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Reflecting on the final report of the O'Neill Review on Antimicrobial Resistance.

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Reflecting on the final report of the O'Neill Review on Antimicrobial Resistance

To resolve the crisis of antimicrobial resistant infections and dearth of new treatments, the Review on Antimicrobial Resistance makes ten wide-ranging recommendations in their final report.¹ Implementation of the recommendations is to be achieved by increasing awareness, tackling supply of new treatments, preventing infections, using current treatments better, and reducing antibiotic use in agriculture and pollution of the environment. By 2050, they estimate the societal and financial cost of not tackling the crisis will be US\$100 trillion. The Review reveals that, at roughly \$30 billion, implementing all proposed recommendations is far cheaper than allowing the crisis to worsen until many infections are untreatable.

The disciplines of microbiology and infectious diseases, and antimicrobial discovery, **research and development** have suffered from many years of underinvestment by the public and private sectors. Consequently, there is a lack of reward for these scientists and physicians; this is reflected by lower measures of esteem and salaries compared with other disciplines and so a shortage of expertise. The Review indicates that the crisis of antimicrobial resistance will not be tackled effectively without increasing the numbers of health-care professionals with specialist knowledge to provide leadership on the use of antimicrobials in people, and scientists to discover and research new treatments to feed into the commercial sector for development.

A global public awareness campaign is recommended. This will inform everybody, irrespective of demographic group, of globally consistent core messages to reduce patient demand and antimicrobial use in animals. As it takes a long time to discover, research, develop, and manufacture new drugs, the Review recommends making better use of existing treatments. This is an approach taken by the British Society for Antimicrobial Chemotherapy (BSAC) Antibiotic Action initiative,² which has networked with like-minded groups (eg, ReAct, CDDEP, APUA, and WAAAR). Recently, BSAC, in collaboration with the University of Dundee and FutureLearn, launched a so-called Massive Open Online Course on antimicrobial stewardship for health-care professionals across the world.³

Prevention of infection is far better than cure; especially as new antimicrobials to treat all drug-resistant infections could be decades away. A major factor in the development and spread of antimicrobial resistance is that globally many people live in unhygienic conditions without access to clean water. The Review recognised that good sanitation is crucial to preventing the spread of infection. They recommend monitoring the levels of antimicrobial-resistant microbes and that infection prevention and control is embedded globally in all health-care and agricultural systems. Furthermore, consumption of antimicrobials should be measured in people and animals. Antibiotics are also frequently released into the environment, including into rivers near manufacturers' production facilities. Therefore, introduction of a target for the maximum amount of antimicrobials allowable in wastewater is recommended and that this is monitored via a regulatory framework.

To further prevent infection and reduce antimicrobial use, the Review recommends increased use of existing vaccines in people and in animals particularly in low-income countries and research to develop, manufacture, and provide new ones. Other ways to treat or prevent infections including alternative treatments such as phage therapy or repurposing of other therapeutics warrant close scrutiny and research.⁴

New antimicrobials will still be needed because this is a form of medicine acceptable to patients and health-care professionals. However, compounds that were readily druggable have already been made into medications. Finding inhibitors of drug-resistant pathogens, particularly Gram-negative bacteria and *Mycobacterium tuberculosis*, is technically difficult and it is hard to translate inhibitors from the laboratory into a new treatment. Since 2000, most new discoveries and much preclinical research has been done in academia or Small Medium Enterprises but the lack of return of investment is a barrier to Big Pharma developing some of these inhibitors. Therefore, working in collaboration with the IMI-funded project DRIVE-AB, the Review has suggested that the market be stimulated to develop and sell new antimicrobials by providing a reward system to those producing new treatments that will be of huge benefit to society even if they are not used. They also suggest the parallel development of new diagnostic tests to quickly and accurately diagnose infections at the time of treatment.

There has been a dearth of funding for antimicrobial-resistance research including for new treatments^{5,6} and public funding agencies did not fill the void when pharmaceutical companies started merging and divesting themselves of this area of activity. Therefore, the Review recommends that a Global Innovation Fund for antimicrobial resistance should be established to pay for early stage research; the UK Prime Minister and the President of China have already indicated their intention to jointly contribute £100 million. Most antimicrobial-resistance researchers are in high-income countries and the continual depletion of expertise will need to be stemmed so that they can share their expertise and provide training to individuals in low-income and medium-income countries.

The Review observed that when there are perceived global infection crises—eg, Ebola virus disease—governments and public funding agencies quickly respond and provide billions of dollars (including for research). The antimicrobial-resistance crisis has arisen stealthily; therefore, increased funding has not been seen as necessary. However, the findings of the Review team make it eminently clear that globally the antimicrobial-resistance crisis overshadows recent threats by many orders of magnitude.

The ability of the Review to interact and influence the World Health Assembly, the G20, and the United Nations to act on their recommendations cannot be underestimated. If all the recommendations are fully implemented and antimicrobial resistance is overcome, this will be one of the most significant achievements of the 21st century, will save countless weeks and months of lost productivity, and will avert unnecessary deaths due to difficult and untreatable infections.

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No conflicts to declare.

LJVP is the BSAC Chair in Public Engagement and Director of the Antibiotic Action initiative. She was an advisor to the AMR Review.

- 1 The Review on Antimicrobial Resistance. [Title]. <http://amr-review.org/Publications> [Ed to update to full reference]
- 2 Piddock, LJV. The crisis of no new antibiotics—what is the way forward? *Lancet Infect Dis* 2012; **12**: 249–53.
- 3 FutureLearn. Free online course—Antimicrobial stewardship: managing antibiotic resistance <https://www.futurelearn.com/courses/antimicrobial-stewardship> (accessed 11 May, 2016)
- 4 Czaplewski, L, Bax, R, Clokie, M *et al*. Alternatives to antibiotics—a pipeline portfolio review. *Lancet Infect Dis* 2016; **16**: 239–51.
- 5 Bragginton, EC, and Piddock, LJV. UK and European Union public and charitable funding from 2008 to 2013 for bacteriology and antibiotic research in the UK: an observational study. *Lancet Infect Dis* 2014; **14**: 857–68.
- 6 Kelly R, Zoubiane G, Walsh D, Ward R, Goossens H. Public funding for research on antibacterial resistance in the JIPAMR countries, the European Commission, and related European Union agencies: a systematic observational analysis. *Lancet Infect Dis* 2016; **16**: 431–40.

[Margin links]

For more on the **British Society for Antimicrobial Chemotherapy Antibiotic Action initiative** see <http://antibiotic-action.com/>

For more on **Action on Antibiotic Resistance** see <http://www.reactgroup.org/>

For more on the **Alliance for the Prudent Use of Antibiotics** see <http://emerald.tufts.edu/med/apua/>

For more on the **World Alliance Against Antibiotic Resistance** see <http://www.ac2bmr.fr/index.php/en/>

For more on **The Centre for Disease Dynamics, Economics and Policy** see <http://www.cddep.org/>

For more on **Driving reinvestment in Research & Development for antibiotics and advocating their responsible use** see <http://drive-ab.eu/>