

1 A Governance Framework for Development and Assessment of 2 National Action Plans on Antimicrobial Resistance

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7 8 **Summary**

9 Strengthening governance is an essential strategy to tackling antimicrobial resistance (AMR) at all
10 levels; global, national, regional and local. To date, no systematic approach to governance of AMR
11 national action plans (NAPs) exists. To address this, we aimed to develop the first governance
12 framework to offer guidance for both the development and assessment of AMR national action plans
13 (NAPs). We reviewed health system governance framework reviews to inform the basic structure of
14 our framework, international guidance documents from the WHO, FAO, OIE and the EU, and sought
15 the input of over 25 experts from international organizations, government ministries, policy institutes
16 and academic institutions to develop and refine our framework. The framework consists of 18
17 domains with 52 indicators that are contained within three governance areas: "policy design",
18 "implementation tools", and "monitoring and evaluation". To consider the dynamic nature of AMR,
19 the framework is conceptualized as a cyclical process, which is responsive to the context and allows
20 for continuous improvement and adaptation of AMR NAPs.

21 22 **Key messages**

- 23 • Antimicrobial Resistance (AMR) is one of the most pressing and complex issues today, with
24 multi drug-resistant, extensively drug-resistant, and even pan drug-resistant organisms
25 emerging.
- 26 • AMR is driven by inter-related dynamics in the human, animal, and environmental health
27 sectors, which makes governance challenging.
- 28 • Strengthening governance of AMR policies at all levels; global, national, regional and local, is
29 essential to tackling AMR. To date, no comprehensive framework for the governance of AMR
30 National Action Plans (NAPs) has been developed.
- 31 • To our knowledge, this is the first study that has developed a governance framework for AMR
32 NAPs, based on a systematic review of the literature, international guidance, and over 20
33 experts from various international organizations, government ministries, policy institutes and
34 academic institutions
- 35 • The framework is conceptualized as a cyclical process between the three governance areas;
36 policy design, implementation tools, and monitoring and evaluation.
- 37 • Within policy design, improving strategic vision, coordination, participation, accountability,
38 responsibility, sustainability, and equity were identified as key to strengthening governance.
- 39 • Implementation, surveillance, antimicrobial stewardship, infection prevention and control,
40 education, public awareness, medicines regulation, and fostering R&D and facilitating market
41 access to novel products were all identified as essential tools.
- 42 • To ensure NAPs can adapt and continually improve, feedback mechanisms, reporting and
43 research to understand the drivers of AMR, were identified as crucial components to allow
44 monitoring and evaluation.

45 • To build on this governance framework, there is a need for international leadership to
46 develop consensus and engagement from national policy-makers to strengthen governance in
47 AMR NAPs.

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49 Words: 3274 excluding tables and figures.

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51 Introduction

52 The problem of antimicrobial resistance (AMR) is one of the most pressing and complex current public
53 health issues. Today, multi drug-resistant, extensively drug-resistant, and even pan drug-resistant
54 organisms are a challenge for healthcare-systems of varying stages of development. If not combatted
55 timely and effectively, AMR can potentially lead to millions of preventable deaths per year and to
56 hundreds of billions of economic costs annually, due to losses in international trade or livestock
57 production and increased healthcare expenditure.¹ Following the adoption of the Global Action Plan on
58 AMR by the World Health Assembly in 2015,² many countries have refined or developed their AMR
59 national action plans (NAPs) in accordance with the internationally recognized ‘One Health’ approach
60 which requires policies to be developed and implemented inter-sectorally across human, animal, and
61 environmental health. Here, we present an AMR governance framework with a dual purpose: as a tool
62 for policy-makers to both develop and improve AMR NAPs, and to also facilitate an objective
63 assessment of AMR NAPs to increase accountability.

64 Defining Governance

65 Definitions of governance have their origins in the multilateral development institutions of the late
66 1980s and 1990s. However, defining governance remains challenging and complex. It is helpful to start
67 by defining what governance is not, i.e. it is not synonymous with government. Addressing governance
68 issues therefore does not exclusively rest on actions of governments, but also on other societal
69 organizations, how they relate to the public, and how decisions are taken.³ Various efforts to define
70 governance have been undertaken and two widely referenced definitions have been outlined by the
71 United Nations Development Programme (UNDP) and the WHO. The UNDP encompasses “five good
72 governance principles”: legitimacy and vote, direction, performance, accountability, and fairness.⁴ The
73 definition recognizes that these principles sometimes overlap and might even be conflicting, their
74 implementation is dependent on the context, the application of these principles is complex, and that
75 good governance needs to consider how power is exercised.

76 Beside this more general definition, governance has been defined more explicitly from a health-systems
77 perspective, starting with the World Health Report 2000.⁵ Here, governance is discussed as a form of
78 stewardship, seen as “the careful and responsible management of the well-being of the population”.
79 The role of the government is outlined as one of “oversight and trusteeship”, which requires “vision,
80 intelligence and influence”. In 2002, the WHO defined governance further by outlining six domains or
81 sub-functions; generation of intelligence, formulating strategic policy direction, ensuring tools for
82 implementation (powers, incentives and sanctions), building coalitions / partnerships, ensuring a fit
83 between policy objectives and organizational structure and culture, and ensuring accountability.⁶ Later,
84 within the 2007 WHO Framework for Action, these principles were cemented as one of the six key
85 building blocks of a health system,⁷ under the domain of ‘leadership and governance’.

86 Governance in the context of AMR National Action Plans

87 Understanding what good governance translates to within the context of AMR national action plans is
88 a different matter. The complex nature of the emergence and spread of AMR globally and the political-
89 economic features of health systems pose challenges that mandate effective governance for successful
90 implementation of AMR policies.^{8,9} AMR is driven by inter-related dynamics in the human, animal, and
91 environmental health sectors, so actions to address AMR should include mechanisms that coordinate
92 AMR policy inter-sectorally. Previous lack of international agreement regarding the direction of efforts
93 to tackle AMR has allowed the discussion to be shaped by a “war on superbugs” or “post-antibiotic
94 apocalypse” discourse, which has put much emphasis on the discovery of new antimicrobials through
95 pharmaceutical innovation and too little priority on reduction of antimicrobial use, and on prevention

96 and control of infections. Furthermore, the complexity of AMR also necessitates policies that range in
97 diversity from surveillance, awareness, to regulation, stewardship, and infection prevention and
98 control, each in the context of human, animal, and environmental health.

99 Given these challenges, there has been considerable interest in governance within AMR policy. In an
100 analysis of AMR policies in 29 European Union/European Economic Area (EU/EEA) countries, the Third
101 Report on Implementation of the Council Recommendation on prudent use of antimicrobial agents in
102 human medicine suggested the need for prioritising governance within national policies to contain
103 AMR.¹⁰ The Food and Agriculture Organization of the United Nations (FAO), the World Organisation for
104 Animal Health (OIE) and the World Health Organization (WHO) together form a tripartite which has
105 produced a manual for developing NAPs on AMR that emphasizes the establishment of a governance
106 mechanism and the undertaking of a thorough situational analysis as key for the development of
107 NAPs.¹¹ The global tripartite database on country progress has been a first step towards monitoring
108 AMR NAPs on a global scale.¹² The goal of the database is to provide “baseline information on the status
109 of countries” regarding the implementation of the Global Action Plan and actions to address AMR
110 across all sectors. It provides crucial initial information such as the existence of a ‘One Health’ NAP,
111 surveillance of antibiotic use in human and animal health, training of veterinary and health personnel
112 and the presence of public awareness campaigns, although to date its data collection is broad and lacks
113 detail.

114 In 2018, a discussion paper on AMR NAPs from the Interagency Coordination Group on Antimicrobial
115 Resistance (IACG) has concluded that in most countries, the greatest challenge is not writing a NAP but
116 implementing it and demonstrating sustained action, and that the following factors make the
117 implementation of NAPs particularly difficult: awareness and political will, finance, coordination,
118 monitoring and data and technical capacity.¹³ The IACG framework for action,¹⁴ highlights system
119 strengthening, governance, coordination, coalition building and political commitment as key enablers
120 for sustainable action at both global and national levels. In the IACG’s final report to the secretary-
121 general of the United Nations (UN),¹⁵ the need to accelerate the development and implementation of
122 One Health AMR NAPs is again highlighted. The IACG rightly emphasises that strengthening governance
123 at all levels of AMR policy; global, national, regional and local, is essential to tackling AMR. Linking global
124 and national governance, the IACG has recommended that tripartite agencies strengthen One Health
125 actions based on country priorities and needs supported by the urgent establishment of a “One Health
126 Global Leadership Group” on AMR.¹⁵ The IACG has also recommended that the UN secretary-general,
127 in close collaboration with the tripartite agencies, UN Environment and other international
128 organizations, convene an independent panel on evidence for action against AMR to support member
129 states to develop evidence based policies.¹⁵

130 In summary, the inherent complexities of the drivers of AMR demand a systematic approach to
131 governance. However, to date, no comprehensive framework for the governance of NAPs has been
132 developed and there is a need for increased clarity in this area. To address this unmet need, this paper
133 presents the development of an AMR governance framework for NAPs and the methods used during
134 its development.

135 **Methods**

136 We approached the objectives in four stages (Table 1). First, we searched Medline, EMBASE, and Global
137 Health databases to identify pre-existing AMR governance frameworks. We then performed a second
138 search of systematic and non-systematic reviews of health-related governance frameworks again
139 searching Medline, EMBASE, and Global Health databases to inform the initial development of the
140 framework. To be included, the publications had to provide sufficient information on the domains
141 within the frameworks included and had to be related to health. We choose to analyse systematic and

142 non-systematic reviews as health system governance is a previously well-researched area, and this
143 strategy allowed us to comprehensively review a large body of evidence in an efficient manner. Both
144 searches were performed up to 30th April 2018; their search strategies can be found in the
145 supplementary material.

146 Data was abstracted from each identified framework using a standardized extraction form. The
147 following information was collected: 1) first author name; 2) year and country of publication; 3) name
148 of the framework; and 4) all domains that constitute the framework. The search and data extraction
149 process were independently performed and agreed upon by the co-authors. We included domains in
150 the initial framework if they were included in more than a third of the frameworks reviewed (appendix
151 A). This approach was taken to capture the most commonly utilised governance principles, and the co-
152 author's judged the cut-off value to be high enough to provide sufficient inclusiveness.

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156 **Table 1. Stages of Developing and Refining the AMR Governance Framework.**

STAGE	AIMS	METHODS USED	
I. Search for existing AMR governance frameworks	To identify previously published AMR governance frameworks	<p>Search of Google Scholar, Medline, Embase, Global Health using the search terms “antimicrobial”, “antimicrobic”, “antibiotic”, “antibacterial”, and “governance”.</p> <p>Academic publications, reports, and grey literature considered</p>	
II. Systematic review of health system governance framework reviews	To identify previously published health system governance frameworks	<p>Search of the literature using Medline, Embase, Global Health using the search terms “governance”, and “framework”.</p> <p>Academic publications, reports, and grey literature considered</p>	
III. Review of international guidance documents	<p>To identify all relevant policy options and strategies</p> <p>To ensure comprehensiveness of implementation tools</p>	<p>Review of key international guidance documents:</p> <ul style="list-style-type: none"> • WHO: Global Action Plan on Antimicrobial Resistance (2015)² • The OIE Strategy on Antimicrobial Resistance and the Prudent Use of Antimicrobials (2016)¹⁶ • The FAO Action Plan on Antimicrobial Resistance 2016-2020 (2016)¹⁷ • FAO/OIE/WHO: A Manual for developing National Action Plans (2016)¹¹ • EU: A European One Health Action Plan against Antimicrobial Resistance (2017)¹⁸ 	
IV. Expert review of draft framework and synthesis	<p>To expand and revise the domains and indicators in all governance areas</p> <p>To validate the framework and potential value for a range of stakeholders</p> <p>To refine and propose final framework</p>	<p>Experts consulted from:</p> <p>5 International Organizations 8 Government Departments 8 Universities 2 Policy Institutes 10 Countries 5 Continents</p> <p>(See Supplementary Material)</p>	<p>Expert consultations through:</p> <p>Written review feedback Teleconferences</p>

157 *WHO, World Health Organization; **OECD, Organisation for Economic Co-operation and Development; ***LSE, London
 158 School of Economics and Political Science.

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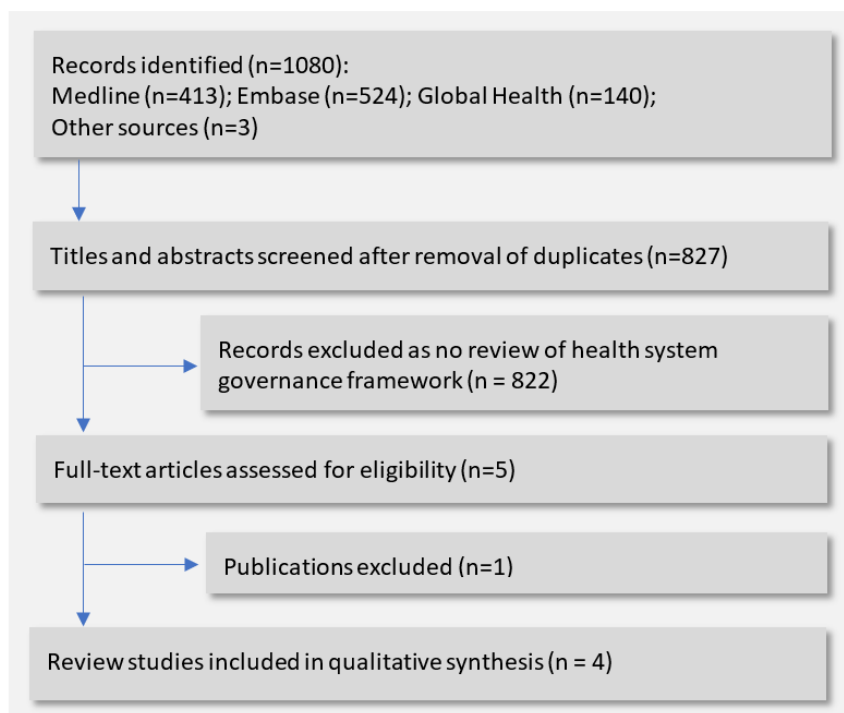
162 To account for the distinctive aspects of governance in the context of national AMR policy, we expanded
163 and refined the AMR governance framework in the third stage by reviewing the five most recent
164 guidance documents from four key international organizations – the WHO, the OIE, the FAO as well as
165 the EU. These four organisations are major actors in international AMR policy development and have a
166 precedent of producing guidance regarding national AMR policies for their member states.

167 To increase the validity of the framework and to develop pre-existing and additional indicators we
168 sought review of the framework and its components by experts from multiple sectors, disciplines, and
169 geographies in the fourth stage. A judgement sample was used for this purpose.¹⁹ Experts were
170 approached based on a combination of factors such as the length of their experience in the field of
171 AMR, their wide perspective on the development of AMR NAPs (both policy-makers and academics),
172 and their interest in governance challenges associated with AMR policy. In total, a range of experts from
173 five international or intergovernmental organisations (WHO, PAHO, OECD, European Commission,
174 European Centre for Disease Prevention and Control), eight universities, eight government ministries,
175 and two policy institutes (Chatham House and PEW Charitable Trust) provided feedback (see
176 acknowledgements). The final step of stage IV involved synthesizing the feedback and findings from the
177 preceding steps to produce a refined and final framework.

178 Results

179 *Stages I and II: Systematic review of AMR governance frameworks and health system governance*
180 *framework reviews*

181 The main results of all stages are summarized in Table 2. The systematic search for previous AMR
182 governance frameworks yielded no results (see supplementary material). The process of identification
183 and study selection for the systematic review of health system governance reviews is summarized in
184 Figure 1.



185 **Figure 1. Flow chart of study selection (stage II)**

186 From a total of 827 records that were title- and abstract-screened, 822 were excluded as they were not
187 reviews of health system governance frameworks. The full text of the remaining four publications were

188 reviewed, leading to the inclusion of three non-systematic reviews and one systematic review for
 189 qualitative assessment.²⁰⁻²³ Twenty-six governance frameworks were identified in those four
 190 publications and the 11 most frequent key governance domains across these frameworks were
 191 identified. The criteria for the inclusion of commonly used governance domains were present in more
 192 than a third of governance frameworks, a cut-off agreed upon by consensus of co-authors
 193 (supplementary material). The final component of stage II was the formation of the basic structure of
 194 the framework by grouping these eleven domains in three broader governance areas: 'Policy Design',
 195 'Implementation tools', and 'Monitoring and Evaluation'.

196 **Table 2. Summary of development of the AMR Governance Framework**

STAGE	MAIN RESULTS								
I. Search for existing AMR governance frameworks	No AMR governance frameworks identified								
II. Systematic review of health system governance reviews	<p>Review of 26 health system governance frameworks → Basic structure of AMR governance framework (3 governance areas, 11 governance domains):</p> <table border="1" data-bbox="560 857 1396 1220"> <thead> <tr> <th data-bbox="560 857 869 898">Area</th> <th data-bbox="869 857 1396 898">Domains</th> </tr> </thead> <tbody> <tr> <td data-bbox="560 898 869 1055">Policy design</td> <td data-bbox="869 898 1396 1055">Strategic Vision, Participation, Coordination, Accountability, Transparency, Sustainability, Equity</td> </tr> <tr> <td data-bbox="560 1055 869 1133">Implementation tools</td> <td data-bbox="869 1055 1396 1133">Generation of Information and Intelligence, Regulation</td> </tr> <tr> <td data-bbox="560 1133 869 1220">Monitoring and evaluation</td> <td data-bbox="869 1133 1396 1220">Effectiveness, Responsiveness</td> </tr> </tbody> </table>	Area	Domains	Policy design	Strategic Vision, Participation, Coordination, Accountability, Transparency, Sustainability, Equity	Implementation tools	Generation of Information and Intelligence, Regulation	Monitoring and evaluation	Effectiveness, Responsiveness
Area	Domains								
Policy design	Strategic Vision, Participation, Coordination, Accountability, Transparency, Sustainability, Equity								
Implementation tools	Generation of Information and Intelligence, Regulation								
Monitoring and evaluation	Effectiveness, Responsiveness								
III. Review of international guidance documents	<p>Domains</p> <ul data-bbox="560 1272 1396 1467" style="list-style-type: none"> • 7 domains added: Surveillance, Stewardship, Infection Prevention and Control, Education, Public Awareness, Fostering R&D of Novel Antimicrobials/Alternatives, AMR Research • One domain removed: Generation of Information and Intelligence. Replaced by the following domains: Surveillance, AMR research, and Fostering of R&D of Antimicrobials/Alternatives <p>Indicators</p> <ul data-bbox="560 1496 1396 1534" style="list-style-type: none"> • 34 indicators developed (see supplementary material) 								
IV. Expert review of draft framework and synthesis	<p>Domains</p> <ul data-bbox="560 1585 1396 1720" style="list-style-type: none"> • 4 domains renamed: Antimicrobial Stewardship, Medicines Regulation, Feedback Mechanisms, Fostering R&D and Facilitating Market Access to Novel Products • One domain added: Reporting <p>Indicators</p> <ul data-bbox="560 1749 1396 1825" style="list-style-type: none"> • 34 indicators reformulated/reworded and explanatory text added • 18 indicators added <p>Agreement on basic structure of the framework</p>								

197 *Stage III: Review of international guidance documents*

198 Reviewing the five international guidance documents resulted in the addition of seven domains:
199 'Surveillance', 'Stewardship', 'Infection Prevention and Control', 'Education', 'Public Awareness',
200 'Fostering the research and development (R&D) of Novel Antimicrobials/Alternatives', 'AMR Research',
201 some of which replaced the previous domain; 'Generation of Information and Intelligence' as well as
202 the extraction of 34 initial indicators (see supplementary material). These domains and indicators were
203 selected as the first step towards developing a governance framework for the specific context of AMR
204 NAPs.

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

209 *Stage IV: Expert review of draft framework and synthesis*

210 Throughout several iterations of the governance framework, we received expert feedback via email and
211 teleconferences. In three cases we received consolidated feedback based on the responses of multiple
212 individuals in those organizations (see acknowledgements). The experts agreed on the general
213 structure of three governance areas and most domains. Instead, experts primarily focused their
214 feedback on the improvement and development of the indicators. This resulted in the reformulation
215 and rewording of initial 34 indicators, the addition of 18 further indicators as well as the addition of one
216 further domain ('Reporting') to feed into the final 'AMR Governance Framework'.

217 **Governance Framework**

218 Eighteen separate domains were incorporated into the framework within three governance areas:
219 'Policy Design', 'Implementation Mechanisms', and 'Monitoring and Evaluation' (Figure 2). At the
220 structural level, the framework represents an ongoing cycle of review and evaluation processes. The
221 aim of this cyclical design is to conceptualize AMR governance not as a static but dynamic and ongoing
222 process that constantly improves and adjusts, according to lessons learned from monitoring and
223 evaluation.

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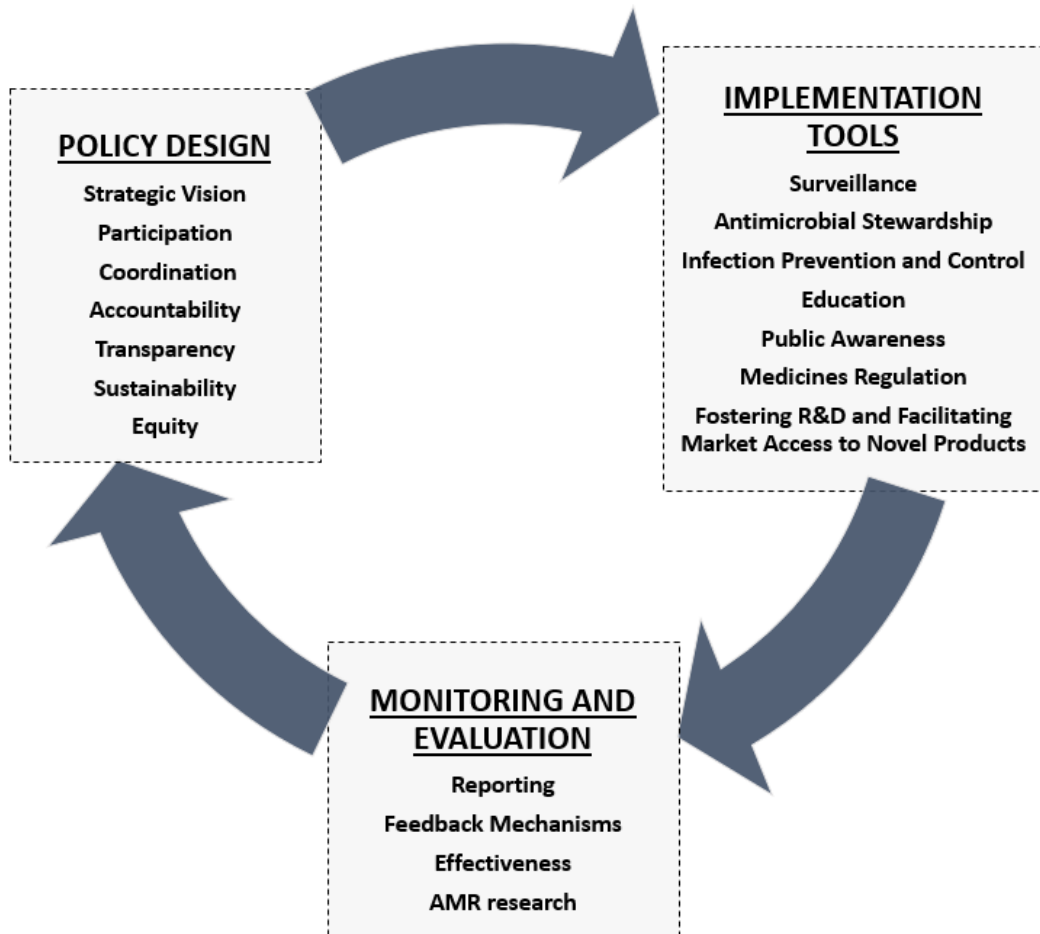


Figure 2 AMR governance framework: three areas and 18 domains.

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226 The first governance area – ‘Policy design’ – is concerned with general and procedural issues of AMR
 227 NAPs, such as wide participation in the development of NAPs, coordination across the multiple sectors,
 228 and levels of service delivery (at national and sub-national levels), transparency, sustainability and
 229 equity implications of AMR policies as well as determining who is ultimately accountable to the
 230 government for achieving the objectives of the NAP (Table 3).

231 The second governance area - ‘Implementation tools’ – consists of crucial interventions contained
 232 within WHO/FAO/OIE/EU guidance. Here, three of the domains determine whether surveillance,
 233 antimicrobial stewardship programmes, and infection prevention and control measures are
 234 implemented across the ‘One Health’ spectrum. Other domains in this governance area encompass
 235 further fundamental AMR tools such as education of relevant professionals, public awareness activities,
 236 and medicines regulation. ‘Implementation tools’ also examine whether there are appropriate policies
 237 and incentives in place to encourage research and development of novel antimicrobials and alternatives
 238 (Table 4).

239 Domains within the third governance area – ‘Monitoring and Evaluation’ – include reporting and
 240 feedback mechanisms that allow for regular review and evaluation of AMR NAPs, as well as the
 241 effectiveness and cost-effectiveness dimensions of different aspects of the NAPs. Finally, the non-
 242 therapeutic AMR research domain considers whether there is a national multidisciplinary ‘One Health’
 243 research agenda which aims to understand the drivers of and potential strategies to combat AMR (Table
 244 5).

245 For each of the 18 domains, multiple indicators were developed to signal whether the requirements for
246 the domains are fulfilled. In total, 52 indicators were derived and are outlined in detail, including an
247 explanation of their rationale in Tables 3–5.

Table 3. AMR Governance Framework, Area 1 - Policy Design

Area 1 - Policy Design		Key Issues
Domains & Indicators		
1 - Strategic Vision		
Indicator 1	<i>Has a situational analysis been conducted to determine the prevalence and incidence of AMR organisms in the country?</i>	<p>In the context of AMR, strategic vision is the overarching platform and the statement of goals and ideas central to the NAP.²⁴ It is important to consider whether a NAP has drawn on an up-to-date country specific situational analysis regarding the extent of AMR and its drivers. A situational analysis may also inform the objectives outlined in each national plan, where each objective should be specific, measurable, and time-bound. Additionally, 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 this may only be the case in more advanced NAPs. For lesser developed plans, there should be an incremental plan in place to improve surveillance capability to facilitate the measurement and implementation of quantitative targets.</p>
2	<i>Organisms a national action plan (NAP) in place, if not what is the timeframe for developing and implementing the NAP?</i>	
3	<i>Are the objectives contained within the NAP specific, measurable and time-bound?</i>	
4	<i>Are there quantitative targets for AMR/antimicrobial use outlined in the NAP?</i>	
2 - Coordination		
5	<i>Is coordination between sectors and across different levels of each sector considered?</i>	<p>The WHO, the FAO, and the OIE 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 organizations and farmer/agricultural organizations, food and pharmaceutical industries, and wholesale and retail distributors, through a multi-sectoral 'One Health' policy approach.^{11,25,26} Additionally, recent reviews 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. For example in human health, across primary, secondary, and long-term care and in animal health across both companion animals and livestock sectors.^{26,27} Lastly, it is an important consideration to clarify if there is an intersectoral committee or ministry responsible for implementing and coordinating the NAP. It may be the case that intersectoral is chaired by a ministry with overarching responsibility for coordination.</p>
6	<i>Is there a ministry and/or intersectoral committee responsible for coordination and implementation?</i>	
3 - Participation		
<p>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</p>		

7	Was a high level of stakeholder participation facilitated throughout the development of the NAP?	<p>a 'One Health' approach. This 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 organizations, farmer/agricultural organizations, 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.</p>
8	Are the activities in the NAP inclusive across all 'One Health'-related sectors? If so, how, and if not, why not?	
9	Was there support from a technical advisory group or subject matter experts during development of the NAP?	
4 - Accountability		<p>Accountability is a crucial aspect of governance in any context. Being accountable means 'having the obligation to answer questions regarding decisions and/or actions' and can be understood to have two parts; 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, it is crucial that whichever entity is responsible for coordination and implementation is accountable to a higher body in government. Furthermore, to improve accountability, there should be a person nominated within each sector responsible for implementation.</p>
10	Is there an ministry and/or intersectoral committee responsible for coordination and implementation which is accountable to the Government?	
11	Is a responsible person nominated in each sector and do agreements exist regarding what happens if objectives are not met?	
5 - Transparency		<p>Transparency can be understood as ensuring AMR policy development, implementation, and evaluation occur in an open and accessible manner. In terms of AMR NAPs, it is important the plan itself, progress reports, and funding allocations are published with open access to the public, subject to agreement of contributors to the plan. 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 greater political awareness and civil society involvement in AMR policy.³⁰</p>
12	Is the complete NAP publicly available?	
13	Are all progress reports publicly available?	
14	Is all funding information publicly available?	
15	Is all AMR/antimicrobial use surveillance data publicly available?	
6 - Sustainability		<p>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, it is likely that actors will have limited resources to implement AMR policies. Furthermore, strategic consideration of budget allocation</p>

16	<i>Is there either a written mandate or voluntary agreement from all relevant sectors in place to implement the NAP?</i>	<p>and assessment for potential gaps in funding is desirable. The sustainability of an AMR NAP may also rely upon its legitimacy, which is crucial for the ongoing engagement of all stakeholders. This can be achieved 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 remains evidence-based and utilizes all recent findings from monitoring and evaluation processes. Finally, 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 (NHPSPs),³¹ National Action Planning for Health Security (NAPHS),³² and the UN Sustainable Development Goals (SDGs).³³</p>
17	<i>Are there dedicated budgets in place to implement specific activities in the NAP?</i>	
18	<i>Is there an assessment of future budget requirements for different activities listed in the NAP?</i>	
19	<i>Is there ongoing support from a technical advisory group or subject matter experts during implementation, monitoring and evaluation of the NAP?</i>	
7 - Equity		
20	<i>Does the NAP include both encouraging responsible use and facilitating equitable access to existing essential antimicrobials?</i>	<p>In all countries, it may be the case that certain communities do 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. Moreover, high out-of-pocket payments can create an incentive for providers to inappropriately prescribe antibiotics and/or result in inequitable access to antimicrobials.³⁷ Therefore, as a key component to tackle AMR, NAPs should consider how best to balance responsible use and equitable access to essential antimicrobials.³⁸</p>

AMR, antimicrobial resistance; FAO, The Food and Agriculture Organization of the United Nations; NAP, national action plan; OIE, World Organisation for Animal Health; WHO, World Health Organization

Table 4. AMR Governance Framework, Area 2 - Implementation Tools

Area 2 - Implementation Tools		Key Issues
Domains & Indicators		
8 - Surveillance		<p>Surveillance is fundamental for the planning, conduct, and evaluation of all other AMR policies.²⁶ It 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 (GLASS) and the work of agencies such as the European Centre for Disease Prevention and Control (ECDC). It is important 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.⁴⁰⁻⁴³ Surveillance metrics should include the overall quantity of antimicrobials used as well as an assessment of both appropriate and inappropriate use. It is also important that there is adequate laboratory capacity and capability supported by a regular programme of external quality assessments.⁴³</p>
Indicator 21	<i>Is there a national surveillance system for resistant organisms across the human, animal, and the environmental health sectors?organism</i>	
22	<i>Is there a national surveillance system for levels of antimicrobial use in animals and humans?</i>	
23	<i>Is there adequate laboratory capacity and capability supported by regular external quality assessments?</i>	
9 - Antimicrobial Stewardship		<p>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 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 utilized 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 may 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 utilised to encourage healthcare professionals to reduce antimicrobial use and</p>
24	<i>Are there stewardship programmes across human and animal health sectors?</i>	
25	<i>Are rapid diagnostic tools widely available and in regularly use? if so, do national guidelines regarding their indication and interpretation exist?</i>	
26	<i>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?</i>	

27	Is there any use of financial and non-financial incentives/penalties in animal and human health to reduce inappropriate use of antibiotics?	adhere to national guidelines. ⁴⁸ However, non-financial incentives such as public reporting and peer comparison can also be utilised. ⁴⁹ Lastly, as discussed in Domain 7 stewardship programmes should both limit inappropriate use of antimicrobials but also facilitate equitable and timely access to appropriate antimicrobials when needed. ⁵⁰
10 - Infection Prevention and Control		Infection prevention and control (IPC) serves as an important policy objective in all settings that aims to reduce the transmission of multi-drug resistant bacteria, minimize the overall risk of infection, and decrease the overall need for antimicrobials. Within AMR NAPs, it is important that the plan includes IPC measures across all sectors including human, animal and environmental health. 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 Whereas in animal health, good husbandry practices and effective biosecurity measures are important. ⁵⁵ Lastly 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 standardize implementation and evaluation within each context. Similarly, 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} Lastly, immunisation programmes can be an effective strategy to reduce burden of vaccine-preventable infections in both human and animal sectors. ⁶⁰
28	Are there IPC policies across all levels of human, animal and environmental health sectors?	
29	Are there up-to-date national guidelines for IPC across human, animal and environmental health sectors?	
30	Are immunisation programmes utilised as an approach to prevent infections across human and animal health sectors?	
31	Are financial and non-financial incentives/penalties for IPC policies utilised across human, animal and environmental health?	
11 - Education		
32	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?	Examples from both the human and the animal health sector have shown how a lack of education can lead to a lack of capacity to adopt standards, facilitate control policies, or implement guidelines sufficiently. ²⁶ It is therefore essential 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. In the human health sector, medical students, physicians, pharmacists,

33	Is there continuing education programmes for all involved groups of professionals to ensure expertise necessary for expanding knowledge and sustained efforts to tackle AMR?	nurses, midwives, 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, education programmes should aim to foster a culture of safety among healthcare workers, administration and decision makers, as part of multimodal strategies to improve IPC and stewardship. ^{63,64} It is equally important for professionals from the animal and environmental health sector to receive training, as well as professionals working in the food industry or environmental agencies. ⁶⁵ Moreover, 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 However, many other professionals such as veterinarians, environmental health officers and biochemists are required to implement AMR policies in animal and environmental health. As such, an essential component of any AMR NAP is a comprehensive workforce strategy responsive to local needs informed by detailed workforce planning.
34	Is there a workforce strategy which aims to deliver the sustainable supply of the necessary workforce required to deliver antimicrobial stewardship and IPC policies?	
12 - Public Awareness		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 Furthermore, 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 multi-modal, utilising 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.
35	Are there multi-modal public awareness campaigns that focus on AMR and educational programmes (including school children) related to AMR?	
36	Do the implemented public awareness campaigns have an ongoing character?	
37	Does the conception of the public awareness campaign consider aspects of behavioural sciences, social science and psychology?	
13 - Medicines Regulation		To conserve the use of currently available antimicrobials, regulation has been utilized in a variety of ways. We interpret regulation as any laws, accreditation or

38	Are there regulations in place to ensure appropriate use of antimicrobials in human health?	financial incentive/penalties in place with the aim of reducing antimicrobial use. For example, many countries have enforced legislation that make antimicrobials “prescription-only status”, that is requiring a mandatory prescription. Another significant example, is the Feed Additives Regulation in the EU, which banned the use of antibiotics as growth promoters in animal feed from January 2006. ⁷⁰ There are also antimicrobials deemed critically important for human health, and regulation should play a key role in ensuring they are not used in animals. ⁷¹ Moreover, 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 which minimizes environmental exposure. ⁷³ Finally, regulation is utilized in many countries to ban direct to consumer advertising (DTCA) of medications, including antimicrobials. This is important as inappropriate DTCA can alter public expectations or prescribing behavior negatively. ⁷⁴ However, presence of regulation alone is not sufficient; effective regulation must be well designed. This involves an appropriate legislative mandate, a clear legal framework and a regulator in place to monitor and implement regulation that is properly accountable. ⁷⁵ These give the full force of law to the regulatory authorities which is key to achieve regulatory objectives.
39	Are there regulations in place to ensure appropriate use of antimicrobials in animal health?	
40	Is there an authority in place to monitor and enforce legislation, if so does this authority have a dedicated budget?	
14 - Fostering R&D and Facilitating Market Access to Novel Products		
41	Is fostering R&D and facilitating market access to novel antimicrobials, diagnostics, vaccines and alternative treatments in both human and animal health listed as a priority in NAP?	Whilst there were significant gains in antibiotic discovery between 1940-1990, research and development (R&D) has shifted to other therapeutics due to a combination of economic, regulatory, and scientific barriers. ^{76,77} A comprehensive AMR NAP should include both fostering R&D 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 R&D, 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 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 R&D 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 alternative business model to facilitate market access for novel antimicrobials. ⁸² Finally, to avoid duplication of efforts on the international level, and given that research of
42	Does the NAP consider how the country can contribute to R&D of novel agents at both a national and international level?	
43	Is there a dedicated national budget for R&D of novel antimicrobials, diagnostics, vaccines, or alternative treatments?	

		novel antimicrobials is not a viable option for all countries, each country should identify potential areas of comparative advantage and seek to harmonize with international efforts.
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AMR, antimicrobial resistance; EU, European Union; IPC, infection prevention and control; NAP, national action plan; R&D, research and development

Table 5. AMR Governance Framework, Area 3 - Monitoring and Evaluation

3 - Monitoring and Evaluation		Key Issues
Domains & Indicators		
15 - Reporting		<p>While it is not realistic for an AMR NAP to be revised on an annual basis, 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 bodies/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. It is also an important aspect of national governance that countries engage with wider international efforts to monitor the extent of AMR globally. Therefore, it is essential that national surveillance systems collaborate with and relay data to international surveillance systems.</p>
Indicator 44	<i>Are annual AMR NAP progress reports published?</i>	
45	<i>Are annual surveillance reports published containing data regarding the incidence of resistant organisms and antimicrobial use?</i>	
46	<i>Is there collaboration with and systematic data transmission to international surveillance systems?</i>	
16 - Feedback Mechanisms		<p>For surveillance to be an effective tool for improvement, data needs to be routinely fed back at regional and organizational level. In practice, this implies involving local stakeholders in analysis of what the data shows, where 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 Domain 1. If progress towards national targets is limited, local stakeholders should be encouraged to produce personalized and time-bound action plans. To improve accountability, a NAP should identify deadlines to review progress of specific actions, as well as arrangements to feedback at both regional and organization level.</p>
47	<i>Are there feedback mechanisms in place which relay surveillance data back at both regional and organisational level?</i>	
48	<i>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?</i>	
17 - Effectiveness		<p>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 healthcare expenditure due to increased morbidity and mortality, likelihood for hospitalization, average hospital length of stay, cost of last-resort treatment options, and productivity losses for patients at work.^{86,87} From a governance perspective, it is important to establish which AMR policies are cost-effective and represent value-for-money. Sources of data could, for example,</p>
49	<i>Have there been efforts to evaluate the effectiveness (e.g. measure of impact on human and animal health) of specific policies and/or interventions implemented?</i>	

50	Have there been efforts to evaluate the cost-effectiveness (e.g. measure of impact on human and animal health) of specific policies and/or interventions implemented?	include surveillance systems, hospitals, clinicians, the agricultural sector, and food-supply chains. Each source provides feedback on the impact of policies in reducing antimicrobial consumption, inappropriate use of antibiotics and antimicrobial resistance rates. Although, estimating the effectiveness and cost-effectiveness of individual interventions and/or policies may be challenging as many factors will contribute to an increase or decrease in antimicrobial use/AMR. Accordingly, 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 (ICER), which can allow comparisons between interventions to rationalize funding decisions.
18 - AMR Research		
52	Is research to understand both the drivers and impact of AMR as well as potential policies and interventions identified as a key priority in the NAP?	‘Generation of information/intelligence’ 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 policies in place to limit them, resistance will develop to new antimicrobials. Research should also consider including modelling exercises to forecast incidence and prevalence of AMR as well as the current and future health and economic impact. Priorities within the national research strategy should be multidisciplinary and potentially defined by an intersectoral committee to ensure a One Health approach. This may include inputs across social sciences, behavioral, economic, and medical research. ⁸⁸ For the long-term sustainability of research activities, it is important to put in place a dedicated budget at the national level.
52	Is there a dedicated national budget for AMR research in place?	

AMR, antimicrobial resistance; ICER, incremental cost-effective ratio; NAP, national action plan

248 **Discussion**

249 *Summary of question, methods, main results*

250 A central challenge to combatting the global threat of AMR is the successful implementation, in each
251 country, of an AMR NAP across the relevant sectors and levels, which can be enabled by a systematic
252 approach to governance. Here, we have developed the first comprehensive framework for the
253 governance of AMR NAPs by synthesising findings from a review of health system governance
254 frameworks, an analysis of the guidance from major international organizations, and extensive input
255 from expert policy-makers, practitioners, and researchers from government ministries, international
256 organizations, policy institutes and academic institutions. Within a cyclical design, our governance
257 framework consists of 52 indicators that are contained within 18 domains and grouped in three main
258 governance areas: “policy design”, “implementation tools”, and “monitoring and evaluation”. It is
259 intended to aid policy-makers to design, implement, monitor, and evaluate AMR NAPs across the ‘One
260 Health’ spectrum, as well as to facilitate objective assessments of countries’ AMR NAPs to increase
261 accountability and stimulate debate.

262 *Strengths*

263 To our knowledge, this is the first study that provides a comprehensive systematic synthesis of available
264 evidence on the governance of AMR NAPs by including information from a systematic review of health
265 system governance frameworks, international guidance, and over 20 experts from various international
266 organizations, government ministries, policy institutes and academic institutions. The AMR governance
267 framework has several strengths. A central and recurring input by experts was the need for usability.
268 By including 52 indicators, and 18 domains the framework balances the right mix of comprehensiveness
269 and usability for policy-makers. This was confirmed by various experts in the fourth stage of the
270 development of the framework. The cyclical design of the framework reflects the dynamic nature of
271 the AMR issue and the corresponding need to be responsive and adaptive, but also ensure that the
272 governance of AMR NAPs itself develops and improves, reflecting the realities observed and lessons
273 learned.

274 *Limitations*

275 The AMR governance framework also has various limitations. Our review of health system governance
276 frameworks prioritised systematic and non-systematic reviews, therefore it is possible that certain
277 governance frameworks were overlooked. It can also be argued that our AMR governance framework
278 would benefit from either reviewing a larger body of international guidance documents or consulting a
279 larger sample of experts. However, the documents reviewed represent the most recent guidance
280 developed by five major international organisations involved in AMR policy. Furthermore, the expert
281 sample was balanced between international organizations, policy institutes, government, and
282 academia, as well as backgrounds relevant to the ‘One Health’ approach.

283 We did not use a structured consensus method during development of the framework.⁸⁹ Our
284 objective is to facilitate international debate around a universally accepted approach to governance in
285 national AMR policy. The establishment of the “One Health Global Leadership Group” on AMR
286 recently recommended by the UN IACG on AMR is one potential forum to develop international
287 consensus.¹⁵ Alternatively, a more detailed assessment of a country’s approach to governance of NAPs
288 could be incorporated into pre-existing initiatives such as the WHO Joint External Evaluation tool,⁹⁰ or
289 the global tripartite database on country progress.

290 A further limitation of our AMR governance framework is related to applicability. A thorough objective
291 application of the framework would be resource intensive due to the broad nature of data sources
292 which would need to be reviewed, as well as challenges with data availability as some policy documents
293 or decisions may not be publicly accessible. As a result, several interviews with multiple stakeholders
294 within each country may need to be conducted. This partially explains why current efforts to assess
295 AMR NAPs such as the global tripartite database on country progress revolve around the use of a self-
296 assessment questionnaire.⁷

297 Conversely, it can also be argued that the 52 indicators and 18 domains only provide a superficial
298 assessment in certain areas, and do not assess quality of governance adequately. For example, a
299 country may offer education to all relevant professionals regarding AMR, but it may be of poor quality
300 and brief, or alternatively a public awareness campaign may be in place, but it is poorly financed with a
301 narrow focus. Cross-country comparisons utilising this governance framework should therefore be
302 made with caution as there are possibilities for misleading conclusions.

303 Finally, the AMR governance framework was developed based upon experience and guidance that
304 applies most typically to high-to-middle income countries. In low income countries with less resources,
305 limited national surveillance and less developed healthcare systems,^{91,92} the application of the
306 framework is possibly ambitious. To address this, we extended the sample size of experts to include
307 perspectives from low-to-middle income countries (LMICs). The feedback was positive, and this
308 resulted in only minor changes to the framework. It was felt this framework was still relevant to lesser
309 developed plans, such as those in some LMICs, as the cyclical nature of this framework captures how
310 shortcomings in pre-existing national action plans can be improved throughout subsequent iterations
311 and repeated applications of the framework.

312 **Conclusion**

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

317

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