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Introduction

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Vaccines and antimicrobial resistance: from science to policy—introduction

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Vaccines for humans and animals represent an attractive means to counter the growing global pandemic of antimicrobial resistance (AMR). However, vaccines are only available against a few key bacterial pathogens, and interactions between the human and veterinary vaccine communities have been limited. In April 2024, a Royal Society Science+ Meeting on 'Vaccines and AMR: from science to policy' was held in London to review the science of how vaccines reduce AMR, identify research gaps in developing AMR vaccines and discuss policy in advancing development and equitable deployment of such vaccines. Taking a One Health approach, the meeting brought together clinical and veterinary experts from academia and industry, policymakers and funders, from high-income countries and from low- and middle-income countries. Articles based on presentations at the Science+ meeting, including an overall summary of the meeting, its outcomes and recommendations, are included in this issue of *Philosophical Transactions of the Royal Society B*. This opening article provides the background, rationale and aims of the meeting.

This article is part of the Royal Society Science+ meeting issue 'Vaccines and antimicrobial resistance: from science to policy'.

1. Background

In 2016, the O'Neill Report, 'Tackling drug-resistant infections globally' [1], commissioned by the UK government, predicted that unless action against antimicrobial resistance (AMR) was taken, by 2050 AMR would be the leading global cause of death, rising from 700 000 annually in 2016 to 10 million deaths annually in 2050. The resulting cumulative loss of economic output between 2016 and 2050 from unchecked AMR was estimated at $100 trillion. The report highlighted the valuable role that vaccines could play against AMR [1].

Separately, in 2017, a World Bank report, 'Drug-resistant infections, a threat to our economic future' [2], concluded that AMR would reduce global gross domestic product (GDP) by 1.1–3.8% by 2050, with an annual global GDP shortfall of $1–3.4 trillion by 2030. The report predicted that the annual reduction in global GDP could be as large as the losses from the 2008–2009 global financial crisis, but would last much longer and would affect low- and middle-income countries (LMICs) the most [2].

The importance of addressing the AMR threat was further highlighted in 2022 when the Institute for Health Metrics and Evaluation (IHME) published a first estimate of deaths from AMR based on real-world data: 1.27 million deaths directly attributed to, and 4.95 million deaths associated with AMR in 2019. This burden of deaths fell heaviest on LMICs [3]. In the same year,

IHME published a first estimate of global mortality associated with bacterial pathogens, the infectious agents that harbour AMR, attributing 7.7 million deaths to 33 such pathogens in 2019, making bacteria the second leading cause of death globally [4].

2. Science

Vaccines reduce AMR via multiple mechanisms but primarily through preventing infections and reducing antibiotic use. Bacterial vaccines directly reduce drug-sensitive and antimicrobial-reistant infections in vaccinated individuals and animals. They indirectly reduce drug-sensitive and antimicrobial-reistant infections in unvaccinated individuals and animals through herd immunity. Both of the above result in a reduction in the development of new resistance. Viral vaccines reduce secondary bacterial infections. Vaccines against infectious agents have the potential to reduce antibiotic prescriptions and use, a key driver of AMR, through reducing the burden of infection in both humans and animals and reducing selection for AMR [5,6].

In contrast to antibiotics, where resistance evolves rapidly and is common, resistance to vaccines is rare owing to their mechanisms of action through the induction of pathogen-specific acquired humoral and cellular immunity [7,8]. However, vaccines are only available against a limited range of human bacterial pathogens and fewer veterinary pathogens. There is currently a limited body of scientific evidence to support the role of vaccines in reducing AMR, particularly in the veterinary field, and our understanding of the current and potential impact of vaccines on AMR is incomplete.

A notable example of recent evidence for the impact of vaccines on AMR comes from the introduction of the typhoid vaccine in Pakistan: in 2021, a typhoid conjugate vaccine was found to be 97% effective against extremely drug-resistant typhoid in Pakistan [9], providing direct evidence that vaccines reduce AMR. This is discussed further in the article by Qamar and colleagues in this issue [10].

3. Policy

The translation of this incomplete scientific evidence on vaccines and AMR into global policy has been challenging. In relation to the holistic problem of AMR, a United Nations (UN) General Assembly High-Level Meeting on AMR was convened in New York in 2016, which resulted in the 2016 UN Declaration on Antimicrobial Resistance, a political declaration adopted by 193 countries, committing to a global response to the threat of drug-resistant infections [11]. Although vaccines were mentioned in the report, the main thrust related to the development of surveillance and regulatory systems to monitor antibiotic sales and use, the development of new antibiotics and diagnostics and raising awareness among healthcare professionals and the public about preventing antimicrobial-reistant infections. A second UN High-level Meeting on AMR was held after this Science+ Meeting in New York in September 2024 [12], with the resulting declaration making several references to vaccines [13].

In recent years, vaccine-specific global policy documents have emerged. The World Health Organization (WHO) Action Framework 'Leveraging vaccines to reduce antibiotic use and prevent antimicrobial resistance' [14] highlighted the importance of expanding the use of licensed vaccines, developing new vaccines that contribute to preventing and controlling AMR and sharing knowledge of vaccine impact against AMR. This key document did not consider animal vaccines. However, in parallel, the role of livestock and fish vaccines in replacing antibiotics and reducing the development of AMR is being explored [15] and is the subject of the articles by Descamps [16] and by Yugeros-Marcos and Etienne [17] in this issue.

4. Rationale and aims

On 29th and 30th April 2024, the Royal Society convened a Science+ meeting in London, 'Vaccines and AMR: from science to policy' [18], which brought together scientists and vaccine developers from the human and animal vaccine communities to understand better how vaccines reduce AMR and help to develop a shared approach to tackling it. Acknowledging that the fields of human and veterinary vaccines usually operate independently, a key concept was that by bringing these together and sharing scientific knowledge of AMR and the role of vaccines in combatting it, common pathways for the development, licensure and use of vaccines to reduce AMR could be identified.

The meeting had two main aims, with the common goals of setting a combined agenda for the use of human and veterinary vaccines to counter AMR, since a joined-up One Health approach is vital for global impact, and informing and guiding the forthcoming second UN High-level Meeting on AMR, which was held in New York in September 2024. The first aim, addressed on Day 1, concerned the science of vaccines and AMR and related to better understanding the current challenges in developing vaccines against human and veterinary antimicrobial-reistant pathogens. The second aim—the focus of Day 2—related to the translation of our scientific understanding of how human and animal vaccines reduce AMR into policy to drive AMR vaccine development and introduction.

5. Participation

Since the problem of AMR is a global one, scientists from LMICs—the countries where the burden of AMR-related disease is greatest [3]—were actively engaged, with speakers and participants drawn from high-income countries and LMICs. BactiVac,

the Bacterial Vaccines Network [19], which partnered in organizing the meeting, provided travel bursaries to facilitate the attendance of early career researchers from LMICs. Solving a problem as enormous as AMR, and indeed the use of vaccines as AMR countermeasures, cannot be accomplished by a single group, so experts and stakeholders were convened from academia and industry, global policymakers, regulators and funders.

Scientific investigation of the problem of AMR and early vaccine development work are often undertaken in universities, requiring a multi-disciplinary approach, involving diverse groups including epidemiologists, microbiologists, immunologists and vaccinologists, who were all invited. However, academics alone cannot develop vaccines through to licensure, and the active involvement of representatives from industry and regulators is vital in relation to product development. Participants included representatives from vaccine manufacturers, both multinational companies and developing country manufacturers. The latter share a business model of high-volume manufacture at low profit margins, which has been key for the production of vaccines for LMICs. Regulatory considerations were addressed through the inclusion of regulators from both the human and veterinary vaccine fields.

Policymakers are key for driving global health human and veterinary vaccine agendas and for their implementation. The meeting was attended by representatives from the UK government, the WHO and World Organisation for Animal Health, the Strategic Advisory Group of Experts on Immunization (SAGE) and Gavi, the vaccines alliance, which acts with UNICEF to procure and distribute vaccines among LMICs. Financial support underpins the execution of research plans and vaccine development. Representatives of key funding agencies, including UKRI (UK Research and Innovation), Wellcome, the Gates Foundation, CARB-X (Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator) and EDCTP (European & Developing Countries Clinical Trials Partnership)/European Commission, were present. Finally, communication is critical to ensure public awareness of the global threat of AMR and the importance of vaccines in dealing with AMR. This is the subject of the article by Hausdorff in this issue [20], and vaccine advocates from both the human and animal health fields were engaged in its discussion.

6. The articles

This issue of the *Philosophical Transactions of the Royal Society B* comprises a series of articles from speakers at the Royal Society Science+ meeting detailing the presentations that they gave. In relation to the burden of AMR, the article by Impalli and colleagues [21] addresses the potential economic impact of a maternal vaccine against *Klebsiella pneumoniae*, a key AMR pathogen with a promising vaccine pipeline but currently no licensed vaccine. Cardinali and colleagues [22] review the current state and future prospects of the diverse array of technologies available for the development of vaccines against antimicrobial-resistant bacteria.

The recent story from Pakistan of typhoid conjugate vaccine and its impact on AMR, together with the more established evidence for pneumococcal conjugate vaccines in countering AMR, is described by Qamar and colleagues [10]. In her article, Anderson takes a broad view of the impact of existing bacterial and viral vaccines on the disease burden of AMR as well as the potential impact of new vaccines targeted against *Clostridium difficile*, Group B *Streptococcus* and *K. pneumoniae* [23]. The development and use of veterinary vaccines against AMR, with special emphasis on regulatory considerations, are discussed from the European point of view by Descamps and colleagues [16] and by Yugueros-Marcos and Etienne from the global perspective [17].

Hatchett and MacLennan [24] cover the 100 Days Mission for developing new vaccines against global pandemics in the aftermath of COVID-19 and they examine what learning can be applied to addressing AMR . Vaccine policy and the importance of AMR in prioritization of vaccine investments are discussed by Jadeja and colleagues in their article [25] from the perspective of Gavi, the Vaccine Alliance. Hausdorff [20] explains the importance of communicating the value of vaccines in combatting AMR while making a call for combination vaccines to facilitate vaccine introductions.

The final article by MacLennan and colleagues provides a summary of the full proceedings of the Science+ meeting across its 2 days [26]. The article outlines the main outcomes and recommendations of the meeting and provides a conclusion to this issue.

Ethics. This work did not require ethical approval from a human subject or animal welfare committee.

Data accessibility. This article has no additional data.

Declaration of AI use. We have not used AI-assisted technologies in creating this article.

Authors' contributions. C.A.M.: conceptualization, funding acquisition, project administration, supervision, writing—original draft, writing—review and editing; S.D.: conceptualization, funding acquisition, supervision, writing—review and editing.

Both authors gave final approval for publication and agreed to be held accountable for the work performed therein.

Conflict of interests. This theme issue was put together by the Guest Editor team under supervision from the journal's Editorial staff, following the Royal Society's ethical codes and best-practice guidelines. The Guest Editor team invited contributions and handled the review process. Individual Guest Editors were not involved in assessing papers where they had a personal, professional or financial conflict of interest with the authors or the research described. Independent reviewers assessed all papers. Invitation to contribute did not guarantee inclusion.

Subsequent to the Royal Society meeting taking place and prior to the publication of this article, C.A.M. became an employee of Pfizer UK.

The authors alone are responsible for the views expressed in this article and they do not necessarily represent the views, decisions or policies of the institutions with which they are affiliated.

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