A governance framework for development and assessment of national action plans on antimicrobial resistance

Michael Anderson, Kai Schulze, Alessandro Cassini, Diamantis Plachouras, Elias Mossialos

Strengthening governance is an essential strategy to tackling antimicrobial resistance (AMR) at all levels: global, national, regional, and local. To date, no systematic approach to governance of national action plans on AMR exists. To address this issue, we aimed to develop the first governance framework to offer guidance for both the development and assessment of national action plans on AMR. We reviewed health system governance framework reviews to inform the basic structure of our framework, international guidance documents from WHO, the Food and Agriculture Organization, the World Organisation for Animal Health, and the European Commission, and sought the input of 25 experts from international organisations, government ministries, policy institutes, and academic institutions to develop and refine our framework. The framework consists of 18 domains with 52 indicators that are contained within three governance areas: policy design, implementation tools, and monitoring and evaluation. To consider the dynamic nature of AMR, the framework is conceptualised as a cyclical process, which is responsive to the context and allows for continuous improvement and adaptation of national action plans on AMR.

Introduction

The problem of antimicrobial resistance (AMR) is one of the most pressing and complex public health issues. Multidrug-resistant, extensively drug-resistant, and even pan drug-resistant organisms are a challenge for healthcare systems of varying stages of development. If not combatted in a timely and effective manner, AMR can potentially lead to millions of preventable deaths per year and to hundreds of billions of pounds in economic costs annually, because of losses in international trade or livestock production and increased health-care expenditure.[1] Following the adoption of the Global Action Plan on AMR by the World Health Assembly in 2015,[2] many countries have refined or developed their AMR national action plans (NAPs) in accordance with the internationally recognised One Health approach, which requires policies to be developed and implemented intersectorally across human, animal, and environmental health. Here, we present an AMR governance framework with a dual purpose: as a tool for policy-makers to both develop and improve AMR NAPs, and to also facilitate an objective assessment of AMR NAPs to increase accountability.

Definitions of governance have their origins in the multilateral development institutions of the late 1980s and 1990s. However, defining governance is challenging and complex. To start by defining what governance is not (ie, governance is not synonymous with government) is helpful. Addressing governance issues therefore does not exclusively rest on actions of governments, but also on other societal organisations, how they relate to the public, and how decisions are taken.[3] Various efforts to define governance have been undertaken and two widely referenced definitions have been outlined by the United Nations Development Programme and WHO. The United Nations Development Programme encompasses five good governance principles: legitimacy and vote, direction, performance, accountability, and fairness.[4] The definition recognises that these principles sometimes overlap and

might even be conflicting, their implementation is dependent on the context, the application of these principles is complex, and that good governance needs to consider how power is exercised.

Beside this general definition, governance has been defined more explicitly from a health-systems perspective, starting with the World Health Report 2000.[5] Here, governance is discussed as a form of stewardship, seen as "the careful and responsible management of the

Department of Health Policy, London School of Economics and Political Science, London, UK (M Anderson MSc, K Schulze MPhil, E Mossialos PhD); MRC Epidemiology Unit, University of Cambridge, Cambridge, UK (K Schulze); and European Centre for Disease Prevention and Control, Solna, Sweden (A Cassini MD, D Plachouras PhD)

Correspondence to:
Michael Anderson, Department of Health Policy, London School of Economics and Political Science, London WC2A 2AE, UK
m.anderson5@lse.ac.uk

Key messages

- Antimicrobial resistance (AMR) is one of the most pressing and complex issues today, with multidrug-resistant, extensively drug-resistant, and even pan drug-resistant organisms emerging
- AMR is driven by interrelated dynamics in the human, animal, and environmental health sectors, which makes governance challenging
- Strengthening governance of AMR policies at all levels (ie, global, national, regional, and local) is essential to tackling AMR; to date, no comprehensive framework for the governance of AMR National Action Plans (NAPs) has been developed
- To our knowledge, this Review is the first study that has developed a governance framework for AMR NAPs, on the basis of a systematic review of the literature, international guidance, and 25 experts from various international organisations, government ministries, policy institutes, and academic institutions
- The framework is conceptualised as a cyclical process between the three governance areas: policy design, implementation tools, and monitoring and evaluation
- Within policy design, improving strategic vision, coordination, participation, accountability, responsibility, sustainability, and equity were identified as key to strengthening governance
- Implementation, surveillance, antimicrobial stewardship, infection prevention and control, education, public awareness, medicines regulation, fostering research and development, and facilitating market access to novel products were all identified as essential tools
- To ensure NAPs can adapt and continually improve, feedback mechanisms, reporting, and research to understand the drivers of AMR, were identified as crucial components to allow monitoring and evaluation
- To build on this governance framework, a need exists for international leadership to develop consensus and engagement from national policy makers to strengthen governance in AMR NAPs

well-being of the population".[5] The role of the government is outlined as one of oversight and trusteeship, which requires vision, intelligence, and influence. In 2002, WHO defined governance further by outlining six domains or sub-functions: generation of intelligence, formulating strategic policy direction, ensuring tools for implementation (powers, incentives, and sanctions), building coalitions and partnerships, ensuring a fit between policy objectives and organisational structure and culture, and ensuring accountability.[6] Later, within the 2007 WHO Framework for Action, these principles were cemented as one of the six key building blocks of a health system,[7] under the domain of leadership and governance.

Governance in the context of AMR NAPs

Understanding what good governance translates to within the context of AMR NAPs is a different matter. The complex nature of the emergence and spread of AMR globally and the political-economic features of health systems pose challenges that mandate effective governance for successful implementation of AMR policies.[8,9] AMR is driven by interrelated dynamics in the human, animal, and environmental health sectors, so actions to address AMR should include mechanisms that coordinate AMR policy intersectorally. Previous absence of international agreement regarding the direction of efforts to tackle AMR has allowed the discussion to be shaped by a so-called war on superbugs or post-antibiotic apocalypse discourse, which has put much emphasis on the discovery of new antimicrobials through pharmaceutical innovation and too little priority on reduction of antimicrobial use, and on prevention and control of infections. Furthermore, the complexity of AMR also necessitates policies that range in diversity from surveillance and awareness to regulation, stewardship, and infection prevention and control, each in the context of human, animal, and environmental health.

Given these challenges, considerable interest in governance within AMR policies exist. In an analysis of AMR policies in 29 countries within the EU and EEA, the Third Report on Implementation of the Council Recommendation on prudent use of antimicrobial agents in human medicine suggested the need for prioritising governance within national policies to contain AMR.[10] The Food and Agriculture Organization of the UN, the World Organisation for Animal Health, and WHO together form a tripartite body that has produced a manual for developing NAPs on AMR that emphasises the establishment of a governance mechanism and the undertaking of a thorough situational analysis as key for the development of NAPs.[11] The global tripartite database on country progress has been a first step towards monitoring AMR NAPs on a global scale.[12] The goal of the database is to provide baseline information on the status of countries regarding the implementation of the Global Action Plan and actions to address AMR across all sectors. The database provides crucial initial information such as the existence of a so-called One Health NAP, surveillance of antibiotic use in human and animal health, training of veterinary and health personnel, and the presence of public awareness campaigns, although to date its data collection is broad and not detailed.

In 2018, a discussion paper[13] on AMR NAPs from the Interagency Coordination Group on Antimicrobial Resistance (IACG) concluded that in most countries, the greatest challenge is not writing a NAP but implementing the NAP and showing sustained action, and that the following factors make the implementation of NAPs particularly difficult: awareness and political will, finance, coordination, monitoring and data, and technical capacity. The IACG framework for action[14] highlights system strengthening, governance, coordination, coalition building, and political commitment as key enablers for sustainable action at both global and national levels. In the IACG's final report to the Secretary-General of the UN,[15] the need to accelerate the development and implementation of One Health AMR NAPs is again highlighted. The IACG rightly emphasises that strengthening governance at all levels of AMR policy (ie, global, national, regional, and local) is essential to tackling AMR. Linking global and national governance, the IACG has recommended that tripartite agencies strengthen One Health actions on the basis of country priorities and needs supported by the urgent establishment of a One Health Global Leadership Group on AMR.[15] The IACG has also recommended that the UN Secretary-General, in close collaboration with the tripartite agencies, UN Environment, and other international organisations, convene an independent panel on evidence for action against AMR to support member states to develop evidence-based policies.[15]

The inherent complexities of the drivers of AMR demand a systematic approach to governance. However, no comprehensive framework for the governance of NAPs has been developed and a need exists for increased clarity in this area. To address this unmet need, this Review presents the development of an AMR governance framework for NAPs and the methods used during its development.

Methods

We approached the objectives in four stages (table). Data were abstracted from each identified framework with a standardised extraction form. The following information was collected: first author name, year and country of publication, name of the framework, and all domains that constitute the framework. The search and data extraction process were independently done and agreed on by two of the co-authors (MA and KS). We included domains in the initial framework if they were included in more than a third of the frameworks reviewed (appendix pp 1–2). This approach was taken to capture the most commonly used governance principles, and the co-author's judged the cut-off value to be high enough to provide sufficient inclusiveness.

See **Online** for appendix

	Aims	Methods used	Main results
Stage one: search for existing AMR governance frameworks	To identify previously published AMR governance frameworks	Search of Google Scholar, MEDLINE, Embase, and Global Health using the search terms "antimicrobial", "antimicrobic", "antibiotic", "antibacterial", and "governance"; academic publications, reports, and grey literature considered	No AMR governance frameworks identified
Stage two: systematic review of health system governance framework reviews	To identify previously published health system governance frameworks	Search of the literature using Medline, Embase, Global Health using the search terms "governance", and "framework"; academic publications, reports, and grey literature considered	Review of 26 health system governance frameworks led to a basic structure of an AMR governance framework with three governance areas (ie, policy design, implementation tools, and monitoring and evaluation) and 11 governance domains (ie, strategic vision, participation, coordination, accountability, transparency, sustainability, equity, generation of information and intelligence, regulation, effectiveness, and responsiveness)
Stage three: review of international guidance documents	To identify all relevant policy options and strategies, and to ensure comprehensiveness of implementation tools	Review of five key international guidance documents: WHO's 2015 global action plan on antimicrobial resistance;[2] the OIE's 2016 strategy on antimicrobial resistance and the prudent use of antimicrobials;[16] the FAO's 2016 action plan on antimicrobial resistance 2016–20;[17] FAO's, OIE's, and WHO's 2016 manual for developing national action plans,[11] and EC's 2017 European one health action plan against antimicrobial resistance[18]	Seven domains added (ie, surveillance, stewardship, infection prevention and control, education, public awareness, fostering research and development of novel antimicrobials and alternatives, and AMR research), one domain removed (ie, generation of information and intelligence) and replaced by three of the new domains (ie, surveillance, AMR research, and fostering of research and development of antimicrobials and alternatives), and 34 indicators developed (appendix p 7)
Stage four: expert review of draft framework and synthesis	To expand and revise the domains and indicators in all governance areas, to validate the framework and potential value for a range of stakeholders, and to refine and propose final framework	Experts consultations (appendix p 12) through written feedback and teleconferences from five international organisations, eight government departments, eight universities, and two policy institutes from ten different countries in five continents	Five domains renamed (ie, antimicrobial stewardship, medicines regulation, feedback mechanisms, fostering research and development, and facilitating market access to novel products), one domain added (ie, reporting), 34 indicators reformulated and reworded and explanatory text added, and 18 indicators added; agreement on basic structure of the framework

AMR=antimicrobial resistance. OIE=World Organisation for Animal Health. FAO=The Food and Agriculture Organization of the UN. EC=European Commission.

Table: Stages of developing and refining the governance framework for antimicrobial resistance with main results outlined

To account for the distinctive aspects of governance in the context of national AMR policy, we expanded and refined the AMR governance framework in the third stage by reviewing the five most recent guidance documents from four key international organisations (WHO, the World Organisation for Animal Health, the Food and Agriculture Organization, and the European Commission). These four organisations are major actors in international AMR policy development and have a precedent of producing guidance regarding national AMR policies for their member states.

To increase the validity of the framework and to develop pre-existing and additional indicators we sought review of the framework and its components by experts from multiple sectors, disciplines, and geographies in the fourth stage. A judgment sample, also known as a purposeful sample, was used.[19] Experts were approached on the basis of a combination of factors such as the length of their experience in the field of AMR, their wide perspective on the development of AMR NAPs (both policy-makers and academics), and their interest in governance challenges associated with AMR policy. In total, a range of experts from five international or inter-governmental organisations (WHO, Pan American

Health Organization, Organisation for Economic Co-operation and Development, European Commission, and European Centre for Disease Prevention and Control), eight universities, eight government ministries, and two policy institutes (Chatham House and Pew Charitable Trust) provided feedback. The final step of stage four involved synthesising the feedback and findings from the preceding steps to produce a refined and final framework.

Results

The main results of all four stages are summarised in the table. The systematic search for previous AMR governance frameworks yielded no results (see appendix p 1). The process of identification and study selection for the systematic review of health system governance reviews is summarised in figure 1.

Stages one and two involved a systematic review of AMR governance frameworks and health system governance framework reviews. From a total of 827 records that were title-screened and abstract-screened, 822 were excluded because they were not reviews of health system governance frameworks. The full text of the remaining four publications were reviewed, leading to the inclusion of one systematic review[20] and three non-systematic
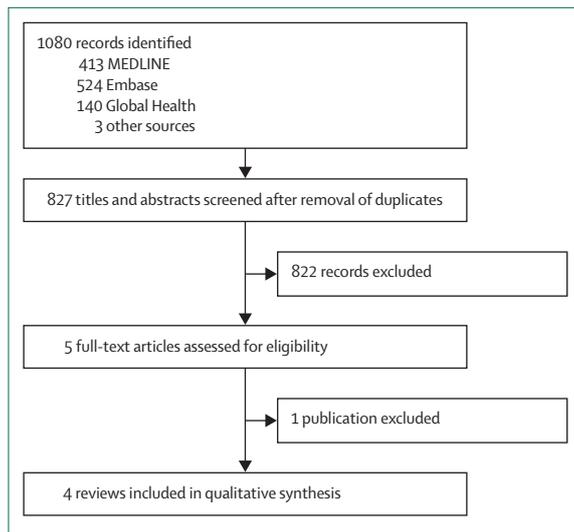
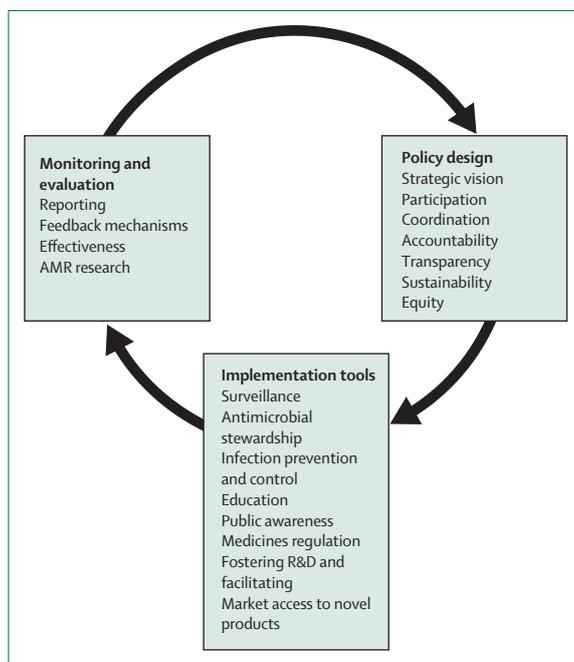*Figure 1:* Flow chart of study selection (stage two)

1080 records identified
    413 MEDLINE
    524 Embase
    140 Global Health
      3 other sources

827 titles and abstracts screened after removal of duplicates

822 records excluded

5 full-text articles assessed for eligibility

1 publication excluded

4 reviews included in qualitative synthesis

Figure 2: Antimicrobial resistance governance framework with three areas and 18 domains

Monitoring and evaluation
Reporting
Feedback mechanisms
Effectiveness
AMR research

Policy design
Strategic vision
Participation
Coordination
Accountability
Transparency
Sustainability
Equity

Implementation tools
Surveillance
Antimicrobial stewardship
Infection prevention and control
Education
Public awareness
Medicines regulation
Fostering R&D and facilitating
Market access to novel products

reviews[21–23] for qualitative assessment. 26 governance frameworks were identified in those four publications and the 11 most frequent key governance domains across these frameworks were identified. The criteria for the inclusion of commonly used governance domains were present in more than a third of governance frameworks, a cut-off agreed on by consensus of co-authors (appendix p 3). The final component of stage two was the formation of the basic structure of the framework by grouping these 11 domains in three broader governance areas: policy

design, implementation tools, and monitoring and evaluation.

Stage three was a review of five international guidance documents and resulted in the addition of seven domains: surveillance, stewardship, infection prevention and control, education, public awareness, fostering the research and development of novel antimicrobials and alternatives, and AMR research. "Some of these domains replaced the previous domain generation of information and intelligence. Stage 3 also resulted in the development of 34 initial indicators (appendix p 7). These domains and indicators were selected as the first step towards developing a governance framework for the specific context of AMR NAPs.

The wording of the indicators was selected in such a way that they could offer binary answers and be applied using a combination of publicly available resources and interviews of country experts to allow a feasible and practical application of the framework to a country's AMR NAP. The justification for each of these indicators is explored further within the framework.

Stage four was expert reviews of draft framework and synthesis. Throughout several iterations of the governance framework, we received expert feedback via email and teleconferences. In three cases we received consolidated feedback on the basis of the responses of multiple individuals in those organisations (appendix p 12). The experts agreed on the general structure of three governance areas and most domains. They primarily focused their feedback on the improvement and development of the indicators. This focus resulted in the reformulation and rewording of the initial 34 indicators, the addition of 18 further indicators, and the addition of one further domain (ie, reporting) to feed into the final AMR governance framework.

Governance framework

18 separate domains were incorporated into the framework within three governance areas: policy design, implementation mechanisms, and monitoring and evaluation (figure 2). At the structural level, the framework represents an ongoing cycle of review and evaluation processes. The aim of this cyclical design is to conceptualise AMR governance not as a static but as a dynamic and ongoing process that constantly improves and adjusts, according to lessons learned from monitoring and evaluation.

The first governance area (ie, policy design) is concerned with general and procedural issues of AMR NAPs, such as wide participation in the development of NAPs, coordination across multiple sectors and levels of service delivery (at national and sub-national levels), transparency, sustainability, equity implications of AMR policies, and determining who is ultimately accountable to the government for achieving the objectives of the NAP (panel 1).

The second governance area (ie, implementation tools) consists of crucial interventions contained within guidance from WHO, the Food and Agriculture Organization, the World Organisation for Animal Health, and the European Commission. Here, three of the domains determine whether surveillance,

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Panel 1: Antimicrobial resistance governance framework: policy design

Domain one: strategic vision
- Has situational analysis been done to determine the prevalence and incidence of AMR organisms in the country?
- Is a national action plan (NAP) in place, if not what is the timeframe for developing and implementing the NAP?
- Are the objectives contained within the NAP specific, measurable, and time-bound?
- Are there quantitative targets for AMR or antimicrobial use outlined in the NAP?
- Key issues and considerations: in the context of AMR, strategic vision is the overarching platform and the statement of goals and ideas central to the NAP;[24] to consider whether a NAP has drawn on an up-to-date, country-specific situational analysis regarding the extent of AMR and its drivers is important; a situational analysis might also inform the objectives outlined in each national plan, in which each objective should be specific, measurable, and time-bound; quantitative targets for improving antibiotic prescription, consumption, and resistance in both human and animal health can be a useful mechanism to focus actors towards a clear objective, although quantitative targets might only be feasible in more advanced NAPs; for lesser developed plans, an incremental plan should be in place to improve surveillance capability to facilitate the measurement and implementation of quantitative targets

Domain two: coordination
- Is coordination between sectors and across different levels of each sector considered?
- Is there a ministry or intersectoral committee, or both, responsible for coordination and implementation?
- Key issue and considerations: WHO, the Food and Agriculture Organization, and the World Organisation for Animal Health have outlined the need for coordination between all relevant ministries, high-quality laboratories, medical and veterinary professions and statutory bodies, research and academic institutes, civil society including patient organisations, food and pharmaceutical industries, and wholesale and retail distributors, through a multi-sectoral One Health policy approach;[11,25,26] reviews from 2016 have highlighted the necessity to coordinate different levels of human and veterinary health care including national, regional, and local, as well as the horizontal dimensions (eg, in human health, across primary, secondary, and long-term care and in animal health across both companion animals and livestock sectors);[26,27] to clarify if an intersectoral committee or ministry is responsible for implementing and coordinating the NAP is an important consideration; the intersectoral committee

might be chaired by a ministry with overarching responsibility for coordination

Domain three: participation
- Was a high level of stakeholder participation facilitated throughout the development of the NAP?
- Are the activities in the NAP inclusive across all sectors related to One Health? If so, how, and if not, why not?
- Was there support from a technical advisory group or subject matter experts during development of the NAP?
- Key issues and considerations: participation both during conception and subsequent implementation is a particularly important aspect of governance in the context of AMR policies,[28] as we move towards a One Health approach; comprehensive participation also improves the legitimacy of AMR NAPs and stakeholder engagement during the implementation and subsequent evaluation phases; WHO guidance states that all relevant ministries, laboratories, medical and veterinary professions and statutory bodies, research and academic institutes, civil society including patient organisations, agricultural organisations, food and pharmaceutical industries, regulatory authorities, and wholesale and retail distributors should be involved;[11] as well as broad stakeholder participation, to promote evidence-based policy, the inclusion of a technical advisory group or subject matter experts from across the human, animal, and environmental health sectors during development offers further credibility

Domain four: accountability
- Is there a ministry or intersectoral committee, or both, responsible for coordination and implementation that is accountable to the government?
- Is a responsible person nominated in each sector and do agreements exist regarding what happens if objectives are not met?
- Key issues and considerations: accountability is a crucial aspect of governance in any context; being accountable means having the obligation to answer questions regarding decisions and actions, and can be understood to have two parts (ie, explanation and sanction);[29] for these processes to work effectively, accountability mechanisms should be as uncomplicated as possible and include mutually agreed measurable outcomes so they can facilitate constructive two-way dialogue; in terms of an AMR NAP, that whichever entity is responsible for coordination and implementation is accountable to a higher body in government is crucial; to improve accountability, a person should be nominated within each sector responsible for implementation

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Domain five: transparency

- Is the complete NAP publicly available?
- Are all progress reports publicly available?
- Is all funding information publicly available?
- Is all AMR and antimicrobial use surveillance data publicly available?
- Key issues and considerations: transparency can be understood as ensuring that AMR policy development, implementation, and evaluation occur in an open and accessible manner; in terms of AMR NAPs, that the plan itself, progress reports, and funding allocations are published with open access to the public, subject to agreement of contributors to the plan, is important; further transparency can be achieved by providing open access to AMR and antimicrobial use data, with adequate consideration of data governance; this information must also be presented in an understandable format to ensure public engagement, which can encourage political awareness and civil society involvement in AMR policy[30]

Domain six: sustainability

- Is there either a written mandate or voluntary agreement from all relevant sectors in place to implement the NAP?
- Are there dedicated budgets in place to implement specific activities in the NAP?
- Is there an assessment of future budget requirements for different activities listed in the NAP?
- Is there ongoing support from a technical advisory group or subject matter experts during implementation, monitoring, and evaluation of the NAP?
- Key issues and considerations: sustainability should be a key objective of any AMR NAP, as any positive change should aim to be consistent and maintained; without a dedicated budget for both the NAP and any intersectoral committee, actors might have restricted resources to implement AMR polices; strategic consideration of budget allocation and

assessment for potential gaps in funding is desirable; the sustainability of an AMR NAP might also rely on its legitimacy, which is crucial for the ongoing engagement of all stakeholders; legitimacy can be enhanced through either the provision of a clear government mandate or a voluntary agreement from all relevant sectors to implement the NAP; the ongoing support of an interdisciplinary technical group can offer further sustainability, ensuring the NAP is evidence-based and uses all recent findings from monitoring and evaluation processes; to achieve ongoing support and promote advocacy, the objectives within AMR NAPs can be aligned with pre-existing initiatives such as National Health Policies, Strategies and Plans,[31] National Action Planning for Health Security,[32] and the UN Sustainable Development Goals[33]

Domain seven: equity

- Does the NAP include both encouraging responsible use and facilitating equitable access to existing essential antimicrobials?
- Key issues and considerations: in some countries, certain communities might not receive appropriate and equitable access to antimicrobials;[34,35] the concepts of responsible use and equitable access are inextricably linked, and the focus should be on facilitating equitable access to the right antimicrobial, at the right time, based on clinical need; shortages of antimicrobials can drive AMR, as prescribers have to resort to less-effective treatments,[36] or to a broader spectrum of antimicrobial than is necessary; high out-of-pocket payments can create an incentive for providers to inappropriately prescribe antibiotics or result in inequitable access to antimicrobials, or both;[37] as a key component to tackle AMR, NAPs should consider how best to balance responsible use and equitable access to essential antimicrobials[38]

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antimicrobial stewardship programmes, and infection prevention and control measures are implemented across the One Health spectrum. Other domains in this governance area encompass further fundamental AMR tools such as education of relevant professionals, public awareness activities, and medicines regulation. Implementation tools also examine whether appropriate policies and incentives are in place to encourage research and development of novel antimicrobials and alternatives (panel 2).

Domains within the third governance area (ie, monitoring and evaluation) include reporting and feedback mechanisms that allow for regular review and evaluation of AMR NAPs, and the effectiveness and cost-effectiveness dimensions of different aspects of the NAPs. Finally, the non-therapeutic AMR research domain considers whether a national multidisciplinary One Health research agenda

that aims to understand the drivers of and potential strategies to combat AMR exists (panel 3).

For each of the 18 domains, multiple indicators were developed to signal whether the requirements for the domains are fulfilled. In total, 52 indicators were derived and are outlined in detail, including an explanation of their rationale in panels 1–3.

Discussion and conclusion

A central challenge to combatting the global threat of AMR is the successful implementation, in each country, of an AMR NAP across the relevant sectors and levels, which can be enabled by a systematic approach to governance. Here, we have developed the first comprehensive framework for the governance of AMR NAPs by synthesising findings from a review of health system governance frameworks, an analysis of the guidance from

Panel 2: Antimicrobial resistance governance framework: implementation tools

Domain one: surveillance
- Is there a national surveillance system for resistant organisms across the human, animal, and the environmental health sectors?
- Is there a national surveillance system for levels of antimicrobial use in animals and humans?
- Is there adequate laboratory capacity and capability supported by regular external quality assessments?
- Key issues and considerations: surveillance is fundamental for the planning, conduct, and evaluation of all other antimicrobial resistance (AMR) policies;[26] surveillance can facilitate accountability mechanisms and the use of consistent metrics are an important tool for cross-country comparisons of progress in reducing AMR,[39] through initiatives such as the Global Antimicrobial Resistance Surveillance System and the work of agencies such as the European Centre for Disease Prevention and Control; that national surveillance systems involve data collection and assessment of both antimicrobial consumption and resistance across human, animal, and environmental health sectors, as well as the provision of adequate laboratories, equipment and technical expertise necessary, is important;[40–43] surveillance metrics should include the overall quantity of antimicrobials used and an assessment of both appropriate and inappropriate use; that adequate laboratory capacity and capability supported by a regular programme of external quality assessments exists is important[43]

Domain two: antimicrobial stewardship
- Are there stewardship programmes across human and animal health sectors?
- Are rapid diagnostic tools widely available and in regularly use?
- If so, do national guidelines regarding their indication and interpretation exist?
- Are there up-to-date national guidelines on antimicrobial use and rapid diagnostic tools across a wide range of settings in animal and human health?
- Is there any use of financial and non-financial incentives or penalties in animal and human health to reduce inappropriate use of antibiotics?
- Key issues and considerations: antimicrobial stewardship is defined as a coherent set of actions designed to use antimicrobials responsibly and refers to all actors and stakeholders seeing their responsibilities, ownership, and interest in the issue;[44] in human health, stewardship programmes can help clinicians to improve patient safety, reduce treatment failure, and increase the use of prophylactic measures;[45] stewardship programmes should be complemented by national guidelines on antimicrobial use and the indication and interpretation of rapid diagnostic tests;[45] in animal health, national guidelines can be used to encourage appropriate antibiotic use and to improve both

terrestrial and aquatic animal health;[46,47] comprehensive national guidelines should cover a wide range of indications, and not only a few common infections; stewardship programmes should also include monitoring adherence to these guidelines, which might require individual physician and patient-level data,[38] or in the case of animal health, the monitoring of farm-level antimicrobial usage and appropriate drug selection and use;[47] financial incentives and penalties have also been used to encourage health-care professionals to reduce antimicrobial use and adhere to national guidelines;[48] however, non-financial incentives such as public reporting and peer comparison can also be used;[49] stewardship programmes should both restrict inappropriate use of antimicrobials but also facilitate equitable and timely access to appropriate antimicrobials when needed as discussed in the equity domain[50]

Domain three: infection prevention and control
- Are there infection prevention and control (IPC) policies across all levels of human, animal, and environmental health sectors?
- Are there up-to-date national guidelines for IPC across human, animal, and environmental health sectors?
- Are immunisation programmes used as an approach to prevent infections across human and animal health sectors?
- Are financial and non-financial incentives or penalties for IPC policies used across human, animal, and environmental health?
- Key issues and considerations: infection prevention and control serves as an important policy objective in all settings that aims to reduce the transmission of multidrug-resistant bacteria, minimise the overall risk of infection, and decrease the overall need for antimicrobials; within AMR national action plans (NAPs), that the plan includes IPC measures across all sectors including human, animal, and environmental health is important; in human health, antimicrobial stewardship programmes have shown to be more effective when implemented in conjunction with IPC measures, especially hand hygiene, than when implemented alone;[51] to support implementation, core components of infection control programmes in both hospital and community settings should be standardised;[52,53] multimodal IPC improvement strategies, including system change, training and education, monitoring and feedback, and reminders and communications have been shown to be effective, feasible, and sustainable across a range of settings in different countries;[54] in animal health, good husbandry practices and effective biosecurity measures are important;[55] waste management programmes should aim to minimise environmental exposure to resistant organisms;[56,57] as part of a NAP, national guidelines for IPC should be developed to standardise implementation and evaluation within each

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context; to antimicrobial stewardship, both financial and non-financial incentives such as public reporting and accreditation can be used to increase adherence to guidelines and reduce the incidence of infections;[58,59] immunisation programmes can be an effective strategy to reduce burden of vaccine-preventable infections in both human and animal sectors[60]

Domain four: education

- Is there certifications or programmes in place to ensure a basic education for all involved groups of professionals to deliver necessary understanding for strategies to tackle AMR?
- Is there continuing education programmes for all involved groups of professionals to ensure expertise necessary for expanding knowledge and sustained efforts to tackle AMR?
- Is there a workforce strategy that aims to deliver the sustainable supply of the necessary workforce required to deliver antimicrobial stewardship and IPC policies?
- Key issues and considerations: examples from both the human and the animal health sector have shown how education is key to developing capacity to adopt standards, facilitate control policies, or implement guidelines sufficiently;[26] for all groups of professionals who are in the position to prescribe antibiotics or influence antibiotic use to receive dedicated education at both undergraduate and postgraduate level about antimicrobial stewardship and infection prevention and control is essential; in the human health sector, medical students, physicians, pharmacists, nurses, midwifes, dentists, and technicians need to be trained to build the capacity that is needed to implement guidelines and objectives;[61,62] at national and institutional level, educations programmes should aim to foster a culture of safety among health-care workers, administration, and decision makers, as part of multimodal strategies to improve IPC and stewardship;[63,64] for professionals from the animal and environmental health sector to receive training, as well as professionals working in the food industry or environmental agencies, is important;[65] workforce shortfalls are a persistent barrier to implementing policies to tackle AMR in many countries, particularly with IPC and antimicrobial stewardship programmes in human health;[66] many other professionals such as veterinarians, environmental health officers, and biochemists are required to implement AMR policies in animal and environmental health; an essential component of any AMR NAP is a comprehensive workforce strategy responsive to local needs informed by detailed workforce planning

Domain five: public awareness

- Are there multimodal public awareness campaigns that focus on AMR and educational programmes (including school children) related to AMR?
- Do the implemented public awareness campaigns have an ongoing character?
- Does the conception of the public awareness campaign consider aspects of behavioural sciences, social science, and psychology?
- Key issues and considerations: public awareness campaigns can be used in a variety of settings to raise awareness and promote best practices for prevention of AMR; several countries have found a reduction in the number of antibiotic prescriptions following campaigns to raise awareness about prudent use of antibiotics and AMR;[26,67,68] campaigns should be implemented at national, regional, and local levels to ensure widespread coverage, and should be ongoing, rather than one-off efforts; educational campaigns within school-based curriculum should be considered to raise awareness about AMR from a young age;[57] communicating the concept of One Health can improve the public understanding of the drivers of AMR; to achieve sustainable behavioural and cultural change, the most effective public awareness campaigns have been shown to be multimodal, using a combination of print and mass media, guidelines, and feedback back to individual prescribers;[69] ideally all awareness and education campaigns should be based on findings in behavioural science, pedagogy, and other behavioural disciplines to increase effectiveness

Domain six: medicines regulation

- Are there regulations in place to ensure appropriate use of antimicrobials in human health?
- Are there regulations in place to ensure appropriate use of antimicrobials in animal health?
- Is there an authority in place to monitor and enforce legislation, if so does this authority have a dedicated budget?
- Key issues and considerations: to conserve the use of available antimicrobials, regulation has been used in a variety of ways and we interpret regulation as any laws, accreditation, or financial incentive or penalties in place with the aim of reducing antimicrobial use (eg, many countries have enforced legislation that make antimicrobials prescription-only status [ie, requiring a mandatory prescription], or the Feed Additives Regulation in the EU, which banned the use of antibiotics as growth promoters in animal feed from January, 2006);[70] antimicrobials deemed critically important for human health also exists, and

(Continues on next page)

major international organisations, and extensive input from expert policy-makers, practitioners, and researchers from government ministries, international organisations, policy institutes, and academic institutions. Within a cyclical design, our governance framework consists of 52 indicators that are contained within 18 domains and grouped in three main governance areas: policy design, implementation tools, and monitoring and evaluation.

(Panel 2 continues from previous page)

regulation should play a key part in ensuring that they are not used in animals;[71] in some countries, large quantities of substandard, expired, or counterfeit antimicrobials are sold,[72] either in-person or online, and effective regulation is essential to reduce this practice; regulation is also required to ensure disposal of antimicrobials takes place in a manner that minimises environmental exposure;[73] regulation is used in many countries to ban direct to consumer advertising of medications, including antimicrobials, which is important as inappropriate direct to consumer advertising can alter public expectations or prescribing behaviour negatively;[74] presence of regulation alone is not sufficient and effective regulation must be well designed, which involves an appropriate legislative mandate, a clear legal framework, and a regulator in place to monitor and implement regulation that is properly accountable[75]

Domain seven: fostering research and development and facilitating market access to novel products
- Is fostering research and development and facilitating market access to novel antimicrobials, diagnostics, vaccines, and alternative treatments in both human and animal health listed as a priority in the NAP?
- Does the NAP consider how the country can contribute to research and development of novel agents at both a national and international level?
- Is there a dedicated national budget for research and development of novel antimicrobials, diagnostics, vaccines, or alternative treatments?

- Key issues and considerations: although substantial gains existed in antibiotic discovery between 1940 and 1990, research and development has shifted to other therapeutics because of a combination of economic, regulatory, and scientific barriers;[76,77] a comprehensive AMR NAP should include both fostering research and development and facilitating market access to novel products,[78,79] such as antimicrobials, diagnostics, vaccines, and alternative treatments such as probiotics, metals, or antimicrobial peptides;[80,81] to foster research and development, NAPs can include the use of financial incentives in the form of push incentives such as research grants, or pull incentives such as monetary rewards, reimbursement premiums, or patent buy-outs by governments;[82] to fund these financial incentives many countries have dedicated budgets;[83] to maximise allocative efficiency, financial incentives should also be linked to predefined public health needs and target product profiles;[84] comprehensive research and development should also address preclinical scientific challenges in antimicrobial development, spanning basic drug discovery science to translational research to clinical trials;[85] to meet the sometimes conflicting aims of improving patient access and promoting stewardship, NAPs should consider an alternative business model to facilitate market access for novel antimicrobials;[82] to avoid duplication of efforts on the international level, and given that research of novel antimicrobials is not a viable option for all countries, each country should identify potential areas of comparative advantage and seek to harmonise with international efforts

This framework is intended to aid policy makers to design, implement, monitor, and evaluate AMR NAPs across the One Health spectrum, and to facilitate objective assessments of countries' AMR NAPs to increase accountability and stimulate debate.

To our knowledge, this Review is the first study that provides a comprehensive systematic synthesis of available evidence on the governance of AMR NAPs by including information from a systematic review of health system governance frameworks, international guidance, and 25 experts from various international organisations, government ministries, policy institutes, and academic institutions. The AMR governance framework has several strengths. A central and recurring input by experts was the need for usability. By including 52 indicators and 18 domains the framework balances the right mix of comprehensiveness and usability for policy-makers. This feature was confirmed by various experts in the fourth stage of the development of the framework. The cyclical design of the framework reflects the dynamic nature of the AMR issue and the corresponding need to be responsive and adaptive, but also ensure that the governance of AMR NAPs itself

develops and improves, reflecting the realities observed and lessons learned.

The AMR governance framework also has various limitations. Our review of health system governance frameworks prioritised systematic and non-systematic reviews, and certain governance frameworks might therefore have been overlooked. That our AMR governance framework would benefit from either reviewing a larger body of international guidance documents or consulting a larger sample of experts might also be argued. However, the documents reviewed represent the most recent guidance developed by five major international organisations involved in AMR policy. Furthermore, the expert sample was balanced between international organisations, policy institutes, government, and academia, as well as backgrounds relevant to the One Health approach.

We did not use a structured consensus method during development of the framework.[89] Our objective is to facilitate international debate around a universally accepted approach to governance in national AMR policy. The establishment of the One Health Global Leadership Group on AMR recommended by the UN IACG on

Panel 3: Antimicrobial resistance governance framework: monitoring and evaluation

Domain one: reporting

- Are annual antimicrobial resistance (AMR) national action plans (NAPs) progress reports published?
- Are annual surveillance reports published containing data regarding the incidence of resistant organisms and antimicrobial use?
- Is there collaboration with and systematic data transmission to international surveillance systems?
- Key issues and considerations: although for an AMR NAP to be revised on an annual basis is not realistic, annual progress reports are a useful mechanism to monitor and evaluate AMR policies in the interim; these progress reports can also be used by other countries to inform their AMR policies and provide feedback to international public health agencies on national achievements; annual reports on data collected by national AMR surveillance systems can improve accountability and transparency, facilitate regular monitoring and evaluation, and feed into AMR NAP progress reports; that countries engage with wide international efforts to monitor the extent of AMR globally is also an important aspect of national governance; that national surveillance systems collaborate with and relay data to international surveillance systems is essential

Domain two: feedback mechanisms

- Are there feedback mechanisms in place that relay surveillance data back at both regional and organisational level?
- Are there regular deadlines in place to review progress of specific actions within the NAP, and arrangements to feedback at both regional and organisation level?
- Key issues and considerations: for surveillance to be an effective tool for improvement, data needs to be routinely fed back at the regional and organisational level; in practice, effective feedback mechanisms require involving local stakeholders in analysis of what the data shows, in which improvement is needed, and their specific data needs; to assess relative performance, these feedback mechanisms should also be aligned with nationally set targets and deadlines as discussed in the strategic vision domain; if progress towards national targets is minimal, local stakeholders should be encouraged to produce personalised and time-bound action plans; to improve accountability, a NAP should identify deadlines to review progress of specific actions, and arrangements to feedback at both the regional and organisation level.

Domain three: effectiveness

- Have there been efforts to evaluate the effectiveness (eg, measure of effect on human and animal health) of specific policies or interventions, or both, implemented?
- Have efforts been made to evaluate the cost-effectiveness (eg, measure of effect on human and animal health) of specific policies or interventions implemented?
- Key issues and considerations: under monitoring and evaluation, methods of measuring AMR policy effectiveness should be outlined within a NAP, and if possible also cost-effectiveness; AMR is a driver of health-care expenditure because of increased morbidity and mortality, likelihood for admission to hospital, average hospital length of stay, cost of last-resort treatment options, and productivity losses for patients at work;[86,87] from a governance perspective, to establish which AMR policies are cost-effective and represent value-for-money is important; sources of data could, for example, include surveillance systems, hospitals, clinicians, the agricultural sector, and food-supply chains; each source provides feedback on the effect of policies in reducing antimicrobial consumption, inappropriate use of antibiotics, and antimicrobial resistance rates; estimating the effectiveness and cost-effectiveness of individual interventions or policies might be challenging as many factors will contribute to an increase or decrease in antimicrobial use and AMR; technical advisory and support groups should be involved in the process, and cost-effectiveness analysis should ideally result in a comparative measure such as an incremental cost-effective ratio, which can allow comparisons between interventions to rationalise funding decisions

Domain four: AMR research

- Is research to understand both the drivers and effect of AMR and potential policies and interventions identified as a key priority in the NAP?
- Is there a dedicated national budget for AMR research in place?
- Key issues and considerations: generation of information is a vital aspect of governance; in the context of national AMR policy, a national research strategy is required to provide an evidence base for AMR policies; without a thorough understanding of the drivers of AMR and polices in place to restrict them, resistance will develop to new antimicrobials; research should also consider including modelling exercises to forecast incidence and prevalence of AMR and the current and future health and economic effect; priorities within the national research strategy should be multidisciplinary and potentially defined by an intersectoral committee to ensure a One Health approach; this research should include inputs across social sciences, behavioural, economic, and medical research;[88] a dedicated budget at the national level is important for the long-term sustainability of research activities

AMR is one potential forum to develop international consensus.[15] Alternatively, a detailed assessment of a country's approach to governance of NAPs could be incorporated into pre-existing initiatives such as the WHO Joint External Evaluation tool,[90] or the global tripartite database on country progress.

Search strategy and selection criteria

We searched the Medline, Embase, and Global Health databases to identify pre-existing AMR governance frameworks using the keywords "antimicrobial", "antimicrobic", "antibiotic", "antibacterial", and "governance". We then did a second search of systematic and non-systematic reviews of health-related governance frameworks again searching the Medline, Embase, and Global Health databases using the keywords "governance" and "framework". Both searches were restricted to English language publications and done from database inception to April 30, 2018, and the full search strategies and results can be found in the appendix pp 1–2. We screened titles and abstracts of all retrieved citations for relevance, removed duplicates, and reviewed full articles that met our selection criteria. To be eligible, the publication had to be a systematic or non-systematic review containing more than one governance framework, provide sufficient information on the domains within each framework, and had to be related to health. We considered grey literature such as policy reports, working papers, and conference proceedings. We also reviewed the reference list of all included publications. We choose to analyse systematic and non-systematic reviews exclusively as health system governance is a previously well-researched area, and this strategy allowed us to comprehensively review a large body of evidence in an efficient manner.

A further limitation of our AMR governance framework is related to applicability. A thorough objective application of the framework would be resource intensive because of the broad nature of data sources that would need to be reviewed, and challenges with data availability because some policy documents or decisions might not be publicly accessible. As a result, several interviews with multiple stakeholders within each country might need to be conducted. These factors might explain why efforts to assess AMR NAPs, such as the global tripartite database on country progress, primarily involve self-assessment.[7]

Conversely, it can also be argued that the 52 indicators and 18 domains only provide a superficial assessment in certain areas. For example, a country might offer education to all relevant professionals regarding AMR, but the education might be of poor quality and brief, or alternatively a public awareness campaign might be in place, but the campaign is poorly financed with a narrow focus. Cross-country comparisons using this governance framework should therefore be made with caution as possibilities for misleading conclusions exist.

Finally, the AMR governance framework was developed on the basis of experience and guidance that applies most typically to high-to-middle income countries. In low-income countries with less resources, less national surveillance and less developed health-care systems,[91,92] the application of the framework is possibly ambitious. To address this issue, we extended the sample size of experts to include perspectives from low-to-middle income countries. The feedback was positive, and resulted in only minor changes to the framework. This framework was felt to still be relevant to lesser developed plans, such as those in some low-to-middle income countries, as the cyclical nature of this framework captures how shortcomings in pre-existing NAPs can be improved throughout subsequent iterations and repeated applications of the framework.

Defining and assessing governance of AMR NAPs are challenging. Despite certain limitations, this AMR governance framework is the first attempt at developing a tool for policy makers to improve the governance of AMR NAPs, and to facilitate the objective assessment of countries' NAPs to increase accountability and stimulate debate.

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