UK AND EU PUBLIC FUNDING FOR BACTERIOLOGY AND ANTIBIOTIC RESEARCH IN THE UK 2008–13

APPG ON ANTIBIOTICS

Preface

Bacteriology and antibiotic research are the bedrock on which new antibiotics are developed. With the inexorable spread of antibiotic resistance, such research is assuming ever greater importance. It is therefore important to know whether current research activity in these fields is sufficient to meet current and future challenges posed by antibiotic-resistant bacteria.

On behalf of the All-Party Parliamentary Group on Antibiotics, we therefore audited current research activity in these areas, analysing publicly funded research in the UK (and EU-funded research being carried out in the UK) for the period 2008–13. Websites and databases were systematically searched using a specific set of criteria to identify research in bacteriology and antibiotics supported by UK funding agencies.

This report provides a summary of our findings. An academic paper is also being prepared to describe our analysis in more detail.

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Executive summary

Out of **£13.8bn** total funding, **£269.2m** (1.9%) was committed to bacteriology and **£95m** (0.69%) to research on antibiotics.

Antibiotic resistance is a world health crisis that threatens to compromise our ability to control infectious disease and to undertake many currently routine medical interventions.

Antibiotic resistance is a complex issue, requiring concerted and coordinated action across many fronts. The World Health Organisation (WHO), European Union and UK Government have launched strategies to tackle antibiotic resistance at global, regional and national levels.

In particular, there is an urgent need for new antibiotics, following a two-decade gap during which the development of new antibacterial drugs has slowed to a trickle.

Bacteriology and antibiotic-related research are critical components of the battle against antibiotic resistance. Such research identifies new targets and generates new leads for antibiotic development, provides insight into microbial biology important to antibiotic development, and sheds light on mechanisms of resistance. It also underpins the development of diagnostic tools, and supports more effective surveillance of antibiotic resistance and enhanced infection control.

Bacteriology and antibiotic-related research are typically carried out in universities, research institutes and hospitals, funded by public sector funding agencies such as the Research Councils and the National Institute for Health Research (NIHR) and medical research charities; the EU is also an important supporter of biomedical research in the UK.

An analysis of funding provided by these organisations in 2008–13 has revealed very low levels of support for bacteriology and antibiotic-related research. Out of £13.8bn total funding, £269.2m (1.9%) was committed to bacteriology and £95m (0.69%) to research on antibiotics.

Hence, although bacteriology and antibiotic-related research are supported by a range of public sector funding agencies in the UK, none commits more than 5% of its budget to these critical fields of research.

This level of support for bacteriology and antibiotic-related research is not consistent with the current health and economic burden of antibiotic resistance, nor does it reflect the major future challenges posed by antibiotic-resistant organisms.

The UK has set out ambitious plans to tackle antimicrobial resistance. Current levels of funding for bacteriology and antibiotic-related research are unlikely to be adequate to enable these targets to be achieved.

Additional funding is urgently needed. If extra resources are not available, public sector funding agencies should consider prioritising bacteriology and antibiotic-related research within their existing budgets, in response to national and international need.

Given the interdisciplinary nature of bacteriology, greater coordination between funding agencies would be beneficial, to promote work towards shared priorities and to avoid duplication of effort. A joint expert group on antibiotic resistance should be established to provide advice across the UK's funding agencies.

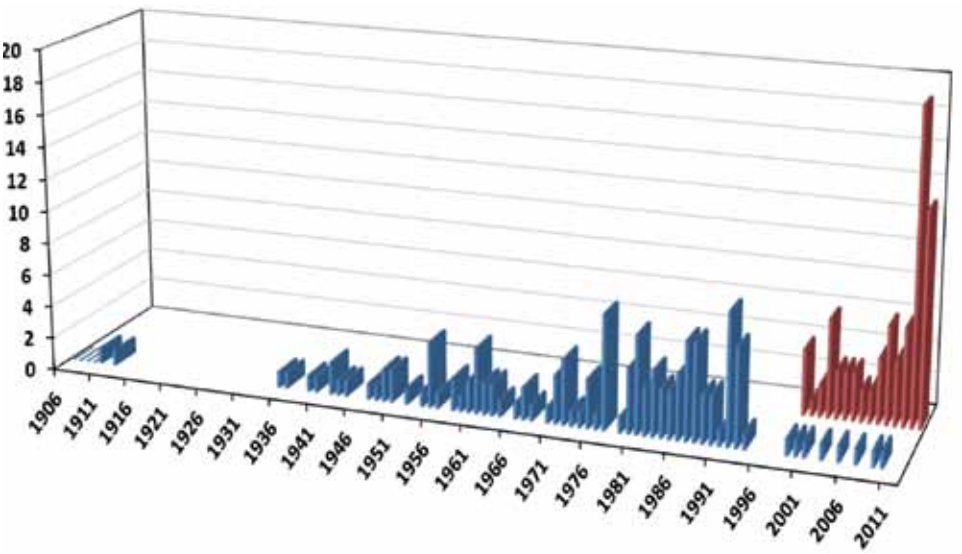
Background

Antibiotic resistance has emerged as a global public health crisis. Worldwide, bacteria are becoming resistant to commonly used antibiotics, forcing doctors to resort to less effective alternatives or drugs with damaging side-effects. The rise of antibiotic resistance threatens our ability not just to treat infections, but also to carry out the invasive procedures typical of modern medicine, which depend on the use of antibiotics to control infection. Chief Medical Officer Professor Dame Sally Davies has drawn attention to the very real prospect that some common treatments may have to be abandoned because of our inability to control infections[1].

Antibiotic resistance is a global issue. It is a particular problem in many parts of the developing world, exacerbated by the ready availability and excessive use of antibiotics and unsanitary conditions that promote the spread of bacteria that cause infections. The World Health Organisation (WHO) has recognised the global threat posed by antibiotic resistance. Antimicrobial resistance was the theme of its World Health Day in 2011 and, publishing its strategy for dealing with antimicrobial resistance in 2012[2], WHO Director General Dr Margaret Chan warned that the world was facing "the end of modern medicine as we know it".

Antibiotic resistance is also a major concern for European countries. In 2011, the European Commission launched an action plan to combat the rising threat of antimicrobial resistance, which estimated that antimicrobial resistance was responsible for around 25,000 deaths a year in Europe and cost €1.5bn[3]. In the UK, the Chief Medical Officer's Annual Report for 2011, published in 2013, provided a stark picture of the challenges the country faces from infections and the rise of antimicrobial resistance. Indeed, a mountain of literature is building on antimicrobial resistance, the threat it poses, and strategies by which it can be tackled – a global chorus that has yet to translate into tangible new antibiotics (Figure 1).

Figure 1: UK and international publications on antibiotic resistance (red columns) and the number of new drugs released onto the pharmaceutical market (blue columns). Despite the burgeoning literature (Appendix 1), the number of new antibiotic products remains alarmingly low.



[1] Davies SC. Annual Report of the Chief Medical Officer, Volume Two, 2011: Infections and the rise in antimicrobial resistance. London: Department of Health; 2013.

[2] World Health Organisation. 2012. The evolving threat of antimicrobial resistance: Options for action. http://www.who.int/patientsafety/implementation/amr/publication/en/

Losing the battle?

In the post-war years, hopes were high that infectious disease would be consigned to history. In the so-called 'golden age of antibiotic discovery'[4] up until 1960, a plentiful supply of new antibiotics transformed treatment of infectious disease. Yet in his Nobel Lecture in 1945, Sir Alexander Fleming had drawn attention to the possibility that drug resistance could arise[5]. His prediction has turned out to be highly prescient.

One solution when resistance arises is to switch to an alternative treatment. However, the rate at which bacteria are becoming resistant has overtaken the rate at which new therapeutics have been developed, reducing the number of options available. Over the past 20–30 years, there has been an alarming decline in the development of new antibiotics. Those that have been launched have typically been variants of existing drugs – generating a 'discovery void' lasting more than 20 years in which no new families of drugs have been developed. Just when they are most needed, the supply of new antibiotics has dried up.

Industry is responsible for the development of most medicines, including antibiotics. For various reasons, antibiotic development has not been a high priority for industry. Important steps are being taken globally to boost industrial investment in antibiotic research and development.

However, many leads for antibiotic development, and the scientific understanding of antibiotic action and resistance that improve antibiotic design or suggest new therapeutic strategies, are generated within publicly funded universities, research institutes and hospitals. This research generates the 'raw material' on which new antibiotics – and potentially entirely new therapeutic strategies – will be based. It also provides an understanding of mechanisms of resistance, insight that may enable resistance to be prevented or overcome.

Given this critical role, it is important to know whether current funding of bacteriology and antibacterial research is consistent with the existing burden of antibiotic resistance and its likely future impact. This analysis therefore set out to assess current funding levels for bacteriology and antibiotic research by the UK's main public sector and charitable funders.

[3] European Commission. Communication from the Commission to the European Parliament and the Council: Action plan against the rising threats from antimicrobial resistance; 2011. http://ec.europa.eu/health/antimicrobial_resistance/policy/index_en.htm

[4] Davies J. Where have all the antibiotics gone? *Can J Infect Dis Med Microbiol* 2006;17:287–90

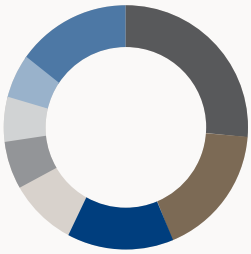
[5] Fleming A. Nobel Lecture: Penicillin. http://www.nobelprize.org/nobel_prizes/medicine/laureates/1945/fleming-lecture.html

UK research activity 2008–13

Across all UK funders, 609 projects related to bacteriology were identified, 196 of which were for antibiotic-related research. These projects accounted for £269.2m of funding, or 1.9% of total funding over the same period. Antibiotic-associated research amounted to 0.69% of total funding.

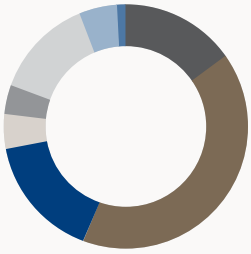
Among the funders, the Biotechnology and Biological Sciences Research Council (BBSRC) supported the greatest number of projects related to antibiotic research (53), while the Wellcome Trust committed the largest sums (£38.2m; Figure 2).

Figure 2: Breakdown of funding by funding agency in terms of number of grants awarded (top) and value of grants awarded (below) to antibiotic-related research.



Number of grants awarded (196 total)

- BBSRC: **53 (27%)**
- Wellcome Trust: **34 (17%)**
- MRC: **26 (13%)**
- TSB: **18 (9%)**
- Defra: **13 (7%)**
- NIHR: **12 (6%)**
- EPSRC: **11 (6%)**
- Others: **29 (15%)**

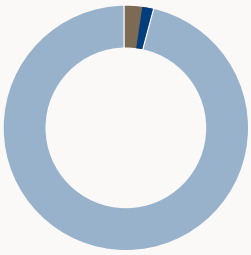


Value of grants awarded

- BBSRC: **£14.0m**
- Wellcome Trust: **£38.2m**
- MRC: **£15.1m**
- TSB: **£5.8m**
- Defra: **£5.0m**
- NIHR: **£11.5m**
- EPSRC: **£3.6m**
- Others: **£1.8m**

Others: Organisations awarding less than £1m for antibiotic research during 2008–13.

In addition to UK agency funding, the European Commission's Framework Programme 7 (FP7) provided £96.2m funding for antibiotic research in the UK.



Medical Research Council (MRC)

Remit: To encourage and support research with the aim of maintaining and improving human health.

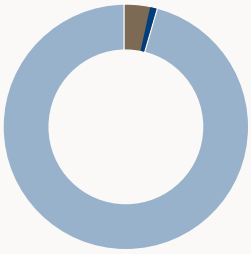
Total funding 2008–13*: **£1253.9m**

- Bacteriology research: **£47.45m (3.78%)**
- Antibiotic-related research: **£15.11m (1.22%)**
- Other: **£1206.45m (96.22%)**

No. of antibiotic-related projects: **26**

*1 April 2008 – 31 March 2013.

Most of the MRC's funding in these areas was for basic research funded by its Infection and Immunity Research Board. Some funding was provided through the Developmental Pathway Funding Scheme, which supports more translational research, and through partnerships with other UK and international funding bodies.



Biotechnology and Biological Sciences Research Council (BBSRC)

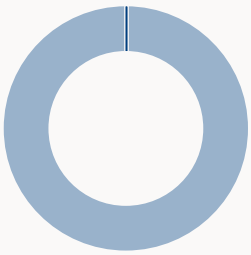
Remit: To invest in world-class bioscience research and training on behalf of the UK public.

Total funding 2008–13*: **£2257.8m**

- Bacteriology research: **£96.19m (4.26%)**
- Antibiotic-related research: **£14.02m (0.58%)**
- Other: **£2161.61m (95.74%)**

No. of antibiotic-related projects: **53**

*1 April 2008 – 31 March 2013.



Engineering and Physical Sciences Research Council (EPSRC)

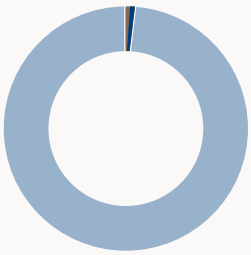
Remit: The EPSRC is the UK's main agency for funding research in engineering and the physical sciences.

Total funding 2008–13*: **£3806m**

- Bacteriology research: **£3.70m (0.10%)**
- Antibiotic-related research: **£3.62m (0.10%)**
- Other: **£3802.3m (99.90%)**

No. of antibiotic-related projects: **11**

*1 April 2008 – 31 March 2013.



Technology Strategy Board (TSB)

Remit: To accelerate economic growth by stimulating and supporting business-led innovation.

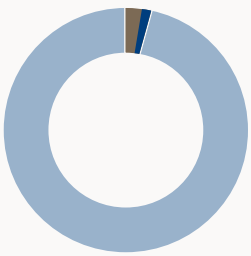
Total funding 2008–13*: **£1427m**

- Bacteriology research: **£11.56m (0.81%)**
- Antibiotic-related research: **£5.76m (0.41%)**
- Other: **£1415.44m (99.19%)**

No. of antibiotic-related projects: **18**

*1 April 2008 – 31 March 2013.

The MRC and TSB jointly run the Biomedical Catalyst grant programme, open to academic groups and small and medium-sized enterprises (SMEs). In its first three rounds, it awarded £4m for antibiotic-related research out of total funding of £180m.



Department of Environment, Food and Rural Affairs (Defra)

Remit: The UK government department responsible for policy and regulations on environmental, food and rural issues.

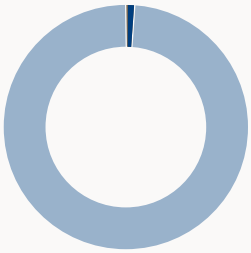
Total funding 2008–13*: **£526.7m** (core funding)

- Bacteriology research: **£18.90m (3.59%)**
- Antibiotic-related research: **£4.97m (0.95%)**
- Other: **£507.80m (96.41%)**

No. of antibiotic-related projects: **13**

*1 April 2008 – 31 March 2013.

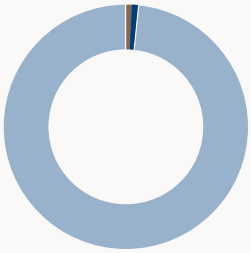
All funding in bacteriology and antibiotic-related research was awarded in the area of Animal Health and Welfare.



National Institute for Health Research (NIHR)
Remit: To maintain a health research system in which the NHS supports outstanding individuals, working in world class facilities, conducting leading edge research focused on the needs of patients and the public.
Total funding 2008–13*: **£879.9m**
(research programme funding)
- Bacteriology research: **£12.78m (1.45%)**
- Antibiotic-related research: **£11.55m (1.31%)**
- Other: **£867.12m (98.55%)**

No. of antibiotic-related projects: **12**
*1 April 2008 – 31 March 2013.

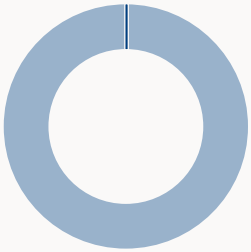
NIHR support included funding through the Invention for Innovation programme (i4i; £0.9m), Health Technology Assessment programme (HTA; £9.8m) and programme grants for applied research (£2.1m).



Wellcome Trust
Remit: To achieve extraordinary improvements in human and animal health.
Total funding 2007–12*: **£3487.6m**
- Bacteriology research: **£73.27m (2.10%)**
- Antibiotic-related research: **£38.17m (1.10%)**
- Other: **£3414.33m (97.90%)**

No. of antibiotic-related projects: **34**
*1 October 2007 – 30 September 2012.

Some £16.2m was awarded for bacteriology and antibiotic-related research through the Seeding Drug Discovery programme, the Translation Fund and the Affordable Healthcare in India initiative.



European Commission Framework Programme 7
Remit: FP7, which ran from 2007 to the end of 2013, was the European's Commission main mechanism for funding research.
Total funding 2007–13: **£43bn (€50bn)**
- Bacteriology research: **£96.2m (0.22%)**
- Antibiotic-related research: **£96.2m (0.22%)**
- Other: **£42.9bn (99.78%)**

No. of antibiotic-related projects: **24**

Figures refer to grants awarded to international consortia with at least one UK partner.

In 2012, the European Union's Innovative Medicines Initiative (IMI) launched a 'New Drugs for Bad Bugs (ND4BB)' initiative focused on antibiotic resistance. It provided funding of £194.1m (€225.7m) to support two projects, COMBACTE (Combating Bacterial Resistance in Europe) and TRANSLOCATION (focusing on the molecular basis of bacterial cell wall permeability). The EU provided £85.1m (€99m) funding, with the remainder coming from industrial sources.

Others
A range of organisations, such as British Society for Antimicrobial Chemotherapy (BSAC), Healthcare Infection Society (HIS), the Royal Society and Action Medical Research, also provide funds for research in this area. Collectively, these bodies provided £5.3m for research on bacteriology and £1.8m for antibiotic-related research in 2008–12.

Discussion

Bacteriology and antibiotic-related research represent just a small fraction of the total funding portfolio of each of the major UK funding agencies. Of the £13.8bn funding analysed here, less than 1% is devoted to antibiotic-related research. Even considering the broader category of bacteriology, none of the UK's major life science funding agencies commits more than 5% of its research expenditure to this field of research.

A similar analysis undertaken by Head and colleagues, based on a wider definition of antimicrobial resistance during 1997–2010, reported similarly low levels of support for antimicrobial research (which includes antibacterial, antiviral, antifungal and antiparasitic research) as a proportion of total agency funding in the UK (5.5% of total studies, 3.9% of total spend)[6].

These figures are all the more anomalous given the growing calls for more to be done to tackle the threat of antibiotic resistance. There appears to be no correlation between research funding and the burden of antibiotic-resistant infections, their impact on medicine, and their social and economic impact more generally. There are few signs that the alarm calls being sounded by policy-makers and public health officials are influencing the behaviour of major funding agencies.

That said, there have been specific initiatives launched recently with a focus on antibiotic resistance. As well as the EU IMI projects described above, in June 2013 the Defence Science and Technology Laboratory launched a Centre for Defence Enterprise themed call, 'Innovation in Drug Development Processes', to encourage the development of new antimicrobials. However, the scheme is providing only short-term funding for small projects. The NIHR has also launched a themed call for proposals in antimicrobial research, using existing funds.

Antibiotic-related projects will also be funded through the ninth and tenth EU IMI calls, which again included the ND4BB topic, and possibly in future rounds of MRC/TSB Biomedical Catalyst funding.

The EU IMI projects, and moves to enhance the economic incentives for industrial research and development in new antibiotics, recognise the important role industry has in delivering effective and safe new medicines. Indeed, most new funding has focused on public–private partnerships.

However, more basic research has an important role to play in the long-term battle against antibiotic resistance. A greater understanding of bacterial biology can identify targets for new medicinal chemistry and therapeutic development. Research in key areas such as bacterial cell wall structure and function may suggest new ways in which drugs can gain access to targets within bacteria. In addition, a better understanding of mechanisms of resistance will shape strategies to minimise the risks of antibiotic resistance when new treatments become available.

The UK five-year antimicrobial resistance strategy has recently been published by the Department of Health in collaboration with Defra and the devolved administrations[7]. It begins by saying: "There are few public health issues of greater importance than antimicrobial resistance in terms of impact on society." It also identifies three strategic aims:

- to improve the knowledge and understanding of antimicrobial resistance,
- to conserve and steward the effectiveness of existing treatments,
- to stimulate the development of new antibiotics, diagnostics and novel therapies.

Research is integral to the first and third of these strategic aims, and the second will be informed by research-based evidence. Yet our analysis suggests that funding policies and decisions are not reflecting these national priorities.

In an era of constrained budgets, it may be difficult to argue for new funding. However, even within existing financial envelopes there is considerable scope for funding agencies to alter their priorities to reflect the strategic importance of this area. Much of the research required is interdisciplinary and there would be benefits in a more coordinated approach among UK funders, to focus pooled resources and prioritise research in areas in which the UK has well-established strengths.

One practical step forward would be to establish a single advisory board comprising experts in antibiotic research to make recommendations to the appropriate committees of each funding agency. This would help to establish priority areas and avoid duplication of efforts.

Bacteria greatly outnumber humans. Although only a minority cause us harm, their speed of reproduction and evolution make them formidable foes. For 70 or so years, antibiotics and other measures have given us the upper hand. Unless we continue to invest to understand and counteract our enemies, this period may come to be the last in which we held the balance of power.

[6] Head MG *et al*. Systematic analysis of funding awarded to antimicrobial resistance research to institutions in the United Kingdom, 1997–2010. *J Antimicrob Chemother* (in press)

[7] Department of Health. UK five year antimicrobial resistance strategy 2013–2018; 2013 https://www.gov.uk/government/publications/uk-5-year-antimicrobial-resistance-strategy-2013-to-2018

Appendix: National and international reports on antibiotic/antimicrobial resistance

1. House of Lords Science and Technology. Seventh Report; Session 1997–98. Resistance to antibiotics and other antimicrobial agents; 1998. http://www.parliament.the-stationery-office.co.uk/pa/ld199798/ldselect/ldsctech/081vii/st0702.htm

2. Department of Health Standing Medical Advisory Committee Sub-Group on Antimicrobial Resistance. The path of least resistance; 1998. [available at http://antibiotic-action.com/wp-content/uploads/2011/07/Standing-Medical-Advisory-Committee-The-path-of-least-resistance-1998.pdf]

3. National Audit Office: Report by the Comptroller and Auditor General. The management and control of hospital acquired infection in acute NHS trusts in England; 2000. http://www.nao.org.uk/wp-content/uploads/2000/02/9900230.pdf

4. Department of Health. UK antimicrobial resistance strategy and action plan; 2000. http://webarchive.nationalarchives.gov.uk/20130107105354/http:/www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_4078448.pdf

5. Department of Health. Better prevention, better services, better sexual health: The national strategy for sexual health and HIV; 2001. http://webarchive.nationalarchives.gov.uk/20130107105354/http:/www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4003133

6. Department of Health. Getting ahead of the curve: A strategy for combating infectious diseases; 2002. http://webarchive.nationalarchives.gov.uk/+/www.dh.gov.uk/en/publicationsandstatistics/publications/publicationspolicyandguidance/dh_4007697

7. House of Commons Health Select Committee. Third Report; Session 2002–03. Sexual health volume I: Report, together with formal minutes; 2003. http://www.publications.parliament.uk/pa/cm200203/cmselect/cmhealth/69/6902.htm

8. House of Lords Session Science and Technology Committee. Fourth Report; session 2002–03. Fighting infection; 2003. http://www.parliament.the-stationery-office.co.uk/pa/ld200203/ldselect/ldsctech/138/13801.htm

9. Department of Health. Winning ways: Working together to reduce healthcare associated infection in England; 2003. http://webarchive.nationalarchives.gov.uk/+/www.dh.gov.uk/en/publicationsandstatistics/publications/publicationspolicyandguidance/dh_4064682

10. National Audit Office. Report by the Comptroller and Auditor General; Session 2003-2004. Improving patient care by reducing the risk of hospital acquired infection: A progress report; 2004. http://www.nao.org.uk/report/improving-patient-care-by-reducing-the-risk-of-hospital-acquired-infection-a-progress-report/

11. Department of Health. Stopping tuberculosis in England: An action plan from the Chief Medical Officer; 2004. http://webarchive.nationalarchives.gov.uk/+/www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4090417

12. Health Protection Agency. Health protection in the 21st century: Understanding the burden of disease; 2005. http://www.hpa.org.uk/Publications/CorporateReports/CorporateAndStrategicPlans/0510HealthProtection21CUnderstandingBurdenofdisease/

13. House of Lords Science and Technology Committee. Fourth Report; Session 2005–06. Pandemic influenza; 2005. http://www.publications.parliament.uk/pa/ld200506/ldselect/ldsctech/88/8802.htm

14. Office of Science and Innovation. Foresight: Infectious diseases: Preparing for the future; 2006. http://www.bis.gov.uk/assets/foresight/docs/infectious-diseases/d1_id_future_vision.pdf

15. Royal Society and Academy of Medical Sciences. Pandemic influenza: Science to policy. Policy document 36/06; 2006. http://royalsociety.org/policy/publications/2006/pandemic-influenza/

16. Department of Health, Cabinet Office. Pandemic flu: A national framework for responding to an influenza pandemic; 2007. http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1238055320501

17. Department of Health. Clean, safe care: Reducing infections and saving lives; 2008. [http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_081719.pdf]

18. UK Clinical Research Collaboration. Developing microbiology infectious diseases research in the UK: Report of the UK Clinical Research Collaboration Strategic Planning Group on Microbiology and Infectious Diseases Research; 2008. http://www.ukcrc.org/index.aspx?o=1510

19. Department of Health. High quality care for all: NHS Next Stage Review Final Report; 2008 http://webarchive.nationalarchives.gov.uk/20130107105354/http:/www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_085828.pdf

20. HM Government. Health is global: An outcomes framework for global health 2011–2015; 2011 https://www.gov.uk/government/publications/health-is-global-an-outcomes-framework-for-global-health-2011-15--2

21. Medical Research Council and National Institute for Health Research. Public health infections research strategy workshop report; 2009. http://www.nihr.ac.uk/files/pdfs/Public%20Health%20Infection%20Research%20Strategy%20-%20Annex%204%20Workshop%20Report.pdf

22. Royal Society. An integrated approach to infectious diseases in the UK; 2009. http://royalsociety.org/policy/publications/2009/infectious-disease-UK/

23. British Society for Antimicrobial Chemotherapy. The urgent need: Regenerating antibacterial drug discovery development; 2010. http://bsac.org.uk/wp-content/uploads/2013/10/Combined-report-for-stakeholder-day.pdf

24. World Health Assembly. Emerging and other communicable diseases: Antimicrobial resistance (WHA51.17); 1998 http://apps.who.int/medicinedocs/index/assoc/s16334e/s16334e.pdf

25. World Health Organisation. Antimicrobial resistance monitoring: Information exchange and opportunities for collaboration: Report of the second joint WHO/IFPMA meeting Geneva 2–3 April 1998 (WHO/EMC/BAC/98.4); 1998. http://apps.who.int/medicinedocs/index/assoc/s16208e/s16208e.pdf

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