House of Commons Health & Social Care Select Committee: inquiry on antimicrobial resistance (AMR)

Response by the Wellcome Trust – September 2018

Summary

- Since its inception in 2013, the UK Government's AMR Strategy can be viewed as having achieved some notable successes. A wide range of domestic and international initiatives have been put in place.

- Significant new resources have been made available to researchers in the UK and beyond; this approach should be maintained with the renewal of the Strategy, and efforts to coordinate funding activities strengthened in the UK and internationally.

- The UK's global leadership on AMR has brought this issue to the world stage, and must continue if we are to see a successful global response. This is particularly important on issues of global governance, R&D, and surveillance.

Introduction

1. Wellcome has supported researchers in the UK and beyond for many years to understand the development and spread of drug-resistant infections. Since 2004, Wellcome has invested more than £300m in AMR-related grants. These awards supported a broad array of activities from basic research looking to unravel the mechanism for pathogen resistance, to the development of new technologies to detect and treat resistant infections. Between 2014 and 2016 we worked with the UK Government to host and fund the work of Lord O'Neill's Review on Antimicrobial Resistance.

2. In 2017, we announced a new five-year, £175m commitment to tackling drug resistance as one of a handful key priority programmes for Wellcome. This programme represents a step-change in Wellcome's proactive work to confront the challenge of AMR across four areas:

   a. **Evidence for decision-making –** supporting a global portfolio of open research and data to help guide national and global strategies for tackling drug-resistant infections;

   b. **New treatments** – working with partners, we are funding the development of potential new antibiotics, diagnostics and preventive approaches;

   c. **Faster clinical trials** – we are developing models for global clinical trials networks for antibiotics, to innovate and standardise protocols and make trials more efficient;

   d. **Global governance** – working with policy-makers to support the development of a global framework to coordinate, monitor and evaluate progress in the global response to AMR.

3. Wellcome's AMR programme is inherently global in its focus, although we engage closely with the UK Government and recognise that we have a shared agenda on a number of key issues. This written evidence focuses on these areas of overlap – particularly the Government's role in supporting research activities and its engagement

in the global response to AMR – with comparatively less discussion of the Government's domestic response to AMR.

The UK Government's AMR strategy, 2013-18

4. The UK has been at the forefront of efforts to achieve consistent and coordinated action through multilateral forums including the World Health Organization (WHO), the United Nations (UN), the G7 and G20. The UK Government deserves particular credit for this, and the credibility and goodwill that this has established for the UK in key quarters in the global health community should not be underestimated.

5. The Government's commissioning of Lord O'Neill's Review on Antimicrobial Resistance (in partnership with Wellcome) was a transformative step in the global discussion about AMR. It re-shaped the global discourse on drug-resistant infections, shifting the issue from one focussed on scientific and technical discussions to one which is understood and engaged with far more broadly, including within the upper echelons of governments around the world. Although progress within the UK with the delivery of Lord O'Neill's recommendations has been variable, the global impact of the Review has been substantial.

6. The priority afforded to AMR within the UK Government's research funding programmes has similarly been very positive. For instance:

   a. The establishment of the UK AMR Funders' Forum was a step forward to coordinate and prioritise the UK's research response to the strategy and to align research activities across different governmental departments in a One Health approach.

   b. The launch of the UKRI AMR cross-council initiative (£44m) tackling AMR in a One health approach was a step change for the UK research agenda in supporting AMR. Additional funding through the Newton Fund and Global Challenge Research Fund have provided opportunities for UK researchers to engage with the international research agenda in particular with lower and middle income countries.

   c. Despite some delays in its setup, the Fleming Fund (£267m) is supporting important efforts in key countries to build surveillance capacity – addressing a major weakness in the global capability to respond to AMR. This includes efforts to develop understanding of the global burden of AMR, an investment in partnership with the Wellcome Trust and Bill & Melinda Gates Foundation.

   d. The establishment of the Global AMR Innovation Fund, and its recent commitment of £10m to the CARB-X partnership (alongside the US Government, Wellcome Trust, and Bill & Melinda Gates Foundation) to support early-stage antibiotic development, are important steps to support key R&D issues globally.

Recommendation 1: maintaining global leadership

7. While we recognise that the refreshed UK AMR strategy must place domestic activities and priorities at its core, the Government should be encouraged to retain – and restate – its commitment to international leadership on AMR.

8. It is clearly important to ensure that other countries – particularly those in the 'global south' – now follow the UK's lead in also taking ownership of the emerging global response to AMR. Similarly, there is a pressing need to ensure broader, global civil society buy-in to the issue. Continued leadership from the UK Government in multilateral forums – such as the G20 and the UN – can play an important role in achieving these things. Active support from (senior) Ministers will be particularly important in this respect, as a means of providing cut-through in an environment where multilateral, cooperative action faces substantial challenges.

9. To this end, we are glad that the UK Government (along with the governments of Ghana and Thailand, and the UN Foundation) worked closely with Wellcome as a host of last year's global Call to Action Conference on AMR, held in Berlin. Ministers have recently confirmed that the UK Government will also work with us as co-hosts of the second Call to Action conference, to be held in Accra, Ghana in November 2018. Convening such a major conference in West Africa provides an unprecedented opportunity to re-balance the discourse around AMR towards the global south, and to showcase African leadership on the issue. The conference will also support a more action-focused discussion on AMR between global government and non-government leaders.

10. Continued UK leadership on AMR is particularly important over the next 12-24 months as we see the development of the UN process around AMR. The UN Inter-Agency Coordination Group (IACG) will make its recommendations to the UN Secretary General in the summer of 2019, with an as-yet undefined UN process to follow. These discussions, most likely as part of the UN General Assembly, will shape the immediate future of global governance arrangements around AMR. As an influential voice within the UN system, the UK Government has an important role to play in this process, ensuring that the level of ambition is kept high but realistic, and that it delivers meaningful and effective change.

Recommendation 2: advancing support for antibiotic development

11. Notable progress has been made since 2013 in stimulating early-stage antibiotic development around the world. The UK Government has played an important role in this, through carefully-targeted funding calls led by the Research Councils and Innovate UK; and latterly through investments in the Global Antibiotic Research & Development Partnership (GARDP) and CARB-X. These complementary initiatives have helped contribute to a modest resurgence of early-stage commercial antibiotic research, largely amongst small- and medium-sized enterprises (SMEs), some of them UK-based.

12. However, the development pipeline of antibiotics remains perilously weak, and certainly insufficient for future needs. Moreover, the path to market for these promising early-stage products remains deeply uncertain: as well as the considerable technical challenges of antibiotic development, the continued absence of assured, predictable commercial returns on investment for antibiotic developers mean that these products risk being starved of funding as they enter the more expensive later stages of development.

13. Lord O'Neill's 2016 report highlighted the nature of these commercial challenges, as have numerous other reports (including the more recent European DRIVE-AB report.) The UK Government has publicly acknowledged the fact that these commercial challenges present a serious threat to the sustainability of antibiotic development: it was recognised within the original national strategy, and the UK was central to statements by the G7 and G20 leaders (in 2016 and 2017 respectively) that action to address the failed market is required.

14. However, despite the fact that the commercial challenges of antibiotic development (and possible interventions to address these) are well-recognised and well-documented in the UK and internationally, progress in addressing these challenges has been slow. The need to address the market failures described by Lord O'Neill is increasingly urgent: the recent withdrawals of Sanofi, Allergan and Novartis from antibiotic/infectious disease R&D provide evidence of the risk of continued decline in global pharmaceutical companies' engagement with the development and distribution of antibiotics. If the number of top-tier global pharmaceutical companies with active antibiotics businesses (now only four – GSK, Pfizer, Roche and MSD) dwindles further, this will place the continued viability of SME-led early-stage antibiotic R&D programmes in doubt.

15. The Government should therefore be considering how it can use its renewed AMR strategy to prioritise further interventions to address the commercial challenges of antibiotic development. This should include continued – and extended – 'push' funding for early stage antibiotic development, in a similar vein to the Government's efforts in this area to date. However, they should also seek to go further, faster in progressing with the implementation of so-called 'pull' incentives which rectify the problematic commercial characteristics of the antibiotics market. This should include:

    a. **Implementing a pilot within the NHS of so-called 'de-linked' purchase models for new-to-market antibiotics**, i.e. models of reimbursement that do not depend on volume of sales. While the NHS is in many respects unique, and the UK market for antibiotics too small to 'move the needle' on the global market, the successful negotiation of such a model between government and pharmaceutical companies would send a powerful signal about the feasibility of such approaches in other healthcare systems around the world.

    b. **Renewing efforts in multilateral forums (such as the G20) to promote new incentive models for antibiotic development.** Although the feasibility of truly global mechanisms of reimbursement for antibiotics is doubtful, further collaboration is needed between governments to resolve issues of how to coordinate efforts to stimulate the global market for antibiotics. Doing so will address questions around global 'free rider' issues; how to shape incentive systems according to global, prospectively-defined needs; and allow consideration of important issues of how to improve national-level stewardship and access.

    c. **Supporting the development of a robust evidence base**, that guides governments and other health system actors within the UK and beyond on how to address outstanding technical and practical issues on the implementation of new reward models for antibiotics. This might include, for instance, further exploration of how to value and assess the cost effectiveness of antibiotics – something that cannot currently be adequately done using established health technology assessment (HTA) models utilised by NICE and comparable agencies elsewhere.

16. Alongside this, the UK Government should consider how it can work with other national governments, and non-government partners (like Wellcome), to initiate 'contingency planning' for a total or near-total withdrawal of major pharmaceutical companies from the antibiotics marketplace. This would have severe implications for the future development and global availability of antibiotics; the Government should begin working with others to consider how the established role of pharmaceutical companies in the late-stage development and global marketing of antibiotics might be replaced. This is work that must look to a lengthy (10 year or more) time horizon, but which needs to be initiated now so as to mitigate the worst potential future impacts.

Recommendation 3: continue to engage in the global coordination of research and surveillance activities

17. Since 2013, we have seen the emergence of multiple new coordination mechanisms intended to align AMR R&D efforts globally. These have included technical coordination mechanisms such as the Joint Programming Initiative on AMR (JPIAMR), and recently, more strategically-focussed initiatives such as the Global AMR R&D Hub.

18. Such initiatives have considerable value: a truly global threat such as AMR requires a global response, so it is vital that the UK works with international partners and takes a worldwide perspective to its research investments. Doing so maximises the protection afforded to UK citizens from the rising threat of drug resistance.

19. The UK should therefore continue to engage in forums such as the Global AMR R&D Hub hosted by the German Government and JPIAMR, and use the insights that these

groups generate to guide its prioritisation decisions about the use of research funds. In doing so, the Government should seek to ensure that it maintains a balanced range of R&D priorities in the AMR field – recognising global as well as domestic needs, and ensuring that it has a truly 'one health' approach to the activities it supports, across human health, animal health, and environmental aspects of AMR.

20. The Virtual Research Institute (VRI) currently being developed by the JPIAMR aims to reinforce alignment of AMR research through connecting institutes, centres and infrastructures in a global larger network to avoid duplication and strengthen collaboration. This provides a good opportunity for the UK Government to continue its leadership role through closer engagement with the VRI and support shaping its priorities.

21. It is also important for consideration to be given to how the successes of R&D coordination initiatives can be applied to other areas of the AMR problem where improved coordination and collaboration is required, such as the surveillance of drug-resistant infections.

22. As a country with some of the most developed AMR surveillance capabilities in the world, and the credibility afforded through its global partnership working and resources provided via the Fleming Fund, the UK could play a vital leadership role in helping to raise standards globally. Concerted, international efforts are required to strengthen conventional public sector disease surveillance capabilities. The UK, working with existing global collaboration structures, could lead the way in raising global standards in this way.

23. Beyond this continued emphasis on the strengthening of standard surveillance capabilities, further efforts are needed to liberate more novel approaches to the surveillance of AMR involving the collection and sharing of data held by the private sector (pharmaceutical companies or healthcare providers). For example, Wellcome is already working with the Open Data Institute to explore mechanisms to use data held by pharmaceutical companies in this way; commitment from the UK Government to supporting such efforts to open up privately-held data on drug resistance for the public good would be a powerful catalyst towards making better use of a valuable yet largely-untapped resource.

Conclusion

24. Rising rates of drug-resistant infections pose an exceptional threat both to modern healthcare and to society at large. The multi-sectoral nature of AMR, and the truly global that it presents, means that a comprehensive response is required from governments around the world: one which places an emphasis on effective cross-government mobilisation, and concerted international engagement.

25. The UK Government deserves credit for the way in which its first AMR strategy has achieved these domestic and international goals. Beyond its domestic activities, the leadership that the UK Government has shown internationally in championing global action on AMR has been highly influential in defining the global discourse on drug resistance.

26. In refreshing its AMR Strategy for the coming years, there is an opportunity for Ministers to re-state their commitment to prioritising (and ensuring proper, sustainable funding for) action on AMR both domestically and on the global stage.

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