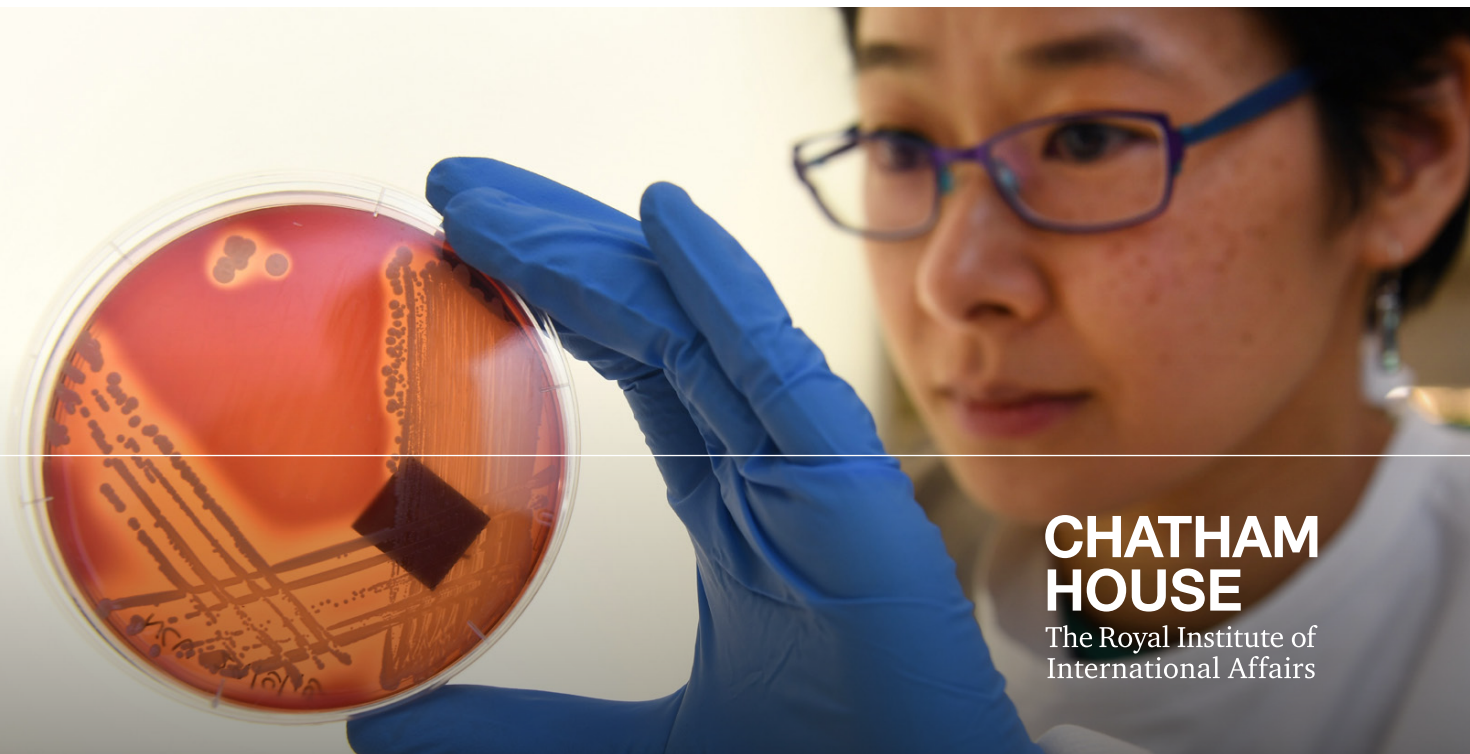


Research Paper

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Centre on Global Health Security | October 2019

Review of Progress on Antimicrobial Resistance



**CHATHAM
HOUSE**

The Royal Institute of
International Affairs

Summary

- The 2016 Review on Antimicrobial Resistance has had a global impact: as an advocacy tool, in raising the profile of antimicrobial resistance (AMR) on the international agenda, and in helping to stimulate a number of new initiatives, in particular relating to the funding of early-stage research.
- However, there has been very little progress on the review's central and most expensive recommendations for transforming research and development incentives for antibiotics, vaccines and diagnostics.
- There have been significant advances in reducing antibiotic use in agriculture, particularly in high-income countries, but there is a long way to go in low- and middle-income countries (LMICs).
- There has been greater investment in awareness raising but questions remain about its impact and effectiveness in changing behaviour.
- Proposals to restrict over-the-counter sales of antibiotics, as recommended by the Review, have foundered in the face of poor living conditions and access to healthcare in LMICs.
- A major reason for the use of antibiotics in LMICs is the prevalence of unhygienic conditions in the community and in healthcare facilities, which contribute to infection and limit the impact of messages about awareness and infection prevention and control.
- Providing quality healthcare to all and moving towards universal health coverage in LMICs will be crucial in addressing the problems of both adequate access to antibiotics and in restricting over-the-counter sales.
- A greater emphasis on investments in water, sanitation and housing will be central to reducing reliance on antibiotics in LMICs in the longer term. This agenda should inform the operations of governments and funding agencies such as the International Monetary Fund (IMF) and the World Bank.
- Investments have been made in improving surveillance of antibiotic use and resistance, particularly for humans, but more effort is required to create surveillance systems that provide data sufficiently accurate to influence policy and action. This applies also to antibiotics and resistant genes circulating in the environment.
- The emerging innovations in the global governance of AMR need to lead to action rather than more words.

Foreword

Jim O'Neill

Being Chair of both Chatham House and the AMR Review, as well as leading the full-day roundtable discussion among experts to examine the impact of the AMR Review for this paper, has tested my abilities to the full.

I have often said that chairing the AMR Review was the most interesting professional challenge in my long and varied career. Not least because within our small team we felt we were having an influence and were being listened to right from the outset. During a previous review that I led for the City Growth Commission, an experienced person suggested to me that the most effective reviews are those that have policymakers trying to implement your ideas before you have even finished. I certainly felt this was true of the AMR Review, which was very gratifying.

Before we had completed the Review, the UK government took action on surveillance with the announcement of the UK Fleming Fund, and improved support for new research through the UK–China innovation fund, which is worth £50 million. AMR also found its way on to the G20 agenda as early as the 2015 G20 summit in Turkey, and in subsequent years the G20 summits in China and Germany paid considerable attention to the challenge. I also think we contributed materially to the passing of the UN political declaration on AMR in September 2016.

The two big numbers that came from our initial paper published in 2014 about the consequences of no action on antimicrobial resistance (AMR) – namely, that around the world it will cause the deaths of 10 million people a year by 2050 and result in an accumulated cost of \$100 trillion for the global economy – have been widely referenced ever since. While some experts dispute our estimates, these figures continue to be cited regularly in most articles on the subject of AMR.

Now, these initiatives might have happened if our Review had not existed, but I suspect not. A number of further policy developments have occurred since our Review finished, which I also doubt would have happened without our existence. In the agricultural sphere, the Review team have been positively surprised. The UK has adopted our precise recommended target of 50 mg of antibiotics used per kilogramme of livestock body weight (which it subsequently achieved). Health ministers at the 2018 Argentina G20 released a statement that members should phase out the use of antibiotics for growth promotion in livestock, and in the past year, both China and India have announced a ban on the use of colistin in animals. Furthermore, in the US and the UK, major food producers and distributors are shifting their strategies with respect to the AMR threat, and those at the forefront of these initiatives have told me personally that it is due to our Review.

I have publicly discussed on a number of occasions that of the 10 broad areas of policy relevance highlighted in the Review – which I often term, the 10 commandments of AMR – there has been some progress on seven of them, and in three areas (diagnostics, vaccines and the market for new drugs) there has been virtually none, despite endless talk.

At the May 2019 roundtable we organized for this paper, participants were asked to score, from one to five, the progress that has been made on each of the Review's recommendations. Unsurprisingly, average scores all tended towards the middle or lower end of that range; and, individually, I believe many of them gave scores that mirrored these middle- to lower-end values. This was a true challenge for me as chair of the roundtable and the Review, as I had quite different scores in my head. But I thought it was important that I did not try to influence the participants.

This experience reminded me of some advice I was given towards the start and end of the formal Review. One experienced adviser encouraged me to create a formal advisory group, but I quickly decided, after consulting my team, that this would not be a good idea. Instead we developed a loose set of advisers that we generally talked to individually when we needed specific advice in their areas of expertise. I believed this would be preferable to organizing collective meetings. After all, I was chosen deliberately as an outsider, a non-health, non-scientist professional, to think differently from those immersed in the AMR world. We wanted to be truly independent, especially in terms of our approach and idea creation, otherwise we would likely have come up with recommendations that had already been suggested. I had joked to Sally Davies (the chief medical officer for England) in the first weeks of the Review that, given how much the experts seemed to know about the issue, it was not immediately obvious why they needed me? But the answer soon became apparent. Towards the end of the Review, we organized meetings involving those with different expertise and were often intrigued to realize that many did not know each other.

As we were concluding the Review, the same adviser tried to encourage me to delay the publication of our final recommendations in May 2016, arguing that the then prime minister could not play a role in promoting our findings as he would be solely engaged in the EU referendum in the UK. I resisted this advice, not least because many thought there was a real possibility that the prime minister might lose. Considering the urgency of tackling AMR, I decided to take the risk and publish the Review.

I highlight these two examples to make a broader point about something I often say when talking publicly about the challenge of AMR and finding effective solutions: unless key players are prepared to behave differently and make bolder decisions, the challenge is never going to be solved, whether that be policymakers, drug companies, doctors, farmers and, ultimately, all 8 billion of us.

Let me now turn back to the seven areas where I believe there is evidence of progress. In my view, the two biggest shifts are related: the number of AMR researchers and the amount of money that is now going into early-stage research. Indeed, from what I can tell, the amount of money that has since been announced, if not completely committed yet, is already equal (if sustained) to what we said was necessary by 2021. I am not sure what more could be done here, and I applaud all those involved in making this possible for their wise judgement.

This also gives me hope that more progress can still be achieved in the other areas, so long as crucial participants are prepared to think creatively.

On public awareness, for example, where there has clearly been some progress, why don't key organizations, such as the World Health Organization (WHO) and the UN, approach major social media companies to pursue a full-blown AMR awareness campaign with their users? In addition to approaching familiar Western companies, this strategy should also include WeChat, the Chinese social media giant, which is now trying to expand significantly in Africa.

Another idea is to persuade key governments to start allowing AMR to be cited as a cause of death on national death registers. While somewhat macabre, this would certainly communicate the fact that AMR does kill.

Progress in agriculture, although limited, has occurred sooner than I had thought possible. But there is still a long way to go. Why don't governments of the West do more to ban the use of so-called last-resort antibiotics, just as China and India apparently have? I continue to have occasional dialogue with major food distributors and I suspect that the momentum developed, probably

due to pressures from changing consumer habits, is set to continue. This is something that could lead to obvious new initiatives such as, for example, colour-labelling on food products to reflect antibiotic usage.

On cleanliness and infection control, an obvious idea that the now head of the Global Fund to Fight AIDS, Tuberculosis and Malaria, Peter Sands, discussed with me is to encourage the International Monetary Fund to pressure all member countries to include their health systems and water and sanitation investments, along with the usual macro-economic criteria, in their regular Article IV assessments. These assessments are something countries typically take very seriously, not least because they can affect credit ratings and the markets.

While progress on surveillance and international cooperation has been made, it is clear that momentum needs to be picked up again on both.

The three areas where there has been no progress are remarkably disappointing, given how much attention we paid to them during our Review and how often AMR circles discuss them, especially the commercial market for antibiotics.

At the heart of all three is the issue of money. We recommended the introduction of market entry rewards to incentivize the development of antibiotics and vaccines against critical new pathogens; and, crucially, affordable key point-of-care diagnostics. The few analysts who have studied the market-failure challenge that lies at the heart of these problems have essentially embraced this recommendation, or some variant of it.

What is missing, despite endless words, is a firm commitment of monies from governments or pharmaceutical companies. At times, I cynically suspect that – based on the experience of past epidemics – governments are waiting for the crisis to escalate to a point where they can most easily justify providing large-scale financial assistance to stimulate companies to develop the antibiotics, vaccines and diagnostics necessary to tackle AMR. Similarly – and here my cynicism is stronger – I suspect that companies that find the antibiotics business increasingly unattractive are simply adhering to their own risk-return calculations, which suggest it is worth waiting until governments panic and throw more money at the challenge than they are apparently ready to do today.

As I think the Review and some others have shown, comparisons to previous epidemics are not applicable as the consequences of continued inaction on AMR will be much more serious. We need a major government decision-maker to be decisive, and either be prepared to spend taxpayers' money themselves or use it to change the risk-reward calculations for pharmaceutical companies. Perhaps a UK initiative on delinking payments for antibiotics from the volume of use announced earlier in 2019 might be the beginning of something serious. If not, our much-discussed 'Pay or Play' policy recommendation – whereby all pharmaceutical companies would be obliged to pay a charge if they do not have active antibiotic R&D programmes – is still a viable option.

I would like to thank everyone who participated in the expert roundtable and, of course, my friends at Wellcome for suggesting the idea. I hope it leads them, and others, to do as I have proposed – to think differently about their own role in the solution. I would especially like to thank and congratulate Charles Clift for the diligence and wisdom he has shown in putting this research paper together, despite having me to contend with.

Introduction

The Review on Antimicrobial Resistance (AMR Review), chaired by Lord Jim O'Neill, was commissioned in July 2014 by the then UK Prime Minister David Cameron. The establishment of the Review reflected a renewed concern at the highest political levels in the UK about antimicrobial resistance (AMR), catalysed by the sustained advocacy of Dame Sally Davies, England's chief medical officer. The choice of Jim O'Neill, an economist without a health or scientific background who had spent much of his career at Goldman Sachs, was surprising to some. However, it reflected the view that tackling the AMR crisis was not just a scientific and medical challenge but an economic and social one too. Moreover, a key factor was the feeling that Jim O'Neill could be instrumental in building connections with emerging economies, which were perceived to be critical players in addressing AMR on a global scale. This perspective is reflected in the Review's emphasis on the potential leadership role of the G20 group of countries, alongside that of the UN and the G7.¹

Box 1: AMR Review recommendations

1. A massive global public awareness campaign;
2. Improve hygiene and prevent the spread of infection;
3. Reduce unnecessary use of antimicrobials in agriculture and their dissemination in the environment;
4. Improve global surveillance of drug resistance in humans and animals;
5. Promote new, rapid diagnostics to cut unnecessary use of antibiotics;
6. Promote the development and use of vaccines and alternatives;
7. Improve the numbers, pay and recognition of people working in infectious disease;
8. Establish a Global Innovation Fund for early-stage and non-commercial research;
9. Better incentives to promote investment for new drugs and existing ones; and
10. Build a global coalition for real action – via the G20 and the UN.

The final report of the Review was published in May 2016. The Review set out why AMR is such a huge threat as antimicrobial drugs become less effective and too few new ones are developed. It found that not enough was being done to reduce unnecessary use of antimicrobials in human healthcare and in agriculture, nor to curb their presence in the environment. The Review estimated that if no action is taken AMR could cause the deaths of 10 million people worldwide every year by 2050, with a cumulative economic impact of around \$100 trillion lost from global GDP.²

The Review made proposals covering the 10 main areas in which action was required to address the imminent threat posed by AMR (see Box 1). In total it made 29 specific sub-recommendations across those 10 areas. In the run up to the final report, the Review published eight separate reports in 2014–16 on different aspects of tackling the AMR crisis. These reports were informed by many supporting documents commissioned by the Review.³

¹ O'Neill, J. (2018), 'Two years on: an update on achievement towards the recommendations of the antimicrobial resistance report', *Journal of Applied Microbiology*, 125(2), pp. 308–312, <https://doi.org/10.1111/jam.13933> (Note: All URLs accessed 10 Sep. 2019).

² AMR Review (2016), *Tackling Drug-Resistant Infections Globally: final report and recommendations*, London: AMR Review, https://amr-review.org/sites/default/files/160525_Final%20paper_with%20cover.pdf.

³ AMR Review (n.d.), 'Publications', <https://amr-review.org/Publications.html>.

The purpose of this research paper is to assess progress on AMR against the recommendations of the Review to identify opportunities for further action and key obstacles that need to be overcome. The analysis is based on a review of available literature and other materials documenting developments in the AMR field, particularly since 2016. This is supplemented by the insights of participants in a Chatham House expert roundtable held in May 2019 and by interviews with other stakeholders.

Impact of the AMR Review

The Review made an impact well before the publication of its final report in May 2016. The estimates of deaths and economic costs in its first report in December 2014 have since been widely used to justify urgent action to tackle AMR. While the estimates have been queried, the number of times the figures have been quoted is a testament to the large advocacy impact the Review has achieved. For example, a Google search for ‘10 million deaths globally 2050 drug-resistant’ on 30 September 2019 produced 5.92 million results. In its major report on the economic impact of AMR in 2017, the World Bank described the Review’s report and background papers as ‘remarkable’.⁴

The Review, and the lobbying efforts of the UK and other governments, certainly played a role in raising the international political profile of AMR and in stimulating a number of initiatives, even before the report was completed. One example is the launch of the UK’s Fleming Fund in 2015.⁵ The declaration on AMR from G7 health ministers in October 2015 specifically referred to the Review’s estimate of 700,000 deaths annually from AMR⁶ and the G20 made its first reference to AMR in the Antalya summit communique in November 2015.⁷ The Review probably also made a material contribution to the passing of the UN Political Declaration on AMR in September 2016.⁸ The declaration reflected many of the themes identified in the Review including, for instance, ‘the importance of delinking the cost of investment in research and development on antimicrobial resistance from the price and volume of sales’ and the need to mobilize predictable and sustainable funding to address all aspects of AMR.

As host of the 2017 G20 meeting, Germany made AMR one of its priorities and undertook substantial preparatory work to seek agreement on the appropriate use of antibiotics as well as to coordinate on incentives for improved research and development (R&D). One major input was a report by the Boston Consulting Group (BCG) that made proposals for new incentives and financing for R&D, drawing heavily on many of the proposals in the Review.⁹ A second was a report from the Organisation for Economic Co-operation and Development (OECD) and the Tripartite agencies – the Food and Agriculture Organization (FAO), the World Organisation for Animal Health (OIE) and the World Health Organization (WHO) – on tackling AMR and ensuring sustainable R&D. This also drew substantially on the analysis in the AMR Review and the BCG report.¹⁰

⁴ World Bank (2017), *Drug-Resistant Infections: A Threat to Our Economic Future*, Washington DC: World Bank, <http://documents.worldbank.org/curated/en/323311493396993758/pdf/final-report.pdf>.

⁵ The Fleming Fund (n.d.), ‘About the Fleming Fund’, <https://www.flemingfund.org/about-us/>.

⁶ G7 (2015), ‘Declaration of the G7 Health Ministers’, 8–9 October 2015, Berlin, <http://www.g8.utoronto.ca/healthG8/2015-berlin.pdf>.

⁷ G20 (2015), ‘G20 Leaders’ Communiqué Antalya’, 16 November 2015, <http://www.g20.utoronto.ca/2015/151116-communicue.html#annex>.

⁸ United Nations (2016), ‘Political Declaration of the High-Level Meeting of the General Assembly on Antimicrobial Resistance’, A/71/L.2, 22 September 2016, <https://digitallibrary.un.org/record/842813?ln=en>.

⁹ Boston Consulting Group (2017), *Breaking through the Wall: A Call for Concerted Action on Antibiotics Research and Development*, Berlin: BCG/Federal Ministry of Health, https://www.bundesgesundheitsministerium.de/fileadmin/Dateien/5_Publikationen/Gesundheit/Berichte/GUARD_Follow_Up_Report_Full_Report_final.pdf.

¹⁰ OECD, WHO, FAO, OIE (2017), *Tackling antimicrobial resistance: Ensuring sustainable R&D*, Final note prepared by OECD, WHO, FAO and OIE, 29 June 2017, <https://www.oecd.org/els/health-systems/G20-AMR-Final-Paper-2017.pdf>.

However, compared with all this comprehensive preparatory work, the G20 leaders' declaration in July 2017 in Hamburg was decidedly muted. The one concrete proposal was to call for the establishment of an international R&D Collaboration Hub but when it came to the detailed proposals put forward by BCG and the OECD/Tripartite for stimulating R&D, the declaration simply said, 'we will further examine practical market incentive options'.¹¹ The outcome of the 2017 G20 summit seems to have marked a turning point in the global political commitment to take concrete action on AMR. To the extent that statements made by the G7 and G20 are important in moving the global agenda forward, and the Review certainly thought they were, these peaked in 2017 when it became clear there was a political impediment in moving from 'examining practical market incentives' to proposing concrete steps to make these a reality.

This lack of forward momentum contrasts with the political impetus that resulted in the G7 summit in Okinawa in 2000 setting in motion steps that led to the establishment of the Global Fund to Fight AIDS, Tuberculosis and Malaria.¹² The Global Fund to date has disbursed more than \$40 billion, which is the amount the Review estimated would be needed over a decade to address AMR.¹³ Current political and economic circumstances are very different from those that prevailed in 2000 but it is apparent that the pressure arising from civil society, key governments, individuals and WHO, allied with the obvious severity of the AIDS pandemic and millions of lives immediately at risk, resulted in effective action at the level of the G7 in 2000 and the mobilization of large-scale financial resources.¹⁴ While many of these elements are present in the case of AMR, they have so far failed to generate financial commitments on the scale that the Review and many others believe is required. It appears that the threat, in spite of many warnings, is not perceived to be sufficient to merit the exceptional policy action many consider necessary.

Assessment of progress

A massive public awareness campaign

While resources have flowed into awareness campaigns, as recommended by the Review, there is very limited evidence regarding their impact on antibiotic use, in countries at all levels of development. How to tailor messages to local circumstances, and the appropriate content of those messages, is not well established. More resources are needed to assess impact. There should be a clearer focus on the factors that influence the behaviour of potential and actual patients, doctors and other prescribers, and on what interventions could cause changes in behaviours that lead to inappropriate use. People (including health professionals, veterinarians and farmers) need suggestions about specific things they can do to achieve impact.¹⁵

Achieving sustainable change requires the involvement of groups in civil society (including, for example, consumers, professional societies and investors) to create the demand and pressure for change. Incorporating more guidance on AMR in general and professional education is also very important for sustainable impact.

¹¹ G20 (2017), 'G20 Leaders' Declaration. Shaping an interconnected world', 7–8 July 2017, <https://www.oecd.org/els/health-systems/G20-leaders-declaration.pdf>.

¹² Global Fund (2017), 'Japan and the Global Fund', Geneva: Global Fund, https://www.theglobalfund.org/media/1493/donor_japan_report_en.pdf?u=636918787320000000.

¹³ The Global Fund (n.d.), 'Financials', <https://www.theglobalfund.org/en/financials/>.

¹⁴ Liden, J. (2013), *The Grand Decade for Global Health: 1998–2008*, Working Group on Governance, Paper 2, London: The Royal Institute of International Affairs, https://www.chathamhouse.org/sites/default/files/public/Research/Global%20Health/0413_who.pdf.

¹⁵ Huttner, B., Saam, M., Moja, L., Mah. K., Sprenger, M., Harbarth, S. and Magrini, N. (2019), 'How to improve antibiotic awareness campaigns: findings of a WHO global survey', *BMJ Glob Health*, 4(3), pp. 1–9 doi:10.1136/bmjgh-2018-001239.

The Review also recommended robust regulations, properly enforced, to prevent antibiotic sales without a prescription. The realities of living conditions and access to healthcare in most low- and middle-income countries (LMICs) makes the enforcement of regulations on prescribing, and the translation of awareness into behaviour change, highly problematic.¹⁶ One reason is the inadequacy of healthcare systems for much of the population and the consequent incentives for patients and sellers of antibiotics to go outside the system. Another is that antibiotics are often used as a ‘quick fix’ in the absence of effective measures to resolve underlying structural problems in healthcare systems, housing, water and sanitation, and agriculture that contribute to infections.¹⁷

It is not simply a question of regulating inappropriate use but also recognizing that the lack of access to quality antibiotics is a major concern responsible for millions of deaths annually. Regulation is therefore important, but it is necessary to address the inadequacies in healthcare systems and the social and economic circumstances that predispose to infection to bring about sustainable change in appropriate use and access. Providing quality healthcare to all and moving towards universal health coverage would be crucial in addressing the problems of adequate access to antibiotics and in restricting non-prescription sales.¹⁸

Improve hygiene and prevent the spread of infection

The Review recommended that healthcare systems embed infection prevention and control (IPC) as a top priority at all levels; that studies on effectiveness of interventions and inducing positive behaviour change in healthcare workers be supported; and that investment in water and sanitation in LMICs be encouraged.

Measures to improve IPC need to be viewed in terms of their importance for public health rather than just through an AMR lens. Compliance with IPC measures is often low, even in well-resourced settings and there is also a lack of good quality evidence on the effectiveness and cost-effectiveness of different IPC interventions.¹⁹ IPC is often ignored for a variety of reasons, including pressures on health professionals and the absence of basic facilities such as clean water and sanitation.²⁰ This is particularly the case in LMICs. IPC is not an issue just for healthcare facilities but also for the wider community, where the absence of adequate water, sanitation and housing is a primary driver of the spread of infectious diseases and hence antibiotic use.²¹ As a result, there is a need for a multi-sectoral approach. At the roundtable, participants discussed whether funders such as the IMF and World Bank should lend their weight to the cause of IPC by integrating public health concerns, including combatting AMR, in their agendas and dialogue with countries. Such a dialogue should include investment in water and sanitation.

¹⁶ Haenssger, M. J., Xayavong, T., Charoenboon, N., Warapikuptanun, P. and Khine Zaw, Y. (2018), ‘The Consequences of AMR Education and Awareness Raising: Outputs, Outcomes, and Behavioural Impacts of an Antibiotic-Related Educational Activity in Lao PDR’, *Antibiotics*, 7(4), 95, <https://doi.org/10.3390/antibiotics7040095>.

¹⁷ Denyer, W. L. and Chandler, C. (2019), ‘Quick fix for care, productivity, hygiene and inequality: reframing the entrenched problem of antibiotic overuse’, *BMJ Global Health*, 4(4), doi:10.1136/bmjgh-2019-001590.

¹⁸ Bloom, G., Merrett, G. B., Wilkinson, A., Lin, V. and Paulin, S. (2017), ‘Antimicrobial resistance and universal health coverage’, *BMJ Global Health*, 2(4), <http://dx.doi.org/10.1136/bmjgh-2017-000518>.

¹⁹ European Centre for Disease Prevention and Control (2017), *Economic evaluations of interventions to prevent healthcare-associated infections*, Stockholm: ECDC, doi: 10.2900/4617.

²⁰ World Health Organization and the United Nations Children’s Fund (2019), *WASH in health care facilities: global baseline report 2019*, Geneva: WHO/UNICEF, <https://apps.who.int/iris/bitstream/handle/10665/311620/9789241515504-eng.pdf>.

²¹ World Health Organization and the United Nations Children’s Fund (2017), *Progress on drinking water, sanitation and hygiene: 2017 update and SDG baselines*, Geneva: WHO/UNICEF, <https://washdata.org/sites/default/files/documents/reports/2018-01/JMP-2017-report-final.pdf>; Collignon, P., Beggs, J. J., Walsh, T. R., Gandra, S. and Laxminarayan, R. (2018), ‘Anthropological and socioeconomic factors contributing to global antimicrobial resistance: a univariate and multivariable analysis’, *Lancet Planet Health*, 2, pp. 398–405, [https://doi.org/10.1016/S2542-5196\(18\)30186-4](https://doi.org/10.1016/S2542-5196(18)30186-4); Population Correction Unit: roughly mg/PCU = mg/kg of animal.

Reducing unnecessary use in agriculture

The Review recommended that surveillance of antibiotic use and resistance be urgently improved, and that steps be taken to reduce unnecessary antibiotic use in animals by setting targets at the country level, beginning in 2018.

In several high-income countries, particularly in Europe, there has been considerable success in reducing antibiotic use in agriculture.²² The evidence suggests that, with the right policies, the costs to producers of transitioning to low antibiotic use can be relatively small or negligible if compensated by improvements in animal hygiene, herd management and biosecurity.²³ The situation is different in LMICs. In less-regulated environments, producers are inclined to resort to antibiotics as they move to more intensive farming methods. Moreover, there is a lack of accurate information on antibiotic use and the level of AMR in animals. One study, based on this inadequate data base, projected that global antimicrobial consumption in agriculture will rise by 67 per cent by 2030, and will nearly double in Brazil, Russia, India, China and South Africa.²⁴ Because of the diversity of livestock development business models in LMICs, identifying solutions for cost-effectively reducing antibiotic use is difficult. More research, as advocated by the Review, could certainly open up new policy options relevant to LMICs.

The Review's emphasis on aggregate target-setting was criticized by some participants at the roundtable because it failed to take account of the diversity of animal species and of antibiotic use in different species. Moreover, the proposed timescale, with country targets being established in 2018, failed to recognize the lack of data on use, on AMR levels and indeed on production systems in LMICs. Nevertheless, the fact that targets have played a significant role in the successful reduction strategies in a number of European countries suggests they could be an important element in strategies elsewhere.

A major gap in developing effective strategies to reduce unnecessary use in agriculture is the lack of accurate data on antibiotic use and on AMR, without which target-setting is redundant.²⁵ Therefore, as the Review recommended, a priority must be to improve surveillance systems and undertake more research, including on how to promote the transition to lower antibiotic use in LMICs.

Consumer groups and others have played an important role in addressing unnecessary antibiotic use in the food chain. Where voluntary approaches are inadequate to promote changes on the scale required, governments could play a greater role by setting mandatory standards for antibiotic use in agriculture. However, standards are only as effective as the enforcement system. The OIE reports that many LMICs have insufficient or non-existent regulatory systems to address antibiotic use in agriculture.²⁶ For those LMICs that are exporters of animal products, regimes in importing countries can be an important influence on production practices and antibiotic use. Namibia, a major beef exporter, banned the use of hormones and antibiotics for growth promotion in the beef industry as long ago as 1991, presumably to bolster its export credentials.²⁷

²² European Medicines Agency (2018), *Sales of veterinary antimicrobial agents in 30 European countries in 2016: Trends from 2010 to 2016*, EMA/275982/2018, London: EMA, https://www.ema.europa.eu/en/documents/report/sales-veterinary-antimicrobial-agents-30-europe-an-countries-2016-trends-2010-2016-eighth-esvac_en.pdf.

²³ Laxminarayan, R., Van Boeckel, T. and Teillant, A. (2015), 'The Economic Costs of Withdrawing Antimicrobial Growth Promoters from the Livestock Sector', *OECD Food, Agriculture and Fisheries Papers*, No. 78, Paris: OECD, <https://doi.org/10.1787/5js64kst5wvl-en>.

²⁴ Van Boeckel, T. P., Brower, C., Gilbert, M., Grenfell, B. T., Levin, S. A., Robinson, T. P., Teillant, A. and Laxminarayan, R. (2015), 'Global trends in antimicrobial use in food animals', *Proceedings of the National Academy of Sciences*, 112(18), pp. 5649–5654, <https://doi.org/10.1073/pnas.1503141112>.

²⁵ World Organisation for Animal Health (2018), *The Third OIE Annual report on the use of antimicrobial agents in animals*, Paris: OIE, http://www.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/AMR/Annual_Report_AMR_3.pdf.

²⁶ *Ibid.*

²⁷ World Health Organization (2017), 'Namibia's ban on antibiotics in healthy animals drives meat exports', 14 November 2017, <https://www.who.int/news-room/feature-stories/detail/namibia-s-ban-on-antibiotics-in-healthy-animals-drives-meat-exports>.

Reducing dissemination in the environment

The Review recognized the potential impact of the circulation of antibiotics and resistant genes in the environment as a result of animal, human and manufacturing waste. The Review decided to confine its recommendations to discharges from pharmaceutical manufacturing. It proposed that regulators should set enforceable targets for discharges and companies should improve monitoring of emissions and reduce discharges and support voluntary and transparent commitments to that end.

There is little evidence that governments or regulators have sought to introduce measures to enforce limits on discharges of antibiotics by pharmaceutical companies. Environmental pollution does not currently feature in regulations relating to Good Manufacturing Practice (GMP) for pharmaceuticals. WHO and others have made efforts to introduce such provisions but these have yet to come to fruition.²⁸ The EU considered introducing such regulations in 2018 but appears to have pulled back following pressure from the pharmaceutical industry.²⁹ Revising the GMP framework to incorporate emission targets is worth pursuing but it would likely be a slow process.

Early in 2018, the AMR Industry Alliance agreed on a voluntary framework that promotes responsible antibiotic manufacturing and, in September 2018, published a list of discharge targets to guide environmental risk assessments for the manufacture of antibiotics.³⁰

There has therefore been considerable progress in addressing pharmaceutical discharges on a voluntary basis. A review by the Access to Medicines Foundation in 2018 found that, while 15 out of 18 companies had some form of environmental risk-management strategy, only eight applied limits on factory discharges and none of them made data available on actual discharges. Moreover, only four firms extended these limits to third-party manufacturers (e.g. of active pharmaceutical ingredients (APIs)). Nor are monitoring data made public. There was a lack of transparency about the measures the industry took in their supply chains.³¹ In the absence of government regulation, one avenue would be to reward firms with good environmental practices in procurement processes.

There is much uncertainty about the impact of antibiotic-resistant bacteria and genes in the environment, the relationship with the development of AMR and therefore the priorities for addressing the problem in ways that would maximize the impact on AMR. Moreover, there is a lack of proven technologies that are known to be feasible and cost-effective in preventing the entry of antibiotics into the environment, and in their removal from the environment.³² In such circumstances, it is probably most effective to promote measures that address known hotspots, such as hospitals or manufacturing plants, and to continue to investigate the complexities of the environmental spread of AMR with a view to identifying the priorities and cost-effective mechanisms for mitigating the threat.

²⁸ World Health Organization (2019), *Environmental aspects of Good Manufacturing Practices: Points to consider for manufacturers and inspectors in the prevention of antimicrobial resistance*, Geneva: WHO, https://www.who.int/medicines/areas/quality_safety/quality_assurance/qas19_802_environmental_aspects_of_GMP.pdf?ua=1.

²⁹ *Guardian* (2018), 'Antibiotic apocalypse: EU scraps plans to tackle drug pollution, despite fears of rising resistance', 1 June 2018, <https://www.theguardian.com/environment/2018/jun/01/antibiotic-apocalypse-eu-scraps-plans-to-tackle-drug-pollution-despite-fears-of-rising-resistance>.

³⁰ AMR Industry Alliance (2018), 'AMR Industry Alliance Antibiotic Discharge Targets', <https://www.amrindustryalliance.org/shared-goals/common-antibiotic-manufacturing-framework/>.

³¹ Access to Medicines Foundation (2018), *Antimicrobial Resistance Benchmark 2018*, Amsterdam: ATMF, https://accesstomedicinefoundation.org/media/uploads/downloads/5bc5edd8367eb_Antimicrobial-Resistance-Benchmark-2018.pdf.

³² Larsson, D. G. J., Andreumont, A., Bengtsson-Palme, J., Brandt, K. K., de Roda Husman, A. M., Fagerstedt, P., Fick, J., Flach, C. F., Gaze, W. H., Kuroda, M., Kvint, K., Laxminarayan, R., Manaia, C. M., Nielsen, K. M., Plant, L., Ploy, M. C., Segovia, C., Simonet, P., Smalla, K., Snape, J., Topp, E., van Hengel, A. J., Verner-Jeffreys, D. W., Virta, M. P. J., Wellington, E. M. and Wernersson, A. S. (2018), 'Critical knowledge gaps and research needs related to the environmental dimensions of antibiotic resistance', *Environment International*, 117, pp. 132–138, DOI: 10.1016/j.envint.2018.04.041.

Improve global surveillance of drug resistance in humans and animals

The Review asked WHO to provide global leadership to improve surveillance of drug-resistant infections and governments and other stakeholders to promote data sharing between public and private organizations.

As part of its Global Action Plan on AMR, WHO has established the Global Antimicrobial Resistance Surveillance System (GLASS).³³ There has been substantial progress, but the experience has demonstrated the significant challenges in building up effective surveillance systems (for both humans and animals) that provide data relevant to clinical practice and research, particularly in LMICs but even in high-income countries.³⁴ Such efforts need to continue. Surveillance is critical to the fight against AMR – without surveillance, efforts to combat AMR are essentially flying blind. Effective surveillance systems are needed to provide the evidence base upon which treatment guidelines and national, regional and global strategies can be developed. It is also through these systems that the impact of interventions can be measured. Much more effort and funding are needed to address root causes of ineffective surveillance systems, such as the shortage of laboratory professionals and technicians to increase coverage, the lack of quality assurance systems to ensure proficiency, and insufficient use of digital technologies and artificial intelligence to translate surveillance data into clinical decision-support tools for patient management.

Alongside this there is a need to strengthen systems for monitoring use in humans and animals. Several monitoring programmes on human antibiotic consumption have been launched in high-income countries and LMICs, by the European Centre for Disease Prevention and Control (ECDC), the Centers for Disease Control and Prevention (CDC) and WHO, but different numerators and denominators are used to express antibiotic use in outpatients and inpatients, and standardization of the methods and indicators is needed. There is much more work to be done in generating data on antibiotic use and resistance in agriculture in LMICs. There is also much to be done on surveillance and understanding of the spread of AMR in the wider environment.

Promote new rapid diagnostics to cut unnecessary use

The Review recommended that high-income countries support point-of-care rapid diagnostics, including measures to make their use mandatory, where they are available, by 2020. For LMICs it advocated a subsidy to manufacturers to promote development and use.

In spite of a number of initiatives to stimulate the development of diagnostics, such as prizes offered in Europe,³⁵ the UK³⁶ and the US,³⁷ a multitude of barriers limit the use of diagnostics in clinical practice and hinder the development of new ones. This applies in countries at all income levels but is particularly acute in LMICs. Even existing rapid diagnostic tests, such as that for detecting levels

³³ World Health Organization (2019), *Global Antimicrobial Resistance Surveillance System (GLASS) Report: Early implementation*, Geneva: WHO, <https://apps.who.int/iris/bitstream/handle/10665/279656/9789241515061-eng.pdf?ua=1>.

³⁴ Ashley, E., Recht, J., Chua, A., Dance, D., Dhorda, M., Thomas, N. V., Ranganathan, N., Turner, P., Guerin, P. J., White, N. J. and Day, N. P. (2018), 'An inventory of supranational antimicrobial resistance surveillance networks involving low- and middle-income countries since 2000', *Journal of Antimicrobial Chemotherapy*, 73(7), pp. 1737–1749, <https://doi.org/10.1093/jac/dky026>; Tacconelli, E., Sifakis, F., Harbarth, S., Schrijver, R., van Mourik, M., Voss, A., Sharland, M., Rajendran, N. B. and Rodríguez-Baño, J. on behalf of the EPI-Net COMBACTE-MAGNET Group (2018), 'Surveillance for control of antimicrobial resistance', *The Lancet Infectious Diseases*, 18(3), pp. 99–106, [https://doi.org/10.1016/S1473-3099\(17\)30485-1](https://doi.org/10.1016/S1473-3099(17)30485-1).

³⁵ European Union (n.d.), 'Horizon prize for better use of antibiotics', https://ec.europa.eu/info/research-and-innovation/funding/funding-opportunities/prizes/horizon-prizes/better-use-antibiotics_en.

³⁶ Longitude Prize (n.d.), 'About the prize', <https://longitudeprize.org/about-us/about-prize>.

³⁷ National Institutes of Health (n.d.), 'Antimicrobial Resistance Diagnostic Challenge', <https://dpcpsi.nih.gov/AMRChallenge>.

of C-reactive protein, are underutilized in clinical practice for reasons that include mistrust of results, risk aversion, time pressure and cost.³⁸ There is no diagnostic test that meets the desirable target product profile that would enable prescribers to avoid empirical prescribing.³⁹

An important overriding barrier in development is the lack of a viable prospective market, partly as a result of barriers to the use of diagnostic tests in clinical practice. The current access pathway from diagnostics R&D through regulatory approval and policy development for implementation of novel diagnostics is complex and lengthy in many countries. Regulatory systems for approval of diagnostic tests are complex, lack clarity and are not harmonized, unlike what has happened to some extent in the regulation of medicines. The problem therefore has to be addressed on several different levels if new diagnostics are to be developed and used. Following the model of Gavi or the Global Fund, organizations such as UNITAID, which already works to stimulate the development of diagnostics for tuberculosis and HIV, could extend work to cover other antimicrobials and antibiotics and help create markets.

Promote the development and use of vaccines and alternatives

The Review recommended promoting the uptake of existing vaccines for humans and animals more widely and initiating 'pull' funding schemes to promote uptake and development.

There has been considerable activity directed at enhancing the role of vaccines in combatting AMR. These include a Chatham House workshop,⁴⁰ a Wellcome report,⁴¹ the formation of a working group at WHO (VAC-AMR)⁴² as well as contributions from academics and industry.⁴³ Gavi, the Vaccine Alliance, has incorporated the impact on AMR as a criterion in compiling its latest investment strategy.⁴⁴ Vaccines that might have a particular impact on AMR by averting future antibiotic treatment include those for seasonal influenza⁴⁵ and typhoid,⁴⁶ as well as respiratory syncytial virus⁴⁷ and Group A streptococcus.⁴⁸ They might be particularly important for diseases such as gonorrhoea where

³⁸ Wellcome (2016), *Four diagnostic strategies for better-targeted antibiotic use*, London: Wellcome, <https://wellcome.ac.uk/sites/default/files/diagnostic-strategies-for-better-targeted-antibiotic-use-wellcome-jul15.pdf>.

³⁹ Dittrich, S., Tadesse, B. T., Moussy, F., Chua, A., Zorzet, A., Tängdén, T., Dolinger, D. L., Page, A. L., Crump, J. A., D'Acremont, V., Bassat, Q., Lubell, Y., Newton, P. N., Heinrich, N., Rodwell, T. J. and González, I. J. (2016), 'Target Product Profile for a Diagnostic Assay to Differentiate between Bacterial and Non-Bacterial Infections and Reduce Antimicrobial Overuse in Resource-Limited Settings: An Expert Consensus', *PLoS ONE*, 11(8), <https://doi.org/10.1371/journal.pone.0161721>; Dailey, P., Osborn, J., Ashley, E. A., Baron, E. J., Dance, D. A. B., Fusco, D., Fanello, C., Manabe, Y. C., Mokomane, M., Newton, P. N., Tessema, B., Isaacs, C. and Dittrich, S. (2019), 'Defining System Requirements for Simplified Blood Culture to Enable Widespread Use in Resource-Limited Settings', *Diagnostics*, 9(10), <https://doi.org/10.3390/diagnostics910010>.

⁴⁰ Clift, C. and Salisbury, D. (2017), 'Enhancing the role of vaccines in combatting antimicrobial resistance', *Vaccine*, 35(48), Part B, pp. 6591–6593. <https://doi.org/10.1016/j.vaccine.2017.09.053>.

⁴¹ Boston Consulting Group, Wellcome (2019), *Vaccines to tackle drug resistant infections: An evaluation of R&D opportunities*, London: BCG/Wellcome, <https://vaccinesforamr.org/read-the-report/>.

⁴² World Health Organization (2019), 'Value Attribution Framework for Vaccines against Antimicrobial Resistance', Presentation on 3 July 2019, https://www.who.int/immunization/research/meetings_workshops/5_Hasso_Prudden_AMR_PDVAC_2019.pdf?ua=1.

⁴³ Bloom, D. E., Black, S., Salisbury, D. and Rappuoli, R. (2018), 'Antimicrobial resistance and the role of vaccines', *Proceedings of the National Academy of Sciences*, 115(51), pp. 12868–12871, <https://doi.org/10.1073/pnas.1717157115>.

⁴⁴ Gavi (n.d.), 'Evaluation criteria for vaccines for endemic disease prevention through routine immunisation', <https://www.gavi.org/about/strategy/vis/evaluation-criteria-for-vaccines-for-endemic-disease-prevention-through-routine-immunisation/>.

⁴⁵ Knight G. M., Clarkson M. and de Silva, T. I. (2018), 'Potential impact of influenza vaccine roll-out on antibiotic use in Africa', *Journal of Antimicrobial Chemotherapy*, 73(8), pp. 2197–2200, <https://doi.org/10.1093/jac/dky17>.

⁴⁶ Andrews, J. R., Baker, S., Marks, F., Alsan, M., Garrett, D., Gellin, B. G., Saha, S. K., Qamar, F. N., Yousafzai, M. T., Bogoch, I. I., Antillon, M., Pitzer, V. E., Kim, J. H., John, J., Gauld, J., Mogasale, V., Ryan, E. T., Luby, S. P. and Lo, N. C. (2019), 'Typhoid conjugate vaccines: a new tool in the fight against antimicrobial resistance', *Lancet Infect Dis.*, 19(1), pp. 26–30, [https://doi.org/10.1016/S1473-3099\(18\)30350-5](https://doi.org/10.1016/S1473-3099(18)30350-5).

⁴⁷ Fleming-Dutra, K. E., Hersh, A. L., Shapiro, D. J., Bartoces, M., Enns, E. A., File, T. M., Finkelstein, J. A., Gerber, J. S., Hyun, D. Y., Linder, J. A., Lynfield, R., Margolis, D. J., May, L. S., Merenstein, D., Metlay, J. P., Newland, J. G., Piccirillo, J. F., Roberts, R. M., Sanchez, G. V., Suda, K. J., Thomas, A., Woo, T. M., Zetts, R. M. and Hicks, L. A. (2016), 'Prevalence of inappropriate antibiotic prescriptions among us ambulatory care visits, 2010–2011', *JAMA*, 315(17), pp. 1864–73, doi:10.1001/jama.2016.4151.

⁴⁸ Berkely S. (2019), 'We're Not Using One of Our Best Weapons against Drug-Resistant Microbes', *Scientific American*, blog, 8 February 2019, <https://blogs.scientificamerican.com/observations/were-not-using-one-of-our-best-weapons-against-drug-resistant-microbes/>.

treatment options are now extremely limited.⁴⁹ While it is self-evident that vaccination should help to reduce AMR, it is a challenge to demonstrate the magnitude and value in ways that would convince policymakers that AMR is a reason to assign a much higher priority to vaccine use and development than they already do.

As with diagnostics, a fundamental issue, alongside scientific challenges in vaccine development, is the absence of an effective market that provides incentives for the development of vaccines relevant to fighting AMR. WHO is already working towards establishing a list of priorities to guide R&D along the lines of the list it developed to guide R&D on antibiotic development. It should also develop target product profiles for priority vaccines. Such an effort would need to be supported by funding agencies in order to help create a viable market. The current Global Vaccine Action Plan, which runs from 2011 to 2020, does not mention the role of vaccines in combatting AMR – this highlights the need for international bodies (such as WHO’s Strategic Advisory Group of Experts (SAGE) on Immunization) as well as national advisory committees to mainstream AMR as a factor in their decision-making.

Improve the numbers, pay and recognition of people working in infectious disease

The Review recommended expanding funding and training opportunities for healthcare workers and scientists and improving their pay, recognition and standing.

Much would be achieved in improving research capacity if the current enhanced level of push funding directed at early-stage research were maintained or further enhanced and if effective pull mechanisms could be implemented to draw resources into late-stage product development, where there is currently the biggest bottleneck. Market forces, as modified by public intervention, would naturally improve the numbers, pay and recognition of researchers in the area. Regarding clinicians and other health workers, the need is for the incorporation of AMR-relevant training at all levels of professional education and for creating paths for career progression in those specialisms most relevant to stewardship of antibiotics.

Funding for early-stage and non-commercial innovation

The Review recommended establishing a Global Innovation Fund for this purpose, with an endowment of \$2 billion over five years.

While a fund, as such, has not been established there has been a proliferation of new funding initiatives and new institutions in recent years. Prominent among these are:

- The US Biomedical Advanced Research and Development Authority (BARDA);
- The Bill and Melinda Gates Foundation;
- CARB-X – the Combatting Antibiotic Resistant Bacteria Biopharmaceutical Accelerator;
- The Global Antibiotic Research & Development Partnership (GARDP);
- UKAID – including the Global AMR Innovation Fund (GAMRIF) and the Fleming Fund;
- Federal Ministry of Education and Research (Germany);
- The EU’s Innovative Medicines Initiative (IMI) – New Drugs for Bad Bugs project;
- The EU’s Joint Programming Initiative on Antimicrobial Resistance (JPIAMR);

⁴⁹ Edwards, J. L., Jennings, M. P. and Seib, K. L. (2018), ‘Neisseria gonorrhoeae vaccine development: hope on the horizon?’, *Current Opinion in Infectious Diseases*, 31(3), pp. 246–250, DOI: 10.1097/QCO.0000000000000450.

- The US National Institutes of Health;
- REPAIR Impact Fund, established by Novo Holdings; and
- Wellcome.

These new initiatives and institutions have contributed to positive developments in the funding of early-stage research and significantly more funding from a variety of sources, almost on a par with what the Review called for. However, there is limited evidence that the pipeline of products in development has significantly improved, particularly with respect to new classes of antibiotics needed to address identified priority pathogens.⁵⁰ Moreover, there remains a massive problem in financing later-stage development, and in bringing promising products to marketing approval and beyond.

Better incentives to promote investment in new drugs and existing ones

The Review called for the design and implementation of a global system of ‘market entry rewards’ to incentivize developers of new antibiotics to meet a specified unmet medical need. It also called for the harmonization of regulatory pathways for antibiotics and the strengthening of clinical trial networks to streamline the process and reduce the time and cost of antibiotic development. It estimated the cost of a market entry reward system at \$16 billion over 10 years.

The ideas in the Review have been elaborated by subsequent reports such as that of the BCG and the DRIVE-AB consortium.⁵¹ Recent announcements in the UK⁵² and the US⁵³ have indicated a willingness to reform the way antibiotics are paid for to delink payments from sales volume and to increase the rewards available for delivering new antibiotics. However, on the key issue of a global scheme of market entry rewards on the scale considered necessary by the Review it is now becoming clear, following the recent G20 meeting in Osaka, that there is little, if any, progress being made towards a substantive outcome.⁵⁴

Meanwhile, the market for antibiotics continues to deteriorate, as illustrated by the demise of Achaogen⁵⁵ and the difficulties in other biopharmaceutical companies.⁵⁶ This applies equally to vaccines and diagnostics, for which companies face similar challenges.

That being the case, there is a need to look for and develop alternative ways to address the problem of insufficient investment in R&D.

Build a global coalition for real action via the G20 and the UN

The Review recommended that the G20 take the leadership role, particularly in developing and implementing new incentive models for new antibiotics, diagnostics and vaccines. It recommended that rapid work be undertaken to consider global coordinated structures to develop and implement

⁵⁰ Pew Charitable Trusts (2019), ‘Tracking the Global Pipeline of Antibiotics in Development’, 5 March 2019, <https://www.pewtrusts.org/en/research-and-analysis/issue-briefs/2019/03/tracking-the-global-pipeline-of-antibiotics-in-development>.

⁵¹ DRIVE-AB (2018), *Revitalizing the antibiotic pipeline: Stimulating innovation while driving sustainable use and global access*, London: Drive-AB, <http://drive-ab.eu/wp-content/uploads/2018/01/CHHJ5467-Drive-AB-Main-Report-180319-WEB.pdf>.

⁵² Department of Health and Social Care (2019), ‘Development of new antibiotics encouraged with new pharmaceutical payment system’, 9 July 2019, <https://www.gov.uk/government/news/development-of-new-antibiotics-encouraged-with-new-pharmaceutical-payment-system>.

⁵³ Verma, S. (2019), ‘Aligning Payment And Prevention To Drive Antibiotic Innovation For Medicare Beneficiaries’, *Health Affairs*, blog, 2 August 2019, <https://www.healthaffairs.org/doi/10.1377/hblog20190802.505113/full/>.

⁵⁴ G20 (2019), ‘G20 Osaka Leaders’ Declaration’, 29 June 2019, <http://www.g20.utoronto.ca/2019/2019-g20-osaka-leaders-declaration.html>.

⁵⁵ Farrar, J. (2019), ‘We ignore the disaster in the antibiotics market at our peril’, *Financial Times*, 21 April 2019, <https://www.ft.com/content/4da1c6e4-603d-11e9-9300-0becfc937c37>.

⁵⁶ Outtersson, K. (2018), ‘Current Market Conditions for Antibiotics’, Presentation, 11 December 2018, <https://www.antibioticresearch.org.uk/wp-content/uploads/2019/04/APPG-Outtersson-11-Dec-2018.pptx?x16182>.

financial support for development and use of products to combat AMR. It also called for work to identify ways to finance a long-term global response to AMR, including innovative mechanisms such as hypothecated taxes on antibiotics and/or healthcare products.

Possibly influenced by the Review, the 2016 UN political declaration on AMR called for an interagency coordination group ‘to provide practical guidance for approaches needed to ensure sustained effective global action to address antimicrobial resistance’. The Interagency Coordination Group (IACG) published its report in 2019.⁵⁷ Its main recommendation was the urgent establishment of a ‘One Health Global Leadership Group on Antimicrobial Resistance’ supported by a small secretariat. The suggested group would consist of past and present political leaders, heads of UN and international agencies and the regional banks and other prominent global leaders in relevant fields. This group would be complemented by an Independent Panel on Evidence for Action against Antimicrobial Resistance, along the lines of the Intergovernmental Panel on Climate Change (IPCC). Finally, it recommended that work on the Global Development and Stewardship Framework to Combat Antimicrobial Resistance, which had been called for in the 2015 World Health Assembly resolution adopting the Global Action Plan and reiterated by the 2016 UN Political Declaration, be expedited.

The UN secretary-general has thus far not responded publicly to the recommendations of the IACG report. One possible concern is that both the new bodies proposed – the Leadership Group and the Independent Panel – sound, as described, rather unwieldy. There is a danger that they might become a forum for more talk rather than action. It is also not encouraging that discussions on the Global Development and Stewardship Framework⁵⁸ have so far been inconclusive. Furthermore, the Global AMR R&D Hub, the only concrete innovation in global AMR governance, appears to have failed as yet to find an effective role.

However, there are signs that the Tripartite agencies are mobilizing. A secretariat has been formally established based in WHO but including staff designated by the FAO and OIE in Rome and Paris. The hope is that it can become the driving force for converting words into action and have a much greater operational role and impact than hitherto.

⁵⁷ Interagency Coordination Group on Antimicrobial Resistance (2019), *No Time to Wait: Securing the future from drug-resistant infections*, <https://www.who.int/antimicrobial-resistance/interagency-coordination-group/final-report/en/>.

⁵⁸ World Health Organization (2018), *Global Framework for Development & Stewardship to Combat Antimicrobial Resistance*, Geneva: WHO, https://www.who.int/phi/news/WHO_OIE_FAO_UNEP_Working_paper_of_the_framework_FINAL.pdf?ua=1.

Acknowledgments

Covering all the aspects of Review and all aspects of the AMR issue was a challenge and could not have been done without the help of, and inputs from, many people. Special thanks are due to:

- Wellcome for funding this work and sharing their extensive expertise in the Drug-resistant Infections Programme team – in particular Jeremy Knox and Rebecca Sugden, who provided help and advice throughout.
- Colleagues at Chatham House for their help and assistance in producing and editing this report.
- Participants at the May roundtable, many of whom also commented on the draft of this report.
- Further experts who also provided valuable peer review comments on the draft of this report.

It was a pleasure to work with Jim O'Neill. He largely left me to my own devices and did not attempt to steer the research paper in any particular direction while clearly having his own views, as he has expressed above, as well as elsewhere!

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Cover image: A PhD student at Melbourne's Doherty Institute inspects the superbug *Staphylococcus epidermidis* on an agar plate, 4 September 2018.

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ISBN 978 1 78413 368 9

This publication is printed on FSC-certified paper.



Typeset by Soapbox, www.soapbox.co.uk

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