Supporting appropriate recognition and action for vaccination in AMR National Action Plans

November 2021

Charles River Associates (CRA) was asked by the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) to analyze the current level of support for vaccination in Antimicrobial Resistance (AMR) National Action Plans (NAPs) and identify how this support could be strengthened in terms of recognizing the role of vaccination and committing to corresponding actions.

Vaccination has a key role to play in combating AMR

AMR is a serious and increasing threat to global health security and threatens much of the modern medicine we have come to rely on, made possible by our ability to prevent and treat infections. Today, over 700,000 people die every year of resistant infections globally. If no action is taken to combat AMR, deaths attributable to AMR could rise to 10 million people a year by 2050, costing the global economy as much as $100 trillion.[i]

To address the challenge of AMR, the World Health Organization (WHO) published a Global Action Plan in 2015[ii] calling for countries to develop NAPs on AMR addressing the five objectives of the Global Action Plan:

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

2. Strengthen the knowledge and evidence base through surveillance and research

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

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

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

NAPs are intended to outline commitments on improving AMR education and awareness, implementing effective antimicrobial stewardship programs, and support the development of much-needed new antimicrobials. However, the role of preventative methods in AMR NAPs, such as vaccination, has received minimal attention. Vaccination is a complementary tool in the fight against AMR as it can help reduce the use of antibiotics by: (i) preventing commonly acquired bacterial infections that require antibiotic treatment and (ii) reducing misuse of antibiotics by preventing viral infections for which antibiotics are inappropriately prescribed.[iii,iv,v] Vaccination also reduces the circulation of strains that could propagate further resistance.[vi]

Given that AMR NAPs drive policies to mitigate AMR, there is a clear case for recognizing vaccination as a key pillar for change and outlining well-defined goals for vaccination in NAPs to ensure AMR is approached in a holistic and sustainable manner.

The inclusion of vaccination in NAPs

To determine the extent of inclusion of human vaccination[1] in NAPs, a structure was developed to assess the level or recognition, prioritization, and evidence of impact (Box 1). This structure was based on the WHO's Action Framework on leveraging vaccination to combat AMR.[vii] Within each pillar of the structure, the plans were analyzed based on the three goals in the WHO Action Framework: increasing vaccine uptake, vaccine research and development (R&D) and generating and sharing data on the impact of vaccines in combating AMR.

This analysis comes in the wake of the 2021 AMR Preparedness Index, which assessed broad progress in the fight against AMR by 11 of the largest global economies, including their national strategies.[viii] The aim of this work analyzing NAPs is to provide more detailed, preliminary insight on the acknowledgement of vaccination in select NAPs. To allow comparison across countries, systematic assessment criteria were applied.

The structure and assessment criteria were used to analyze the positioning of vaccination in two international (WHO, European Union (EU)) and 11 national AMR action plans (Brazil, China, France, Germany, India, Italy, Japan, Saudi Arabia, South Africa, United States (US), United Kingdom (UK)) (see Appendix). Countries were selected that represent each WHO region and after an initial review were hypothesized to cover a range of level of detail of vaccination acknowledgement in their NAPs.

Box 1: Structure for analyzing vaccination positioning in NAPs

Ambition	**1. Vaccination Recognition**
	• Acknowledgement of the role of vaccination in combating AMR through increasing vaccine uptake, accelerating AMR-relevant vaccine R&D, and generating data on the impact of vaccination in combating AMR
	• Recognition of the role different types of AMR-relevant vaccines play in combating AMR
	• Link to country immunization policies and programs or other infection control and prevention plans
	2. Vaccination Prioritization & Goals
	• Dedication of specific sections, goals, or objectives for leveraging vaccines to combat AMR, including increasing uptake, accelerating R&D and data generation
	• Specific policies/action steps outlining how vaccination strategies will be implemented
	• Country commitment to implementation
Evidence	**3. Evidence of Impact**
	• Evidence of implementation of vaccination strategies
	• Evidence of effort to measure the implementation and effectiveness of vaccination strategies

Source: CRA analysis

This analysis aims to assess the positioning of vaccination in NAPs; the broader environment of uptake and R&D of AMR-relevant vaccines may differ from the level of recognition and prioritization in NAPs and further analysis is needed to assess this. With

---

[1] This analysis focuses on the positioning of human vaccination in NAPs. In this report, where "vaccines" or "vaccination" are mentioned, this refers to human vaccination unless otherwise specified.

respect to NAPs, while this review identifies where improvements are needed in the positioning of vaccination, further understanding and research are also needed to set out how this should be done; for example, by drawing learnings from how NAPs have successfully led policy development in other areas (e.g., antimicrobial stewardship).

It should also be noted that the NAPs analyzed were developed at different points in time since the WHO Global Action Plan was published. Since publication of these NAPs, knowledge on the impact of vaccines on AMR has grown greatly and the WHO Action Framework has provided a structure for policy discussions in this area. It is therefore important to analyze NAPs with a view to the level of knowledge and state of the debate at their time of publication, and to monitor the positioning of vaccines in future NAP revisions.

Lessons on the role of vaccination in AMR plans

Although all AMR plans analyzed include reference to vaccination, there are major gaps across all three pillars of recognition, prioritization, and impact. As shown in Figure 1, the relative performance of the 13 AMR plans analyzed can be grouped as follows:

- Some plans have a high level of recognition and prioritization of the role of vaccination in AMR, where future efforts should focus on implementation. These include the France, US, and WHO plans.

- In some plans, there is a high level of recognition of vaccination but with a need to translate recognition into clear priorities, goals, actions, and efforts to implement. These include the EU, Italy, and UK plans.

- In some plans, prioritization of vaccination has been acknowledged with some corresponding actions, but they require broader and consistent recognition of the role of vaccination in AMR and a focus on implementation. These include the Brazil and Japan NAPs.

- Some plans lack recognition and prioritization of the role of vaccination in AMR, where efforts should focus on improving recognition. These include the China, Germany, India, Saudi Arabia, and South Africa NAPs.

In this section, we discuss lessons drawn from comparing the different plans across the three pillars of the framework, country examples and how global and national policy efforts could improve the positioning of vaccination in AMR to ensure effective and coordinated action to optimize how vaccination could be used to combat the growing threat of AMR.

Figure 1: Summary of relative vaccination positioning in AMR plans
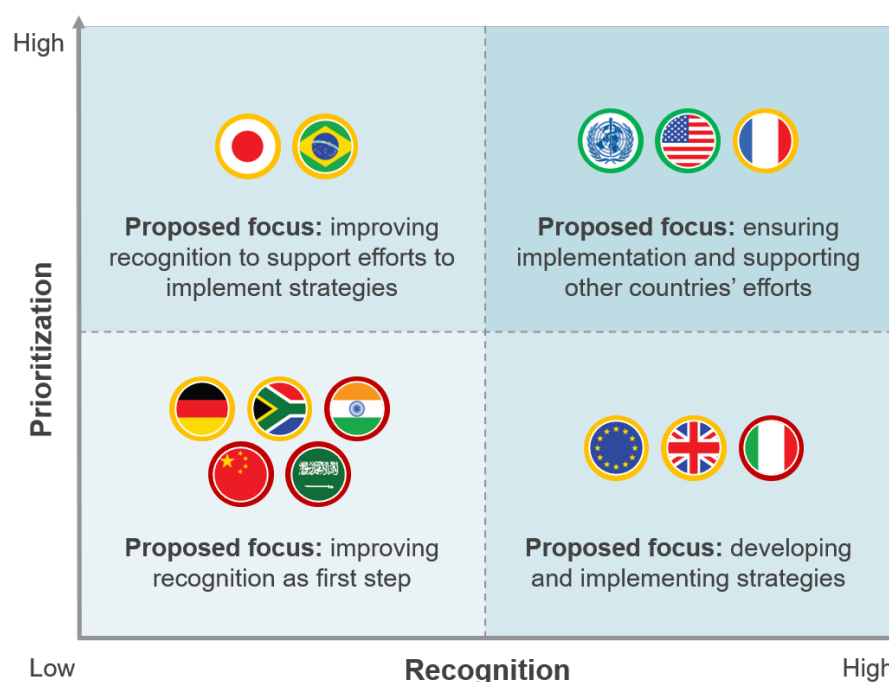
Source: CRA analysis. Colored flag borders indicate relative level of evidence of implementation and impact of vaccination strategies in AMR plans. Red=low, amber=medium, green=high.

Recognition of vaccination in NAPs

Findings

Most AMR plans acknowledge or mention the importance of vaccination in the context of AMR in at least one of the three key areas (Box 2). However, many plans that identify the need to increase vaccine uptake and R&D do not explicitly elaborate on the role and importance that this has for combating AMR or include explicit strategies to increase this. The WHO, EU and UK plans are the only ones to explicitly acknowledge the importance of both increasing vaccine uptake and R&D for combating AMR.

Furthermore, most plans either do not mention or lack specificity around the range of vaccine types (high priority bacteria, common bacterial pathogens, viral pathogens) that combat AMR. Only the UK plan lists examples of high priority bacterial strains in the context of vaccination. Some plans recognize the role of vaccination for common and resistant bacterial pathogens in combating AMR but fewer explicitly recognize the role of vaccination for viral pathogens.

Most of the evaluated plans (nine out of 13) mention an immunization policy or program or other infection plan. However, in many cases the immunization plans do not reciprocally link to AMR plans, indicating a disconnect between AMR and infection control/vaccination policy.

Box 2: NAP recognition of the need for action on vaccination for AMR

- **Vaccine uptake:** All but four plans acknowledge the role of human vaccines in combating AMR through increasing vaccine uptake.

- **R&D:** All plans, except France, acknowledge the role of vaccine R&D. However, there is a lack of specificity around vaccine R&D, regarding which vaccines to prioritize and how vaccine R&D combats AMR.

- **Data generation:** All plans, except France, acknowledge the role of vaccine R&D. However, there is a lack of specificity around vaccine R&D, regarding which vaccines to prioritize and how vaccine R&D combats AMR.

Source: CRA analysis

Policies to improve the recognition of vaccination:

- AMR NAPs should explicitly recognize the role of vaccination in AMR tailored by vaccine type (against AMR priority, common bacterial, and/or viral pathogens), as each have different roles and require different actions to appropriately combat AMR. In general, greater recognition of the value of viral vaccines to reduce inappropriate antibiotic use is needed.

- NAPs should include greater recognition of the need for specific actions aimed at increasing the impact of vaccination against AMR (uptake, R&D, data on vaccination impact) to ensure prioritization of vaccination. There is a particular need for increased recognition of the importance of generating data on the impact of vaccination on AMR and using it to improve awareness and understanding.

Prioritization of vaccination in NAPs

Findings

Overall, all plans analyzed (except Germany, Italy, and China) have at least one general goal or objective dedicated to vaccination. However, only the WHO, the US, Brazil, and Japan plans have specific goals or objectives for two of the three key components: vaccine uptake, R&D, and data generation (Box 3).

Inclusion of specific policies for how vaccination-related goals will be achieved and of stakeholder roles and responsibilities related to vaccination goals is mixed. Seven of the analyzed plans include policies to achieve vaccination goals, but some are lacking assigned stakeholders or detail regarding roles and responsibilities to operationalize the strategies.

Box 3: NAP prioritization of goals and strategies related to vaccines for AMR

- **Vaccine uptake:** Although most plans have a commitment to action for increasing vaccine uptake, fewer than half have dedicated objectives on this, indicating low priority. In addition, these goals are mostly focused on increasing coverage of existing vaccines rather than updating vaccination recommendations/schedules (e.g., to include additional vaccines or to include additional groups in existing recommendations).

- **R&D:** The only two plans not to include commitments to action on human vaccine R&D are France and Germany. However, the level of detail and prioritization varies: some plans only include vaccines in a list of new technologies for which development is needed (e.g., diagnostics and novel antimicrobials). In contrast, the UK NAP lists priority bacteria where vaccine development is needed.

- **Data generation:** Only two plans commit to generating data on the impact of vaccination on AMR: Italy and the US. Only Italy has an action for specific studies to evaluate the impact of vaccination on AMR.

Source: CRA analysis

Regarding commitment to implement vaccination-related goals, five indicators were evaluated: (1) inclusion of timelines, (2) allocated funding, (3) numeric targets/indicators, (4) up-to-date plan and (5) publication of progress reports. Across all these indicators, only two countries (France and the US) demonstrate a high degree of commitment. Only five plans include specific timelines for vaccination-related activities and only two NAPs and the WHO and EU plans have evidence of funding identified and allocated for vaccination strategies. Only the US NAP defines indicators for vaccination-related goals and specific targets for success, despite the existence of these for anti-infectives in many NAPs. Finally, four countries have not published progress reports or other details pertaining to progress on their vaccination strategies.

Policies to improve the prioritization of vaccination:

- To improve the prioritization of vaccination, AMR plans should have clear objectives and goals across three key areas: increasing vaccine uptake, promoting R&D, and generating and sharing data on the impact of vaccination on AMR.

  - One of the key priorities should focus on data generation on the impact of vaccination on AMR to further support actions including future policy prioritization of vaccination to combat AMR (both uptake and R&D), targeted immunization policies for AMR, and vaccine R&D investments.

  - Prioritization of vaccination in NAPs needs to be increased to reflect the importance of vaccination in combating AMR.

- Objectives related to vaccination need to have specific policies associated to them with clear stakeholder roles and responsibilities assigned for implementation.

  - Where AMR plans draw from high-level goals set out by international organizations (e.g., WHO Global Action Plan on AMR), these should be coupled with locally tailored objectives and strategies and achievable, measurable targets for implementation.

- Vaccination strategies within AMR plans should be assigned appropriate funding and other ancillary resources (such as toolkits for guidance and support from vaccination experts) to aid implementation.

Collecting evidence on implementation of vaccination policies

Findings

There is evidence of implementation of vaccination strategies across all AMR plans except China and Saudi Arabia. However, only the WHO, EU, US, and the UK have specifically linked implementation of vaccination-related strategies to their AMR plans. There is evidence of efforts to implement vaccination related strategies (e.g., increasing uptake) in Italy, Brazil, Japan, South Africa, and India, for example through national vaccine plans, but this has not been linked explicitly to the NAPs by government sources.

Countries vary in the extent to which they measure implementation of vaccination strategies in their NAPs, and the extent to which this data is used to assess the impact of these strategies. Most countries do not track implementation of vaccination-related strategies, or when they are tracked, they are not linked to AMR plan implementation, particularly for vaccine R&D activities. Only the WHO and US plans have systematic reporting of implementation activities and tracking of performance. Across countries, there is limited measurement of the impact of vaccination-related strategies on AMR development.

Box 4: Implementation of vaccination strategies from AMR plans

- **Vaccine uptake:** Although many countries are making efforts to increase vaccination coverage, such as by national vaccine plans, this is often not linked to AMR action plans.

- **R&D:** There is limited evidence on effort to implement vaccine R&D strategies outside the WHO, EU, US, and UK, despite existence of these strategies in many NAPs.

- **Data generation:** The overall lack of recognition and prioritization in this area translates to very little action to generate data on the impact of vaccination on AMR.

Policies to improve the implementation and monitoring of vaccination strategies in AMR plans:

- In order to track the impact of including vaccination in NAPs it is important that AMR plans include quantifiable metrics for evaluation of implementation of vaccination strategies (such as coverage of priority AMR-relevant vaccines, number/stage of AMR priority vaccines in development, levels of resistance of vaccine-preventable diseases).

- Measurement of vaccine uptake and efforts to increase uptake should be more explicitly linked to AMR objectives and AMR should be integrated in other immunization efforts.

- Implementation of vaccination strategies in NAPs should be clearly monitored and reported and outcomes used to inform future AMR and vaccination policy.

Authors

Tim Wilsdon
Vice President
+44-207-664-3707
twilsdon@crai.com

Artes Haderi
Principal
+44-207-664-3743
ahaderi@crai.com

Anna Robson
Consulting Associate
+44-207-664-3713
arobson@crai.com

Appendix: AMR Action Plans Analyzed

Country/Region	Main AMR Plan analyzed
WHO	Global Action Plan on Antimicrobial Resistance (2015)
European Commission	European One Health Action Plan against Antimicrobial Resistance (AMR) 2017
United Kingdom	UK 5-year national action plan: Tackling antimicrobial resistance 2019-2024
France	France Inter-ministerial Roadmap for Controlling Antimicrobial Resistance (2016)
Germany	German Antibiotic Resistance Strategy 2015-2020 (DART 2020)
Italy	Italy National Action Plan on Antimicrobial Resistance (PNCAR) 2017-2020
United States	US National Action Plan for Combating Antibiotic-Resistant Bacteria: 2020-2025
Brazil	National Action Plan for Prevention and Control of Antimicrobial Resistance Within One Health: 2018-2022
Saudi Arabia	Kingdom Saudi Arabia National Action Plan on Combatting Antimicrobial Resistance: 2017
South Africa	Antimicrobial Resistance National Strategy Framework 2018-2024
India	National Action Plan on Antimicrobial Resistance (NAP-AMR) 2017-2021
China	National Action Plan to Contain Antimicrobial Resistance (2016-2020)
Japan	Japan National Action Plan on Antimicrobial Resistance (AMR): 2016-2020

References

[i] O'Neill, J. (2016) *Tackling drug-resistant infections globally: final report and recommendations*. Review on Antimicrobial Resistance. Available at: https://amr-review.org/sites/default/files/160525_Final%20paper_with%20cover.pdf [Accessed 20 October 2021]

[ii] World Health Organization (2015) Global action plan on antimicrobial resistance. Available at: https://apps.who.int/iris/handle/10665/193736 [Accessed 20 October 2021]

[iii] Lipsitch, M. & Siber, G. R. (2016) How can vaccines contribute to solving the antimicrobial resistance problem? *mBio.* 7 (3), e00428-16. doi.org/10.1128/mBio.00428-16

[iv] Bloom, D. E., Black, S., Salisbury, D. & Rappuoli, R. (2018) Antimicrobial resistance and the role of vaccines. *PNAS.* 115 (51), 12868–12871. doi.org/10.1073/pnas.1717157115

[v] Clift, C. & Salisbury, D. M. (2017) Enhancing the role of vaccines in combatting antimicrobial resistance. *Vaccine.* 35 (48B), 6591–6593. doi.org/10.1016/j.vaccine.2017.09.053

[vi] Baker, S. J., Payne, D. J., Rappuoli, R. & De Gregorio, E. (2018) Technologies to address antimicrobial resistance. *PNAS.* 115 (51), 12887–12895. doi.org/10.1073/pnas.1717160115

[vii] World Health Organization. (2020) *Leveraging Vaccines to Reduce Antibiotic Use and Prevent Antimicrobial Resistance: An Action Framework.* World Health Organization. Available at: https://www.who.int/publications/m/item/leveraging-vaccines-to-reduce-antibiotic-use-and-prevent-antimicrobial-resistance [Accessed 20 October 2021]

[viii] Global Coalition on Aging & Infectious Diseases Society of America. (2021) *2021 AMR Preparedness Index.* Available at: https://globalcoalitiononaging.com/wp-content/uploads/2021/06/GCOA-AMR-Preparedness-Index_FINAL.pdf [Accessed 20 October 2021]