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Vaccines and antimicrobial resistance: from science to policy—summary and outcomes

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In April 2024, the Royal Society convened a Science+ meeting in London on 'Vaccines and antimicrobial resistance: from science to policy'. The purpose

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was to review the science of how vaccines reduce antimicrobial resistance (AMR) and discuss policy in advancing development and equitable deployment of such vaccines. The meeting adopted a One Health approach with international speakers presenting from both human and veterinary perspectives. Presentations on Day 1 focused on scientific aspects of the AMR threat and the role of vaccines as counter measures. On Day 2, presentations covered associated policy implications based on this scientific understanding. A closing panel discussion looked towards the United Nations High-Level Meeting on AMR in New York in September 2024. This article is the closing contribution to an issue of *Philosophical Transactions of the Royal Society B* based on the meeting. It serves as a summary of the two days of proceedings, including key outcomes and recommendations, and provides an overall conclusion to the meeting.

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

1. Introduction

On 29 and 30 April 2024, the Royal Society held a Science+ meeting in London to discuss 'Vaccines and antimicrobial resistance: from science to policy' organized by Professor Calman MacLennan and Dame Sally Davies [1]. Global experts were assembled from academia and industry, together with economists, regulators, policy-makers and funders from high-income countries and low- and middle-income countries (LMICs) working in the fields of human and veterinary vaccines against bacterial pathogens of global antimicrobial resistance (AMR) concern.

Vaccines have increasingly been recognized as important tools to counter the global pandemic of AMR. However, the scientific evidence base for their effectiveness as countermeasures has been limited to date and often poorly articulated, particularly within the AMR community as a whole. Furthermore, translation of such scientific knowledge into policy at both the national and global level is slow, resulting in limited integration of vaccines into AMR strategies. Although the importance of using vaccines to address AMR is appreciated in both human and veterinary health, these two communities, for the most part, operate independently. It is critically important that the two work together, and this was a key element of the meeting.

The overall purpose of the meeting was to bring together key stakeholders in vaccines and AMR over two days to review the current scientific evidence concerning the relationship between vaccines and AMR, and discuss the translation of this evidence into policy. Day 1 addressed the scientific evidence of how vaccines are a key tool against AMR, acting both directly, by reducing antibiotic-sensitive and AMR infections, and indirectly, by reducing antibiotic use, which constitutes an enormous problem in the veterinary field where antibiotics are commonly used as growth enhancers among livestock. Day 2 focused on how this evidence can be used to drive policy, culminating in a discussion on recommendations for the United Nations High Level Meeting on AMR to be held in New York in September 2024. The full agenda for the meeting is shown in table 1.

For a full background to the meeting, please see the article by MacLennan & Davies in this issue of *Philosophical Transactions of the Royal Society B* [2].

2. Antimicrobial resistance and vaccines—the scientific evidence

Day 1 of the Royal Society Science+ meeting focused on scientific aspects of vaccines and AMR. The meeting was introduced by Calman MacLennan, Director of BactiVac, the Bacterial Vaccines Network [3], who emphasized the importance of translating our scientific understanding of the impact of vaccines on AMR into policy for the benefit of both human and animal health. MacLennan highlighted the relevance of this to the United Nations High-Level meeting on AMR in New York in September 2024.

3. Global burden of antimicrobial resistance

The first talks addressed the overall global burden of AMR, beginning with Ramanan Laxminarayan (One Health Trust) who highlighted the need for sustainable access to effective antibiotics and the role of vaccines in reducing the need for antibiotics and thereby lowering the burden of AMR. Annual global deaths from non-tuberculosis (TB) bacterial infections have been estimated at 7.7 million [4], with deaths associated with bacterial AMR at 4.95 million and those attributable to bacterial AMR at 1.27 million [5]. However, from a global perspective, lack of access to priority antibiotics causes more deaths than AMR itself [6].

Laxminarayan raised several areas of concern, including AMR complicating neonatal sepsis, which has been highlighted by several recent multi-country epidemiological studies [7–9]; the threat of AMR on the United Nation's Sustainable Development Goals [10]; and the increasing threat of AMR infections in animals, particularly in LMICs, a key component of the One Health theme of this meeting. He explained that while the development of new antibiotics, a priority of the Global North, is no longer economically viable in the absence of incentives, programmes to address AMR in the Global South are severely underfunded compared with other comparable global health threats [6].

Turning to the role of vaccines in tackling AMR, he showed results of a new modelling analysis which estimated that universal coverage with existing priority paediatric vaccines could prevent 181 500 AMR-associated deaths through direct prevention of resistant infections and reductions in antibiotic consumption [11]. In relation to introducing new vaccines, Laxminarayan highlighted RSV, TB and *Klebsiella pneumoniae* as priority targets where new or improved vaccines could have

Table 1. Agenda of the Royal Society Science+ meeting on 'Vaccines and antimicrobial resistance: from science to policy' held on 29 and 30 April 2024 in London. Talk and session titles are in bold.

DAY 1 Monday 29 April 2024—Science				DAY 2 Tuesday 30 April 2024—Policy			
SESSION 1		**SESSION 2**		**SESSION 3**		**SESSION 4**	
09.05	Ramanan Laxminarayan ***Burden of disease evidence for impact of AMR***	**13.30**	Richard Adegbola & Farah Qamar ***Pneumococcal & typhoid vaccine AMR impact***	**09.00**	Gordon Dougan ***Translating science on AMR & vaccines into policy***	**13.30**	David Kaslow & Rory Cooney ***The regulatory perspective on AMR vaccines***
09.30	discussion	**14.00**	discussion	**09.30**	discussion	**14.00**	discussion
09.45	Juan Pablo Uribe & Anthony McDonnell ***The economic burden of AMR***	**14.15**	Roberto La Ragione & Duncan Colquhoun ***Vaccine impact against AMR in the food chain/aquaculture***	**09.45**	Richard Hatchett ***Lessons from Covid / The 100 Days Mission & AMR***	**14.15**	Ed Buurman & Renee Larocque ***Supporting AMR vaccine R&D***
10.15	discussion	**14.45**	discussion	**10.15**	discussion	**14.45**	discussion
10.30	break	**15.00**	break	**10.30**	break	**15.00**	break
11.00	Katherine O'Brien ***Scientific evidence for how vaccines reduce AMR***	**15.30**	Annaliesa Anderson & Frédéric Descamps ***The manufacturers' perspective***	**11.00**	Javier Yugueros-Marcos ***Animal vaccines & AMR: an underutilised tool***	**15.30**	Bill Hausdorff ***AMR vaccines: communication and trust***
11.30	discussion	**16.00**	discussion	**11.30**	discussion	**16.00**	discussion
11.45	Rino Rappuoli ***Technologies for AMR vaccine development***	**16.15**	*Early-stage researchers* ***Science poster session***	**11.45**	Marta Tufet ***AMR vaccine implementation***	**16.15**	panel discussion/overview ***Setting course to the UN General Assembly on AMR Vaccines***
12.15	discussion			**12.15**	discussion		

great impact on AMR infections. His modelling estimates that a maternal vaccine against *K. pneumoniae* could prevent $6.9 billion costs from disability-adjusted life years (DALYs) each year in LMICs, work which is published in a separate article in this issue [12]. These findings demonstrate the economic burden that accompanies one global AMR pathogen and the potential savings which could result from the introduction of an effective vaccine.

Anthony McDonnell (Center for Global Development) expanded on the economic burden of AMR in the second talk, highlighting predicted economic costs from AMR for 2050 ranging from $2–4 trillion to $6.9 trillion [13]. However, these figures are outdated and there is a lack of recent and detailed studies on which to base revised economic estimates, particularly at the country level and in relation to impact on farming productivity. (Note that, since the Royal Society Science+ meeting, a comprehensive analysis of the economic burden of AMR has been published [14].)

McDonnell outlined modelling efforts currently underway to update economic estimates on the burden of AMR, including health system costs modelling and economic resilience modelling which could predict the cost of each AMR infection by country and help project costs into the future. He described work on a macroeconomic model which would estimate the costs and benefits of different interventions to stop AMR, including vaccines [15].

Juan Pablo Uribe (World Bank) continued the theme of AMR economic burden from the perspective of the World Bank, emphasizing the importance of addressing AMR to achieve its vision of a world free of poverty in a liveable planet. Referring back to World Bank estimates from 2017, he explained that AMR left unchecked could cost the global economy 3.8% of global gross domestic product (GDP) by 2050 and push an additional 28 million people, mostly in LMICs, into poverty by 2030 [13].

Looking forward, he explained the role of the World Bank in responding to this 'terrifying and expensive' challenge through financing and policy, knowledge and advocacy, and stewardship. He explained the importance of multisectoral working to overcome the challenges of AMR through 20 intervention areas across the health, water, agriculture, food and environment sectors. The need for a long-term sustainable effort was emphasized.

4. Evidence for the impact of vaccines on antimicrobial resistance

The meeting then moved on to examine the evidence for how vaccines reduce AMR with Katherine O'Brien (WHO) explaining that this is through prevention of infections, preventing individuals and communities from becoming ill, decreasing antibiotic use and supressing the evolution of AMR. However, O'Brien acknowledged that despite their potential, the impact of vaccines on AMR has been consistently underestimated and underutilized. She outlined the focus of the WHO in this area with its policy document, 'Leveraging vaccines to reduce antibiotic use and prevent AMR: an action framework' which covers expanding the use of licensed vaccines against AMR, developing new vaccines to address AMR and expanding and sharing knowledge on the impact of vaccines against AMR [16].

O'Brien highlighted the importance of evaluating the role of vaccines in reducing AMR at all stages of vaccine development, approval and introduction, and discussed evaluation of vaccine impact on AMR through averted health burden, change in AMR prevalence, averted antimicrobial use and reduction in AMR-related economic burden [17]. Examples from the field were given. Highly resistant outbreaks of cholera and typhoid in Zimbabwe between 2017 and 2019 were controlled through campaign administration of typhoid and cholera vaccines [18]. A multi-country clinical trial of a maternal RSV vaccine found a reduction in antimicrobial prescriptions of 12.9% for any diagnosis and 16.9% for acute lower respiratory tract infections in infants born to vaccinated mothers [19].

In an ecological observational study, the introduction of universal free seasonal influenza vaccination in Ontario, Canada, in 2000 reduced respiratory antibiotic prescriptions by 64% [20] and reduced secondary bacterial infections, including pneumonia and otitis media. Through an analysis of demographic health surveys combined with mathematical modelling, pneumococcal conjugate vaccine and rotavirus vaccine introductions had prevented an estimated 23.8 and 13.7 million antibiotic-treated illnesses annually, with potential for the prevention of an additional 21.7 and 18.3 million antibiotic-treated illnesses if 90% global coverage with these vaccines was attained [21].

The need for further research to strengthen the evidence base for vaccines impacting AMR, particularly through the collection of data on antibiotic use in vaccine trials, was emphasized, together with the importance of studying the impact of vaccination included in national action plans (NAPs) against AMR. However, although a review of NAPs indicated that 87% mention vaccines, only a minority (43%) have implemented indicators to capture the impact of vaccination [22], preventing translation of measurable impact into action and failing to integrate vaccines with other AMR interventions.

Priority new and improved vaccines to counter the AMR pandemic were highlighted including vaccines against *Mycobacterium tuberculosis* (TB), *Streptococcus pneumoniae*, *K. pneumoniae*, *Escherichia coli* and *Staphylococcus aureus*, which would together have the potential to avert over 50 000 deaths a year [17]. Improved TB vaccines and a group A *Streptococcus* vaccine could respectively reduce antimicrobial use by 1200-1900 million and 72 million defined daily doses annually [17]. The article by Anderson in this issue provides a summary of the evidence for vaccine impact on AMR [23].

5. Vaccine technologies

Rino Rappuoli (Fondazione Biotecnopolo di Siena) reviewed the current technologies available for AMR vaccine development which are covered in detail in his article [24]. He opened his talk by stating that, unlike antibiotics, vaccines are 'evolution proof', with resistance to them rarely developing, but emphasized that optimal deployment of both vaccines and antibiotics is key for controlling AMR, with potential for monoclonal antibodies against AMR bacteria in both preventative and therapeutic roles.

In relation to vaccine development, Rappuoli explained that bacteria are complex organisms and this complexity can hamper development efforts. However, over the last 40 years, several innovative technologies have allowed the development and licensure of previously 'impossible' vaccines against AMR bacteria. He reviewed the range of vaccine technologies from traditional whole cell approaches to more recent subunit options including glycoconjugates, protein-based vaccines, nanoparticles, use of novel adjuvants, and, more recently, mRNA-based candidate bacterial vaccines, with examples against Lyme disease and TB that have reached the clinic.

Rappuoli covered the use of reverse vaccinology for antigen discovery which was one way used to develop meningococcal group B vaccines [25]. He outlined his laboratory's current approach to antigen discovery, termed 'reverse vaccinology 2.0', which involves isolating peripheral blood mononuclear cells from donors convalescing from a specific infection, using these cells to produce monoclonal antibodies and then identifying the target antigens of the most broadly cross-reactive antibodies.

Addressing the need for a vaccine against gonorrhoea, which is now associated with very high levels of AMR, he explained how an outer membrane vesicle (OMV)-based vaccine developed against group B meningococcus was found to protect against gonorrhoea. With effectiveness of 31% [26], this example indicates the potential for vaccine cross-protection against different bacterial species. Linking back to earlier talks, he described current efforts to develop a vaccine against *K. pneumoniae*, another highly antibiotic-resistant bacterial pathogen, where development is focusing on the polysaccharide capsule and O-antigen of lipopolysaccharide as key antigenic targets.

6. Success stories of vaccines against antimicrobial resistance

Farah Qamar (Aga Khan University) and Richard Adegbola (Nigerian Institute of Medical Research) followed with examples of success in deploying vaccines against AMR bacteria in LMIC settings. Qamar described the problem of typhoid in Pakistan where, following years of increasing resistance, extensively drug-resistant (XDR) *Salmonella* Typhi emerged resulting in outbreaks which could not be controlled by third-generation cephalosporins.

These outbreaks coincided with the first approval by WHO in 2018 of a typhoid conjugate vaccine (TCV). Pakistan became the first country to use TCVs in an outbreak response campaign in Hyderabad in 2018. This resulted in a 45% reduction in suspected typhoid cases, with 95% vaccine effectiveness against culture-confirmed *S*. Typhi and 97% effectiveness against culture-confirmed XDR *S*. Typhi [27]. TCVs were also used in an outbreak response campaign in Karachi. In November 2019, Pakistan became the first country to introduce TCVs into its national immunization programme. Following the success in Pakistan, TCVs have been introduced in 10 other countries but ongoing surveillance is key to monitoring impact on AMR. The full story is reported by Qamar [28].

Adegbola described the impact of pneumococcal conjugate vaccines on AMR and *S. pneumoniae* (pneumococcus) which is a leading cause of invasive disease globally with 30–40% of invasive pneumococcal disease caused by AMR strains. Pneumococcal conjugate vaccines have resulted in the reduction of pneumococcal infections caused by both sensitive and AMR strains of pneumococcus in countries where they have been introduced, such as South Africa [29]. These vaccines also reduce nasopharyngeal carriage of pneumococci and can impact pneumococcal AMR by curtailing the carriage of resistant serotypes [30].

However, despite their effectiveness, uptake of pneumococcal conjugate vaccines has been poor in some settings. Another challenge is serotype replacement when disease due to pneumococcal serotypes not present in pneumococcal conjugate vaccines becomes more prevalent. As mentioned by O'Brien, expanded use of pneumococcal conjugate vaccines could have an enormous impact on reversing AMR through reduced pneumococcal infections and carriage, and reduced antibiotic prescriptions and use. Further details are reported separately in this issue [28].

7. Use of vaccines in reducing antibiotic use and antibiotic resistance in livestock, poultry and aquaculture

With the One Health emphasis of the meeting, Roberto La Ragione (University of Surrey) and Duncan Colquhoun (Norwegian Veterinary Institute) addressed the issue of vaccines and AMR in animals, with La Ragione focusing on livestock and poultry vaccines and Colquhoun addressing vaccine use in aquaculture. La Ragione explained the observed inverse relationship between livestock and poultry vaccine sales, and antibiotic sales, alongside responsible use of antimicrobials in animals [31]. He explained that vaccines are essential for improving animal health, welfare and productivity, while also safeguarding human health and global economies.

However, although there are some highly efficacious vaccines available for priority pathogens, challenges are present in relation to uptake due to cost, delivery, licensing, efficacy and short available time windows for delivery. Further research on the impact of animal vaccines on AMR, together with funding for animal vaccine development were highlighted as gaps in the field [32].

Aquaculture is the fastest growing food-producing sector in the world and Norway is the leading producer of farmed Atlantic salmon worldwide, with over 1.5 million tons produced in 2022 [33]. However, in the 1980s/early 1990s, serious bacterial infections caused significant losses resulting in the use of large quantities of antibiotics, peaking at almost 50 tonnes of antibiotics in the production of less than 100 000 tonnes of farmed salmon in 1987. AMR to several antibiotic classes rapidly emerged.

Colquhoun described the huge success story of vaccination in addressing AMR in the Norwegian salmon farming industry where 100% vaccine coverage has been achieved. Vaccines against the major bacterial diseases were first introduced in 1985

resulting in an increase in salmon production, with further increases in production and large reductions in use of antibiotics when oil-adjuvanted vaccines were introduced in 1993. Only 425 kg of antibiotics were used in the whole of Norwegian aquaculture in 2022 [34]. AMR surveillance is conducted routinely but is now only occasionally detected in Norway among bacteria which are pathogenic to fish [35].

8. Advances in antimicrobial resistance-associated vaccine development

Vaccines against AMR can only be implemented if they have been developed, manufactured, licensed and are available for use. Annaliesa Anderson (Pfizer) discussed vaccine development from a manufacturer perspective, highlighting that both viral [36] and bacterial vaccines [37] contribute to reducing AMR at the population level, and explained that developing a new vaccine takes around 10 years through to introduction.

Anderson outlined the need for and development of a vaccine against *Clostridioides difficile*, a bacterium responsible for a large burden of diarrhoea cases and linked to the use of antibiotics which kill protective gut bacterial flora. In a phase 3 trial, although a toxoid vaccine did not meet its primary endpoint, it was 100% efficacious against medically attended *C. difficile* infection. Another bacterial AMR pathogen with no current licensed vaccine is group B *Streptococcus* which causes invasive disease in infants, particularly in LMICs. A 6-valent polysaccharide conjugate vaccine against group B *Streptococcus* is under development for maternal immunization to protect neonates through the passive transfer of antibodies across the placenta. The identification of an immunological correlate of protection against Group B *Streptococcus* has good potential to facilitate licensure. Further details are provided in Anderson's article [23].

Frédéric Descamps (Zoetis) covered the manufacturers' perspective on animal vaccines. Use of antimicrobials in food-producing animals has significantly decreased in the European Union in the recent past in response to pressure, implementation measures and incentives [38]. However, it is widely recognized and reported that specific veterinary vaccines may contribute to reducing antimicrobial use and indirectly reduce the risk of antimicrobial gene selection and/or AMR development [39]. Descamps explained that increasingly food-producing animal vaccines are live vaccines, and that vaccine development in this sector needs to be encouraged because vaccines are still not available for many veterinary infectious diseases. He reviewed the current status of veterinary vaccines, covering opportunities as well as technical and regulatory challenges, and expands on this theme in his article in this issue [40].

9. Translating to policy

On Day 2, the presentations and discussion moved from science to policy implications. This theme was introduced by Gordon Dougan (University of Cambridge) who addressed translating scientific understanding of AMR and vaccines into policy. He used specific examples to illustrate how a combination of epidemiological information and vaccine development can be used to tackle AMR in a direct and indirect way and explained how this science is translated into action and policy.

Tackling AMR at a policy level requires a multi-faceted approach which integrates prevention measures, accurate pathogen identification and proper treatment. Dougan gave examples of policy decisions to implement vaccines against AMR, citing the first introduction of typhoid conjugate vaccine to address XDR typhoid in Pakistan, linking back to Qamar's presentation on Day 1 and her article in this issue [28]. Concluding this introduction to policy implications, he emphasised the importance of combining action and policy to tackle the spread of AMR pathogens across the globe.

10. The 100 Days Mission

Richard Hatchett (Coalition for Epidemic Preparedness Innovations; CEPI) provided insights into how to engage, inform and advance policy on AMR vaccines, using lessons from the COVID-19 pandemic and the example of the CEPI 100 Days Mission. The 100 Days Mission has been created to enable the development of vaccines and other medical countermeasures within 100 days of a new pandemic threat being recognized. Tackling new pandemics will require sustained, focused international collaboration at all levels, from community health workers, to health and social policy-makers, and innovative scientists. Hatchett shared concepts from the 100 Days Mission that could be relevant to the global battle against AMR.

The importance of non-pharmaceutical interventions was highlighted together with the use of statistical models based on epidemiological data to track transmission routes of microbial pathogens, stop transmission networks associated with epidemics, and reduce the number of disease cases and mortality rates. Hatchett also emphasized the need for speed in vaccine development and deployment, which, in the COVID-19 pandemic, could have saved millions more lives, prevented trillions of dollars of economic damage, and limited or possibly prevented the emergence of the challenging SARS-CoV-2 variants circulating today.

The establishment of a vaccine library against priority viral families, manufacture of working seed material and development of exemplar vaccine candidates are being undertaken in order to accelerate future pandemic responses. The application of these steps to the development of vaccines against AMR pathogens was discussed and further details are in Hatchett's article [41].

11. Animal vaccines as an underutilized tool against antimicrobial resistance

Returning to animal health, Javier Yugueros-Marcos (World Organization for Animal Health; WOAH) discussed, from a policy perspective, animal vaccines as an underutilized tool against AMR. In a world with competing priorities and scarce public

resources, he argued the importance of identifying those areas of greatest impact first, alongside fostering synergies to mobilize private investments into vaccine development and implementation.

WOAH has produced a series of documents prioritizing diseases for which vaccines could reduce antimicrobial use in animals, providing information regarding the opportunities, challenges, needs, new approaches and potential solutions for the development of such vaccines [39,42]. Yugueros-Marcos gave an overall view of priorities, focusing on the high priority areas for investment to optimize the use of antimicrobials and the setting up of complementary initiatives, including vaccines, to curb AMR. He explained how WOAH performs surveillance of antimicrobial use among livestock across the globe through ANIMUSE, a global database on ANImal antiMicrobial USE [43,44].

Results from this surveillance demonstrate a reduction of around 35% in antimicrobial use among animals over the years, after the implementation of strategic actions. However, antibiotics are still used as animal growth promoters by a concerning number of countries. Yugueros-Marcos covered the importance of vaccines to reduce antimicrobial use, exemplified by the livestock vaccines developed against theileriosis and brucellosis [45,46]. These vaccines have reduced mortality rates among bovines, confer protection against these diseases and reduce the costs associated with animal health. Nevertheless, replacing antibiotic use with vaccines is not straightforward and there are challenges, but, from a policy perspective, when shown to be cost-effective for the farmers and governments such a move has great potential to reduce AMR.

Yugueros-Marcos finished by presenting 'Accelerating action against AMR: closing the gaps in the animal health sector', a WOAH report to inform stakeholders involved in discussions for the United Nations High-Level Meeting on AMR [47]. The document outlines WOAH perspectives on current gaps in addressing AMR, highlighting four priority issues for an international dialogue on animal health: cross-sectoral coordination, resourced surveillance systems, prevention and sustainable financing. Yugueros-Marcos and Floriane Etienne expand on the theme of animal vaccines as an underutilized tool against AMR in their article [48].

12. Vaccine implementation

Marta Tufet (Gavi) covered how to leverage vaccine policy and investment to address the AMR challenge. She described Gavi's worldwide activities to foster and support the implementation of vaccines against infectious diseases which are recognized as the major threats to global public health. Immunization equity is key to the mission of Gavi [49].

Since 2000, Gavi has offered support for routine immunization in 78 lower-income countries. This support is through three key financing levers: health system strengthening, procurement of vaccines and technical assistance. To ensure equitable access to vaccines, the Gavi model includes long-term funding, pooling demand from the lowest-income countries, accelerating access to vaccines, shaping markets for affordable vaccines, strengthening vaccine delivery platforms, and sustaining immunization and transition.

Tufet highlighted the importance of vaccines in reducing AMR. Increased pneumococcal conjugate vaccine (PCV) coverage in Ethiopia through Gavi support averted an estimated 718 000 treatment failures, and reduced AMR-associated deaths by 28% between 2011 and 2017. Over its lifetime, the number of vaccines available for support has increased and so Gavi created the Vaccine Investment Strategy (VIS) to determine which vaccines should be included in its funding portfolio.

The VIS takes an evidence-based approach to determine immunization investments. Vaccines are selected through an extensive analytical process which results in an evaluation framework that considers various ranking criteria, such as health impact, which includes the impact of vaccines on AMR, value for money, equity and social protection, economic impact and antibiotic use prevented. Gavi is committed to addressing global AMR because it views vaccines as cost-effective ways to prevent mortality and morbidity from AMR. Further details are included in the article by Tufet [50].

13. Regulatory considerations

Regulatory perspectives on vaccines and AMR were provided by David Kaslow (US Food and Drug Administration, FDA) for human vaccines and Rory Cooney (Veterinary Medicines Directorate, VMD) for veterinary vaccines. Kaslow explained that well-defined regulatory pathways exist at the FDA for vaccines with indications to prevent diseases caused by infectious agents. Postmarketing studies are carried out to confirm the benefits and monitor for safety signals of approved products. He elaborated on criteria for approval and explained the strategic importance of evidence for potential impact on AMR in defining the regulatory pathway, including considerations for accelerated approval of vaccines.

Cooney provided the regulatory position on AMR from a UK veterinary medicines perspective, explaining how the VMD adopts a One Health policy approach to tackling AMR within a 20 year vision and a 5 year National Action Plan. He explained that antibiotic sales for animals in the UK had fallen by 59% in 2022 compared with 2014, with a reduction of 74% for pigs alone. One of the biggest challenges to reducing antibiotic use in animals is changing behaviour. With regards to vaccine strategies for curbing AMR in animals, VMD supports the authorization of animal vaccines, alongside innovation, novel therapies and technologies as alternatives to antimicrobials.

14. Funding vaccine development

Ed Buurman (CARB-X) explained that the priority of CARB-X (Combating Antimicrobial-Resistant Bacteria Biopharmaceutical Accelerator) [51] vaccine funding is the development of vaccines targeted against pathogens with high morbidity and mortality

rates associated with AMR. CARB-X had funded 101 projects at a combined cost of $459 million since its inception, of which $83 million has been for preventive interventions. He explained that vaccines are a key component of the funding portfolio at CARB-X, including maternal vaccines targeting neonatal sepsis. The first CARB-X-funded vaccine against invasive non-typhoidal *Salmonella* (iNTS) and typhoid fever is in clinical development.

The CARB-X funding model is non-dilutive (i.e. does not require giving up any equity or ownership) and follows a Stewardship and Access Plan so that products can reach those who need them most. He explained the need for products funded by CARB-X to be relevant to LMICs where the burden of AMR is greatest. Buurman also outlined other strategies at CARB-X to drive vaccine development. These include, for example, a business development council that helps companies secure funding for advanced vaccine development beyond phase 1 clinical trials and whole genome sequence databases of relevant pathogens to ensure presence and conservation of selected antigens.

Renée Larocque (International Development Research Center, IDRC), speaking on innovation in veterinary vaccine development for the prevention of AMR, discussed the challenges of developing animal vaccines, explaining that AMR is an evolving threat and climate change means that burden of disease is unpredictable. Among the challenges for livestock vaccines against neglected tropical diseases, she described the high risk of failure. To overcome these challenges, Larocque suggested reducing the time from antigen discovery to scientific proof of concept, through moving into target species faster and offering research support in product development to research teams. She outlined the characteristics of an ideal vaccine for LMICs, explaining, among other things, that it should be cost-effective and thermostable.

15. Communication

The importance of communication and trust in advocating for vaccines against AMR was covered by William Hausdorff (PATH). Effective communication of the value of vaccines as tools to combat AMR presupposes that we have carefully determined their true value, but unfortunately there is lack of consensus about this, even within the medical community. Vaccines have been ignored in many review articles and editorials about AMR, both in the popular press and the scientific literature, in favour of discussions of potential new antibiotics, bacteriophages and better antimicrobial stewardship, implying that the impact of vaccines on AMR is marginal.

However, vaccines are equally effective against resistant and sensitive pathogens, as demonstrated by the use of typhoid conjugate vaccine to address XDR typhoid in Pakistan, covered earlier in the talk by Qamar. Hausdorff emphasized the need for continued accrual of similar data, coupled with the knowledge that technologies, as outline by Rappuoli, are being employed to develop vaccines against a range of AMR bacteria, in order to inform and change the views of policy-makers. To underline the importance of communication, Hausdorff demonstrated how a simple experiment on *Shigella* vaccine acceptability in LMICs resulted in greater acceptance when the ability of the vaccine to prevent AMR and stunting was communicated. This indicated awareness of AMR and willingness to prioritize vaccines once there is clarity that vaccines help to reduce AMR [52].

Hausdorff cautioned that vaccines directed against single pathogens only prevent the AMR and antimicrobial use associated with that pathogen, and many national immunization schedules are already crowded. He therefore advocated for combination vaccines, arguing that the potential value of vaccines against AMR will only be achieved if multiple vaccines, identified as public health priorities, can be delivered within a minimal number of separate administrations. The importance of clear and focused communication on the benefit of vaccines against AMR that addresses policy-makers' specific information needs and concerns is further discussed in Hausdorff's article in this issue [53].

16. Setting course on the UN General Assembly on antimicrobial resistance vaccines

The meeting concluded with a panel discussion chaired by Dame Sally Davies on knowledge gaps and research priorities for AMR vaccines to inform the United Nations High-Level Meeting on Antimicrobial Resistance. Davies started by asking panel members their expectations for the high-level meeting. Rakan Khalid Bin Dohaish (Ministry of Health, Saudi Arabia) expressed his desire for continued discussions and commitments by member countries and the establishment of an independent scientific panel on how to best implement vaccine strategies. He raised the need for access and affordability, including stewardship, data generation and capacity building.

Yugeros-Marcos would like movement to go beyond what was agreed at the last United Nations High-Level Meeting on AMR, held in 2016, and emphasized the need for interventions that adopted a One Health approach. Peter Borriello (Food Standards Agency, UK) also wanted to see vaccines from a One Health context that are pre-authorized with commitment to assess quality post-authorization, including surveillance to ensure these vaccines are effective. At a policy level, he wanted an easier way to demonstrate confidence in vaccines. Tufet supported innovation in vaccine delivery, including microarray patches and determination of optimal combinations of vaccines.

Dohaish emphasized the need for improved financing and advocacy processes and greater clarity for people who allocate finances, as there is often a lack of understanding of what is happening in science. Kaslow mentioned the need to impress how vaccines not only reduce infection and AMR but how they impact other United Nations sustainable development goals (SDGs), in order to give a higher-level view of the impact of vaccines. Davies pointed out that ReACT, a global network dedicated to the problem of AMR, had undertaken work on the SDGs in relation to AMR [54]. Yugeros-Marcos explained the need to speak the same language as diplomats, explaining that countries had developed NAPs and might need guidance on prioritizing AMR, re-emphasizing the importance of good communication in advocating for vaccines as countermeasures for AMR.

Subsequent to this Science+ Meeting, the second UN High-level Meeting on AMR took place in New York in September 2024 [55], with the resulting declaration making several references to vaccines [56].

17. Conclusion

On 29 and 30 April 2024, 250 people attended the two-day Royal Society Science+ meeting on 'Vaccines and antimicrobial resistance: from science to policy' with a further 450 joining online [1,3]. The burden of the AMR pandemic was clearly articulated from both burden of disease and economic perspectives, as were the consequences of failing to take appropriate countermeasures against AMR. From the talks and discussion, the importance of vaccines in addressing AMR was appreciated by those present at the meeting. However, among the broader global community, it is apparent that the role for vaccines in preventing AMR is underestimated. Of concern, such lack of understanding often extends to healthcare professionals and policy-makers resulting in underutilization of available vaccines and lack of demand for the development of new vaccines, and highlighting the need for effective communication concerning vaccines and AMR.

There is a growing body of evidence that vaccines reduce AMR both in relation to reducing infections by AMR bacteria and reducing antibiotic use. In human health, such evidence has accumulated over many years with the widespread introduction of pneumococcal conjugate vaccines and more recently with TCV. Similarly, evidence has emerged for impact on antibiotic use with the introduction of viral vaccines against influenza, rotavirus and RSV. Although discussion at the meeting was restricted to bacterial and viral vaccines, newly licensed malaria vaccines present an opportunity to counteract increasing drug-resistance of the malaria parasite, *Plasmodium falciparum*.

The impact of vaccines on reducing AMR is also apparent in animal health, for example against AMR among *Salmonella* in the poultry industry. In aquaculture, the use of bacterial vaccines in the Norwegian salmon industry provides a compelling exemplar of the huge impact vaccines can have in reducing antibiotic use and AMR while increasing salmon production. Nevertheless, further evidence is required in order to continue to build a convincing and compelling case for the prioritization of investment in vaccine development and use, and the inclusion of clear vaccine strategies within national action plans on AMR. Such evidence comes from clinical trials demonstrating vaccine efficacy, and post vaccine introduction studies demonstrating effectiveness on the prevalence of AMR, and the use and consumption of antibiotics.

New technologies now exist to enable the development of vaccines against key AMR bacteria for which vaccine development has been challenging in the past and against which no licensed vaccines are currently available. Important examples of such pathogens with vaccine candidates currently in clinical development include *K. pneumoniae*, group B *Streptococcus*, *C. difficile* and *Neisseria gonorrhoeae*. However, there are many remaining bacterial pathogens relevant to human and animal health that lack vaccines. Unlike antibiotics, vaccines are usually pathogen-specific. Both observations highlight the need for a coordinated approach to tackling AMR in which vaccines play an important role alongside other interventions including the development of new antimicrobials, use of diagnostics and implementation of water, sanitation and hygiene improvements.

In relation to policy, initiatives by WHO, such as its three-point action plan to introduce, develop and inform about vaccines and AMR, will help focus global attention on the role of vaccines in addressing AMR. WOAH provides a parallel voice for vaccines against AMR in the context of animal health. In multiple respects, the meeting served to highlight converging approaches within human and animal health to vaccines and AMR. Such a holistic One Health approach will be important for maximizing the global impact of vaccines in relation to health and economics, as well as helping to address many of the United Nations SDGs.

The importance of equity in the development and deployment of vaccines against AMR was highlighted by the acknowledgement that the major burden of AMR falls on LMICs. Engagement and collaboration between the Global North and South will be critical as we journey forward so that no country is left behind. This has been particularly important in the implementation of available vaccines to curb AMR. Gavi support has been critical here, though funding constraints will potentially limit the opportunity to make vaccines available for those that need them most in the control of AMR. Indeed, limited funding and budget cuts are issues which negatively impact all aspects of vaccine development and deployment, within academia, policy-making bodies, such as WHO, funding bodies themselves and even pharmaceutical companies.

In summary, progress is being made at both the scientific and policy level regarding vaccines and AMR. However, much more effort and support are required for the development of new vaccines that are currently not available, for the introduction of existing vaccines that have been proven to reduce AMR infections in humans and animals, and for ongoing measurement of the impact of these vaccines on AMR. Clear advocacy and communication are needed to help drive the necessary collaboration, financial commitment and sustained effort nationally and internationally to maximize the potential of vaccines as countermeasures to AMR.

18. Key outcomes

A summary of the high-level outcomes of the meeting is provided in Box 1. These include an appreciation of the enormous health and economic burdens from AMR, particularly in LMICs, and the importance of vaccines in addressing and reducing the AMR burden from both a human and animal health perspective. A limited number of vaccines are currently available for key

Box 1. Key outcomes.

- AMR is a One Health problem with devastating health and economic consequences, particularly in LMICs
- The importance of vaccines in addressing AMR is underappreciated
- Vaccines are an effective tool against AMR, both in humans and animals, but more evidence is needed
- Limited vaccines are available against the bacterial pathogens which are responsible for *1.27 million AMR deaths/year*
- There is limited funding to develop new vaccines, despite an estimated economic cost of *US$3–7 trillion/year by 2050* from AMR
- The vaccine community must effectively communicate the role that vaccines play in reducing AMR
- The AMR community must integrate vaccines into AMR strategies, and actively implement them

AMR pathogens. Funding for the development of new vaccines and full implementation of existing vaccines is lacking despite the cost of failing to address AMR properly. Effective communication is required to tackle the lack of investment in vaccines against AMR and vaccines needs to be incorporated into global AMR strategies.

19. Recommendations

Box 2 contains the key recommendations from the meeting. These highlight the importance of a coordinated One Health approach across human and animal health in order to maximize the global impact of vaccines against AMR. Such coordination will require a strengthening of partnership and collaboration across both sectors. Ongoing evidence generation for the impact of vaccines on AMR is needed to gain momentum around the importance of vaccines and provide reliable data to support effective and persuasive communication on the subject. As this is critically underfunded and the burden is greatest amongst populations with the least resources, increasing advocacy is required in order to gain traction and financial support for vaccines against AMR and ensure global equity. Such advocacy and clear messaging need to reach healthcare professionals, policy-makers, funders and governments alike.

Box 2. Recommendations.

- There is a critical need for a coordinated, multidisciplinary One Health global approach to addressing the AMR crisis
- Human and veterinary vaccine fields have a pivotal role to play and must work together in order to achieve this
- The evidence that vaccines reduce AMR needs to be continually strengthened by scientific studies
- Advocacy is required for funding to drive vaccine development and implementation, particularly in LMICs
- Clear messaging is essential to articulate the importance of vaccines in combatting AMR to stakeholders and policy-makers globally

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