatments, ensure clear diagnosis before antimicrobial use is permitted)	Goal 3. Good health and wellbeing Goal 10. Reduced inequalities
2. Develop new drugs, diagnostics and vaccines	Vaccine development	Goal 3. Good health and wellbeing
	Development of new, affordable and robust rapid diagnostic tests	Goal 9. Industry, innovation and infrastructure
	Development of new drugs including the assessment of novel compounds	Goal 10. Reduced inequalities
3. Increase public engagement with AMR	Systematic and meaningful engagement of public and civil society groups	Goal 3. Good health and wellbeing
	Increase public awareness	Goal 4. Quality education
	Education of the public	Goal 5. Gender equality Goal 10. Reduced inequalities
4. Understand AMR in the environment	Responsible handling of waste (pharmaceutical, healthcare, agriculture)	Goal 2. Zero hunger
	Investigate alternative methods of biocontrol, biosecurity and alternatives to antimicrobials in agriculture, farming and aquaculture	Goal 3. Good health and wellbeing Goal 6. Clean water and sanitation
	Reduce or minimize environmental AMR contamination and spread	Goal 9. Industry, innovation and infrastructure
	Investigate the drivers behind AMR outbreaks/hotspots	Goal 13. Climate action Goal 14. Life below water Goal 15. Life on land
5. Reduce and prevent infection in humans and animals	Generic targets to reduce/prevent infection	Goal 2. Zero hunger
	Specific targets for reducing or preventing infection	Goal 3. Good health and wellbeing
	Access to clean water and safe sanitation	Goal 6. Clean water and sanitation
	Responsible and informed animal husbandry	Goal 10. Reduced inequalities
	Education of health professionals on AMR	Goal 13. Climate action Goal 14. Life below water Goal 15. Life on land
6. Optimize AMR surveillance, data management and dissemination	Strengthen knowledge of antimicrobial use, sources and levels of resistance	Goal 2. Zero hunger
	Specific data collection, analytical and reporting methods	Goal 3. Good health and wellbeing
	Design, pilot, refine and evaluate interventions to tackle AMR	Goal 6. Clean water and sanitation
	Monitor, analyse and share data on antimicrobial use in the human, animal and environmental sectors	Goal 9. Industry, innovation and infrastructure Goal 13. Climate action Goal 14. Life below water

			Goal 15. Life on land Goal 17. Partnership for the goals
7.	Increase financial investment in AMR-related activities	Fund or promote AMR research (epidemiology, socioeconomic, behavioural) Increase investment specifically in R&D of new drugs, diagnostics and vaccines Risk-assess AMR, including the financial consequences Develop the economic case for sustainable investment in AMR	Goal 2. Zero hunger Goal 3. Good health and wellbeing Goal 6. Clean water and sanitation Goal 9. Industry, innovation and infrastructure Goal 10. Reduced inequalities Goal 13. Climate action Goal 14. Life below water Goal 15. Life on land Goal 17. Partnership for the goals
8.	Establish strong AMR governance	Accelerate the development of legislation on AMR within the context of the SDGs Establish governance structures to spearhead AMR activities Collaborate at international, national and subnational levels to tackle AMR	Goal 1. No poverty Goal 2. Zero hunger Goal 3. Good health and wellbeing Goal 6. Clean water and sanitation Goal 9. Industry, innovation and infrastructure Goal 10. Reduced inequalities Goal 13. Climate action Goal 14. Life below water Goal 15. Life on land Goal 17. Partnership for the goals

Figure 1. The eight key themes identified from the global and national AMR guidance documents analysed in this study.

(Separate hi-res version on ScholarOne)