strategy&

Antimicrobial resistance

&

The State of the Nation report on UK R&D

pwc

For the past 10 years, Strategy& has analysed R&D investment at the 1,000 biggest-spending public companies in the world, and explored various innovation-related topics based on in depth interviews and surveys with innovation leaders.* This time we have created a snapshot of the current state of the nation of R&D in the UK, focused on tackling the global challenge of antimicrobial resistance.

Foreword

Antimicrobial resistance (AMR) is one of the most important issues facing the global healthcare community. The failure to find a solution threatens the very heart of modern medicine. Without concerted and coordinated international action we could be faced with a situation where common infections are once again fatal.

Here in the UK, we have a real chance to lead the way in combatting AMR. We have a commitment and passion that has already forced the pace of international action. But we will have to do more if we are to make any real impact on this global issue.

At PwC's Strategy&, we are committed to solving important problems. We don't do this alone, but seek to bring people together, recognising that no one sector or organisation can influence something of this scale on their own. We very much hope this report will allow everyone who has a stake in tackling AMR, whether that be the pharmaceutical and life sciences industry, government, or the not-for-profit sector, to take stock of where we are and identify the barriers that we need to overcome.

I look forward to working with all of you who share my passion to make a real difference to this critical global issue.

Jo Pisani
Partner, Pharmaceutical and Life Sciences Consulting Leader

Executive summary

There is an urgent and vital need to tackle antimicrobial resistance (AMR). Existing drugs are losing their efficacy, and without new therapies, there will be an escalating cost in both money and lives.** Over 700,000 people globally are already dying every year, and according to the O'Neill Review into antimicrobial resistance, this will increase to 10 million by 2050 if we don't bring new antibiotics to market and protect the efficacy of our current antibiotics. This would have an overwhelming cumulative cost to world GDP of $100tn.[1]

Tackling AMR is a global challenge and it needs a co-ordinated effort – not just across the world, but across different stakeholders, from government policy-makers to the public, private and philanthropic funders of research, between the different players within the pharmaceutical and life sciences industry and across human and animal health. In other words, we need to 'join up' the international industry, academic and healthcare systems. That basic principle informs the rest of this report. We will, nonetheless, focus specifically on the UK. This is a good place to start, given that the UK has a leading role in research globally through well-established expertise in early-stage research and diagnostics, there is political and industry support for action, and the UK has championed much greater awareness internationally.

This report aims to map the extent of all AMR research activity in the UK, and discuss whether this is likely to be sufficient to meet the scale of the challenge. We map activity from two different perspectives; firstly by geographical region of the UK and secondly by products in different stages of development. We also discuss different R&D strategies.

We have engaged experts from academia, biotech, diagnostics companies, animal health, pharma, charities, and funders to ask whether the current level of activity is sufficient. The consistent answer was 'no', although experts recognise the progress that has been made on reducing unnecessary use of antibiotics (stewardship), raising awareness at the global level, and the importance of commitments by the UN and industry through the Davos Declaration. We include analysis of the level of investment available for R&D in anti-infectives in parts of the UK, which also shows a gap between this and other disease areas.

The report goes on to examine what more can be done to support R&D. We discuss the various interventions available and finally, we make recommendations about what can be done in the UK to make significant progress. Our recommendations are split into funding and other areas.

Summary of recommendations

There are a number of ways to address the gap in funding and in enablers of R&D. In the short term, UK public funders should make R&D in antibiotics a priority for funding as part of an industrial strategy for UK life sciences and the broader review of opportunities to maintain and grow UK life science in the wake of the result from the 'Brexit' referendum.

Specific funding measures which could make a significant difference would include:

1. **Increasing R&D investment** to leverage public-private financing models such as the Dementia Discovery Fund approach
2. **Delivering on existing commitments** such as the $2bn Global Innovation Fund proposed by Lord O'Neill
3. **Implementing new commercial models** to derisk the commercial uncertainty for

antibiotics and 'pull through' products, for example through an insurance-based model that delinks revenues and sales volume

4. **Joining up funding streams** and initiatives in the UK and globally to create a coherent end-to-end funding solution in AMR across public and private sources
5. **Funding to cover the whole range of R&D strategies**, including novel antibiotics, vaccines, investigations into technology that combines old antibiotics with resistance breakers, combining existing antibiotics for clinical efficacy, and protecting those existing antibiotics through better diagnostics.

Addressing AMR isn't just about finding the money; it's about solving the other issues that are currently standing in the way of progress. These include:

1. **Tackling hospital-acquired infections**, by improving awareness, clinical microbiological testing, and identifying combination antibiotic therapies for patients at particular risk
2. **Increasing uptake of Point of Care diagnostics** in the hospital and primary care setting
3. **Reviewing the regulatory framework** for novel antibiotics. For example, more use could be made of accelerated development programmes to bring new products to market faster and therefore reduce cost. Consider a patent pause where manufacturers could pause the period of exclusivity and restart the patent period again when demand has increased. There is also a case for new antibiotics to be licensed more flexibly on a pathogen rather than indication basis, given that a new compound might prove to be effective for a number of conditions, caused by a common pathogen. This would enable the drug to be used more effectively in hospitals
4. **Developing a comprehensive skills strategy** to manage the gap in expertise that has emerged over the last 20 years e.g. through industry/academia secondments, mentoring programmes and incentives to attract and retain PhD level researchers into anti-infectives research
5. **Improving surveillance data** across the UK and globally in order to better understand the spread of resistant strains
6. **Raising awareness** of AMR impact in other disease areas. Many large charities in other disease areas do not understand how the disease they focus on is affected by AMR. For example, patients with cancer can die from infection due to the lack of new antibiotics, even though there may be an effective treatment for their underlying cancer
7. **Improving stewardship** in the UK and globally to preserve the effectiveness of our existing antibiotics including usage in animal health and agriculture. This includes appropriate prescribing, reducing use and patient education.

AMR has potentially catastrophic global consequences. The action taken thus far has been insufficient to turn policy commitments into action on the ground, and the current level of available funding will not be enough to make significant progress. More needs to be done, quickly, and internationally. The UK has both the scientific infrastructure and the necessary skills and expertise to make a significant contribution.

The current situation

The pressing need for new antibiotics

Since the discovery of penicillin in 1928, antibiotics have allowed the world to treat and prevent diseases that had previously been fatal. Antibiotics have become the backbone of modern medicine and are one of its most widely used products.

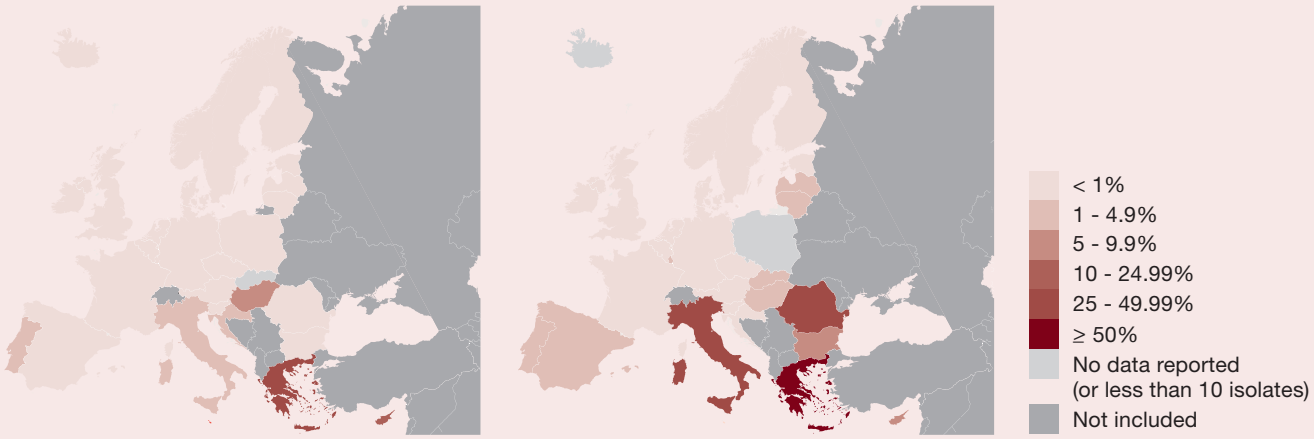
However, antibiotics are becoming less effective as bacteria evolve and develop antibiotic-resistant strains. The antibiotics of last resort are now under threat, raising the prospect that 'superbugs' such as *MRSA*, *C.difficile* and *E.coli*[2] will become untreatable, even by the strongest antibiotic currently available. At the same time, the risk of infection could make it too risky to carry out either routine or life-saving surgical and medical procedures, including chemotherapy, organ transplants, and Caesarian births. In UK hospitals, for example, patients with cystic fibrosis can be refused lung transplants if they carry resistant strains of bacteria, because of the high risk of infection following the operation. In fact, it's impossible to underestimate the long-term consequences of what the Director-General of the World Health Organization has called a 'slow-motion tsunami'.[3]

To take just one example, the chart below shows the worsening trend in Carbapenems resistance. Carbapenems are generally considered the most reliable treatment for multi drug resistant bacteria in hospitalised patients. However the charts below show resistance in Europe from 2010-2014 against *Klebsiella pneumoniae* and also the high variation by country (ranging from 0% to 62% of samples tested).[4]

Worsening Carbapenems resistance in Europe, (2010-2014)

Proportion of Carbapenems resistant *Klebsiella pneumoniae* isolates in participating countries 2010

Proportion of Carbapenems resistant *Klebsiella pneumoniae* isolates in participating countries 2014



Source: European Centre for Disease Prevention and Control (ECDC)

10 million
lives could be lost every year by 2050

at a cumulative cost of
100 trillion dollars

700,000 people
are already dying of resistant infections every year

> ***We are in the biggest crisis that modern medicine has faced … We have to effectively replace 200 antibiotics. There is no other area of medicine that is even approaching this level of disaster.***
> **CEO, Biotech**

And as the graphics show, the price to be paid across the world, both in premature deaths and economic costs, can only escalate. The review of the problem led by Lord Jim O'Neill estimated that 10 million lives could be lost every year by 2050, at a cumulative cost of 100 trillion dollars to world GDP. 700,000 people globally are already dying of resistant infections every year, and the greatest impact is and will be on low and middle-income countries.[5]

Why is this happening? A combination of over-use and misuse is one major factor. Up to 50% of antibiotics are poorly prescribed or misused[6], and the widespread use in global agriculture, especially poultry and pig-farming, could also be contributing to increased levels of resistance. And bacteria continue to evolve, which means antibiotics must evolve to match them.

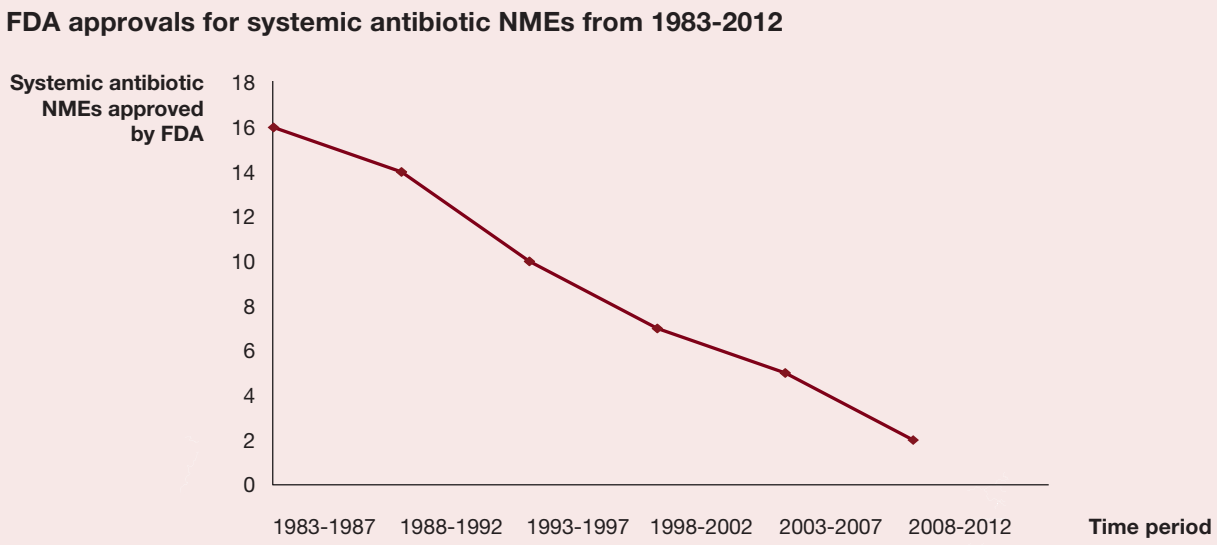
> ***The fact of the matter is that we are running out of antibiotics [and] people are dying. … What is going to end modern medicine is the lack of availability of antibiotics and that is going to happen big time.***
> **CEO, Biotech**

Where are the new antibiotics?

There are three drivers of life sciences research: medical need, commercial return, and scientific feasibility. In the case of antibiotics, there is no question of the scale of the medical need; the barriers are in the second and third criteria.

- **Commercial returns**: Current commercial returns simply aren't great enough to justify the R&D expense involved: it can take $2.6bn and around ten years to take a new compound to market launch.[7] And once on the market, antibiotics sell at a relatively low price compared to other therapies. Furthermore, sales volumes will probably be low because doctors are likely to be sparing in prescribing new antibiotics, to reduce the spread of resistance and ensure there is a drug of last resort. Taking all this into account, our analysis has shown that the sales of any new broad-spectrum antibiotic would not cover its development costs for almost a decade. It is no surprise, therefore, that pharma companies do not see this as an attractive area for investment, and the number of antibiotic new molecular entities (NME) registered has declined.

The number of NMEs registered with the Food and Drug Administration (FDA) in the 1980s compared to today



Source: FDA, Strategy& analysis

We have [had] a gap in antibiotics [R&D] for about 30 years. There needs to be an awful lot of basic research at the academic level before we even get to translational stage.
CEO, Biotech

- **Scientific feasibility**: Not only is it commercially unattractive to develop new antibiotics, it is also very hard to do. Across all disease areas, only 1.5-3.5% of the compounds identified during the early research phase ever make it onto the market. This – combined with a lack of investment – is the main reason why there have only been two genuinely new classes of antibiotics in the last 30 years, cyclic lipopeptides and oxazolidinones, and even these are not effective against 'Gram-negative' bacteria – the most resistant type. The experience of GSK is instructive here; between 1995-2001 they conducted extensive analysis of 67 potential targets screened against between 260,000 and 530,000 compounds in the SmithKline Beecham (now GSK) compound library. This generated a mere 5 leads, which was 4 or 5 times lower than average success rates at this time in other disease areas. Furthermore the leads were either toxic or ineffective against the most important infections (Gram-negative and Gram-positive). The whole process took 7 years but GSK were no nearer to finding a viable new antibiotic.[8]

Growing awareness – but a lack of action

In recent years, the world has become far more aware of just how serious the threat of antimicrobial resistance has become. There has been a Davos Declaration signed by 98 international pharma and biotech companies as of April 2016, and in September 2016, 193 countries signed a UN Declaration in support of concerted action at both government and industry level. The UK has also launched the Fleming Fund, which will develop AMR surveillance in low and middle income countries – to increase global understanding of the issue. The years of awareness-raising efforts led by the UK's Chief Medical Officer Dame Sally Davies, and Lord Jim O'Neill, the former Treasury Minister have been a significant driver of global action.

> ***"From a broader perspective the UK is doing fantastically due to the leadership of Dame Sally Davies and getting this taken forward internationally.***
> **Global research funder**

However, we have reached the point where awareness – certainly among policy-makers and practitioners – is no longer the issue. The issue is translating that awareness into action. There is a WHO Action Plan on Antimicrobial Resistance as well as the UN Declaration and a UK Five Year AMR Strategy, but thus far, little practical action is yet underway. As Margaret Chan, Director-General of the WHO, has said, doctors need to

change the way they prescribe, backed up by more effective tests; consumers need to be better informed, and more responsible; the global food industry needs to reduce its massive use of antibiotics, in both animal husbandry and agriculture. And most importantly of all, scientists need to find the new compounds that will get the world back to where it was in the 1960s.

In the rest of this report we look at ways this might be achieved, with a focus on one key aspect of the problem: the development of new antibiotics.

The purpose of this report

As already discussed, tackling antimicrobial resistance needs a co-ordinated effort – not just across the world, but across different stakeholders, from government policy-makers to the public, private and philanthropic funders of research, and between the different players within the pharmaceutical and life sciences industry. That basic principle informs the rest of this report. We will, nonetheless, focus specifically on the UK. This is a good place to start, given that the UK is already a world leader in early-stage research, there is a growing not-for-profit sector, political and industry support for action, and the UK has championed much greater awareness internationally.

With this in mind, this report will map the extent of R&D activity in the UK, and discuss whether this is likely to be sufficient to meet the scale of the challenge. We will also examine the various interventions available, given the scarcity of investment funding and limitations on capacity. And finally, we will explore how much more will be needed to make significant progress.

To compile the activity map we have performed desk-based research on organisations conducting or funding AMR R&D. We have reviewed grant awards from major funders in this area, and we have used our existing knowledge and internet searches of key words such as 'research into antimicrobial resistance/AMR', 'Funding awards for antimicrobial resistance/AMR', 'biotech antimicrobial resistance/AMR', 'academic research into antimicrobial resistance/AMR' and more, to compile the list. Finally we have consulted experts to identify any gaps and discuss solutions. It should be noted that despite these endeavours, it is possible that we have not captured all the activities underway in the UK.

> ***The UK has raised this as a priority for global action so therefore it is right that we shoulder the responsibility to demonstrate action.***
> **CEO, Industry Association**

> ***The number of UK scientists who have won the Nobel prize per capita [is higher] than anywhere else in the world. We are very innovative.***
> **CEO, Biotech**

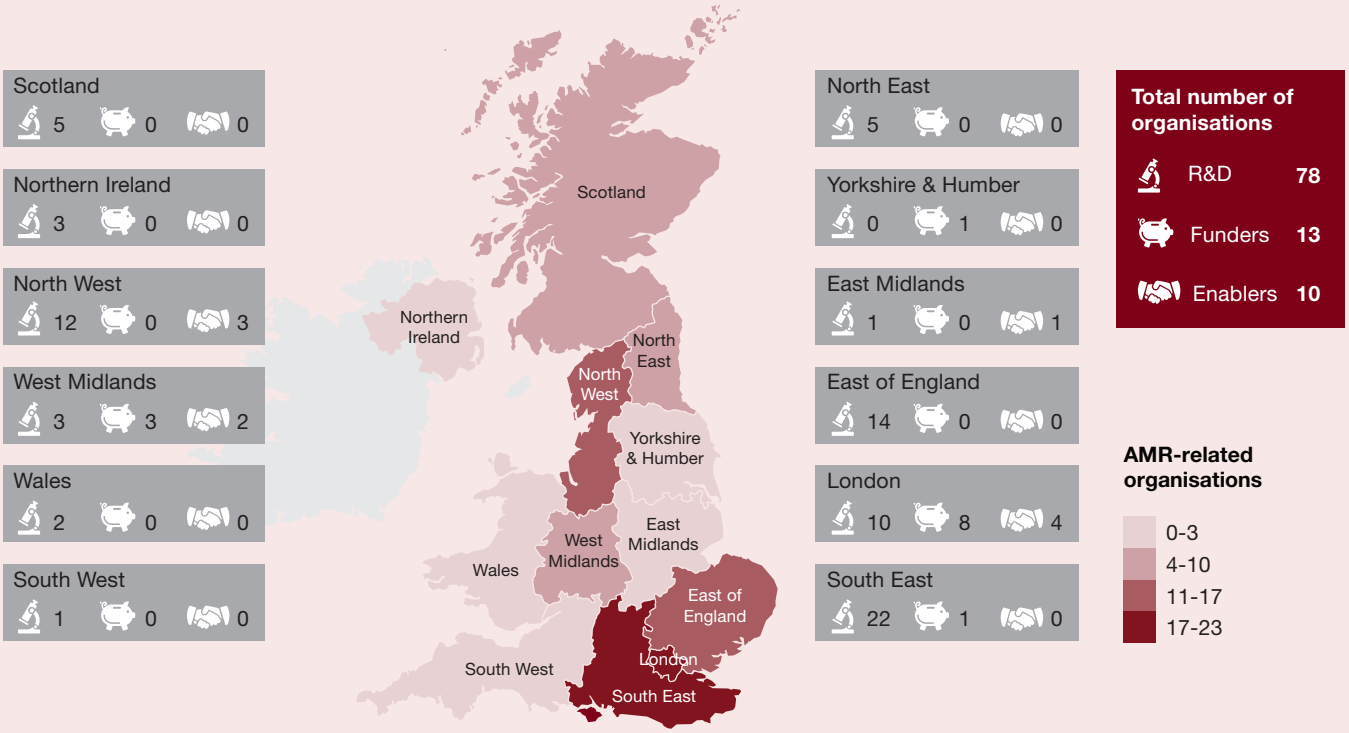
AMR Research & Development in the UK today

The research and development process involves academics, biotech organisations, diagnostics companies, contract research organisations, microbiology labs, medical research charities, and pharmaceutical companies. But all of these organisations need funding, investment, collaborative partnerships, and the right environment to have any chance of success. We will start by discussing R&D activity in the UK, before we move on to discuss funding sources and wider activities that contribute to the AMR landscape in the UK today.

In general, the UK has a strong scientific base and there are active organisations across all stages of R&D. As the map shows, there are 101 organisations working on antimicrobial resistance, of which 78 are engaged in R&D (51 being in drug development), and 23 are either funding that research, or enabling it.

UK geographical map of all AMR organisations

Map of UK organisations involved in AMR



Source: Strategy& analysis

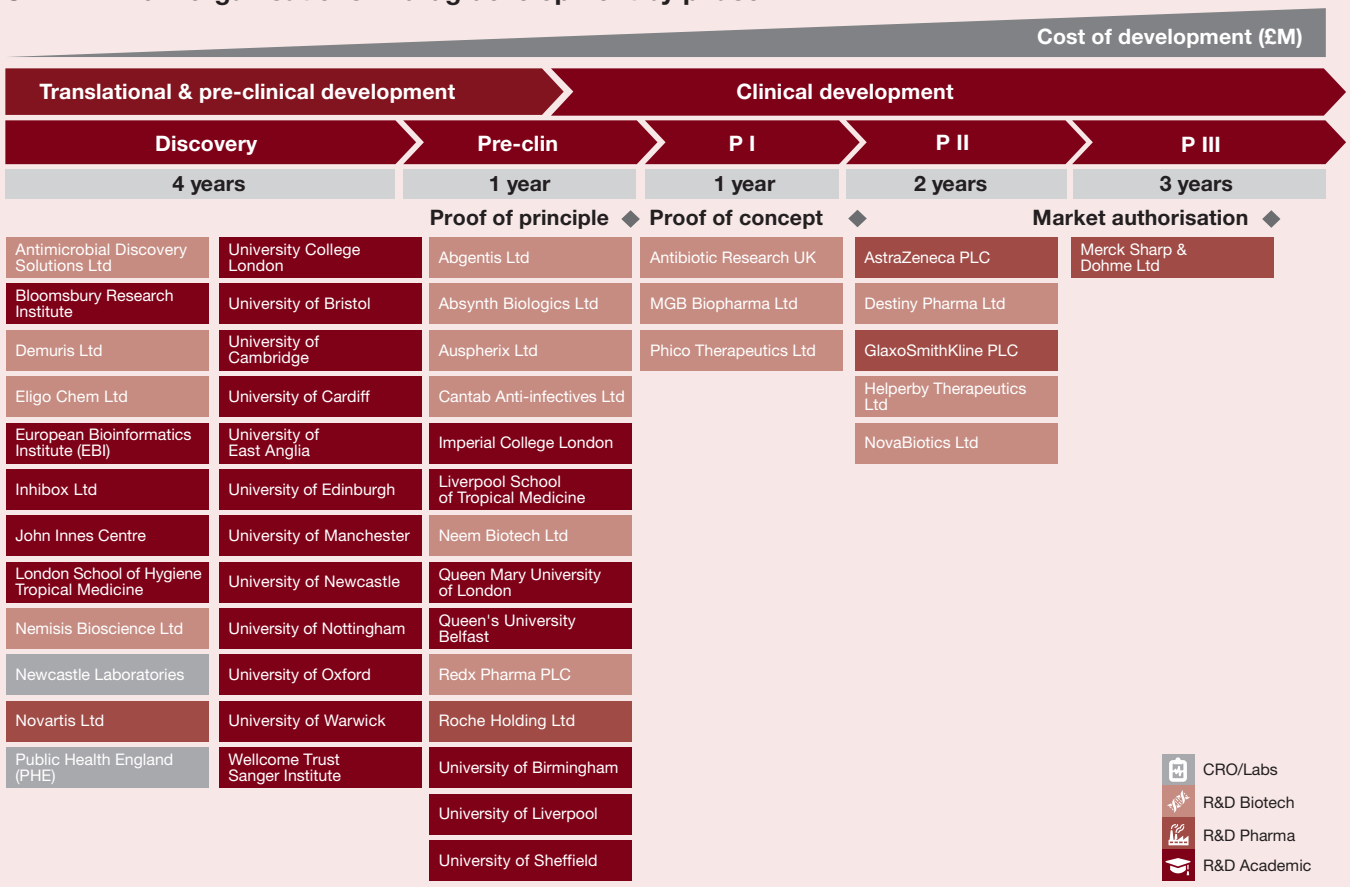
R&D Today

The development of a new drug entails different types of activity at each R&D stage:

- **Discovery research**: Universities and research institutes are typically involved in scientific discovery – this is the earliest stage of research. Microbiology laboratories and contract research organisations are also involved in this work.
- **Pre-clinical and Phase I**: Translating this 'discovery science' into a product that could be used in a clinical setting is usually taken forward by biotech organisations and some

Organisation by phase

UK AMR R&D organisations in drug development by phase



Note: Based on stage of development of lead candidate. We were not able to determine the R&D stage categorisation for the following organisations: Blueberry Therapeutics Ltd, Centauri Therapeutics Ltd, Discuva Ltd, Evotech Ltd and Fixed-Phage Ltd. Roche Holding Ltd is undertaking an early stage research partnership with Discuva Ltd in the UK. Merck Sharp & Dohme Ltd has a UK R&D facility focused on infectious diseases. Novartis Ltd has early stage research partnerships with academia in the UK. AstraZeneca PLC and GlaxoSmithKline PLC are headquartered in the UK and have products in late stage development. To note: AstraZeneca's assets are being acquired by Pfizer Inc. – this deal is in progress at time of publication. Antibiotic Research UK is a NFP funder and also conducts its own research.
Source: Strategy& analysis

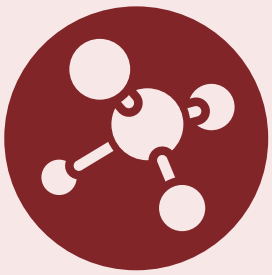
academic institutions. Biotechs work across the whole spectrum from preclinical to Phase I and II, and diagnostic development. Biotech companies are usually either spin-offs from universities, or start-ups led by scientists and business leaders from pharmaceutical companies. They are small in comparison to the mainstream pharma companies and they often cluster together in areas with access to skilled staff and world-class scientific facilities. That is certainly the case in the UK.

- **Late-stage development (Phase II and III)**: 'Big Pharma' tend to acquire products from biotech companies or enter a partnership with those companies to take the product through the most costly stage of development. Phase II and III clinical trials can involve thousands of patients across the globe. The global pharma companies are better placed to do this because they have a global reach, can spread development risk over a much broader portfolio, and benefit from stable investment flows.

In the UK there is 1 organisation with products in Phase III or earlier, 5 with products in Phase II or earlier, 3 in Phase I or earlier and 14 in preclinical. Early research is the most active area with 24 organisations.

With antimicrobial resistance research, a number of different R&D strategies are being followed. For example, organisations like Discuva Ltd and Redx Pharma PLC are trying to develop completely new therapies, while players like Helperby Therapeutics Ltd and charity Antibiotic Research UK (ANTRUK) are exploring the possibilities of combining old antibiotics with other molecules that act as a 'resistance-breaker', thereby restoring the efficacy of the existing drug. Absynth Biologics Ltd is taking another approach, involving the use of vaccines to prevent infection, which would not contribute to the spread of AMR. Likewise, diagnostics companies are developing new ways for clinicians to test patients and determine the cause of infections, which would ensure more effective use of existing antibiotics. Finally, some scientists, such as those at the NIHR Healthcare Protection Research Unit and at Newcastle Laboratories are exploring the potential efficacy of new combinations of existing antibiotics. Some patients who could not be treated elsewhere in the country have received life-saving treatment as a result.

Antibiotic Research UK



Antibiotic Research UK (ANTRUK) has been formed to take a Third Sector approach to tackling AMR through research, education and patient support

R&D strategy

As a not-for-profit it can take a unique approach to R&D, as intellectual property rights and return on investment are not the charity's drivers. ANTRUK's R&D strategy focuses on

1. Repurposing existing drugs as resistance-breakers; and
2. Examining combination therapy with two or more antibiotics targeting Gram-negative bacteria

R&D activity

To date ANTRUK has screened the entire pharmacopoeia and nutraceutical library against pan-resistant bacteria to the five major classes of antibiotics

> ***The charity's first research programmes are focussed on resistance-breakers since we believe these could provide a quick win in our search to find new antibiotic therapies.***
> **Prof Colin Garner, Chief Executive, ANTRUK**

Newcastle Laboratories

Newcastle Laboratories offer clinical analytical services and diagnostics testing to Newcastle Hospitals, GPs, NHS laboratories, private hospitals and other healthcare organisations

R&D strategy

Their AMR research focus is on rapid detection of AMR and screening of patients, as well as developing antibiotic combinations

R&D activity

Newcastle Laboratories provide one of the most comprehensive test portfolios in the UK, a one-stop shop for all Microbiology tests

- They receive samples of resistant isolates across the UK (and the world) and test them using novel agents alone and in combination with other antibiotics infections

> ***We have a wealth of expertise in the UK but there is insufficient testing. We could do more but the funding holds us back. We have a lung transplant centre and have been able to treat patients who carry resistant pathogens and have been denied transplants elsewhere.***
>
> **Prof Kate Gould, Lead Public Health Microbiologist, Newcastle Laboratories**

Discuva Ltd

Cambridge-based drug discovery company focused on the creation of next generation targeted antimicrobials against new emerging and drug-resistant bacterial pathogens

R&D strategy

Discuva's approach seeks novel compound classes which have a narrower bacteriocidal spectrum of activity, and so increases the potential number of bacterial targets available and ultimately reduces the risk of cross-resistance in the clinic

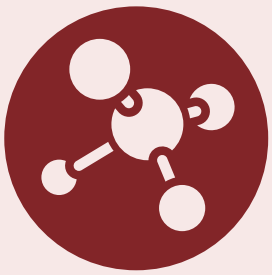
R&D activity

Discuva has several specific antimicrobial programmes mainly focused on Gram-negative bacteria that cause major hospital and community-based infections

- Discuva's proprietary platform technologies, known as SATIN and SILK, allow scientists, using sophisticated molecular network analysis, to select, optimise and develop chemical compounds through to antibiotic drugs based on their molecular targets and resistance mechanisms

> ***We want to be the antibiotics company, focused on no other therapeutic area apart from antibiotics … the challenge is to fund that activity.***
> **Dave Williams, Chief Executive Officer, Discuva Ltd**

Absynth Biologics Ltd



Absynth Biologics Ltd has been created with the initial goal of developing immunological prophylaxis and therapy to combat bacterial infections

R&D strategy

Their current strategy focuses on developing vaccines to prevent infection across vaccine pipeline programmes targeting S. aureus, *C.difficile* and S. pyogenes

R&D activity

The most advanced programmes target S. aureus including its more difficult-to-treat drug-resistant form, methicillin-resistant S. aureus (*MRSA*), which has had significant financial and human costs of in-patients compared to uninfected patients:

- 3 times the length of hospital stay (14.3 vs 4.5 days)
- 3 times the total charges ($48,824 vs $14,141), and
- 5 times the risk of in-hospital death (11.2% vs 2.3%)

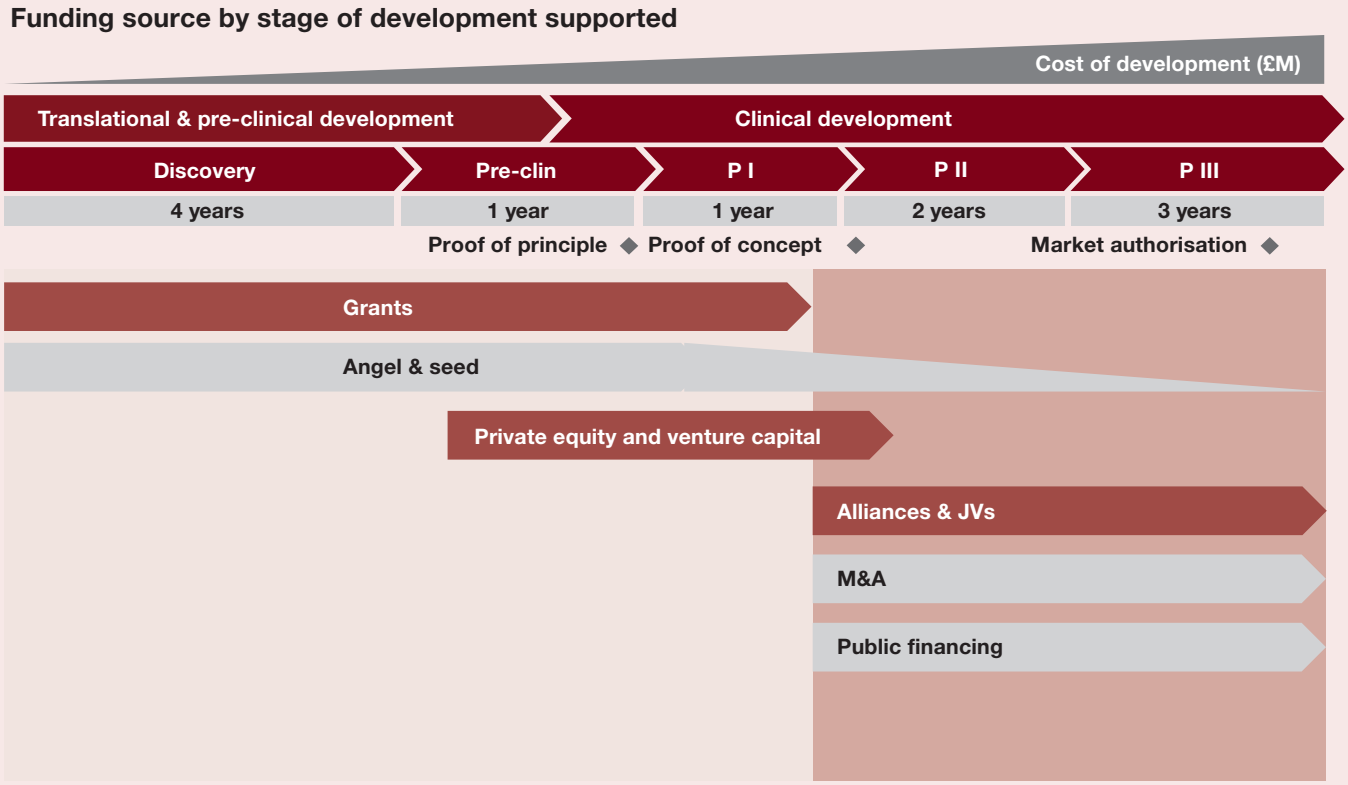
> ***A successful prophylactic vaccine should stimulate an immune response in a way that creates a memory so that when, in the future bacteria invade the bloodstream, the immune system reacts faster and stronger … we expect to be in Phase I in 2019. We need to be focused on investing in a more targeted way and to foster collaboration around translation.***
> **Dr Fiona Marston, Chief Executive Officer, Absynth Biologics Ltd**

Today's R&D funding

Turning to funding, there are currently different funding approaches depending on the stage of development a compound or product has reached. Public funding for the discovery stages of research tends to come from grant-making bodies like the Medical Research Council and the Biotechnology and Biological Sciences Research Council. Not-for-profit organisations such as the Wellcome Trust can also provide funding, as do government agencies like Innovate UK.

These organisations can also provide large grants to biotech companies and major research projects, but biotech organisations usually have to rely on investment from private investors like venture capital firms and private equity. As already discussed, corporate alliances are the most common form of financing in later stages of development, when the major pharma companies typically enter the development process.

Funding source by stage of development supported



Source: Strategy& analysis

In addition, the Longitude Prize is offering £10m of UK government money through Innovate UK and Nesta, to the team who can develop a new test for bacterial infections that would allow health professionals to identify the right antibiotics for each patient, thereby cutting down on unnecessary and ineffective use. Efforts like this have started to raise wider public awareness of the issue.

In addition, following Lord O'Neill's independent review into antimicrobial resistance he has stated the ambition to develop a $2bn global investment fund by 2020 to support the development of new drugs. The fund aims to leverage funding from public, private and not-for profit sources and to build international alliances – including funding from China.[9]

Selected current funding sources

Stage of investment	Funder	Examples of AMR funding commitments
Discovery	Public sector grant funders e.g. Research Councils, Innovate UK Not for profit organisations e.g. Wellcome Trust, Antibiotic Research UK	• Cross-Council Initiative c.£10m, BBSRC £4.5m fund for 6 large UK-China AMR research projects • £10m Longitude prize • 2004-2016 – £287m spent on AMR
Pre-clinical/Phase I-II	Public funders of translation, such as the NIHR, IMI	• NIHR AMR themed call across 8 research programmes with c.£20m in grant awards, HPRU centre investments in Oxford and London • IMI 700m Euros[10] ND4BBs programme (particularly ENABLE and COMBACTE workstreams) • CARB-X $250m, with additional match funding from the Wellcome Trust and AMR Centre
	Private investors e.g. private equity and venture capital firms	• Multiple investments made in small biotech firms specialising in AMR
Late stage	Corporate funding	• Large pharma funding their late stage development of some products e.g. GlaxoSmithKline PLC, Merck Sharp & Dohme Ltd, and AstraZeneca PLC

Source: Strategy& analysis

Today's R&D enablers

In the UK, there are a number of examples of collaborative partnerships that seek to share learning, skills, and talent to support the battle against AMR.

- *Public/Private Partnerships:* As already observed, bringing together many different stakeholders will be crucial in tackling AMR, including the public, private, and not-for-profit sectors. The AMR Centre at Alderley Park is an example of a joint private-public initiative to support and accelerate the development of new antibiotics and diagnostics. The centre will open in January 2017, and will offer facilities and resources to support testing, research, and analytics into tackling anti-infectives. Biotech firms and academics with new ideas will be able to access world-class skills to support their R&D from the pre-clinical stage through to Phase II.

- *Collaborative global partnerships*: Partnerships across the world are as important as partnerships across stakeholder groups. This is, after all, a global challenge. The new CARB-X initiative and the well-established IMI programme New Drugs for Bad Bugs (ND4BBs), are excellent examples of multiple countries coming together to pool ideas, research, scientific advice, and resources to tackle the problem. The programmes aggregate the available funding, and encourage collaborative working to accelerate new drug development. CARB-X will contribute funding with the cash match-funded by the Wellcome Trust, and resources available via the AMR centre.

- *Academic collaborations:* The National Institute for Health Research Health Protection Research Unit (HPRU) create centres of excellence in multi-disciplinary AMR research. A HPRU has been established to tackle healthcare associated infections and AMR that is being led out of Imperial College London in collaboration with the Wellcome Sanger Institute, North West London Academic Health Science Network and the Cambridge Veterinary School. A second HPRU involving the University of Oxford and Public Health England is focused on improving data linkage across hospitals for infectious diseases such as *C.difficile* and tuberculosis (TB) using genomic testing technologies.

> ***[The AMR Centre] can get so much more bang from our buck having an organisation with 80-100 staff than if ten organisations were taking on 15 staff each. It is basically economies of scale in translational R&D.***
> **Peter Jackson, CEO, AMR Centre**

The gap and ways to address it

Does the level of activity match the need?

Although the volume of research initiatives underway, and the number of organisations involved may seem positive, experts share the view that this is insufficient for the scale of the problem. Many suggest that a comparison of all the organisations and R&D activity across all disease areas would show that AMR is chronically underfunded.

The number of organisations often reflects the available investment. Progress has been made in securing new R&D funding for AMR since the O'Neill review. However, many industry participants believe that the money currently available is still nowhere near enough. Even CARB-X aims to get just six products to the clinic, and that's going to cost $250m of funding plus additional match-funding from its partners. As this suggests, there is a chronic gap between the need for funding, and the money available. And this is particularly worrying given how hard the scientific challenge is, and how many new compounds will be needed over time.

> ***"The UK needs to step up its game in terms of the level of funding given the cost of what they want to achieve. It's very welcome to have the funding going into the discovery end, but the expensive nuts and bolts of this game is getting things through translation and into the clinic."***
> **Biotech founder and CEO of AMR Public-Private Partnership**

Analysis of private investment in London and the South East alone has shown that investment in anti-infectives is significantly lower than in other areas like oncology, respiratory, cardiovascular, despite the fact that anti-infectives includes viral infections such as Malaria, Hepatitis, HIV and TB.

There is also the question of how available money is spent. Although the UK is known for having the best end-to-end R&D funding environment in Europe, the funding process is often disjointed, which means that research can get to a certain stage only to find there is no money to get it to the next point. This restricts the ability to make progress quickly: as one biotech CEO we interviewed for this report told us, "You can only move as fast as the amount of money you have."

Likewise, funding decisions and allocations can lack transparency or focus on only a narrow aspect of the challenge. Funders can lack the skills needed to identify the most promising proposals among competing bids. We know that existing funding for AMR is oversubscribed, and therefore prioritising scarce resource is vital.

Although the experts believe that R&D funding should be increased and optimised, R&D funding does not address the longer-term problem of insufficient commercial returns, even for successful compounds. In other words, 'push' funding from the public and private sector needs to be matched by 'pull' incentives for the pharma industry, to make it worth their while to take new compounds through the later stages of development and onto the market. The lack of commercial incentives inhibits the whole R&D cycle: fewer academics are inclined to work in the area, which means fewer new compounds, less funding for biotechs from private investors, and limited enthusiasm from pharma to enter partnerships with developers or acquire the underlying asset. We discuss potential 'pull' approaches shortly.

Finally, funding is needed to protect existing antibiotics, both through diagnostic development and investigating combinations that may be effective against resistant pathogens.

> ***I hope that a lot of money will come in. That will change this area from a backwater to where it needs to be – it must be the largest area of R&D spend on the planet.***
> **CEO, Biotech**

In addition to funding challenges, there is also a shortage of the right skills, which will only get worse over time. Although the UK can draw on a rich pool of scientific talent, many of the people with specific experience and expertise in antibiotic research are now either retired or

> ***Who in the UK has developed an antibiotic?***
> **CEO, Biotech**

> ***There has been no investment in pre-clinical people and facilities for 25-30 years. There just aren't the people around that have the experience of developing antibiotics through pre-clinical.***
> **CEO, Public-Private Partnership on AMR**

nearing retirement. The lack of funding over many years means there is a very limited pipeline of younger scientists to take their place.

Collaboration models remain important as a method of pooling our collective understanding and resources to find new approaches to solving the AMR challenge. For example lessons could be applied from the Structural Genomics Consortium open innovation collaboration model in Oxford.[11] The SGC makes all reagents available to academia, biotech and pharma, in order to facilitate science and thereby drug discovery. They are working with c.250 academic labs and c.10 pharmaceutical companies only on novel human proteins considered to be difficult or intractable.

Also public-private partnerships and private ventures between innovative companies allows organisations to pool risk and share rewards. For example programmes such as Medicines for Malaria Ventures (MMV)[12] combines public and private funding with 400 pharmaceutical and academic partners to fund Malaria research. This effort has successfully brought 9 new products to market since it was established in 1999. Collaborations such as MMV enable a more active sharing of knowledge between different organisations, in different markets, and at different stages of the R&D cycle, from universities, to biotech firms, to large pharma.

Furthermore, the pioneering partnership between Oxford University, Cambridge University, Imperial College London, King's College London, and University College London, has led to promising new drugs candidates to treat HIV, which none of the institutions could have achieved alone. The partnership was facilitated by the National Institute for Health Research.

Models like these could place a similar role in tackling antimicrobial resistance. There has already been some progress in this area, and as a leading academic told us, "The UK is doing well at linking up the disparate groups into effective consortia."

Still more progress could be made by finding better ways to exploit the existing 'bioclusters', or new virtual and physical ways to connect them. This needs to be combined with a concerted campaign to recruit and develop PhDs, as well as experienced and promising research scientists, who can take this work forward. We need to inspire them with the scale of the opportunity to make a major difference.

How can we bridge the gap?

There are a number of ways to address the gap in funding and in enablers of R&D.

Specific funding measures which could make a significant difference would include:

1. **Increasing R&D investment** to leverage public-private financing models such as the Dementia Discovery Fund approach
2. **Delivering on existing commitments** such as the $2bn Global Innovation Fund proposed by Lord O'Neill
3. **Implementing new commercial models** to derisk the commercial uncertainty for antibiotics and 'pull through' products, for example through an insurance-based model that delinks revenues and sales volume
4. **Joining up funding streams** and initiatives in the UK and globally to create a coherent end-to-end funding solution in AMR across public and private sources
5. **Funding to cover the whole range of R&D strategies**, including novel antibiotics, vaccines, investigations into technology that combines old antibiotics with resistance breakers, combining existing antibiotics for clinical efficacy, and protecting those existing antibiotics through better diagnostics.

Addressing AMR isn't just about finding the money; it's about solving the other issues that are currently standing in the way of progress. These include:

1. **Tackling hospital-acquired infections**, by improving awareness, clinical microbiological testing, and identifying combination antibiotic therapies for patients at particular risk
2. **Increasing uptake of Point of Care diagnostics** in the hospital and primary care setting
3. **Reviewing the regulatory framework** for novel antibiotics. For example, more use could be made of accelerated development programmes to bring new products to market faster and therefore reduce cost. Consider a patent pause where manufacturers could pause the period of exclusivity and restart the patent period again when demand has increased. There is also a case for new antibiotics to be licensed more flexibly on a pathogen rather than indication basis, given that a new compound might prove to be effective for a number of conditions, caused by a common pathogen. This would enable the drug to be used more effectively in hospitals
4. **Developing a comprehensive skills strategy** to manage the gap in expertise that has emerged over the last 20 years e.g. through industry/academia secondments, mentoring programmes and incentives to attract and retain PhD level researchers into anti-infectives research
5. **Improving surveillance data** across the UK and globally in order to better understand the spread of resistant strains
6. **Raising awareness** of AMR impact in other disease areas. Many large charities in other disease areas do not understand how the disease they focus on is affected by AMR. For example, patients with cancer can die from infection due to the lack of new antibiotics, even though there may be an effective treatment for their underlying cancer
7. **Improving stewardship** in the UK and globally to preserve the effectiveness of our existing antibiotics including usage in animal health and agriculture. This includes appropriate prescribing, reducing use and patient education.

Dementia Discovery Fund

Set up in 2015, the Dementia Discovery Fund was set up with an initial $100m from both public and private investors

R&D strategy

- The fund provides financing to translate early-stage research into commercialised disease-modifying drugs for dementia patients
- Investment in two companies to date, with one receiving in excess of $29.5m
- Longer-term, strategically-focused fund to build substantial companies without excessive dilution of owner equity and its resultant impact on incentives

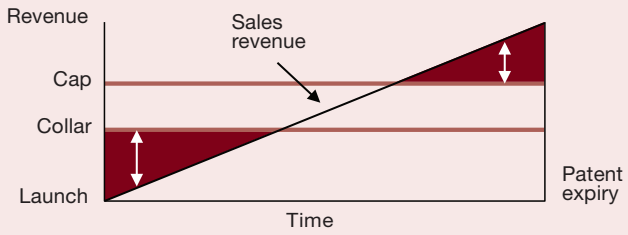
R&D activity

- Pioneering collaboration between charity, government, large pharma and private equity funds
- Mechanism to pool funding sources recognising the mutual interest in bringing new candidates through early stage development
- The limitation of the model is the attractiveness of the fund to pharmaceutical companies, given the business model failure

New commercial model: "cap and collar" to incentivise R&D

Overview

- New commercial models that de-link revenue from volumes. are needed to incentivise R&D in new drugs
- Health systems need new antibiotics, but will keep new antibiotics "on the shelf" to slow the spread of AMR



The cap and collar

- Under a cap and collar model pharma receive "top up" payments to achieve a pre-agreed level of return (the collar)
- If the return increases above an agreed level "the cap" due to increased resistance, pharma rebates the money back to the health system through a "gain-share" agreement

Conclusion

There has been significant political support to tackle AMR over the last five years, and the leadership of people like Dame Sally Davies and Lord O'Neill has made a significant contribution. Awareness has been achieved; commitments have been made. The challenge is to ensure that these are translated into practical action.

> ***We are on the forefront on proposing solutions but we haven't implemented much around the solutions.***
> **CEO, Biotech**

But doing this is a long-term task. In developing new antibiotics the world needs to think in terms of generations, not years. But across the world the current level of activity, and the available funding, are not enough to meet the scale of the challenge.

> ***The will and the capacity is there within the UK. Significant attempts have been made and large funding made available.***
> **Clinical microbiologist**

To summarise: AMR is a global problem, with potentially catastrophic global consequences. The UK has played a leading role so far, and done much of the necessary groundwork in terms of raising awareness and galvanising international consensus. This has been vital. But the action take thus far is inadequate, and the level of available funding will not be enough to make significant progress. More needs to be done, quickly, and internationally.

> ***Yes the UK should be doing more – but so should everyone else. [This is a] global problem and therefore a global solution is needed.***
> **CEO, Biotech**

Appendix

List of organisations involved in the UK R&D landscape

Abbott Diagnostics Ltd	R&D Diagnostics	Maidenhead	South East	www.abbottdiagnostics.com
Abgentis Ltd	R&D Biotech	Abingdon	South East	www.abgentis.com
Abingworth LLP	Funder Private Investor	London	London	www.abingworth.com
Absynth Biologics Ltd	R&D Biotech	Macclesfield	North West	www.absynthbiologics.co.uk
Accelerate Diagnostics Ltd	R&D Diagnostics	London	London	www.acceleratediagnostics.com
Agilent Technologies Ltd	R&D Diagnostics	Manchester	North West	www.agilent.com
Agricultural & Horticultural Development Board (AHDB)	Funder NFP	Coventry	West Midlands	www.ahdb.org.uk
Alere Ltd	R&D Diagnostics	Bedford	East of England	www.alere.com
Alpha Laboratories Ltd	R&D Diagnostics	Southamp-ton	South East	www.alphalabs.co.uk
Antibiotic Research UK (ANTRUK)	Funder NFP	York	Yorkshire & Humber	www.antibioticresearch.org.uk
Antimicrobial Discovery Solutions Ltd	R&D Biotech	Coventry	West Midlands	www.amrdiscovery.solutions
Antimicrobial Resistance Centre (AMR Centre)	Enabler PPP	Macclesfield	North West	www.amrcentre.com
AstraZeneca PLC	R&D Pharma	Cambridge	East of England	www.astrazeneca.co.uk
Auspherix Ltd	R&D Biotech	Stevenage	South East	www.auspherix.com
Becton Dickinson Ltd	R&D Diagnostics	Oxford	South East	www.bd.com
BioCity	Enabler Industry Body	Nottingham	East Midlands	www.biocity.co.uk
BioIndustry Association	Enabler Industry Body	London	London	www.bioindustry.org

Biomedical Catalyst	Funder Public Body	London	London	www.mrc.ac.uk/funding/science-areas/translation/biomedical-catalyst
bioMérieux Ltd	R&D Diagnostics	Basingstoke	South East	www.biomerieux.co.uk
Biotechnology and Biological Sciences Research Council (BBSRC)	Funder Public Body	Swindon	West Midlands	www.bbsrc.ac.uk
Bloomsbury Research Institute	R&D Academia	London	London	www.bloomsburyresearchinstitute.org.uk
Blueberry Therapeutics Ltd	R&D Biotech	Macclesfield	North West	www.blueberrytherapeutics.com
British In Vitro Diagnostics Association (BIVDA)	Enabler Industry Body	London	London	www.bivda.co.uk
Cantab Anti-infectives Ltd	R&D Biotech	Welwyn Garden City	East of England	www.cantabanti.com
Centauri Therapeutics Ltd	R&D Biotech	Sandwich	South East	www.centauritherapeutics.com
Cepheid Ltd	R&D Diagnostics	High Wycombe	South East	www.cepheid.com
Ciga Healthcare Ltd	R&D Diagnostics	Ballymena	N. Ireland	www.cigahealthcare.com
Demuris Ltd	R&D Biotech	Newcastle	North East	www.demuris.co.uk
Destiny Pharma Ltd	R&D Biotech	Brighton	South East	www.destinypharma.com
Discuva Ltd	R&D Biotech	Cambridge	East of England	www.discuva.com
Eligo Chem Ltd	R&D Biotech	Sandwich	South East	www.eligochem.com
Enigma Diagnostics Ltd	R&D Diagnostics	Salisbury	South East	www.enigmadiagnostics.com
European Bioinformatics Institute (EBI)	R&D Academia	Cambridge	East of England	www.ebi.ac.uk
Evotech Ltd	R&D CRO/Labs	Manchester	North West	www.evotec.com

GlaxoSmithKline PLC	R&D Pharma	London	London	www.gsk.com
Hain Lifescience UK Ltd	R&D Diagnostics	London	London	www.hain-research.com
Helperby Therapeutics Ltd	R&D Biotech	London	London	www.helperby.com
Imperial College London	R&D Academia	London	London	www.imperial.ac.uk
Imperial Innovations PLC	Funder PPP	London	London	www.imperialinnovations.co.uk
Inhibox Ltd	R&D Academia	Oxford	South East	www.inhibox.com
Innovate UK	Funder Public Body	Swindon	West Midlands	www.connect.innovateuk.org
Isohelix (Division of Cell Projects Ltd)	R&D Diagnostics	Maidstone	South East	www.isohelix.com
John Innes Centre	R&D Academia	Norwich	East of England	www.jic.ac.uk
Liverpool School of Tropical Medicine	R&D Academia	Liverpool	North West	www.lstmed.ac.uk
London School of Hygiene & Tropical Medicine	R&D Academia	London	London	www.lshtm.ac.uk
Mast Group Ltd	R&D Diagnostics	Liverpool	North West	ww.mastgrp.com
MedCity Ltd	Enabler Industry Body	London	London	www.medcityhq.com
Medical Research Council (MRC)	Funder Public Body	London	London	www.mrc.ac.uk
Medicines Discovery Catapult	Enabler NFP	Macclesfield	North West	www.md.catapult.org.uk
MGB Biopharma Ltd	R&D Biotech	Glasgow	Scotland	www.mgb-biopharma.com
Momentum Bioscience Ltd	R&D Diagnostics	Oxford	South East	www.momentumbio.co.uk
Merck Sharp & Dohme Ltd	R&D Pharma	Hoddesdon	East of England	www.merck.co.uk
National Institute for Health Research (NIHR)	Funder Public Body	London	London	www.nihr.ac.uk

Neem Biotech Ltd	R&D Biotech	Abertillery	Wales	www.neembiotech.com
Nemisis Bioscience Ltd	R&D Biotech	Cambridge	East of England	www.nemesisbio.com
Newcastle Laboratories	R&D CRO/Labs	Newcastle	North East	www.newcastlelaboratories.com
Northern Health Science Alliance (NHSA)	Enabler Industry Body	Manchester	North West	www.thenhsa.co.uk
NovaBiotics Ltd	R&D Biotech	Aberdeen	Scotland	www.novabiotics.co.uk
Novartis Ltd	R&D Pharma	Farnborough	South East	www.novartis.co.uk
OJ-Bio Ltd	R&D Diagnostics	Newcastle	North East	www.oj-bio.com
Oxford Biosystems Ltd	R&D Diagnostics	Oxford	South East	www.oxfordbiosystems.com
Phico Therapeutics Ltd	R&D Biotech	Cambridge	East of England	www.phicotx.co.uk
Public Health England (PHE)	R&D CRO/Labs	London	London	www.gov.uk/government/organisations/public-health-england
Qiagen Ltd	R&D Diagnostics	Manchester	North West	www.qiagen.com
QuantuMDx Group Ltd	R&D Diagnostics	Newcastle	North East	www.quantumdx.com
Queen Mary University of London	R&D Academia	London	London	www.qmul.ac.uk
Randox Laboratories Ltd	R&D Diagnostics	Belfast	N. Ireland	www.randox.com
Redx Pharma PLC	R&D Biotech	Macclesfield	North West	www.redxpharma.com
Renishaw Diagnostics Ltd	R&D Diagnostics	Glasgow	Scotland	www.renishaw.com
Responsible Use of Medicines in Agriculture Alliance (RUMA)	Enabler Industry Body	Worcester	West Midlands	www.ruma.org.uk
Roche Diagnostics Ltd	R&D Diagnostics	Burgess Hill	South East	www.roche-diagnostics.com
Roche Holding Ltd	R&D Pharma	Welwyn Garden City	East of England	www.roche.co.uk

Royal Pharmaceutical Society of Great Britain-Antimicrobial Expert Advisory Group	Enabler NFP	London	London	www.rpharms.com
Sekisui Diagnostics Ltd	R&D Diagnostics	Maidstone	South East	sekisuidiagnostics.com
Siemens Healthcare Diagnostics Ltd	R&D Diagnostics	Farnborough	South East	www.healthcare.siemens.co.uk
SV Life Sciences LLP	Funder Private Investor	London	London	www.svlsa.com
SVB Financial Group	Funder Private Investor	London	London	www.svb.com
TCS Biosciences Ltd	R&D Diagnostics	Milton Keynes	South East	www.tcsbiosciences.co.uk
The British Society for Antimicrobial Chemotherapy (BSAC)	Enabler NFP	Birmingham	West Midlands	www.antibiotic-action.com
Thermo Fisher Scientific Inc	R&D Diagnostics	Basingstoke	South East	www.thermofisher.com
TwistDX Ltd	R&D Diagnostics	Cambridge	East of England	www.twistdx.co.uk
University College London (UCL)	R&D Academia	London	London	www.ucl.ac.uk
University of Birmingham	R&D Academia	Birmingham	West Midlands	www.birmingham.ac.uk
University of Bristol	R&D Academia	Bristol	South West	www.bristol.ac.uk
University of Cambridge	R&D Academia	Cambridge	East of England	www.cam.ac.uk
University of Cardiff	R&D Academia	Cardiff	Wales	www.cardiff.ac.uk
University of East Anglia	R&D Academia	Norwich	East of England	www.uea.ac.uk
University of Edinburgh	R&D Academia	Edinburgh	Scotland	www.ed.ac.uk
University of Liverpool	R&D Academia	Liverpool	North West	www.liverpool.ac.uk

University of Manchester	R&D Academia	Manchester	North West	www.manchester.ac.uk
University of Warwick	R&D Academia	Coventry	West Midlands	www.warwick.ac.uk
University of Newcastle	R&D Academia	Newcastle	North East	www.ncl.ac.uk
University of Nottingham	R&D Academia	Nottingham	East Midlands	www.nottingham.ac.uk
University of Oxford	R&D Academia	Oxford	South East	www.ox.ac.uk
University of Sheffield	R&D Academia	Sheffield	North West	www.sheffield.ac.uk
Wellcome Trust	Funder NFP	London	London	www.wellcome.ac.uk
Wellcome Trust Sanger Institute	R&D Academia	Cambridge	East of England	www.sanger.ac.uk
Woodford Investment Management Ltd	Funder Private Investor	Oxford	South East	www.woodfordfunds.com
Woundchek Ltd	Funder Private Investor	Skipton	North West	www.woundchek.com

Endnotes

* "2016 Global Innovation 1000 Study available at http://www.strategyand.pwc.com/innovation1000."

** "Antimicrobials include therapeutics designed to treat a wide range of infections caused by bacteria, viruses, parasites and viruses. In this report we refer largely to the challenges posed by the growing resistance to antibiotics for bacterial infections, although resistance to viral pathogens such as HIV and TB remains a growing health concern."

[1] "The Review on Antimicrobial Resistance available at https://amr-review.org."

[2] "http://www.nhs.uk/news/2013/03March/Pages/Superbug-threat-is-ticking-time-bomb.aspx."

[3] "http://www.who.int/dg/speeches/2016/antimicrobial-resistance-un/en/."

[4] "European Centre for Disease Prevention and Control (ECDC) available at http://ecdc.europa.eu/en/healthtopics/antimicrobial-resistance-and-consumption/antimicrobial_resistance/database."

[5] "Tackling Drug-resistant Infections Globally: Final Report and Recommendations, May 2016."

[6] "CDC available at http://www.cdc.gov/drugresistance/about.html."

[7] "Tufts 2014 Cost study of 106 randomly selected drugs that were first tested in human subjects anywhere in the world from 1995 to 2007 available at .http://csdd.tufts.edu/news/complete_story/pr_tufts_csdd_2014_cost_study."

[8] "Drugs for Bad Bugs: Confronting the Challenges of Antibacterial Discovery in Nature Reviews Drug Discovery 6(1):29-40 · February 2007."

[9] "https://www.gov.uk/government/news/uk-and-china-start-global-fund-to-tackle-drug-resistant-infections."

[10] "http://www.imi.europa.eu/content/nd4bb."

[11] "http://www.thesgc.org/scientists/groups/oxford/"

[12] "http://www.mmv.org/"

*Appendix list of experts interviewed as part of the report**

First name	Last name	Organisation
Anthony	Coates	Helperby Therapeutics Ltd
Chas	Bountra	Structural Genomics Consortium, Oxford University
Chris	Dowson	University of Warwick
Colin	Garner	Antibiotic Research UK (ANTRUK)
Dave	Williams	Discuva Ltd
David	Brown	Antibiotic Research UK (ANTRUK)
David	Roper	University of Warwick
David	Wareham	Queen Mary University of London
Doris-Ann	Williams	British In Vitro Diagnostics Association (BIVDA)
Fiona	Marston	Absynth Biologics Ltd
Harpal	Dhillon	Merck Sharp & Dohme Ltd
James	Anderson	GlaxoSmithKline PLC
John	Bell	University of Oxford
John	Fitzgerald	Responsible Use of Medicines in Agriculture Alliance (RUMA)
Kate	Gould	Newcastle Laboratories
Neil	Murray	Redx Pharma PLC
Pete	Jackson	Antimicrobial Resistance Centre (AMR Centre)
Steve	Bates	BioIndustry Association
Tim	Jinks	Wellcome Trust

*Please note the interpretation and conclusions of this report are PwC Strategy&'s alone.

About the authors

Jo Pisani
Pharmaceutical and Life Sciences Consulting Leader, EMEA

Jo Pisani is a partner with Strategy& in London. Jo has over 20 years pharma industry & consulting experience. She assists pharma and biotech, CMO, Government & CRO clients with strategy development, valuations & advice. Jo has led projects and thought leadership considering new commercial and innovation models, including structures to incentivise antibiotics R&D.

jo.pisani@strategyand.uk.pwc.com

Rachel Armstrong
Pharma and Life Sciences, EMEA

Rachel Armstrong is a manager in the Pharmaceutical & Life Sciences consulting practice. Rachel specialises in developing strategies for pharmaceutical companies. She previously spent over eight years in the UK civil service and held senior policy roles in the Department of Health and the (former) Department for Business, Innovation & Skills.

rachel.x.armstrong@strategyand.uk.pwc.com

David Weston
Pharma and Life Sciences, EMEA

David Weston is a Senior Associate in the Pharmaceutical & Life Sciences practice, with a special interest in R&D strategy and market access. Prior to joining PwC's Strategy&, David completed a doctorate in Neuroscience.

david.a.weston@strategyand.uk.pwc.com

Contacts

London

Jo Pisani
+44-20-7804-3744
jo.pisani
@strategyand.uk.pwc.com

Rachel Armstrong
+44-77-9048-3521
rachel.x.armstrong
@strategyand.uk.pwc.com

Strategy& is a global team of practical strategists committed to helping you seize essential advantage.

We do that by working alongside you to solve your toughest problems and helping you capture your greatest opportunities.

These are complex and high-stakes undertakings — often game-changing transformations. We bring 100 years of strategy consulting experience and the unrivaled industry and functional capabilities of the PwC network to the task. Whether you're charting your corporate strategy, transforming a function or business unit, or building critical capabilities, we'll help you create the value you're looking for with speed, confidence, and impact.

We are part of the PwC network of firms in 157 countries with more than 223,000 people committed to delivering quality in assurance, tax, and advisory services. Tell us what matters to you and find out more by visiting us at strategyand.pwc.com.

www.strategyand.pwc.com