

Open for Innovation

UK Biopharma R&D Sourcebook 2016



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excerpts from Developing talent and partnerships to create new medicines

* excerpts from The Changing UK Drug Discovery Landscape

+ excerpts from UK Participation in IMI



"In times of change learners inherit the earth; while the learned find themselves beautifully equipped to deal with a world that no longer exists."

Eric Hoffer, 20th century American philosopher and (I'm told) longshoreman, is credited with this clever insight. Others have

gone further to clarify what he means by a "learner" as opposed to the "learned". Apart from the obvious, I like one blogger's description that learners are "open to others' views"¹. The learner is someone collaborative and open in exploration and action.

As the UK prepares to embark on a new path outside of the EU, we will need plenty of learners and the best policies and resources to foster **open innovation**. 'Open Innovation' is a practice first coined by global management thinker, Dr Henry Chesbrough, in 2003². Henry was reflecting on a change in practice by firms in the way that they brought ideas in from outside to innovate and commercialise, as well as sharing ideas externally. This "outside in/inside out" flow of ideas was a contrast to previously closed R&D corporate labs. Regardless of when this practice started (we can find examples across history), for innovation in medicines, the practice has become ever more established and refined. Our 2016 ABPI report commissioned with consultancy TBR, *The Changing UK Drug Discovery Landscape*, documents how this practice has progressed in the UK, and signals how life science innovation in the UK provides a community of "learners" which should continue to be fostered³.

This is why '**Open for Innovation**' is our theme for this year's **UK Biopharma R&D Sourcebook**. The Sourcebook aims to provide a snapshot of some of the key measures by which our industry develops medicines and the context in which this takes place. We have these data grouped in four sections: **Global health and the role of biopharma**, **Investing in innovation**, **Driving clinical research to deliver medicines** and **Collaborating for innovation**. We plan to refine and extend this analysis over the coming years, and so we would welcome feedback on the data shared and the format for the report.

In addition to the core data sections, each year we invite essays from leading experts to contribute their **Viewpoints**. We are thrilled to have **David Roblin**, Chief Operating Officer and Director of Scientific Translation at the Crick, setting out their unique approach to open innovation, as well as **James Wilsdon**, Professor of

Research Policy at the University of Sheffield, exploring the policies and incentives that drive that elusive goal – academic-industry collaboration.

Each year, we will try and introduce new evidence and insights on specific themes that matter to the future for discovery and development of medicines. We hope you will find this year's edition a good read and a reason to come back for more.

Dr Virginia Acha

Executive Director, Research, Medical & Innovation,
Association of the British Pharmaceutical Industry

ABPI would like to thank Clarivate Analytics for their data and analysis used in the UK Biopharma R&D Sourcebook.

About Clarivate Analytics

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1. INTRODUCTION: OPEN FOR INNOVATION



Dr Neil Weir
Senior Vice President,
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The UK has a long tradition of acting as the world's crucible for new ideas in science and philosophy. When one walks through the capital cities of the UK, one gets a rich sense of the history of science,

where scientists and industrialists both clashed and came together to advance our technologies and our worldview. This is perfectly illustrated in the life sciences, where many of the medical interventions we use today trace their invention to a pioneer in the UK.

However, as any pioneer knows, the routes that brought you to where you are today may be very different to the ones you need to follow in the future. That has been the focal challenge for all biopharmaceutical companies over the past decade. We are embarking on new areas of science using the new tools of genomics, advanced analytical technologies and techniques, bioprocessing, bioinformation, gene editing and cell-based treatments. Although this is the frontier of science and failures have to be anticipated, the recent results in terms of new breakthroughs published and new molecular entities approved are reassuring. The number of new molecular entities approved by the FDA in 2015 reached a new high, with 45 new medicines approved in comparison with the average of 28 per year over the previous period, 2006 – 2014.¹ Of these approvals, over one-third were for medicines considered to be “first in class”, and nearly half were for treatments for rare disease.

These results are the fruits of scientific endeavour and investment to which our biopharmaceutical companies contribute substantially, both globally and in the UK. The

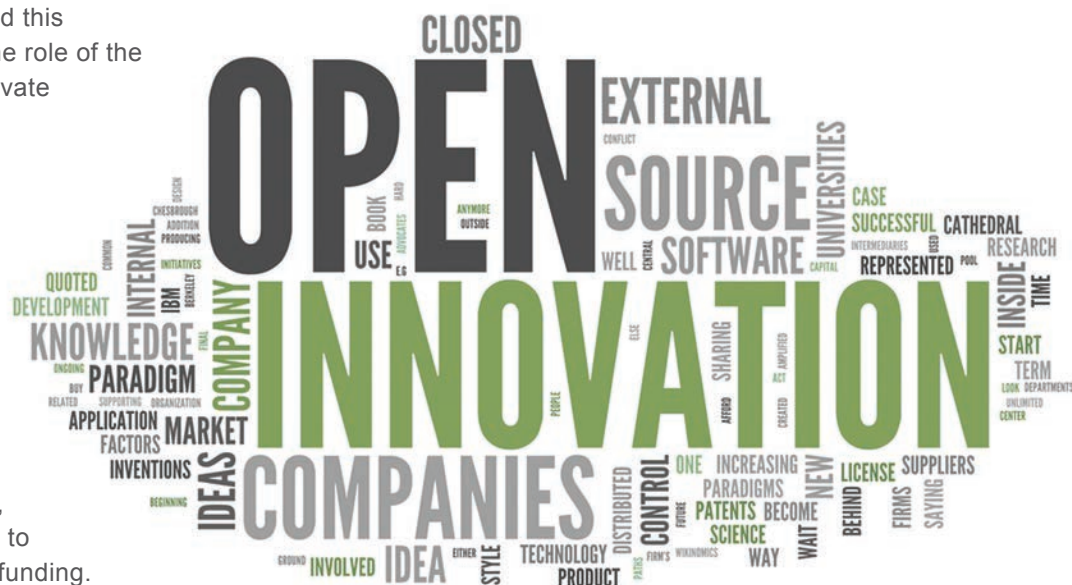
figures presented in this year's UK Biopharma R&D Sourcebook reveal increases in global R&D investment over the last decade - from USD \$108.1 billion in 2006 to \$149.8 billion in 2015² – whilst R&D in the UK by the biopharmaceutical industry had increased to £4.2 billion in 2015³, breaking the trend of recent years. However, this investment does not tell the whole of the story of the progress in the discovery and development of medicines that we have witnessed in these past years. Equally important is how we have changed how we innovate. Although the biopharmaceutical industry has a long history of collaboration with academia to advance our science and our treatments, we are witnessing both an increase in the scale of engagement as well as innovations in the modalities by which we engage. The ABPI recently published *The Changing UK Drug Discovery Environment* which highlighted that many biopharma companies have increased overall investment in discovery activities in the UK through a collaborative and sometimes “open innovation” approach, with over 60% increasing outsourcing and collaborative working over the past decade.⁴ The future for innovation in life sciences, here in the UK and globally, will depend on how well we continue to innovate and collaborate, and what it means to be “open”.



A vital element that has aided this collaborative innovation is the role of the Research Councils and Innovate UK, and the Government's commitment to them. For example, in the recent Autumn Statement the Government committed an additional £2 billion for R&D over and above previously announced funding, much of which will be available to the Research Councils and Innovate UK and will enable, as an example, Innovate UK to substantially increase grant funding.

This follows a previous announcement to extend the biomedical catalyst with an additional £100m until 2020-2021. The continued enhancement and evolution of the funding and capability within these organisations is a key element in a strong and vibrant ecosystem for life sciences innovation.

It is not all uniformly good news, however. Over the last ten years almost all large biopharmaceutical companies have significantly decreased their employment in in-house discovery in the UK. Since these companies have been shown to account for around 75% of all employment in the sector⁴ the impact of this loss is substantial. Indeed, more companies - particularly the biggest - have increased and prioritised R&D investment in the US and continental Europe, as well as new markets in Asia, when compared to the UK. This is a worrying trend for the future of UK medicines research, particularly relating to the training and development of the next generation of discovery scientists given the breadth and scale of research that larger companies have previously offered.



The Government has announced the intention to use the forthcoming industrial strategy to mark our path forward for the UK, particularly given the decision to leave the European Union. We believe that life sciences should be central to that industrial strategy, and that critical to that strategy will be an exploration about how the UK can be a global leader in the practices that will help us to be open for innovation, building on the strengths that we currently have whilst addressing some of the more concerning trends that recent data and reports point to. Some of the clues to how we might achieve this for the life sciences are found in the analysis presented in this Sourcebook, and we look forward to sharing our views on the shape of industrial strategy in the months to come.

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2. VIEWPOINT: OPEN SCIENCE, COLLABORATION AND ACCELERATED DEVELOPMENT: TRANSLATION AT THE CRICK



David Roblin
Chief Operating Officer
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Translation at the Francis
Crick Institute

London Zoo is a great place for a day out. But early last year, away from the animal enclosures and the tourists, it was the surprising setting for a very fruitful meeting indeed. We

had organised something approaching a match-making event for researchers from the newly formed Francis Crick Institute, a large biomedical discovery institute in London, and the pharmaceutical company GSK.

On both sides, the organisers had worried that speed-dating just wouldn't work. What would the researchers find to talk about, would they have anything in common, would they have anything interesting to say, would they even stay for long? I had maintained the need for an open meeting and so no confidential disclosures were in place.

We needn't have worried. It turns out many Crick researchers and GSK scientists have everything to talk about, have lots in common and want to share their different approaches and experiences. It has led to many new ideas for investigating the basic biological processes involved in disease. Over a glass or two of wine, we found soulmates, united in the desire to understand the basics of human health and disease better.

And so was born the Crick's first proper 'open science' partnership with a large pharmaceutical company. We're hoping there will be many more.

Fourteen joint projects are now underway with GSK in areas from HIV and malaria to cancer, with a further two projects being developed. These see Crick researchers working right alongside scientists from GSK in the lab every day – both at the new Crick laboratory in London and at GSK in Stevenage - sharing equipment, resources and expertise. GSK scientists are so embedded they are suggesting avenues for blue-sky exploration.

This open collaboration in early-stage research is one example of the way the Francis Crick Institute has placed an emphasis on 'translation' as a key strategic goal from the start.

The £650 million Francis Crick Institute, next to St Pancras in London, is the biggest biomedical research institute under one roof in Europe, perhaps the world. Research at the Crick aims to discover how and why disease develops in order to find new ways to prevent, diagnose and treat conditions such as cancer, heart disease and stroke, infections and neurodegenerative conditions like motor neurone disease.

I've been leading the development of the Crick's innovation strategy as Director of Scientific Translation, having had extensive experience in running research programmes for some of the largest pharmaceutical firms. My career has travelled from bedside in the NHS as a doctor through development and research in industry where I worked in Pfizer, Bayer and biotech to the bench at the Crick. A few ideas have moved in the opposite direction and become important medicines for patients; ciprofloxacin, moxifloxacin, selzentry, sildenafil and a few more still to come I hope.

In this role at the Crick I have turned from poacher to game-keeper! The UK is acknowledged to be world-leading in its bioscience research but really hasn't punched its weight in translating that into new treatments for patients, new companies, new investment and returns. This needs to change. We need to make the most of our outstanding science research and turn it into new health and wealth benefits for society.

At the Crick, we are pursuing an approach to translation that we think offers something new, offers the best chance of success in providing benefits to patients sooner and can play a role in demonstrating the way to boost innovation arising out of UK science.

It's based on three core principles: open science; accelerating the development of that science into "capable hands" where advanced testing can occur; and keeping patients at the centre of our work. I published recently on this ('The Francis Crick Institute: Scientific Discovery Open to Translation'. *Pharmaceutical Medicine*, 2016; 30(3), 133-135) but reflect further here.

Open science

Society needs better treatments for many pressing health conditions: cancer, neurodegenerative disease and dementia, autoimmune conditions and infectious disease. And it is the basic understanding of the science causing these diseases that is required in order to improve the success rate and speed of developing new treatments.

Through my career I've seen the pharmaceutical industry increasingly collaborating with academia to achieve a better understanding of the underlying biology of disease. Various models have been used in forming these research partnerships.

What we want to do at the Crick is to collaborate openly in the very earliest, pre-competitive stages of research. And we're finding companies are looking for the same and are very willing to form partnerships. It makes sense. It's at this stage that pharma and academia can bring their sometimes different but complementary approaches

and expertise together and make great strides in understanding the fundamental biology involved.

The idea is that only by working closely together will we know more about biological processes that can be targeted with treatment. This is best done - and has most chance of success - if the skills, talents and capabilities from both sectors are applied together in an open way, sharing knowledge.

At this early stage, it's first and foremost about making discoveries about the basic biology rather than filing patents, which usually comes somewhat later. It may be that new treatments could be developed from such work but this is somewhat downstream. That much later stage of research is where pharma and biotech companies come into their own, with their expertise in optimising compounds and taking them through clinical studies. Then we all benefit: the Crick will benefit from its involvement, the drug firm will benefit and in the future society will have better treatments available to it.



Accelerating development

The Francis Crick Institute is very lucky to have core funding from its founding partners – the UK Medical Research Council, Cancer Research UK, Wellcome, UCL (University College London), Imperial College London and King's College London.

This funding means we are better able to move potential innovations further along the path towards patients. By getting to a later stage of development and ensuring that the biology of disease is better understood before needing to find investment, this should increase the chances of success.

I believe that the current technology transfer approach taken by some other institutions can lead to a pressure to do deals early on, perhaps too early on when technologies are as-yet unproven. In addition there is a focus often on early value, with upfronts and early milestones. This is perhaps driven by the need to pay salaries and office costs of independent tech transfer organisations. This together creates a perverse set of incentives which has driven long and time-consuming negotiations.

The Crick's dedicated funding and long-term view means scientists can get on with experiments that provide confidence in a concept instead.

Discoveries can be accelerated further towards clinical studies, learning from each round of research, without feeling investment deals need to be done to suit short-term needs and incentives. So, deals can come later with late milestones and royalties. Our focus is acceleration into the most capable hands, rather than the deal with the highest up-fronts.

The Crick has established a programme to identify a pipeline of research projects ripe for translation. Seed funding from the Medical Research Council is available to carry out pilot investigations. Research group leaders work with the Crick's translation team and submit proposals which are reviewed by a translational advisory group. Some are selected to go forward, others with potential continue to be monitored or developed. Nine projects are currently underway with a further four projects in cancer, malaria and tuberculosis being developed.



Patient benefit

Of course in translation and innovation, there is still one aim: to improve outcomes and quality of life for patients.

I strongly believe that clinical insight – from doctors and patients – is key for progress. For me, translation isn't just the way in which discoveries in the lab become developed into safe and effective new therapies for patients. The process also works in the other direction too, with clinical and patient insight informing basic science in the laboratory – a truly two-way process.

So at the Crick, we are making moves to increase the clinical expertise we have available. Many of our partnerships with the London universities of UCL, Imperial and King's involve working with clinicians. Peter Ratcliffe, our Clinical Research Director, is overseeing the support for clinical academic training provided by the Crick. And we aim to recruit more research group leaders with a clinical background.

We are also looking to carry out more research in human cells and tissues. This is because there is evidence that higher probability of getting to later stage clinical trials goes hand in hand with studies involving the human organism! So having evidence and confidence that the putative drug target or pathway is important in human disease is very important and all efforts should be made to achieve this as early as possible.

Spinout investments take research closer to the clinic

If a biological discovery in the lab is to be developed into a potential new treatment or diagnostic test, it'll need to be optimised and validated before it gets near a patient and clinical trials. That needs significant investment, of course, and one of many ways to achieve that is by forming a new company to develop the technology.

In the autumn, the first spinout companies were launched based on research by Francis Crick Institute scientists.

Achilles Therapeutics is a new company formed by Syncona LLP and Cancer Research Technology with backing of £13.2 million. It brings together research by scientists from the Francis Crick Institute and UCL (University College London) which was funded by Cancer Research UK and the National Institute for Health Research (NIHR).

Charlie Swanton and colleagues discovered unique markers that are present on the surface of all cancer cells in an individual patient's tumour, but not on healthy cells. These markers, or 'truncal tumour neo-antigens', can act as flags to the immune system. Achilles Therapeutics will design lung cancer therapies that target these markers with the aim of destroying tumours without harming healthy tissues.

It could provide a personalised approach to lung cancer therapy, targeting markers that are present on all the patient's cancer cells rather than just a subset of cells. That would make it far less easy for the cancer to escape or become resistant to the treatment.

The second Crick spinout is GammaDelta Therapeutics. Co-founded by Adrian Hayday and Oliver Nussbaumer at King's College London and the Francis Crick Institute, the company aims to exploit the unique activities of gamma delta ($\gamma\delta$) T cells that are found in the body's tissues where cancers and inflammatory diseases take hold. It has received seed funding from the life sciences investment group Abingworth, as well as support from Cancer Research Technology (CRT), King's College London and the Francis Crick Institute.

A culture of success

So the Crick is making progress. But we think there is yet another element that is important to creating success. And that is about getting the culture of an institution right.

To that end, a translation team has been appointed to put the support in place at the Crick for all these efforts. A Translation Advisory Group has been formed with a number of external experts and entrepreneurs in residence to help spark interest and run sessions for PhD students, postdocs and other interested scientists.

And when there are lots of examples of success for other researchers at the Crick to follow, this culture, this entrepreneurial mind-set, will become self-sustaining.

Will it work?

What will the upshot of all this be? Will our approach based on collaboration and open science lead to new ideas and opportunities to pursue? Will developing potential new therapeutics further, faster make them any better investments? Will placing insight from patients and the clinic at the centre of what we do increase the chances of success?

I firmly believe so. But in many ways the experiment is just starting and only time will tell. The Crick is open, the researchers have moved into the new building and the first partnerships and spinouts have been established. We'll learn the outcome in due course and promulgate; we have a role in describing experiments in the way science is done as well as the science itself.

What I do know is: we provide an excellent basis for innovation. The Crick has world-leading science and great research partnerships, and is an attractive offer to investors. There is no shortage of ideas and projects here. We will be judged in the end on the breakthroughs in science we achieve and through delivering new therapies with real benefit for patients. After all, that is why we do all of this.

David Roblin

2. VIEWPOINT: BROKERS AND BOUNDARY SPANNERS: WILL THIS BE THE YEAR THE UK GETS SERIOUS ABOUT COLLABORATIVE SCIENCE AND INNOVATION?



James Wilsdon

Professor of Research Policy and Director of Impact and Engagement in the Faculty of Social Sciences at the University of Sheffield, and chair of the Campaign for Social Science.

He is on Twitter @jameswilsdon

For a group of people dedicated

to the pursuit of breakthrough ideas, the UK's research community can be surprisingly conservative. There is a tendency among our leading universities, national academies and business groups to favour incremental tweaks over radical upheaval of the policies and structures for research funding and collaboration. Disruptive change seems to occur no more than once in a generation.

So in 1965, the Science and Technology Act established the procedures for creating research councils by Royal Charter, as a contribution to Harold Wilson's ambitions for the "white heat of the scientific and technological revolution". In 1993, William Waldegrave as science minister published the *Realising our Potential* White Paper, which called for new partnership between public and private research, and the establishment of six new research councils.

And we're now in a moment of equivalent – perhaps greater – change. The Higher Education and Research Bill – currently making its way through Parliament – will draw all seven research councils, Innovate UK and HEFCE's quality-related funding under the new strategic umbrella of UK Research and Innovation (UKRI).

Informed by Sir Paul Nurse's review of the research councils, and Lord Stern's review of the research excellence framework, this nine-headed hydra will formally spring into life in April 2018. But detailed work is already underway to ensure that it delivers the step change in UK research and innovation performance that Jo Johnson MP, as minister for universities and science, and Sir John Kingman, as inaugural chair of UKRI, have promised.

Collaboration and cross-disciplinarity lie at the heart of the vision for UKRI, which the Government describes in terms of six objectives:

- a greater focus on cross-cutting issues that are outside the core remits of the current funding bodies, such as multi- and inter-disciplinary research;
- a strengthened, unified voice for the UK's research and innovation system;
- improved collaboration between the research base, business and the commercialization of discoveries;

- better mechanisms for the sharing of expertise and best practice – for example, around management of major projects and large capital investment;
- more time for research leaders to focus on strategic leadership through the centralisation of back and middle office functions; and
- improved quality of evidence on the UK's research and innovation landscape through the pooling of multiple datasets.

Elsewhere, Sir John Kingman has spoken about the new funding agency as "nine brains in one body". However, while UKRI's objectives are laudable, there was – until recently – a nervousness in some quarters that they could be realised against the backdrop of largely flat budgets (with the exception of the Global Challenges Research Fund, which will inject an extra £1.5 billion of DfID money into development-linked research by 2020). The grinding uncertainties of Brexit have added to the downbeat mood, casting a shadow over the prospects for EU-funded collaborative research (which in 2014-2015 brought £836 million of research funding into UK universities).

Lord Rees, former president of the Royal Society, gave voice to the UKRI-sceptic case in a *Guardian* article in June 2016. "While there are already so many pressures in the higher education and research environment," Rees argued, "surely we should avoid the risk and distraction of a wholesale and controversial reorganisation. Our research system is working well and needs no more than a little fine-tuning." ¹

But the context for these debates has been altered profoundly by November's Autumn Statement, with its unexpected multi-billion pound boost to R&D funding. By 2020, government spending on R&D will grow by £2 billion above existing spending, with a total additional investment of £4.7 billion by 2020-21 – the largest increase in R&D expenditure in any Parliament since 1979.

This new funding will flow through two streams: a new Industrial Strategy Challenge Fund (ISCF) for collaborative research between industry and academia, targeted at priority technologies; and a broader boost to UK capacity in research and innovation. The challenge-led approach of the ISCF represents the culmination of a revival of interest in activist technology policy in the UK, which has been building since the financial crisis. Earlier steps were tentative and criticised for being sub-scale.

Beyond the headlines, there are plenty of details still to be worked out. How much of the new investment will go to the research councils, and how much to the ISCF, via Innovate UK? How will new challenges and priorities be defined, and with what mix of government, academic, disciplinary and user input?



More will become clear when the Government publishes its industrial strategy in the coming weeks. But there's no doubt that the Autumn Statement represents a transformative statement of intent. Its significance was underlined by Lord Willetts, Jo Johnson's predecessor-but-one as science minister, who described in the *Financial Times* how "gradually the Conservatives came to see that there is a significant role for government in the long journey of a technology from lab to market."

So the prospects for UKRI to deliver real change in the UK's research and innovation performance now look genuinely exciting. And any lingering resistance to the plans is likely to evaporate. To demonstrate the value of UKRI, Jo Johnson simply needs to smile and utter the words "£4.7 billion".

The architecture is clear, the legislation to enable it is proceeding at pace, and the resources to deliver it are secure. Job done?

Unfortunately not; this is where the real work begins. To date, debates about UKRI have been characterised by an enthusiastic, well-intentioned, yet decidedly fuzzy commitment to new forms of collaboration – across disciplines, across sectors and between researchers and research users in business, government or civil society.

Now we have to get serious about new ways of working. To realise the potential of the UKRI reforms, themselves made more acute by the indeterminacies of Brexit, we need to invest time, effort and resource in developing connective tissue across the research and innovation system.

As Gillian Tett reminds us in her recent book *The Silo Effect*: "Silos exist in structures. But they exist in our minds too." Genuinely interdisciplinary research escapes the constraints of our theoretical and methodological prejudices, and highlights the sheer diversity of ways to understand and tackle most problems. Getting users involved in the design phase of

research questions and projects further expands our horizons. Working in these ways isn't easy. Academic reward systems still tend to privilege mono-disciplinary work. Metrics and evaluation systems are underdeveloped. Career paths are less predictable and more risky.

In recent months, there have been several efforts to address these challenges in a UK context. Work by the Academy of Medical Sciences on "team science" and the British Academy's *Crossing Paths* report stand out as particularly helpful. The best – and certainly the most honest – contribution I've enjoyed is *Rethinking Interdisciplinarity*, a short book by Felicity Callard and Des Fitzgerald, based on their experiences, as social scientists, of collaborating with neuroscientists through the Hub at the Wellcome Collection.

As Callard and Fitzgerald describe, they tried to start "from what interdisciplinarity looks like, on the ground, rather than in bureaucratic daydreams. We set out to write about things that usually get pushed under the carpet: the often deeply-etched disparities in institutional power across the social sciences, humanities and neurosciences ... the day-to-day, here-and-now relations and feelings through which collaborative work gets done."²

Such issues need far more attention and discussion as UKRI moves from idealised blueprint to operational reality. And our focus needs to turn to the people who can make collaborations work; and the skills, training and capacity which they and others like them will need.

Some of these people are researchers in universities; others work in knowledge exchange, or in funding agencies. Many more will be found in the businesses, public bodies and NGOs that academics need to partner with, if the UK is to succeed in scaling up the volume and intensity of collaborative, problem-oriented activity across its research and innovation system.

All of them are brokers and boundary-spanners – the "T-shaped people" on which the success or failure of UKRI will ultimately rest. 2017 needs to be their year.

James Wilsdon

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3. GLOBAL HEALTH AND THE ROLE OF BIOPHARMA

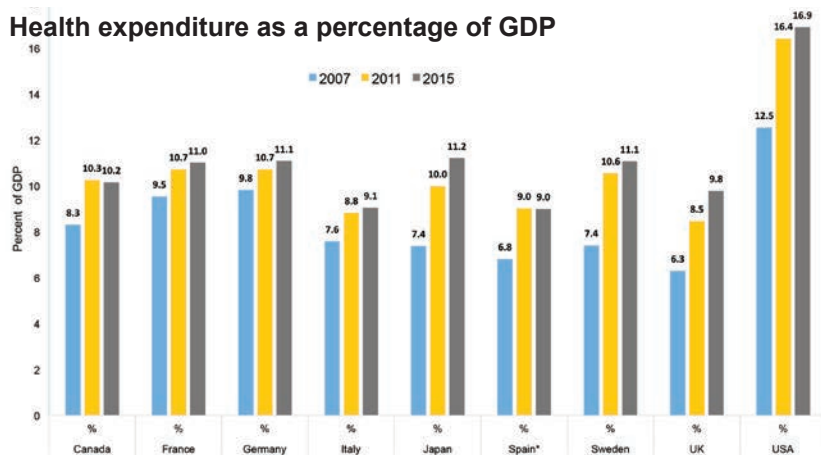
The cost of healthcare to society is a subject rarely out of the media, and was a key discussion in this year's US Presidential election and the EU Referendum. However, although our investment in healthcare has been rising over decades (mirrored accordingly in the improvement in health outcomes and life expectancy), the economic crisis in 2008 initiated a curb

on the growth of the share of investment in healthcare that continues into the present.

In this section, we review some key measures of how the UK aligns with global trends in healthcare investment and pharmaceutical markets, and in that context, how the UK biopharma industry is contributing to UK economic growth and prosperity.

3.1 The growth of total expenditure on health as a share of gross domestic product (GDP) has slowed since 2008 across many countries, according to the OECD. Expenditure has even declined slightly in Canada as a percentage of GDP between 2011 and 2015. Within this peer group, the **UK is third lowest** in terms of its share of health expenditure as a share of GDP, above Spain (lowest) and Italy.

Health expenditure as a percentage of GDP

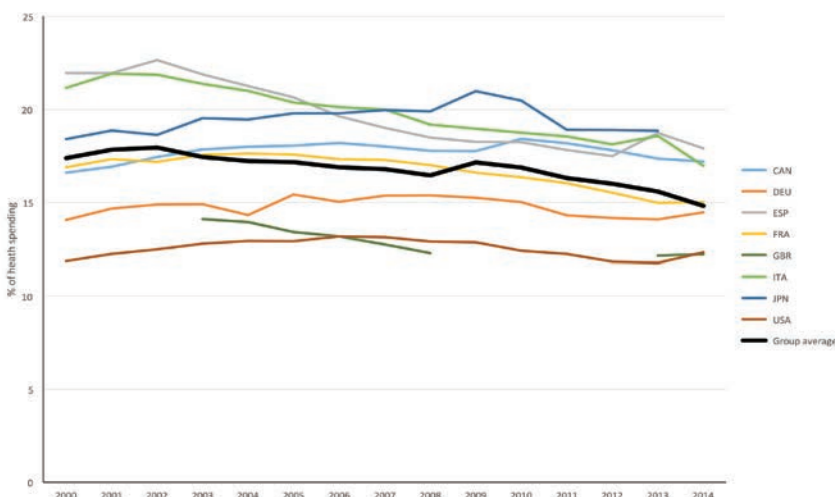


SOURCE: OECD Health Database (accessed 22 September 2016).

NOTES: This statistic measures health expenditure as a % of GDP.

3.2 Pharmaceutical expenditure as a share of health expenditure has declined in the last 15 years for many of the leading OECD economies, and most particularly since 2008, according to the OECD Health Expenditure indicators. Although this data series is incomplete for the UK, figures are available for 2013 and 2014, demonstrating a **significant decline** in pharmaceutical expenditure as a share of total health expenditure. Together with the US (12.3%), **the UK had the lowest pharmaceutical spend as a share (12.2%) of health expenditure in 2014.**

Pharmaceutical spending as a % of health spending 2000-2014

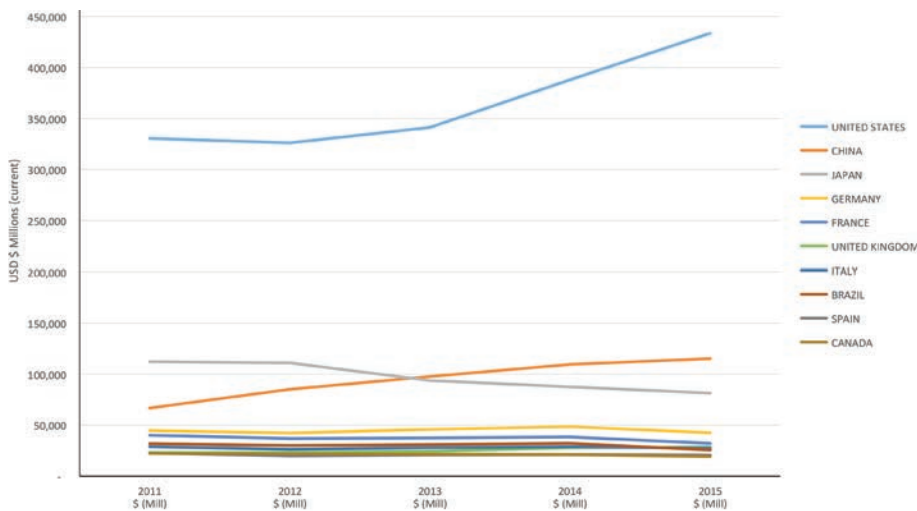


SOURCE: OECD (2016), Pharmaceutical spending (indicator). <https://data.oecd.org/healthres/pharmaceutical-spending.htm>, accessed 19 October 2016.

NOTES: The OECD defines pharmaceutical spending as expenditure on prescription medicines and self-medication, often referred to as over-the-counter products. In some countries, other medical non-durable goods are also included. Pharmaceuticals consumed in hospitals and other healthcare settings are excluded. Final expenditure on pharmaceuticals includes wholesale and retail margins and value-added tax. Total pharmaceutical spending refers in most countries to "net" spending, i.e. adjusted for possible rebates payable by manufacturers, wholesalers or pharmacies. This indicator is measured as a share of total health spending, in USD per capita (using economy-wide PPPs) and as a share of GDP. <https://data.oecd.org/healthres/pharmaceutical-spending.htm>

3.3 Of the top 10 largest markets for pharmaceuticals worldwide, **the United States continues to lead by a widening margin**. However, important growth is also seen in **China**, which swapped places with **Japan** over 2013 to 2014 in terms of the overall value of the market. Of course, the value of the market per capita is still more significant in Japan than in China, but the Japanese market for pharmaceuticals has declined in terms of total sales. The other leading markets are much more closely grouped with less change in overall sales.

Worldwide pharmaceutical markets – top 10 countries

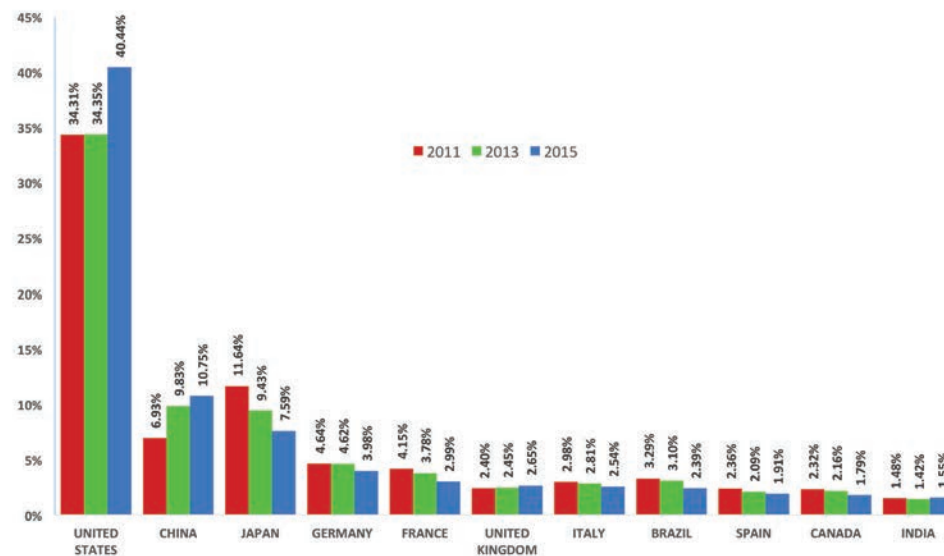


SOURCE: IMS World Review Analyst, accessed 20 September 2016.

NOTES: IMS estimates sales through all distribution channels in all countries, whether these channels are audited by IMS Health or not. These estimates are intended to include both prescription and most non-prescription products. These data are provided in millions of US dollars, current values, at list prices.

3.4 Considering the top 10 markets as a share of the total worldwide pharmaceutical market gives an easier view of the dynamics, particularly if we contrast the figures from 2011, 2013 and 2015. As a share of the worldwide market, the share of the **US market** as part of the total has grown considerably (40.44%), as has the **Chinese** pharmaceutical market (10.75%). The **UK was the only EU “Big 5” (UK, France, Germany, Italy, Spain) market for pharmaceuticals whose share in the total market increased**, although growth was modest and the overall share (2.65%) remains lower than France (2.99%), Germany (3.98%) and Japan (7.59%).

Percentage share of global pharmaceutical sales for leading markets, by sales



SOURCE: IMS World Review Analyst, accessed 20 September 2016.

NOTES: IMS estimates sales through all distribution channels in all countries, whether these channels are audited by IMS Health or not. These estimates are intended to include both prescription and most non-prescription products. These data are provided in millions of US dollars, current values, at list prices.

Share of the global medicines market

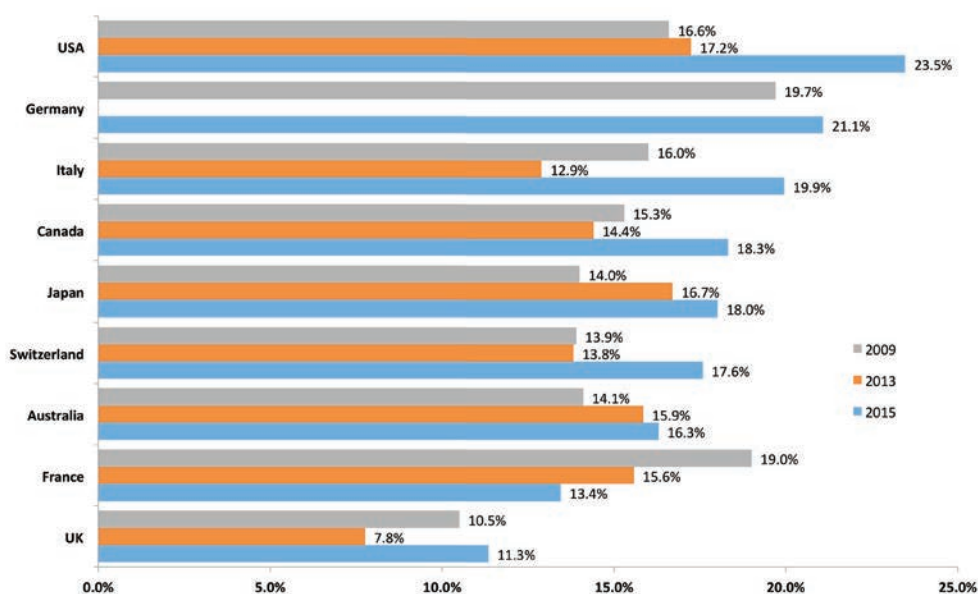
	2011	2012	2013	2014	2015
UNITED STATES	34.31%	33.81%	34.35%	36.55%	40.44%
CHINA	6.93%	8.82%	9.83%	10.32%	10.75%
JAPAN	11.64%	11.52%	9.43%	8.25%	7.59%
GERMANY	4.64%	4.36%	4.62%	4.56%	3.98%
FRANCE	4.15%	3.83%	3.78%	3.61%	2.99%
UNITED KINGDOM	2.40%	2.41%	2.45%	2.62%	2.65%
ITALY	2.98%	2.72%	2.81%	2.71%	2.54%
BRAZIL	3.29%	3.10%	3.10%	3.01%	2.39%
SPAIN	2.36%	2.07%	2.09%	2.00%	1.91%
CANADA	2.32%	2.29%	2.16%	1.97%	1.79%
INDIA	1.48%	1.45%	1.42%	1.43%	1.55%

SOURCE: IMS World Review Analyst, Accessed 20 September 2016.

NOTES: IMS estimates sales through all distribution channels in all countries, whether these channels are audited by IMS Health or not. These estimates are intended to include both prescription and most non-prescription products. These data are provided in millions of US dollars, current values at list prices.

3.5 Considering **only recently launched medicines** (within the previous 5 years), the relative shares of different countries show differences both within the peer group and across the years **2009, 2013 and 2015**. Across this period, all of the OECD countries included in the analysis **increased their relative share for newly launched medicines in 2015**, with the **exception of France**. Although the **UK's market share for products launched in the previous 5 years is the lowest in this group**, the **share increased** in 2015. This is largely explained by launches of significant new classes of medicines, notably new treatments for Hepatitis C, cancer, diabetes and anticoagulation.

Market share for products launched in the previous five years

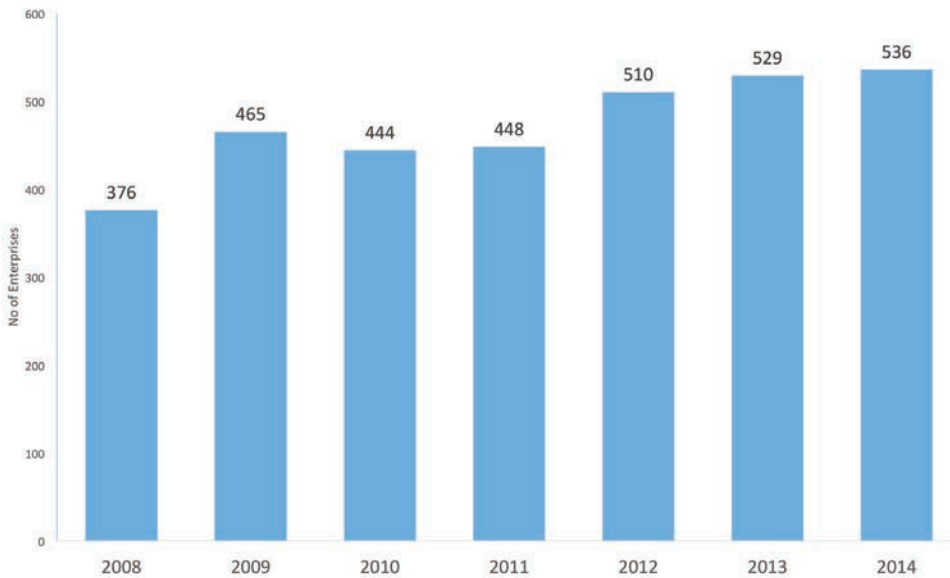


SOURCE: IMS World Review Analyst, accessed September 2016.

NOTES: The analysis above uses list prices and the IMS Midas definition for new products, which is broader than new molecular entities (NMEs) and, for example, will include branded generics. Where possible new branded generics have been excluded (these will be formulations with significant sales). The figure for Germany for 2013 has been omitted due to data issues.

3.6 In the UK, the **biopharmaceutical industry represents an important sector** for economic growth. The **number of pharmaceutical enterprises has been increasing** since 2008. According to the Office for National Statistics, by 2014 the number of enterprises operating in the UK was 536.

Number of pharmaceutical enterprises in the UK

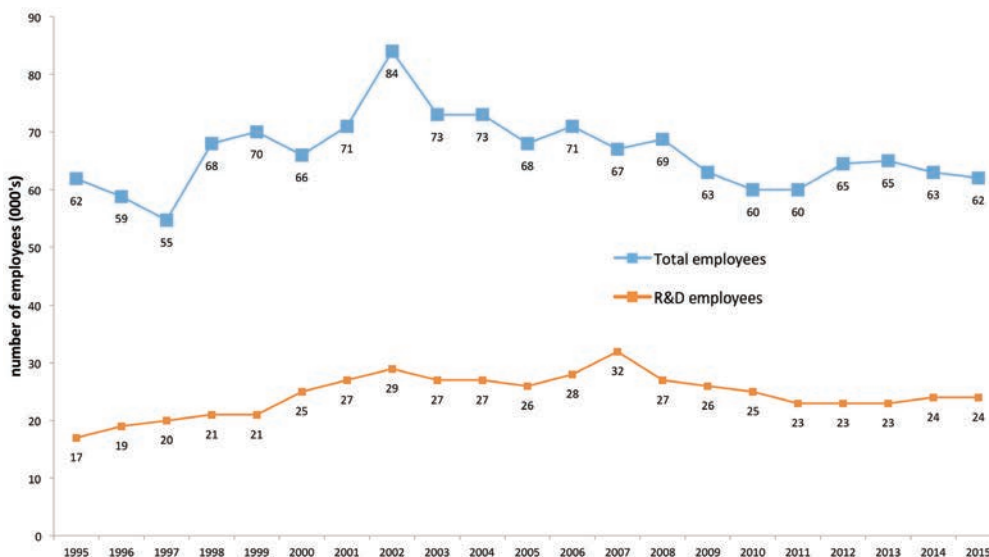


SOURCE: Office for National Statistics Annual Business Survey 2016.

NOTES: The data relate to the manufacture of basic pharmaceutical products and pharmaceutical preparations, SIC (2007) 21. Enterprises here are defined as VAT-registered organisations self-referring as a manufacturer of basic pharmaceutical products and pharmaceutical preparations.

3.7 In the UK, the **biopharmaceutical industry continues to represent an important employer** for high value jobs. The greatest challenge in reporting the figures is defining the right data sources and what to include. The difference between the figures we are publishing this year and last year's figures is due to a change in the source; we are using the Office for National Statistics "Employees by Jobs" which we believe provides a more robust sampling and methodology, as a best approximation of employment in the pharmaceutical industry in the UK. By this assessment, the number of jobs in **2015 was 62,000**, with **24,000 of those jobs dedicated to R&D**.

UK pharmaceutical industry employees (000s) 1995 - 2014

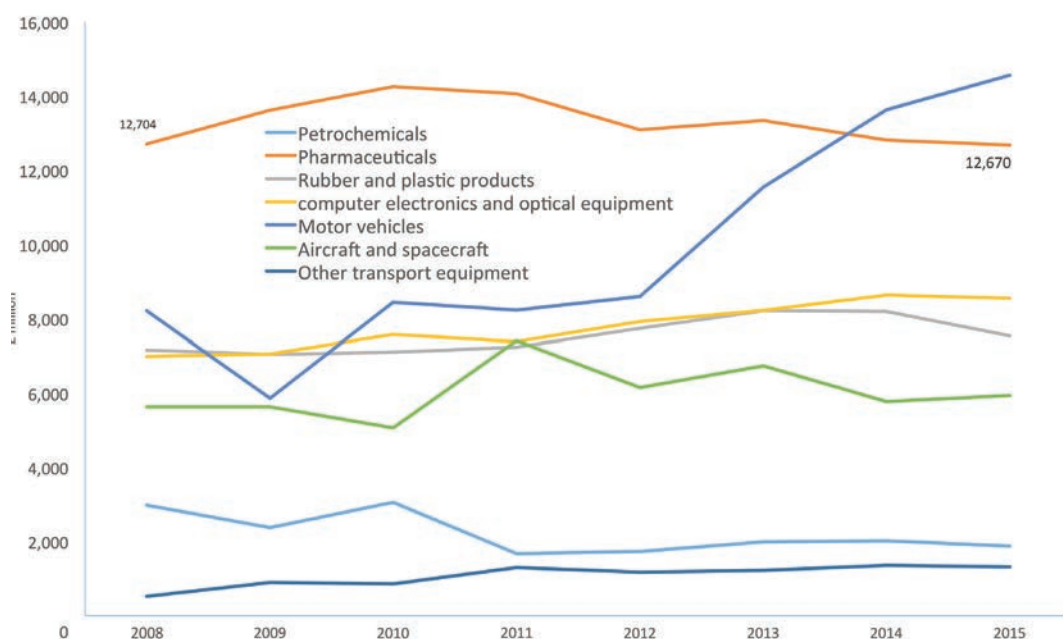


SOURCE: Number of jobs at industry level (manufacturing) are available at: <https://www.ons.gov.uk/employmentandlabourmarket/peopleinwork/employmentandemployeetypes/datasets/employeejobsbyindustryjobs03> [accessed on November 17, 2016], and number of jobs at industry level (R&D) are available at: <http://www.ons.gov.uk/economy/governmentpublicsectorandtaxes/researchanddevelopmentexpenditure/datasets/ukbusinessenterprisesresearchanddevelopment/current> [accessed on November 17, 2016].

NOTES: These total employment and R&D employment figures are differently defined to those presented in the 2015 UK Biopharma R&D Sourcebook. We have provided the full time series here to allow assessment of trends. These figures are drawn from a different ONS dataset which allows for a more robust estimate for jobs in the pharmaceutical industry. Although these are always approximations, this dataset we believe provides a better estimate for our purposes. Also note that the number of jobs is rounded to the thousand.

3.8 In terms of Gross Value Added (GVA) to the UK economy, the pharmaceuticals industry **remains a leading sector contributing to wealth**. However, this contribution has been in **decline since 2010**, reflecting the loss of operations and manufacturing activity from the UK.

Gross value added (GVA) – current price reference year 2013



SOURCE: Office for National Statistics (ONS) per annum GVA figures at industry level are available at: <https://www.ons.gov.uk/economy/grossdomesticproductgdp/datasets/ukgdpolowlevelaggregates>, Accessed on August 2016.

NOTES: ONS estimates the GVA by two independent approaches, Current Price (CP) and Chain Volume Measures (CVM). Differences between both approaches are explained in the spreadsheet available at the link above. The analysis above corresponds with the CP approach calculated for the reference year 2013. This is a different approach than was used for the UK Biopharma R&D Sourcebook 2015. A longer note explaining gross value added analysis (overall and on a per worker basis) is provided in Box 3.1.

BOX 3.1 Methodological note on change in use from Chain Volume Measurements (CVM) to Current Prices (CP) for Gross Value Added (GVA) figures

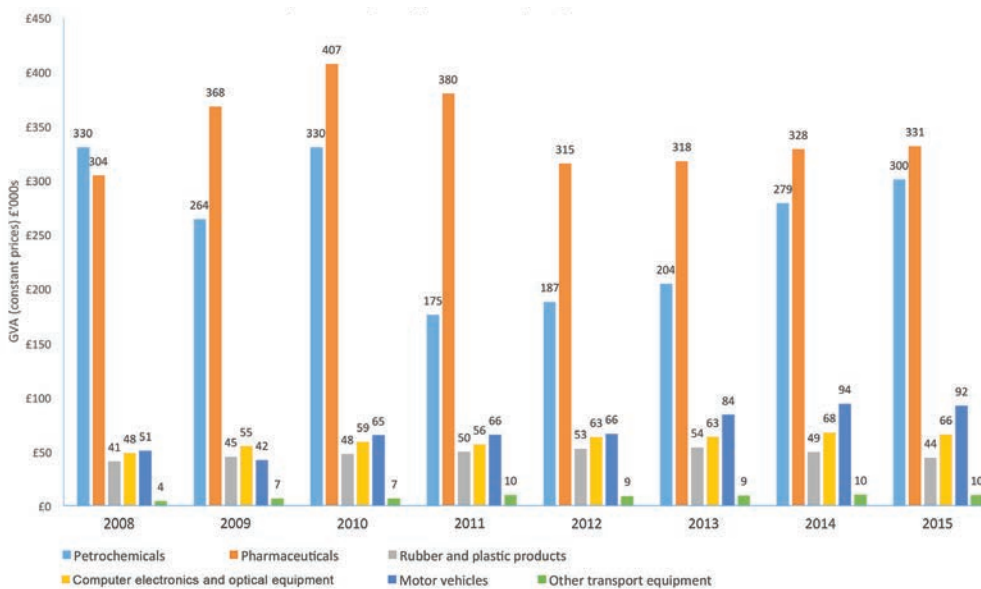
The Office for National Statistics (ONS) publishes annual and quarterly detailed industry level data of UK output gross value added (GVA), “UK GDP(O) low level aggregates”, on a constant and current price basis, in an index and pounds million format. Figures of GVA are broken down by industries following Standard International Classification (SIC) codes. For pharmaceuticals there are the following categories:

- Division 21 Pharmaceutical products and preparations:
- Group 21.1 Basic pharmaceutical products (broadly active pharmaceutical ingredient manufacturing)
- Group 21.2 Pharmaceutical preparations (broadly packaged medicines)

Both approaches are subject to revisions in reported figures as the reference year for calculating prices changes. For instance, the update in 2015 shifted the reference year for prices to 2013 (from 2011). When comparing the impact on the two approaches for measuring GVA, the absolute change in historic figures was smaller using current price (CP) rather than constant price (CVM). This report has therefore switched to using CP in anticipation that future revisions will be minimised. It should be noted that although the absolute values reported using the two approaches are different, the annual trends are comparable.

3.9 GVA per worker across comparative sectors in the UK, **pharmaceuticals provides the highest GVA per worker**, followed by motor vehicles. Although there was a decline in pharmaceutical GVA per worker between 2010 and 2012, **this value has recovered and has increased** in the following years.

GVA (constant prices) per worker (£000s) for selected industries

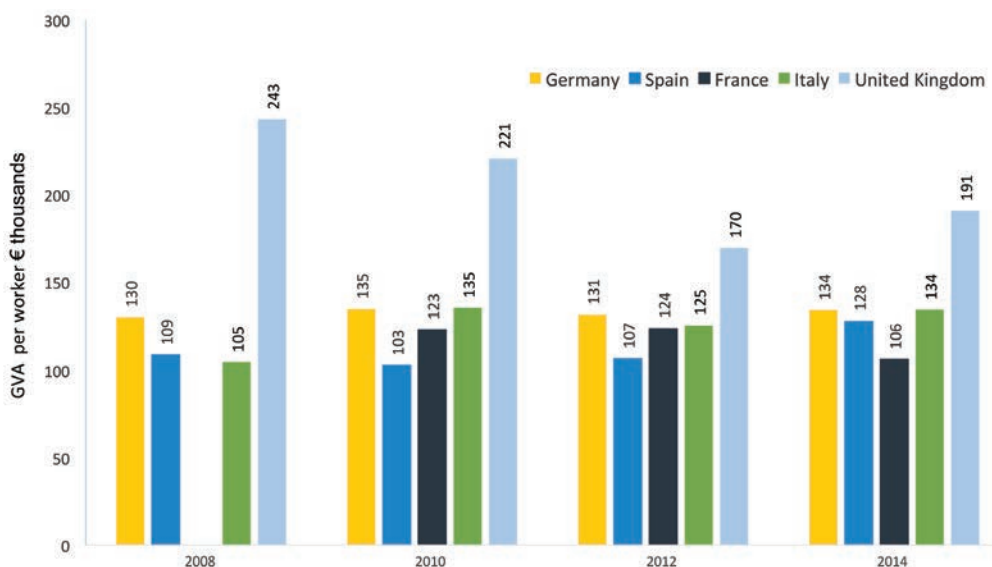


SOURCE: Office for National Statistics (ONS) Per annum GVA figures at industry level are available at: <https://www.ons.gov.uk/economy/grossdomesticproductgdp/datasets/ukgdpowlevelaggregates>. Accessed on August 31, 2016. ONS estimates the GVA by two independent approaches, CP and CVM. Differences between both approaches are explained in the spreadsheet available at the link above. Figures in table and on chart correspond with the CP approach at the reference year 2013. Employment figures at <https://www.ons.gov.uk/employmentandlabourmarket/peopleinwork/employmentandemployeetypes/datasets/employeejobsbyindustryjobs03>, average of four quarters used to calculate an annual figure.

NOTES: "Other transport equipment" includes manufacturing of air and spacecraft. GVA per worker has been calculated as the ratio of GVA (numerator) and year average employment (denominator excludes employment in R&D).

3.10 GVA per worker in the pharmaceutical industry across the European "Big 5" countries (UK, France, Germany, Italy, Spain), the UK retains the highest GVA per worker. Between 2012 and 2014, GVA per pharmaceutical worker in the **UK grew to reach €191,000 per worker**. Although not at the previous values seen in 2008, it is a welcome increase for the British pharmaceutical industry.

Relative performance of pharmaceuticals in the UK compared to other major EU economies: GVA per worker (€000s per person)



SOURCE: Eurostat

NOTES: The data for France were not available for 2008. 2009 and 2011 have been omitted because of data availability issues.

4. INVESTING IN INNOVATION

Innovation in medicines above all requires commitment – commitment of time, resources and continuous endeavour – because this is one of the most uncertain of investments. Biopharma companies have been evolving their approach to drug discovery and development, following the scientific breakthroughs that allow better understanding of human biology and the biology of disease. As the evidence in this section describes, we are already seeing the success of some of these efforts in new candidate medicines and technologies; but the extent of unmet need for treatment is such that there remains so much yet to discover and deliver.

Any candidate medicine begins with the research and investment in discovery research to understand the disease biology, target identification and validation, proof of principle and proof of concept efforts for a lead compound, followed by refinements of the lead compound and pre-clinical safety testing. These candidate treatments are then explored in clinical settings and beyond to

establish how best to further develop and then use these valued treatments. However, the journey from idea to implementation of a treatment for care is fraught with considerable scientific uncertainty and risk, and most ideas never make it through to a patient, although they do play a role in the progress of science.

It takes a long time to make this journey, on average 10 to 12 years, with clinical trials alone taking six to seven years on average¹. Some industry analysts have calculated average costs for developing and licensing a new medicine at well over £1 billion². A recent Tufts Center for the Study of Drug Development (CSDD) study estimated costs could reach \$2.6 billion³. Overall, in 2014, the estimate was that the research-based pharmaceutical industry collectively spent nearly \$141.6 billion on R&D annually⁴.

In this section, we will review the investment made into R&D for health, and specifically medicines, and what role the UK plays in this broader global activity.

4.1 Medicines are only one part of investment in research in healthcare. Global investment in healthcare research is an important component, but a difficult metric to obtain because of the variation in funding types and organisations supporting this work globally. Such a measure includes government, the private sector and the academic/non-profit sectors. It is easiest to identify government funding for R&D related to public health, as defined by the OECD Frascati Manual.

The United States leads by far the amount of **government expenditure on health R&D** expenditure, followed by the United Kingdom (it is roughly one-tenth of the US expenditure). The **UK increased the investment by government in health R&D steadily since 2000, but this tapered off between 2010 and 2014** (particularly noting that these are current value figures).

Government funding in health R&D, selected countries

	Canada	France	Germany	Italy	Japan	Spain	Sweden	UK	US
	US Dollar, millions current prices								
2000	517	785	602	624	823	292	23	1,499	18,766
2001	706	918	708	733	902	132	15	1,623	21,741
2002	856	993	731	..	964	492	15	1,688	24,754
2003	943	921	793	..	1,032	575	24	1,819	27,335
2004	966	937	817	..	1,040	751	24	1,940	29,346
2005	1,084	1,060	859	1,093	1,076	763	24	1,977	29,871
2006	1,141	963	945	1,121	1,133	1,302	31	2,225	29,702
2007	1,336	1,049	1,062	1,664	1,178	1,529	18	2,279	31,080
2008	1,336	1,090	1,056	1,554	1,250	1,380	18	2,507	31,054
2009	1,427	1,283	1,237	1,296	1,246	1,373	30	2,777	43,926
2010	1,471	1,354	1,253	1,274	1,466	1,564	60	2,749	34,206
2011	1,355	1,353	1,394	1,254	1,480	1,500	45	2,756	33,536
2012	1,408	1,326	1,612	1,204	1,663	947	45	2,711	33,924
2013	1,369	1,389	1,637	1,092	1,673	1,308	63	3,193	32,454
2014		1,328	1,729	1,040	1,633	1,276	62	3,196	33,451
2015		1,235	1,703		1,059		76		33,745

SOURCE: OECD STAN database (Science, Technology and Patents) accessed 27 October, 2015.

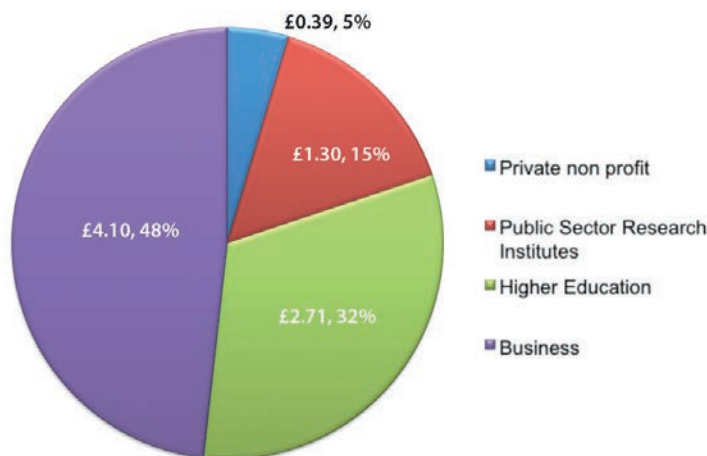
NOTES: The OECD Structural Analysis (STAN) database defines total expenditure on health as the sum of expenditure on activities that – through application of medical, paramedical and nursing knowledge and technology – has goals of: promoting health and preventing disease, curing illness and reducing premature mortality, caring for persons affected by chronic illness who require nursing care, caring for persons with health-related impairments, disability and handicaps who require nursing care, assisting patients to die with dignity, providing and administering public health, providing and administering health programmes, health insurance and other funding arrangements. The key below the diagram provides notes for the different data series, as provided by the OECD.

A: Break in series with previous year for which data are available **B:** Secretariat estimate or projection based on national sources **C:** National estimate or projection **H:** Federal or central government only **S:** Unrevised breakdown not adding to the revised total **V:** The sum of the breakdown does not add to the total

4.2 In the UK, the total national expenditure on all R&D (the Gross Domestic Expenditure on R&D, or GERD) reached **£30.6 billion** in 2014, according to the Office for National Statistics. This represented **1.67% of GDP**, unchanged from the 2013 estimate, and well below the Lisbon target of 3% of GDP⁵. Of this £30.6 billion, business expenditure on R&D (BERD) accounted for 65% of the total.

The most recent data available on UK health research expenditure by performing sector were for 2014. As published in last year's UK Biopharma R&D Sourcebook, the figure below describes the component contributions of the overall **£8.5 billion** health research expenditure by the performing sector. **Business expenditure represented almost half of that total.**

UK health research expenditure by performing sector, 2014

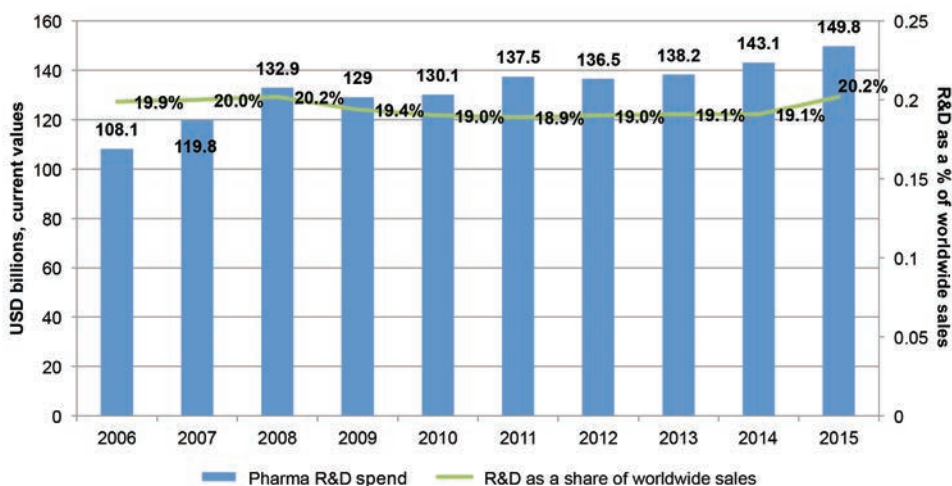


SOURCE: UK Clinical Research Collaboration (CRC), 2015. "UK Health Research Analysis, 2014", pp 21-22. <http://www.ukcrc.org/research-coordination/health-research-analysis/uk-health-research-analysis/>

NOTES: For this analysis, the UK CRC team followed a "top down" approach, using information on total research and development activity across the research performing sectors. This is the second estimation of these figures, following the previous analysis in the 2009/10 report. The estimation is modelled on the GERD, and is detailed in Appendix 4 of the report.

4.3 According to EvaluatePharma⁶, the worldwide biopharmaceutical industry invested over **\$1.3 trillion in R&D** in the decade from 2006 to 2015 and they forecast an annual investment of \$182 billion by 2022. The figures below demonstrate that this investment is **growing moderately**, but steadily. The **R&D intensity** (R&D expenditure as a share of sales) however had been declining, but has **recovered in 2015** to the period high value (**20.2%**). At 20.2%, the biopharma industry has one of the highest R&D intensity measures of any sector globally, reflecting that R&D remains at the core of our innovation. **The US retains the highest share of R&D expenditure. In Europe, the UK has the highest share** if we exclude exchange rate effects.

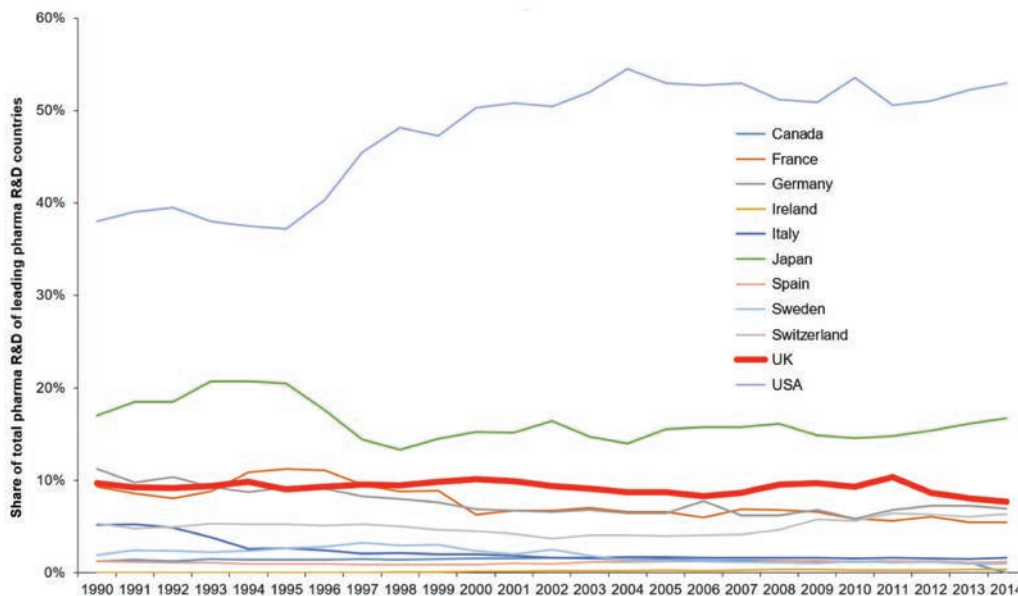
Worldwide biopharma companies R&D expenditure



SOURCE: EvaluatePharma, WORLD PREVIEW 2016: OUTLOOK TO 2022, p. 27.

NOTES: EvaluatePharma date this analysis as August 2016. Industry sales are based on the top 500 pharmaceutical and biotech companies.

Share of the total pharmaceutical R&D expenditure of leading pharma R&D countries

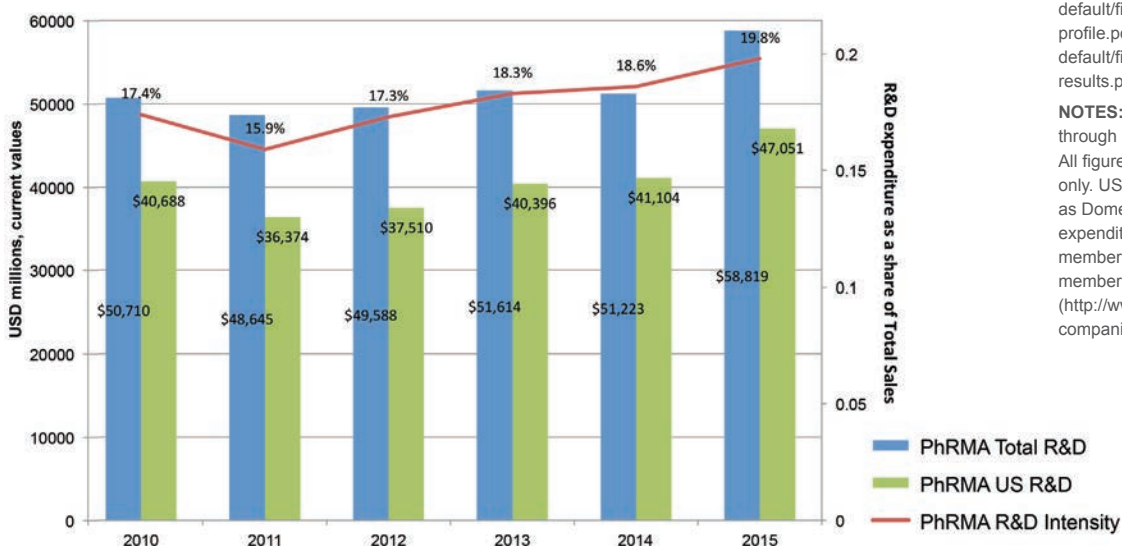


SOURCE: ABPI/Office of health economics calculations based on national trade association reported expenditure figures.

NOTES: The chart figures are based upon national trade association reported expenditure levels and may not reflect official statistics. The chart uses exchange rates fixed at 2000 levels. If actual exchange rates are used, the relative shares of European countries change, with the UK declining in relative value.

- 4.4** The Pharmaceutical Research and Manufacturers of America (PhRMA) association surveys its members annually and it explores the trend in **PhRMA members' total expenditure on R&D**. The figure below describes a moderate growth in total R&D expenditure from **2010 to 2015** by these biopharma companies (**growth averages at 3%** across the 6 years of data). The R&D intensity is also increasing, rather than decreasing over that period, suggesting that the amount of sales for these companies has declined relative to the relatively small growth in R&D expenditure. The survey also explores the R&D expenditure of PhRMA members which is spent in the US (PhRMA US R&D), generally leading global multinational biopharmaceutical companies. For this group of companies, the US retains the great majority of R&D expenditure and this **US share is increasing** (growth averages at 3% across the 6 years of data).

R&D expenditure for PhRMA member companies



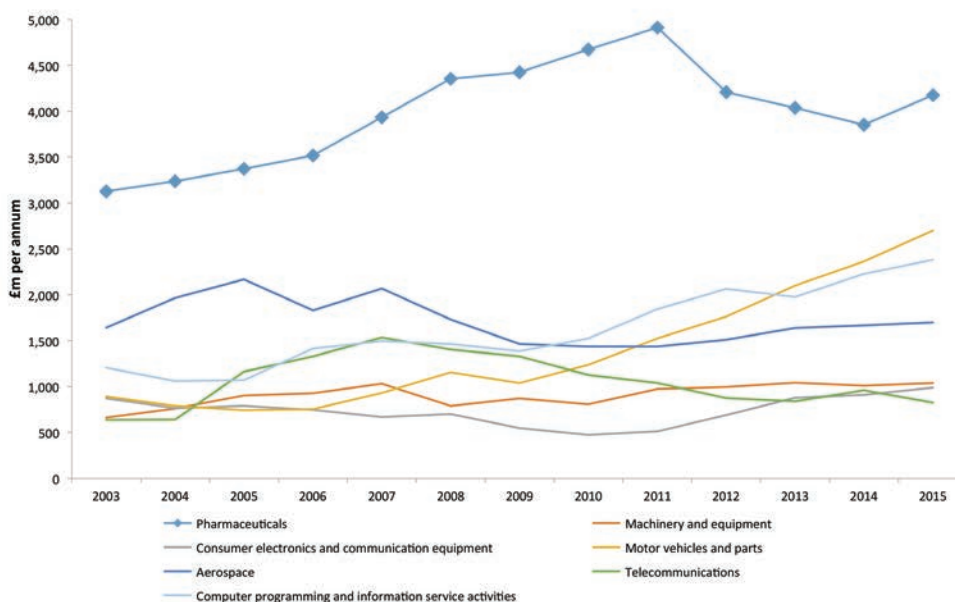
SOURCE: PhRMA 2016 Profile; accessed November 18, 2016. <http://phrma.org/sites/default/files/pdf/biopharmaceutical-industry-profile.pdf> <http://www.phrma.org/sites/default/files/pdf/annual-membership-survey-results.pdf>

NOTES: PhRMA collects this information through its Annual Membership Survey. All figures include company-financed R&D only. US R&D (referred to in the Profile as Domestic R&D) includes all R&D expenditures within the US by all PhRMA member companies. A list of PhRMA member companies is available online (<http://www.phrma.org/about/member-companies>).

4.5 In the UK, biopharmaceuticals remains the highest R&D spending sector, and the level of investment grew by 8% over the previous year to £4.2 billion. The sector reached a peak in its share of overall UK business expenditure on R&D in 2010, with a share of 29% of the total. According to the 2015 survey, the biopharmaceutical industry spent **£4.2 billion** in the UK on R&D⁷. The next largest spending sectors are motor vehicles and parts and computer programming & information services. Aerospace has also seen a return to growth in R&D after a decline. Overall, pharmaceutical R&D represents **20% of all business expenditure on R&D** in the UK in 2015.

The UK is a relatively R&D intensive country for pharmaceuticals, with an intensity (that is, UK R&D expenditure as a share of UK sales) of **38%** in 2015. The only sector with a higher R&D intensity is consumer electronics and communications equipment, which has grown substantially since 2010.

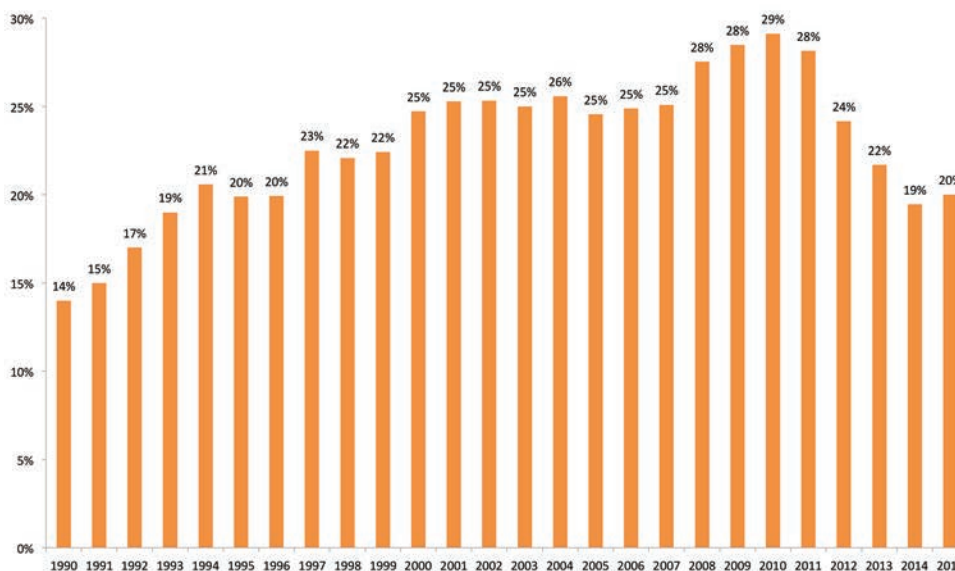
Leading industries for UK R&D expenditure



SOURCE: UK Office for National Statistics (ONS), Business Enterprise Research and Development (BERD) survey 2015.

NOTES: The BERD survey is conducted annually by ONS. As part of the 2015 survey, approximately 5,400 (4,000 Great Britain and 1,400 Northern Ireland) questionnaires were sent to businesses known to perform R&D. This included around 400 of the largest R&D spenders, which accounted for approximately 75% of the 2015 total R&D expenditure estimate. Smaller R&D performers and others believed to be performing R&D were selected using various sampling fractions. Industry product group and business employment size were the stratification variables. Completed questionnaires were returned by 4,600 businesses, representing a response rate of 85%. The data are reported irrespective of the residence of the ultimate owner, but overseas activities of affiliates of UK businesses are not included.

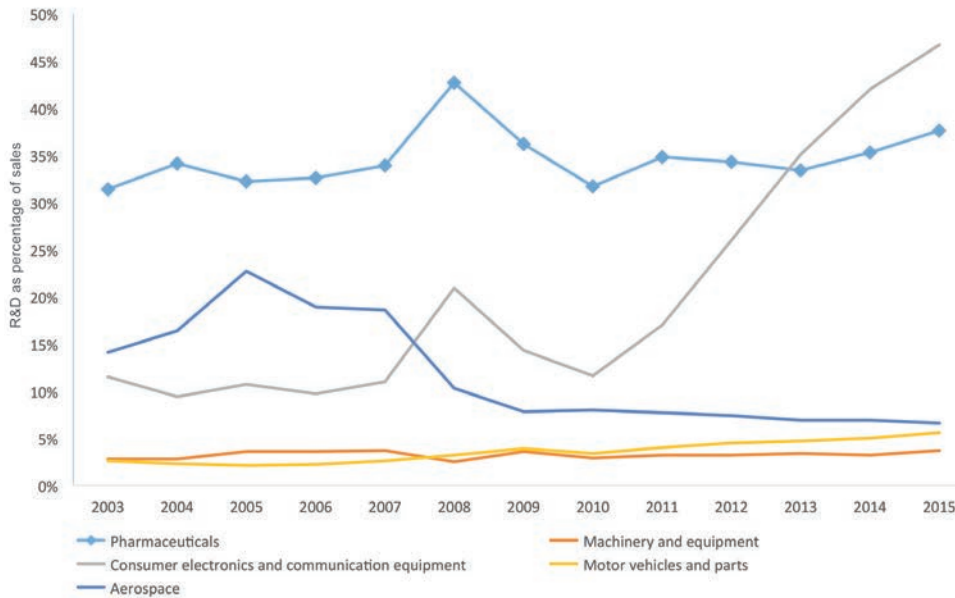
Pharmaceutical R&D as a percentage of all industry R&D



SOURCE: UK Office for National Statistics (ONS), Business Enterprise Research and Development (BERD) survey 2015.

NOTES: The BERD survey is conducted annually by ONS. As part of the 2015 survey, approximately 5,400 (4,000 Great Britain and 1,400 Northern Ireland) questionnaires were sent to businesses known to perform R&D. This included around 400 of the largest R&D spenders, which accounted for approximately 75% of the 2015 total R&D expenditure estimate. Smaller R&D performers and others believed to be performing R&D were selected using various sampling fractions. Industry product group and business employment size were the stratification variables. Completed questionnaires were returned by 4,600 businesses, representing a response rate of 85%. The data are reported irrespective of the residence of the ultimate owner, but overseas activities of affiliates of UK businesses are not included.

UK R&D intensity by industry

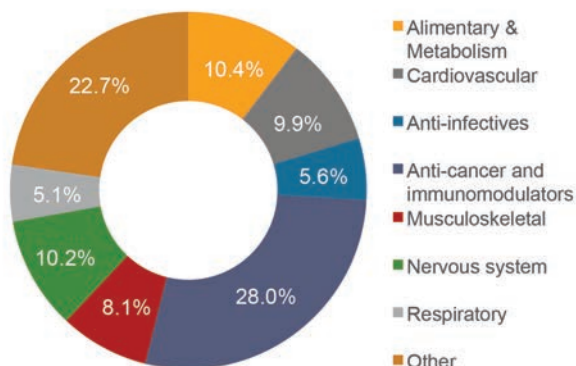


SOURCE: UK Office for National Statistics (ONS), Business Enterprise Research and Development (BERD) survey 2015.

NOTES: The BERD survey is conducted annually by ONS. As part of the 2015 survey, approximately 5,400 (4,000 Great Britain and 1,400 Northern Ireland) questionnaires were sent to businesses known to perform R&D. This included around 400 of the largest R&D spenders, which accounted for approximately 75% of the 2015 total R&D expenditure estimate. Smaller R&D performers and others believed to be performing R&D were selected using various sampling fractions. Industry product group and business employment size were the stratification variables. Completed questionnaires were returned by 4,600 businesses, representing a response rate of 85%. The data are reported irrespective of the residence of the ultimate owner, but overseas activities of affiliates of UK businesses are not included.

4.6 R&D expenditure by therapeutic area in 2015, drawn from the *Clarivate Analytics CMR Pharmaceutical R&D Factbook 2016*, reflects the continuing leading share (28.0%) invested in **anti-cancer and immunomodulators** treatments. The share is virtually unchanged from its value in 2014 (28.7%, see *UK Biopharma R&D Sourcebook 2015*). What has **grown significantly** as a share of investment is the “**other**” category (16.7% in 2014, now 22.7%) and **anti-infectives** (3.7% in 2014, now 5.6%). This reflects a response by biopharma companies to areas of unmet need, and therefore investing in a growing range of treatment areas, including areas for rare disease, and in support of the global priority for anti-infectives, including antibiotics. PhRMA calculates that biopharma companies have **more than 7,000 medicines in development globally**⁸.

Total R&D expenditure in 2015 by therapeutic area



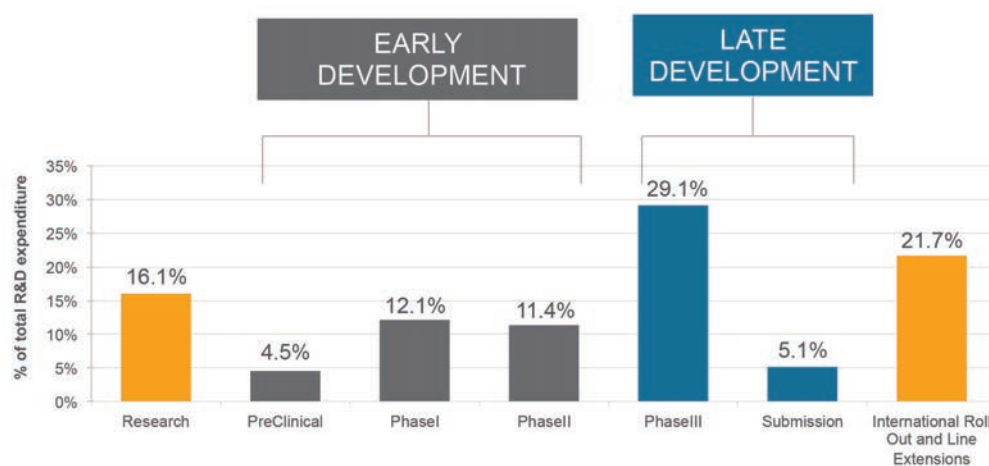
'OTHER' CATEGORY BREAKDOWN	
	%
Blood	3.1
Genitourinary & sex hormones	2.2
Hormones (exc sex hormones & insulin)	0.9
Dermatologicals	2.1
Sensory	0.4
Non TA specific	14

SOURCE: 2016 CMR Factbook from Clarivate Analytics; Drawn from the Industry R&D Investment Programme and reproduced with permission.

NOTES: Clarivate Analytics undertakes a comprehensive benchmarking of international performance metrics, and some of this evidence is reproduced in its annual CMR Pharmaceutical R&D Factbook. For details, please refer to <http://ipsience.thomsonreuters.com/>. Presented is the distribution of total R&D expenditure in 2015 by therapeutic area calculated from data provided by 10 companies (seven Major and three Mid and Other). The total R&D expenditure represented by the figure is US\$ 32.26 billion. Major companies are defined as those spending ≥US\$ 2 billion in 2015 on ethical pharmaceutical R&D. Mid companies are defined as those spending ≥US\$ 0.7 billion and <US\$ 2 billion in 2015 on ethical pharmaceutical R&D. Other companies are defined as those spending <US\$ 0.7 billion in 2015 on ethical pharmaceutical R&D.

4.7 The structure of R&D expenditure by phase of development continues to change annually, reflecting the different stages of the pipeline. In contrast to the figures for 2009 and 2014 presented in last year's *UK Biopharma R&D Sourcebook*, the shares of expenditure in research (15.3% in 2014, now 16.1%) and Phase 1 (8.5% in 2014, now 12.1%) have increased. Although the share categorised as "Research" is less than it was in 2009 (25.5%), the share of Phase 1 research today is higher than it was in 2009 (7.3%). The share of international roll out and line extensions continues to be significant, although less (26.1% in 2014, now 21.7%), as companies seek to extend the value of the medicine beyond the original indication(s).

Proportion of total R&D expenditure in 2015 by phase or R&D



Definitions:

Research: Phase of R&D up to the 'First toxicity dose for the active substance'.

Preclinical: Phase of R&D from 'First toxicity dose for the active substance' to 'First human dose'

Phase 1: Phase of R&D from 'First human dose' to 'First patient dose'

Phase 2: Phase of R&D from 'First patient dose' to 'First pivotal dose'

Phase 3: Phase of R&D from 'First pivotal dose' to 'First submission'

Submission: Phase of R&D from 'First submission' to 'First launch'

International roll out (including Line Extensions): Phase of R&D from 'First launch in first core market' onwards (eg Phase 4 expenditure, regulatory fees, etc for further work to support the launch for the same indication in other markets).

SOURCE: 2016 CMR Factbook from Clarivate Analytics; Drawn from the Industry R&D Investment Programme and reproduced with permission.

NOTES: Clarivate Analytics undertakes a comprehensive benchmarking of international performance metrics, and some of this evidence is reproduced in its annual CMR Pharmaceutical R&D Factbook. For details, please refer to <http://ipscience.thomsonreuters.com/>. Presented is the proportion of R&D expenditure in 2015 by phase of R&D calculated as an aggregate of the data supplied by 13 companies (10 Major and 3 Mid and Other). Major companies are defined as those spending ≥US\$ 2 billion in 2015 on ethical pharmaceutical R&D. Mid companies are defined as those spending ≥US\$ 0.7 billion and <US\$ 2 billion in 2015 on ethical pharmaceutical R&D. Other companies are defined as those spending <US\$ 0.7 billion in 2014 on ethical pharmaceutical R&D.

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5. DRIVING CLINICAL RESEARCH TO DELIVER MEDICINES

Any candidate medicine has to undertake extensive studies in humans to demonstrate its safety profile and efficacy before it can be licensed for use in the UK. Traditionally, there are **three key phases of clinical research** which collectively provide the evidence to support a decision on the relative benefits of a medicine for clinical use in comparison with its risks. **Phase 1** clinical trials are typically conducted with a small number of healthy volunteers to determine the safety, tolerability and how the candidate medicine behaves in the body and the relationship between its molecular structure and effects on volunteers. **Phase 2** clinical trials generally involve patients (eg between 100 and 500 volunteers) to assess the efficacy and dose response of the candidate medicine, as well as identification of potential side effects. **Phase 3** clinical trials then continue assessment of the candidate medicine with a much greater number of patients (eg between 1,000 – 5,000 volunteers) and several clinical trial sites, usually global. A **fourth phase** of clinical research study is also undertaken more commonly these days as part of the post-approval research and monitoring of a medicine, to gather information on the drug's effect in various populations and to monitor safety and long-term side effects in patients using the medicine.

Globally, the biopharma industry undertakes the greatest share of clinical research trials, and this investment makes possible the provision of innovative, novel treatments for a wide range of disease and ill-health as well as for prevention. In addition, the investment in clinical research provides substantial benefits to the health systems and economies in which it is undertaken. A recent study by Battelle investigated the impact of industrial-sponsored clinical research in the United States. They found that in

2013, the biopharmaceutical industry sponsored **6,199 clinical trials of medicines in the US**, involving a total of **1.1 million participants** and delivering **direct expenditure of \$10 billion** in the conduct of trials, and yielding through indirect and induced effects a total of \$25 billion in economic activity in those communities¹.

Industry-sponsored clinical research represents an important share of clinical research in the UK as well. Companies will work with physician researchers to conduct the research with them to a specific plan (the study protocol). Often these studies will be held in several countries around the world simultaneously to collectively provide an evidence base for the medicine. From start to finish, the clinical development phase takes an average of 6 to 7 years, and **historically we have seen less than 12% of candidate medicines that enter clinical testing (at Phase 1) make it to approval**², although data presented later in this chapter show a slightly lower likelihood (9%) which may reflect a difference in estimation. The authors of the 12% estimation also noted a significant decline since their previous analysis a decade ago³; this decline reflects both the significant scientific challenges that face innovation in medicines today as well as growing complexity in clinical design itself⁴.

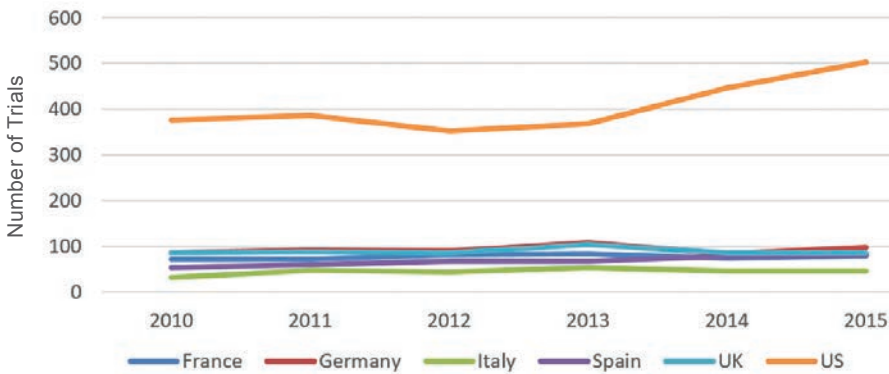
Clinical research is important to countries as a measure of the translational capacity of a healthcare system to bring concepts for new medicinal treatments into care. In the UK, the health research authorities in England, Scotland, Wales and Northern Ireland have been working to improve the environment and procedures for conducting clinical research, and progress is being made. In this section, we will review the measures for clinical research and medicine authorisations, using publicly available measures for the UK and globally.

5.1 Before a medicine reaches a Phase 1 trial, research on the candidate medicine is undertaken to establish “proof of concept” and “proof of mechanism”. This research can involve a small number of volunteers with the aim of determining dose-response, effect size and tolerability. These studies, described as **experimental medicine trials**, often involve state-of-the-art techniques in imaging, biomarkers and genomics. Experimental medicine has been a focus for investment in the UK clinical research environment, with the **UK Clinical Research Collaboration partners dedicating over £134 million** in investment to improve infrastructure, provide funding and develop research networks⁵.

Using **Cortellis Clinical Trial Intelligence data**, the evidence for the number of experimental trials conducted by industry **clearly shows the strength of the US**, relative to EU countries including the UK. In 2015, the US ran **five times more** industry-sponsored experimental trials than the UK.

The overwhelming share of trials undertaken in the US obscures the landscape in Europe. If we consider the peer group for the UK in Europe, the **UK is competitive for experimental clinical trials**. It is a close second to Germany over the time period 2010-2015. Interestingly Spain has increased the number of these trials consistently over the period.

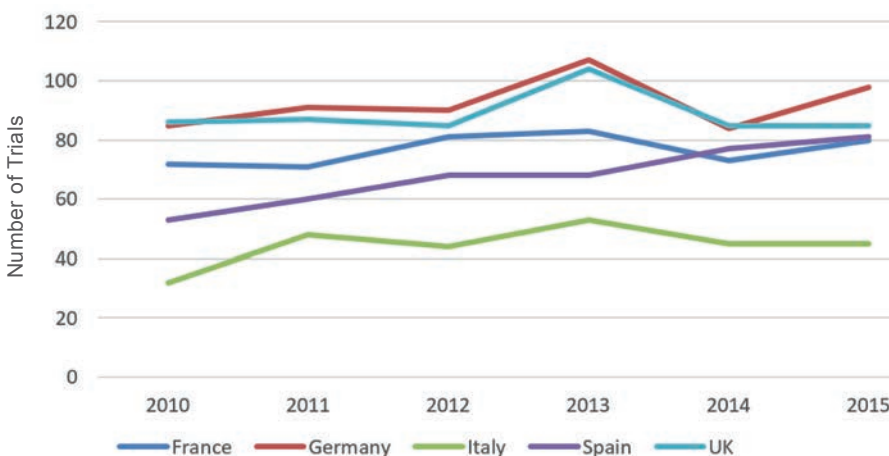
Industry sponsored experimental medicine trials, by year (core EU & US, 2010-2015)



SOURCE: Cortellis Clinical Trial Intelligence from Clarivate Analytics accessed September 2016.

NOTES: Data were collected from the Cortellis Clinical Trial Intelligence from Clarivate Analytics using the following criteria: trial start date (1st January 2010 – 31st December 2015), phase (Phase 0, Phase 1, Phase 1a, Phase 1b, Phase 1/2 and Phase 2a clinical studies) but excluding healthy volunteer studies, and country (UK, Germany, France, Italy, Spain, US). Trials related to pharmaceutical drug development and molecular/ biological entities and pathophysiology and biomarkers studies were included. Only commercially-sponsored trials were included. All therapeutic areas were included in this analysis including oncology.

Industry sponsored experimental medicine trials, European peer group



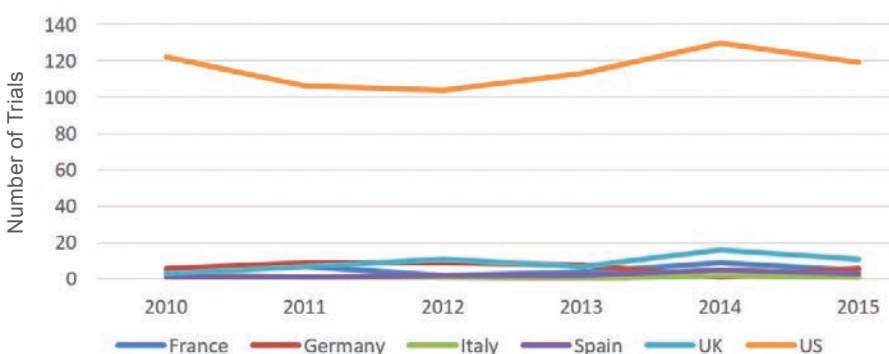
SOURCE: Cortellis Clinical Trial Intelligence from Clarivate Analytics accessed September 2016.

NOTES: Data were collected from the Cortellis Clinical Trial Intelligence from Clarivate Analytics using the following criteria: trial start date (1st January 2010 – 31st December 2015), phase (Phase 0, Phase 1, Phase 1a, Phase 1b, Phase 1/2 and Phase 2a clinical studies) but excluding healthy volunteer studies, and country (UK, Germany, France, Italy, Spain). Trials related to pharmaceutical drug development and molecular/ biological entities and pathophysiology and biomarkers studies were included. Only commercially-sponsored trials were included. All therapeutic areas were included in this analysis including oncology.

Definition: Experimental medicine trials involve "investigation undertaken in humans, relating where appropriate to model systems, to identify mechanisms of pathophysiology or disease, or to demonstrate proof-of-concept evidence of the validity and importance of new discoveries or treatments."⁶⁰

- 5.2** Experimental medicine trials are an important area of development within British universities, and they have been identified as an opportunity for greater academic-industry collaboration. In absolute terms, the total number of collaborative experimental studies between industry and academia is low, according to the Clarivate Analytics analysis. The UK is competitive within Europe for these studies and has increased its share of collaborative research since 2010.

Collaborative industrial-academic experimental medicine trials, by year 2010 - 2015



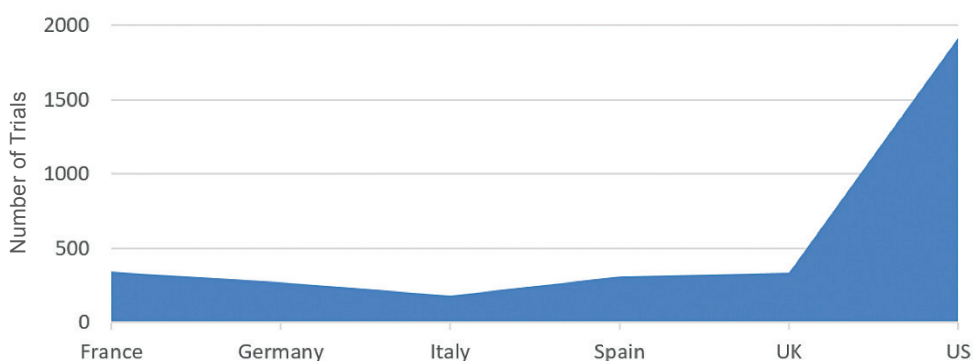
SOURCE: Cortellis Clinical Trial Intelligence from Clarivate Analytics accessed September 2016.

NOTES: Data were collected from the Cortellis Clinical Trial Intelligence from Clarivate Analytics using the following criteria: trial start date (1st January 2010 – 31st December 2015), phase (Phase 0, Phase 1, Phase 1a, Phase 1b, Phase 1/2 and Phase 2a clinical studies) but excluding healthy volunteer studies, and country (UK, Germany, France, Italy, Spain, US). Trials related to pharmaceutical drug development and molecular/ biological entities and pathophysiology and biomarkers studies were included.

Trials were only included as collaborative if they were industry-sponsored and one or more partners were an academic organisation or were academia sponsored and one or more partners were a commercial organisation. All therapeutic areas were included in this analysis including oncology.

5.3 According to the Clarivate Analytics analysis, oncology was the top therapy area for experimental trials for all countries examined. This may reflect the fact that all oncology trials are routinely carried out in patients and not healthy volunteer studies. The UK is competitive across Europe in a number of other therapy areas and **demonstrates expertise in respiratory studies**, which was not a top 10 therapy area for the US.

Oncology experimental medicine trials, 2010 - 2015

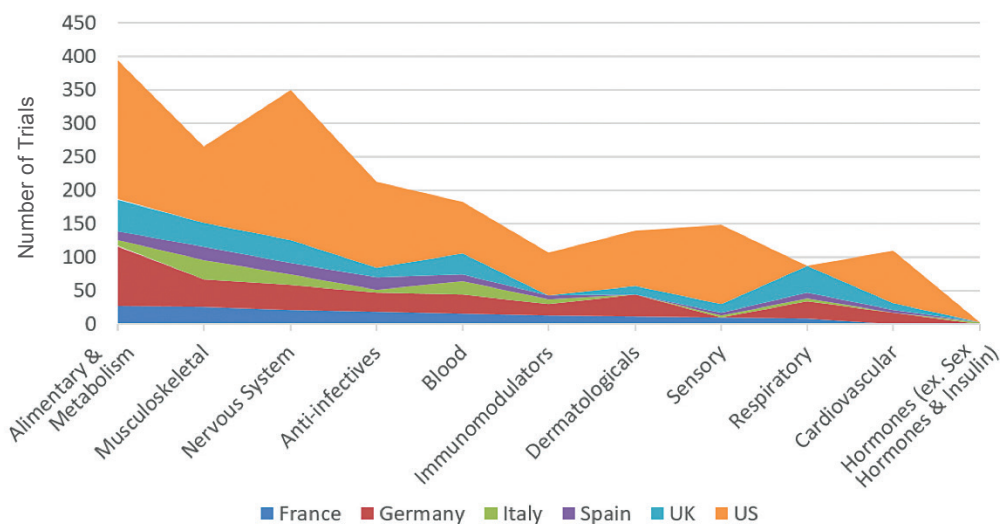


SOURCE: Cortellis Clinical Trial Intelligence from Clarivate Analytics accessed September 2016.

NOTES: Data were collected from the Cortellis Clinical Trial Intelligence from Clarivate Analytics using the following criteria: trial start date (1st January 2010 – 31st December 2015), phase (Phase 0, Phase 1, Phase 1a, Phase 1b, Phase 1/2 and Phase 2a clinical studies) but excluding healthy volunteer studies, and country (UK, Germany, France, Italy, Spain, US). Trials related to pharmaceutical drug development and molecular/ biological entities and pathophysiology and biomarkers studies were included. Only commercial trials were included. Collaborative trials were only included if one or more partners were a commercial organisation. Number of trials identified the top 10 therapy areas for each country, all therapeutic areas were included in this analysis including oncology.

We present the data for oncology trials separately to allow for clearer analysis of trends amongst the other therapeutic areas.

Top 10 experimental medicine trial therapy areas, by country (Core EU & US, 2010 - 2015) - excluding oncology

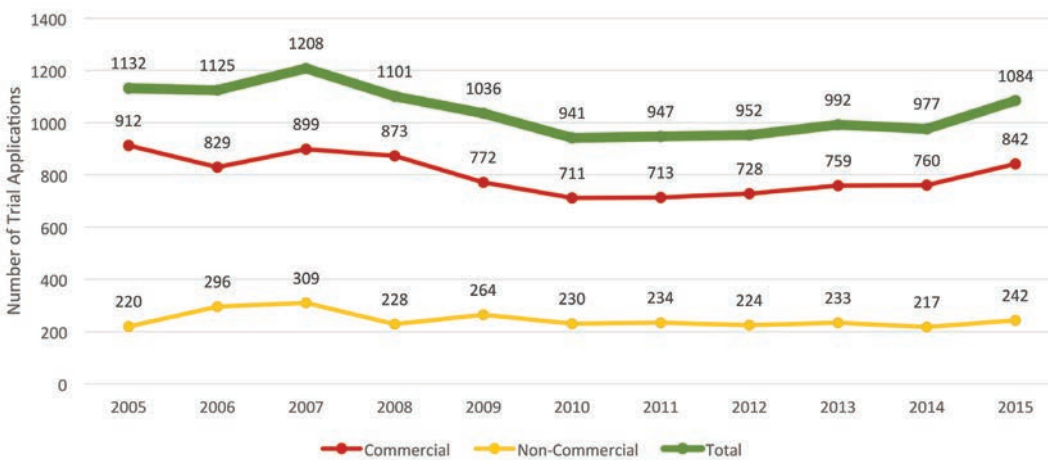


5.4 In the UK, the Department for Business, Innovation and Skills published the second annual series of *Life Science Competitiveness Indicators*⁷, which reviewed the relative shares of patients recruited to global studies across all trial phases. This evidence revealed that the **share of patients recruited to global studies in the UK, rose from 1.6% in 2010 to 2.7% in 2014**. The UK share remains substantially less than the US share, lower than Germany and Poland, and greater than France and the Czech Republic⁷. However, the data reveal that any analysis has to look at trends over a longer period, as there is considerable volatility in the numbers by year.

One way to measure clinical research is to review the clinical trial applications received by the UK regulator, the Medicines and Healthcare products Regulatory Agency (MHRA). According to the MHRA's figures, the **number of applications for clinical trials in the UK has declined since 2005** with the lowest ebb in 2010. Recent years show a **recovery in application numbers**. In 2015, 842 commercial clinical trial applications were received, which is close to the number of applications seen a decade ago.

The UK National Institute for Health Research (NIHR) statistics show that nearly 35,000 participants were recruited to 650 new commercial contract studies taking place through the Network in 2015-16⁸. It is important to take into account a number of factors that could contribute to the differences between the MHRA data and the NIHR statistics. Firstly, not all applications would have been successful – either being totally unsuccessful or requiring further amendments with subsequent delay and secondly, not all commercial research is necessarily conducted via the NIHR clinical research network. However, the conclusion that can be drawn is that both MHRA and the NIHR analyses indicate a continued competitive performance for clinical research in the UK.

UK clinical trial applications received



SOURCE: Adapted from MHRA Clinical Trials for Medicines: authorisation assessment performance.

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/564942/10_Oct_2016.pdf last accessed November 2016.

NOTES: MHRA last updated the data in November 2016. The data set out the number of applications assessed by MHRA split out by phase and commercial and non-commercial sponsors between 2005 and 2015 for all clinical trial phases.

5.5 The MHRA data for clinical trial applications by Phase 1 are a good proxy for clinical trial activity in the UK. If we look at the period as a whole (2005-2015) for **commercially sponsored applications**, there is a marked decline in Phase 2 (-6%) and no growth in Phase 4 applications. However, since 2011, the decline is less marked, with a decline of 4% in Phase 1 trial applications and growth of 6% in Phase 4 applications. However, **between 2011 and 2015**, applications for **Phase 2 and 3 trials grew by 7%**, surpassing in 2015 the number of applications seen in 2007.

UK commercial clinical trial applications by phase



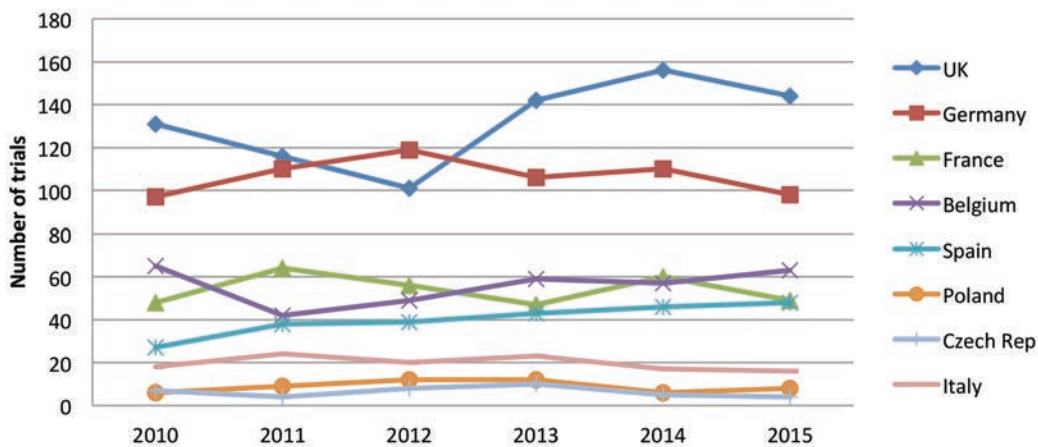
Adapted from MHRA Clinical Trials for Medicines: authorisation assessment performance

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/564942/10_Oct_2016.pdf last accessed November 2016

NOTES: In 2005 and 2006, Phase 4 trials were included together with Phase 2 and III trials. MHRA last updated the data in November 2016. The data set out the number of applications assessed by MHRA split out by phase for commercial sponsors only.

5.6 Using Cortellis Clinical Trial Intelligence data from Clarivate Analytics, the evidence for the number of trials for **Phase 1 clinical research clearly shows the continued strong performance of the UK**, relative to other EU countries including Germany, although in 2015 both Germany and the UK show a decline from the 2014 performance.

Phase 1 clinical trials UK vs Europe

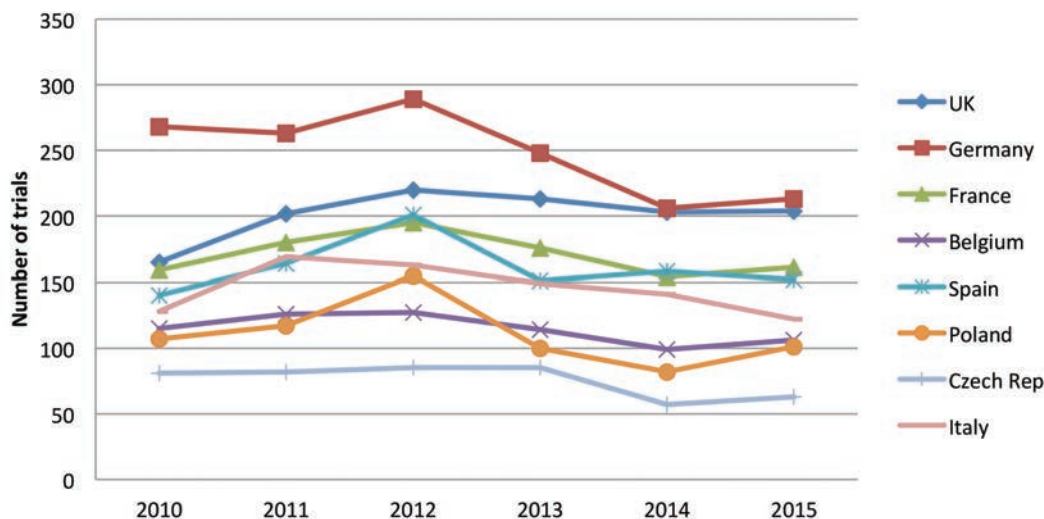


SOURCE: Cortellis Clinical Trial Intelligence from Clarivate Analytics, accessed July 2016.

NOTES: Data were collected from Cortellis Clinical Trial Intelligence, Clarivate Analytics using the following criteria: trial start date (1st January 2010 – 31st December 2015), phase (1, 2, 3), and country (UK, Germany, France, Belgium, Spain, Poland, Czech Republic and Italy). Only trials related to pharmaceutical drug development and molecular/biological entities were included. Only commercial trials were included. Collaborative trials were only included if one or more partners were a commercial organisation. All therapeutic areas were included in this analysis.

5.7 The **UK is competitive for Phase 2 clinical trials** in Europe, according to the Clarivate Analytics Cortellis analysis. By 2015, the number of Phase 2 trials in the UK is roughly matched to that of the leading country, Germany (which has seen a decline in the number of Phase 2 clinical trials over the past few years).

Phase 2 clinical trials UK vs Europe

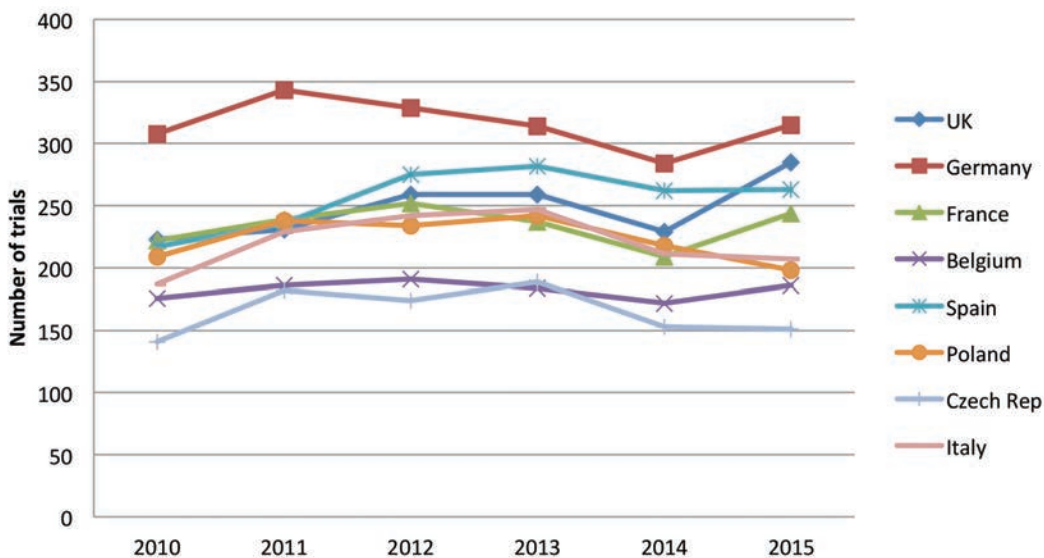


SOURCE: Cortellis Clinical Trial Intelligence from Clarivate Analytics, accessed July 2016.

NOTES: Data were collected from Cortellis Clinical Trial Intelligence, Clarivate Analytics using the following criteria: trial start date (1st January 2010 – 31st December 2015), phase (1, 2, 3, unspecified) and country (UK, Germany, France, Belgium, Spain, Poland, Czech Republic and Italy). Only trials related to pharmaceutical drug development and molecular/biological entities were included. Only commercial trials were included. Collaborative trials were only included if one or more partners were a commercial organisation. All therapeutic areas were included in this analysis.

5.8 According to these data, the **UK is continuing to demonstrate competitive performance in Europe for Phase 3 trials** and has even moved ahead of Spain this year. What is interesting about this evidence is that the decline, seen in 2014 for all compared countries in Europe, seems to have picked up this year. It will be essential over the next few years to monitor whether this is an isolated year or whether it is the beginning of an upward trend for Phase 3 clinical trials in Europe.

Phase 3 clinical trials UK vs Europe

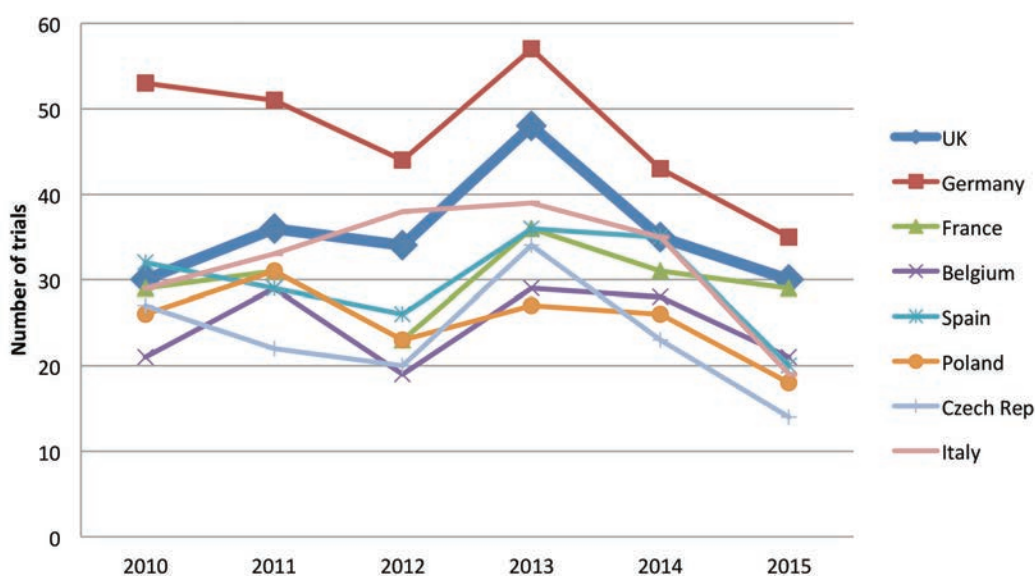


SOURCE: Cortellis Clinical Trial Intelligence from Clarivate Analytics, accessed July 2016.

NOTES: Data were collected from Cortellis Clinical Trial Intelligence, Clarivate Analytics using the following criteria: trial start date (1st January 2010 – 31st December 2015), phase (1, 2, 3) and country (UK, Germany, France, Belgium, Spain, Poland, Czech Republic and Italy). Only trials related to pharmaceutical drug development and molecular/biological entities were included. Only commercial trials were included. Collaborative trials were only included if one or more partners were a commercial organisation. All therapeutic areas were included in this analysis.

5.9 Exploring the data for clinical trials by therapeutic focus, we can see areas where specific countries may have competitive advantage based on scientific excellence and clinical opportunity. For **cardiovascular treatments, Germany and the UK are both significant sites for clinical research; however, we are seeing an overall downward trend** in research in this disease area which is a likely reflection of product pipeline rather than a result of global competition for trials in cardiovascular disease.

Clinical trials for cardiovascular treatments

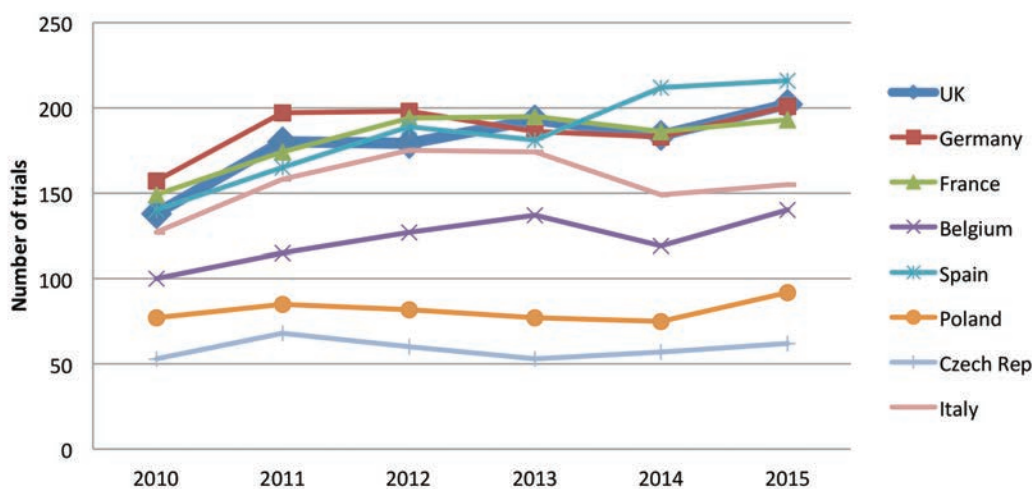


SOURCE: Cortellis Clinical Trial Intelligence from Clarivate Analytics, accessed July 2016.

NOTES: Data were collected from Cortellis Clinical Trial Intelligence, Clarivate Analytics using the following criteria: trial start date (1st January 2010 – 31st December 2015), phase (1, 2, 3, and 4), and country (UK, Germany, France, Belgium, Spain, Poland, Czech Republic and Italy). Only trials related to pharmaceutical drug development and molecular/biological entities were included. Only commercial trials were included. Collaborative trials were only included if one or more partners were a commercial organisation. This analysis focused on cardiovascular treatment trials only. Trials across multiple therapy areas were only included once. The therapy area in which they were included was determined by the trial's main purpose for study.

5.10 Oncology clinical trials represent a higher share of clinical trials in the dataset for all countries. The leadership position in Europe for oncology trials is clearly contested, with an interesting **increase in the number of trials in Spain** over the period. With all types and phases of trials included, it is difficult to explore whether there is any differentiation amongst countries in their comparative advantage for oncology clinical research. However, we note that the UK remains competitive for oncology trials and is on par with Germany and France, with a sustained increase in the number of trials in the UK over the period.

Clinical trials for oncology treatments

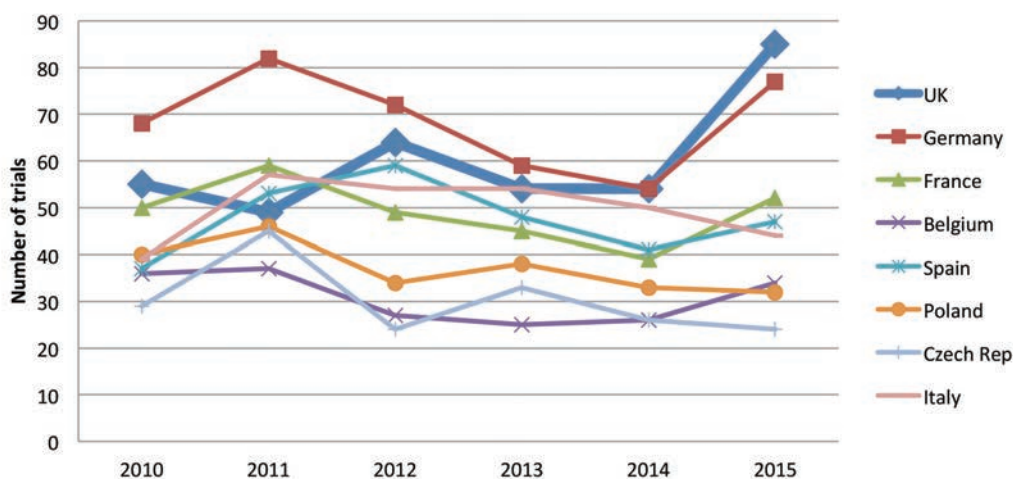


SOURCE: Cortellis Clinical Trial Intelligence from Clarivate Analytics, accessed July 2016.

NOTES: Data were collected from Cortellis Clinical Trial Intelligence, Clarivate Analytics using the following criteria: trial start date (1st January 2010 – 31st December 2015), phase (1, 2, 3, and 4), and country (UK, Germany, France, Belgium, Spain, Poland, Czech Republic and Italy). Only trials related to pharmaceutical drug development and molecular/biological entities were included. Only commercial trials were included. Collaborative trials were only included if one or more partners were a commercial organisation. This analysis focused on oncology treatment trials only. Trials across multiple therapy areas were only included once. The therapy area in which they were included was determined by the trial's main purpose for study.

5.11 This year has seen a notable increase broadly across Europe, in trials for treatments related to **diseases of the nervous system**. Where the preceding years showed a decline which was particularly marked in Germany and France, this year has shown a sharp upturn for the UK, which for the first time conducted more trials in this area than Germany. Overall, the number of trials reported was fewer than for oncology, but more than for cardiovascular disease.

Clinical trials for treatments related to the central nervous system



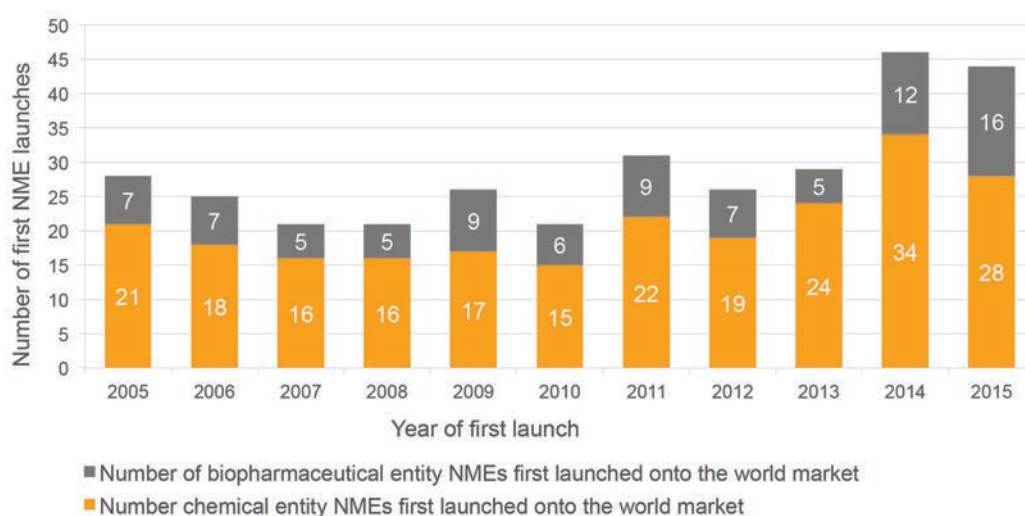
SOURCE: Cortellis Clinical Trial Intelligence from Clarivate Analytics, accessed July 2016.

NOTES: Data were collected from Cortellis Clinical Trial Intelligence, Clarivate Analytics using the following criteria: trial start date (1st January 2010 – 31st December 2015), phase (1, 2, 3, and 4), and country (UK, Germany, France, Belgium, Spain, Poland, Czech Republic and Italy). Only trials related to pharmaceutical drug development and molecular/biological entities were included. Only commercial trials were included. Collaborative trials were only included if one or more partners were a commercial organisation. This analysis focused on central nervous treatment trials only. Trials across multiple therapy areas were only included once. The therapy area in which they were included was determined by the trial's main purpose for study.

5.12 The aim for all clinical research is to provide the evidence needed to secure marketing authorisation.

Over the period 2009 to 2015, industry has seen a **growth in the number of new molecular entities (NMEs), both chemical and biological, launched worldwide**. This is a good measure of the innovative activity of the industry, and the confirmation of welcome new treatments for patients. Over the past two years, the number of new biopharmaceutical molecular entities has increased in particular, and this is anticipated as more of the pipeline includes these technologies.

Number of first NME launches between 2005 - 2015 by active substance type



SOURCE: 2016 CMR Factbook from Clarivate Analytics; Drawn from the Annual Survey of New Molecular Entity First Launches / New Medicine Launches 2015. A complete guide to New Molecular Entities (NMEs) launched worldwide and reproduced with permission.

NOTES: To compile this analysis, annual surveys of the global pharmaceutical industry were undertaken to identify all new molecular entities launched for the first time anywhere in the world between 2005 and 2015.

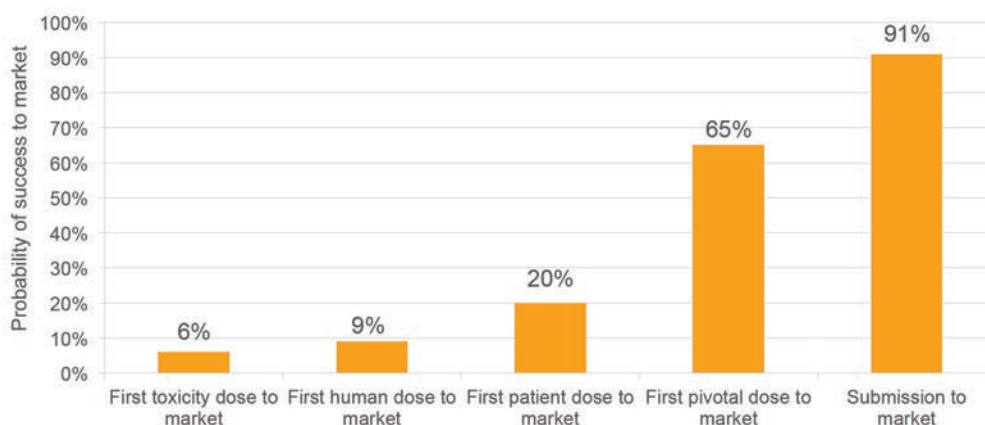
New Biopharmaceutical Entity (NBE): A biological substance that has been produced or extracted from a biological source for therapeutic, prophylactic or in vivo diagnostic use in humans. This includes i) a substance isolated directly from animal tissues eg hormones; ii) a naturally occurring or modified polypeptide, protein, DNA or RNA product (produced by recombinant DNA or hybridoma technology and expressed in cell lines, transgenic animals or transgenic plants).

New Chemical Entity (NCE): A chemical substance that has been created or synthesised using physical or chemical manufacturing methods capable of a high degree of consistency.

5.13 The drug development cycle continues to be challenging and highly uncertain, but there has been some improvement. If we compare the figures from the **CMR Factbook 2015**, to last year's figures (see *UK Biopharma R&D Sourcebook 2015* for 2014), the difficult period that precedes the first pivotal dose to market now shows a greater probability of success. The increases are small but are an important trend (from 5% to 6% for first toxicity dose to market, from 7% to 9% for first human dose to market, and from 17% to 20% for first patient dose to market).

Probability of successfully reaching market authorisation remains unchanged for the last two stages. Upon reaching the **first pivotal dose (eg Phase 3), almost two-thirds of active substances are expected to make it through to market authorisation**, but a third will not progress.

Probability of success to market for active substances

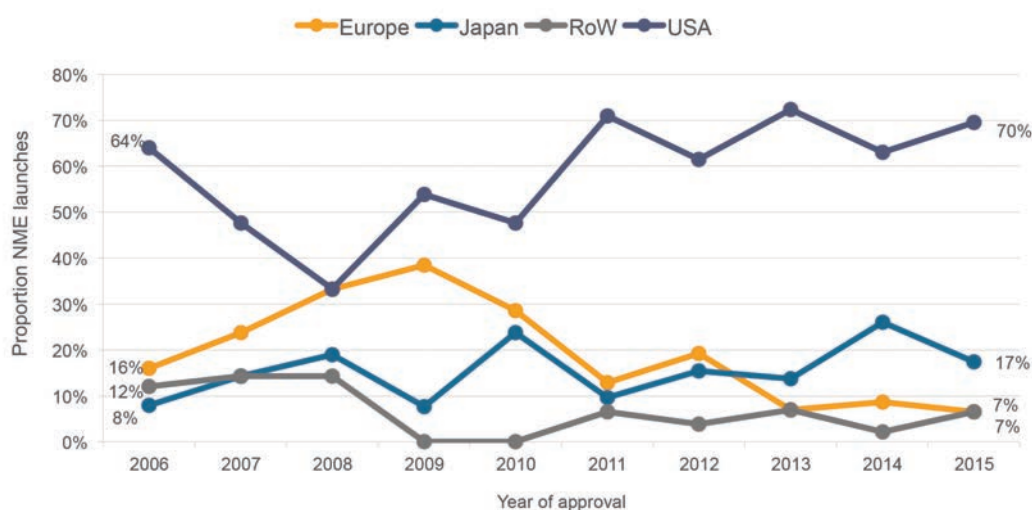


SOURCE: 2016 CMR Factbook from Clarivate Analytics; Drawn from the Global R&D Performance Metrics Programme and reproduced with permission.

NOTES: Between-phase success rates were calculated using the CMR methodology. The fate (progressed/terminated) of active substances that entered phase between 2009 and 2011 were assessed as of 31st December 2014. Displayed are the probability of success to market values, which are a product of the between-phase success rates from the start milestone to market.

5.14 Comparing across regions over the period 2006 - 2015, the **United States has remained the principal region for the first launch of New Molecular Entities (NME)** and this trend has been more pronounced since 2009. The United States retains a key innovative draw for new medicines over other regions around the world. After increasing its share of first launches up to 2009, **Europe now sees very few, with only 7% of NMEs first launched in Europe in 2015.**

Region of first launch for new molecular entities 2006 - 2015



SOURCE: 2016 CMR Factbook from Clarivate Analytics; Drawn from the Annual Survey of New Molecular Entity First Launches / New Medicine Launches 2015. A complete guide to New Molecular Entities (NMEs) launched world-wide and reproduced with permission.

NOTES: Annual surveys of the global pharmaceutical industry were undertaken to identify all new molecular entities introduced for the first time anywhere in the world. Presented is the proportion of each year's output between 2006 and 2015 according to the geographical region of the first launch.

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The theme of this year's Sourcebook is "Open for Innovation". We say this very much in parallel to the more often used phrase, "Open for business". But our goal sets out a change in how we discover, develop, manufacture and deliver new medicines, and, as the analysis in this chapter demonstrates, the change is well underway.

Open innovation isn't a new concept, but, as the Introduction from our Innovation Board chair, Dr Neil Weir, explains, it is also not a static concept. The practices to deliver open innovation, and the infrastructure to support these, continue to evolve and adapt to the opportunities

and the challenges we face. Moreover, open innovation inspires (and is inspired by) a culture and a mind-set that have to be fostered, and leadership that makes the goal clear. Our two Viewpoint essays illustrate these points eloquently.

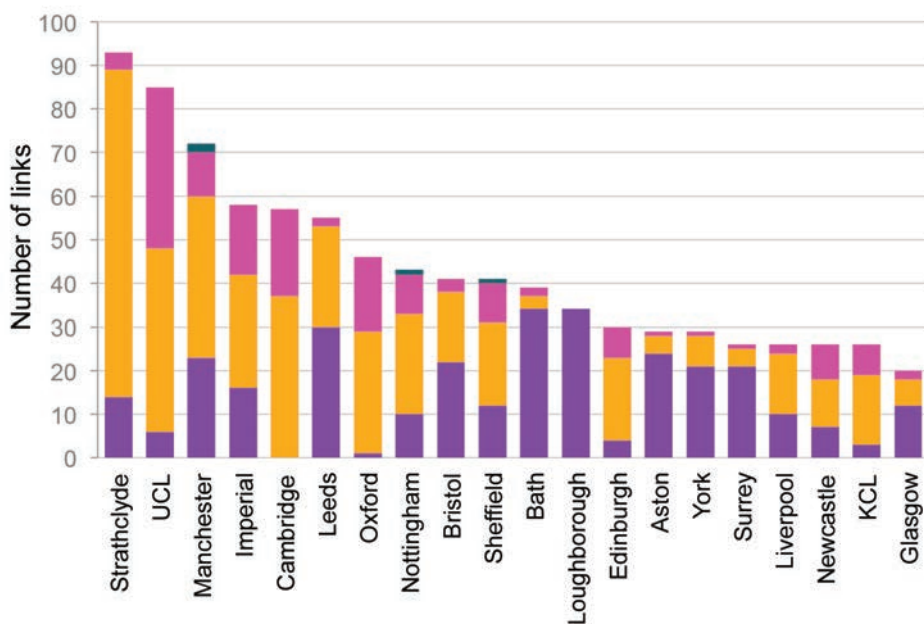
What we will cover in this final section of the *UK Biopharma R&D Sourcebook 2016* is some of the evidence of how the UK is "open for innovation" today. We will include here some new research using bibliometrics to illustrate collaboration, as well as evidence from recently published research by the ABPI on collaboration and the drug discovery environment in the UK.

6.1 Last year's report from Professor Ann Dowling for the Government identified areas for improvement to encourage greater collaboration¹. The study noted that "[t]he UK has a vibrant research environment, with a range of collaborations taking place between universities and business across many disciplines, but there is more to be done to help existing efforts evolve from short-term, project-based collaborations to longer-term partnerships focussed on use-inspired research."¹: p.3

This year, the ABPI undertook its own survey of members to identify links between industry and academia. These links range right across academia from interactions with undergraduates to postdoctoral researchers, fellows and professors.

We collect these data every two years to assess trends in this important work. In this year's survey, data were collected on the number of academic links that were in place as of 31 December 2015 and those that started and finished during 2015 (for example, placements under one year in length).

Overall top 20 academic institutions



SOURCE: Developing talent and partnerships to create new medicines. Published September 15, 2016. <http://www.abpi.org.uk/our-work/library/industry/Pages/Developing-talent-and-partnerships-to-create-new-medicines.aspx>

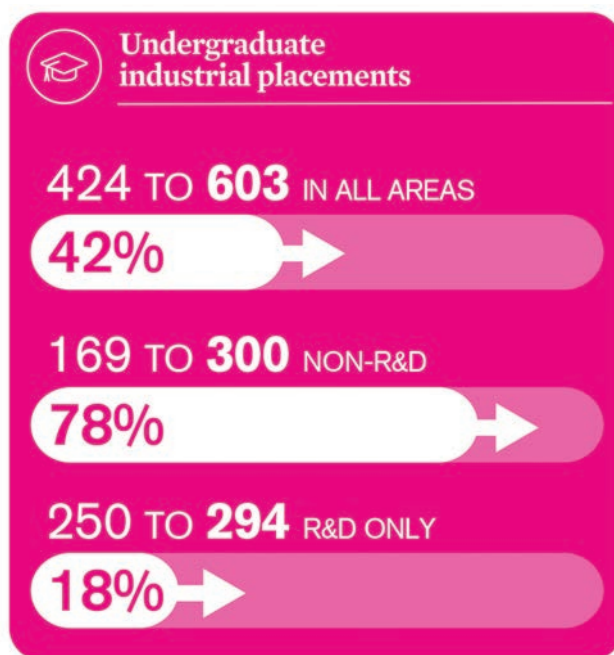
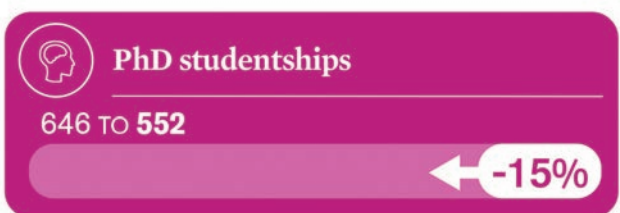
NOTES: The ABPI survey was sent out to all ABPI full members and research affiliates and was intended to capture both R&D and non-R&D interactions, for example those in HR, IT, Finance and other roles across all company sites. The data were collected and analysed by the ABPI.

- Academic posts
- PhD studentships
- Postdoctoral researchers
- Undergraduate IPs

The bar chart and figures below are reproduced from the published report, **Developing talent and partnerships to create new medicines**, and they show some areas of strength but also opportunities that need addressing. The increase in undergraduate industrial placements in research and development (294 placements) was particularly noteworthy, in comparison with the figure in 2013 of 250 placements in R&D), and an even greater increase in non-R&D placements (300 placements in 2015, up from 169 in 2013) in manufacturing and other business areas. This increase in industrial placements stands in contrast to the number of PhDs supported by industry, which is now at its lowest level since 2003. This decline is likely to be driven by a lack of supervisory capacity within pharmaceutical company sites in the UK, many of which have closed or downsized their R&D operations based here.

Moreover, as the first graph demonstrates, these partnerships are happening with a wide range of institutions across the UK. The University of Strathclyde has the highest number of PhD students in partnership with industry (75 PhDs), followed by the next highest-ranked institutions, UCL, Manchester and Cambridge.

The report also illustrates partnerships that are related to collaborative research. For example, the Dundee Division of Signal Transduction Therapy has been continuously supported by several pharmaceutical companies since it was created in 1998. Other partnerships are focused on a specific disease area or more general purpose research, such as validation of therapeutic targets for medicines. The ABPI survey illustrated that the number of major collaborative projects and initiatives is increasing as industry shifts towards long-term open partnerships with academia, charities and other funders.

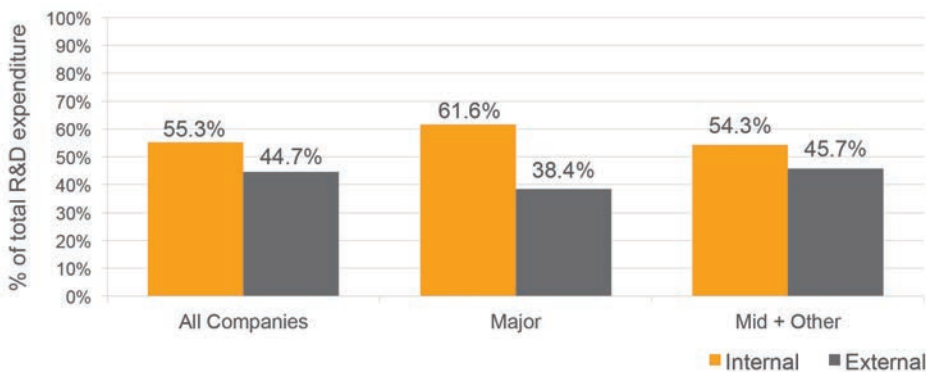


References

- 1 The Dowling Review of Business-University Research Collaborations, Department for Business Innovation & Skills, Editor. 2015, HM Government: London. p. 84.

6.2 Biopharmaceutical companies have been increasing collaboration and extending R&D investment to external projects and partners. In last year's *UK Biopharma R&D Sourcebook 2015*, we presented data from the Thomson Reuters CMR International for 2009 and 2014 that **demonstrated an increase in the share of external spend** within total R&D expenditure from an average of 35% to an average of 41.8% across surveyed companies. This trend has continued with the updated figure for 2015 given as **44.7%**. Although the share of external spend in 2014 was **greatest for the smaller biopharmaceutical companies** ("Mid and other" companies spend less than \$2 billion on R&D), at an average of 54.9%, the difference between "major" and "mid and other" companies was much less in 2015.

Internal and external spend by company size in 2015



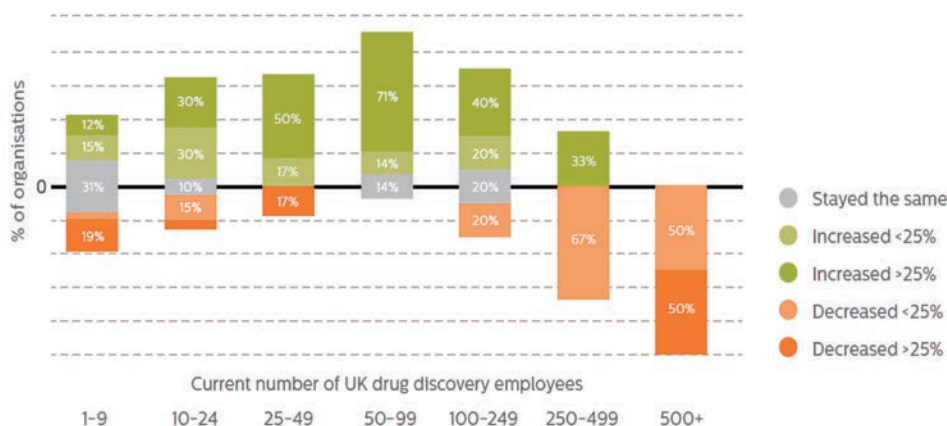
SOURCE: 2016 CMR Factbook from Clarivate Analytics; Drawn from the Industry R&D Investment Programme and reproduced with permission.

NOTES: Presented is the proportion of total R&D expenditure in 2015 allocated either internally or externally, calculated as a median of the data provided by a minimum of five companies. Data are also shown for Major or Mid and Other companies where at least three companies are represented. The data presented in this graph are based on data from 15 companies (11 Major and 4 Mid and Other). Major companies are defined as those spending \geq US\$ 2 billion in 2015 on ethical pharmaceutical R&D. Mid companies are defined as those spending \geq US\$ 0.7 billion and $<$ US\$ 2 billion in 2015 on ethical pharmaceutical R&D. Other companies are defined as those spending $<$ US\$ 0.7 billion in 2015 on ethical pharmaceutical R&D.

6.3 To explore such trends in R&D investment further, the ABPI commissioned economic consultants TBR and CSBL to generate a robust evidence base of the shifting drug discovery landscape in the UK, where there is a particular lack of publicly available data due to difficulties in isolating drug discovery from broader trends in preclinical and clinical development. They made use of a combination of quantitative surveys and expert interviews involving almost 80 organisations across the drug discovery landscape (pharmaceutical companies, biotech companies, contract research organisations (CROs), and academia).

The research shows that there has been a **shift from in-house drug discovery employment in large pharmaceutical companies, to increased employment in smaller and mid-sized companies, CROs, and academia**. The majority of large companies have significantly decreased their number of in-house drug discovery employees in the UK in the last 5 years, whilst there has been an increase in employment in many small and mid-sized organisations.

Change in number of UK drug discovery employees



SOURCE: 2016 The Changing UK Drug Discovery Environment, TBR and CBSL for the ABPI. <http://www.abpi.org.uk/our-work/library/industry/Documents/the-changing-UK-drug-discovery-landscape.pdf>

NOTES: Change in number of UK drug discovery employees in the last 5 years across all organisations: 1-9 n=21 (as % of 26), 10-24 n=18 (as % of 20), 25-49 n=5 (as % of 6), 50-99 n=7 (as % of 7), 100-249 n=5 (as % of 5), 250-499 n=3 (as % of 3), 500+ n=2 (as % of 2). Where columns do not sum to 100% it is because some firms were not able to answer or had not traded for 5 years.

6.4 Almost all organisations have **increased their absolute level of investment in collaborative and outsourced drug discovery** in the UK in the last 10 years, demonstrating a shift towards more open ways of working, and consistent with the trends in overall external R&D spend.

Change in UK drug discovery collaboration investment

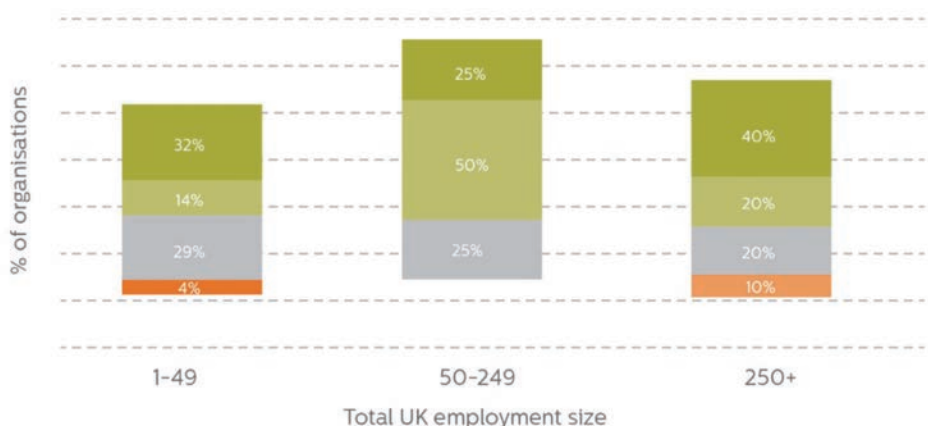


SOURCE: 2016 The Changing UK Drug Discovery Environment, TBR and CBSL for the ABPI. <http://www.abpi.org.uk/our-work/library/industry/Documents/the-changing-UK-drug-discovery-landscape.pdf>

NOTES: Change in UK investment in collaborative and outsourced drug discovery by initiator firms in last 10 years. For Collaborative investment: 1-49 n=18 (as % of 28), 50-249 n=3 (as % of 4), 250+ n=8 (as % of 10). For Outsourced investment: 1-49 n=22 (as % of 28), 50-249 n=4 (as % of 4), 250+ n=9 (as % of 10). Where columns do not sum to 100% it is because some firms were not able to answer or had not traded for 10 years.

- Stayed the same
- Increased <25%
- Increased >25%
- Decreased <25%
- Decreased >25%

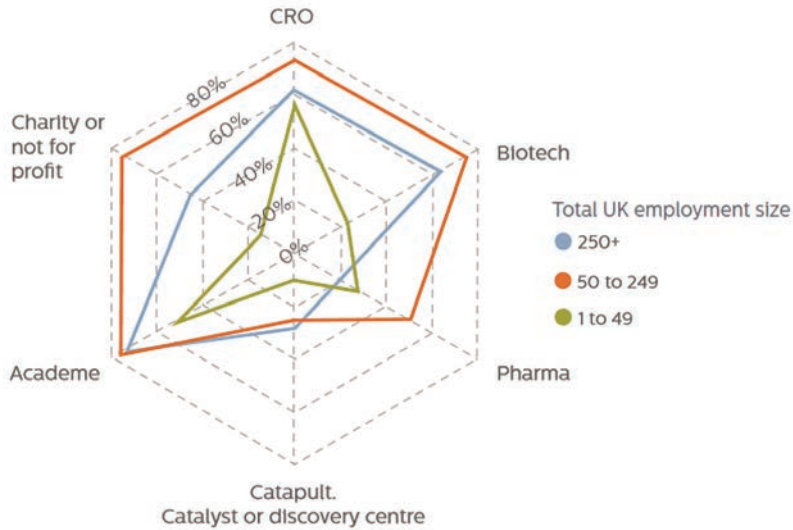
Change in UK drug discovery outsourcing investment



6.5 Companies **work collaboratively with a broad range of organisations** in the UK including academia, CROs, biotech companies, and research charities. Organisations **work via a variety of collaborative models**. One-to-one commercial collaborations are the most common. However, almost as many companies report participating in pre-competitive collaborations with academia or industry as having traditional commercial collaborations.

Mirroring the increase in outsourced drug discovery investment shown above, the large majority of service providers (CROs and some academic units) have seen an increase in commissioned discovery work in the last 5-10 years. As many service providers report clients from the EU and US as the UK, but interestingly few report working for clients based in Asia.

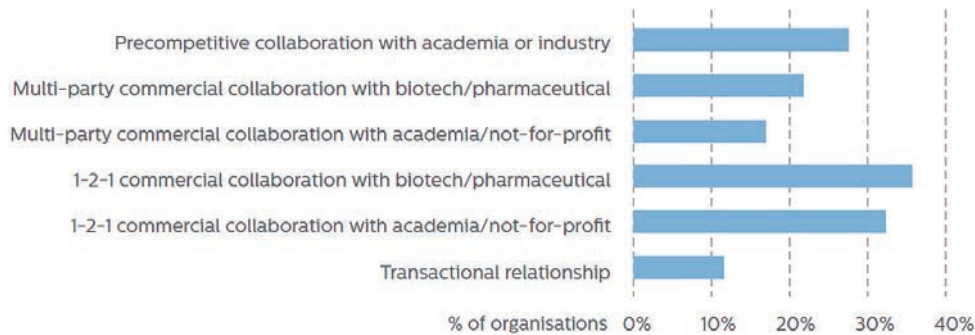
Partnerships made by initiator organisations by size of organisation (total employment) n=48



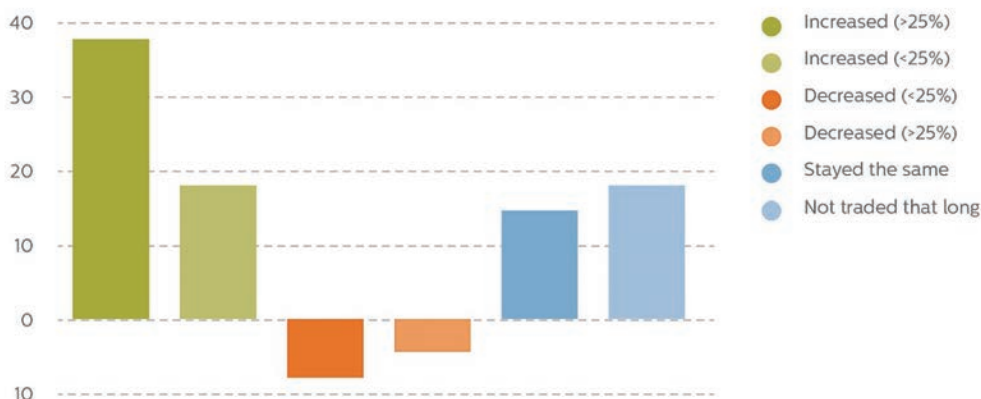
SOURCE: 2016 The Changing UK Drug Discovery Environment, TBR and CBSL for the ABPI. <http://www.abpi.org.uk/our-work/library/industry/Documents/the-changing-UK-drug-discovery-landscape.pdf>

NOTES: For Partnership by size of organisation, number of respondents is 48. For Types of Partnership, number of respondents is 77. For CRO graphs, number of respondents is 28.

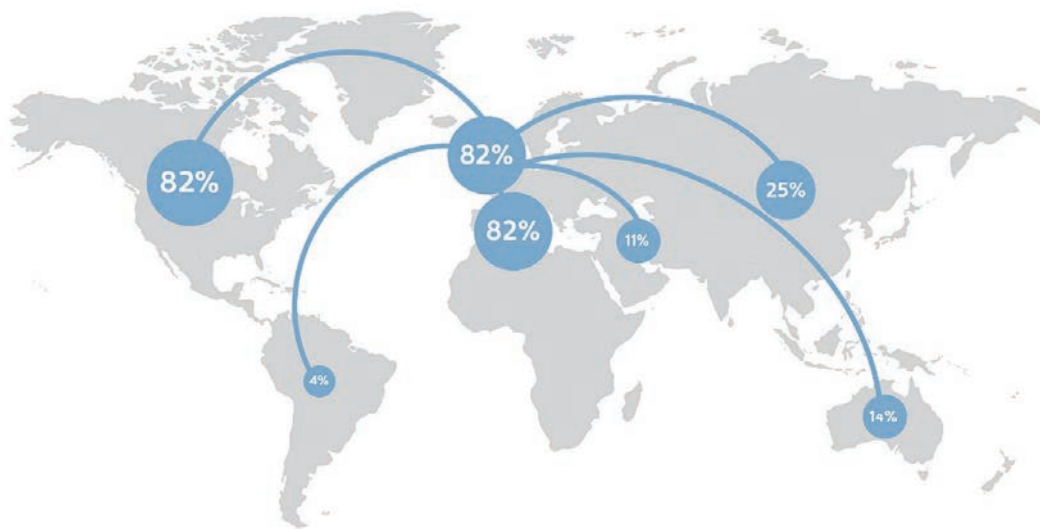
Types of partnership entered into across all organisations n=77



Percentage of CROs reporting change in commissioned activity in the last 5 years, n=28

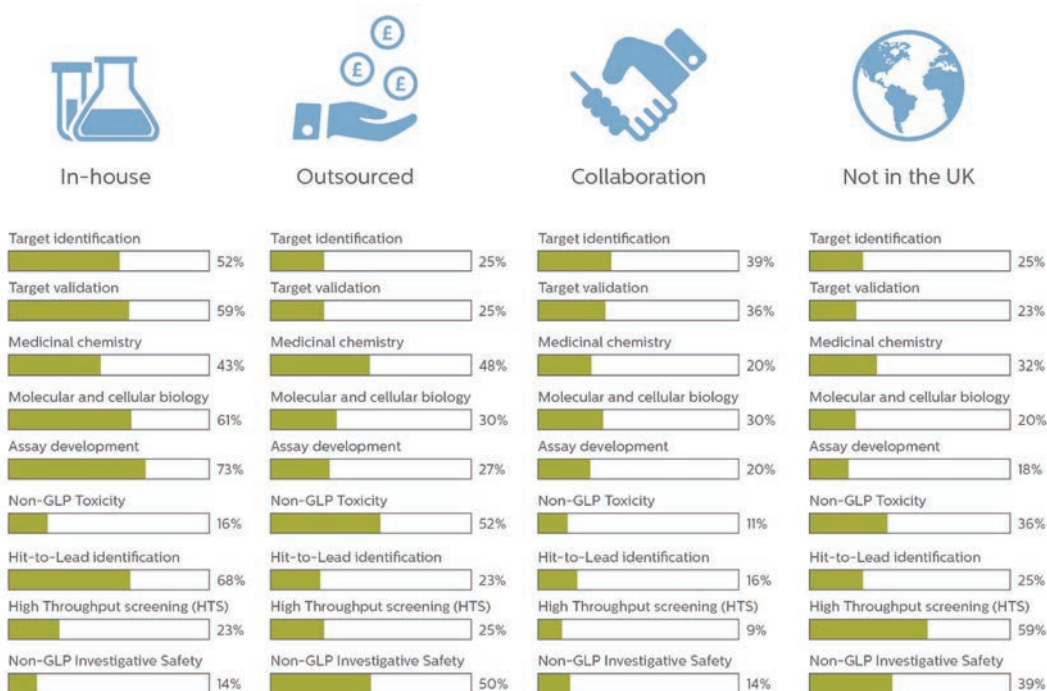


Percentage of CROs reporting they work for customers in different global regions, n=28



6.6 Companies conduct **different parts of the drug discovery process in different ways and in different parts of the world.** Notably, many companies outsource non-GLP safety studies in the UK, whilst many companies conduct target identification and validation in collaboration in the UK, likely reflecting the high quality of UK biological academic research. Almost 60% of companies undertake high throughput screening outside of the UK.

Change in UK collaboration investment



SOURCE: 2016 The Changing UK Drug Discovery Environment, TBR and CBSL for the ABPI. <http://www.abpi.org.uk/our-work/library/industry/Documents/the-changing-UK-drug-discovery-landscape.pdf>

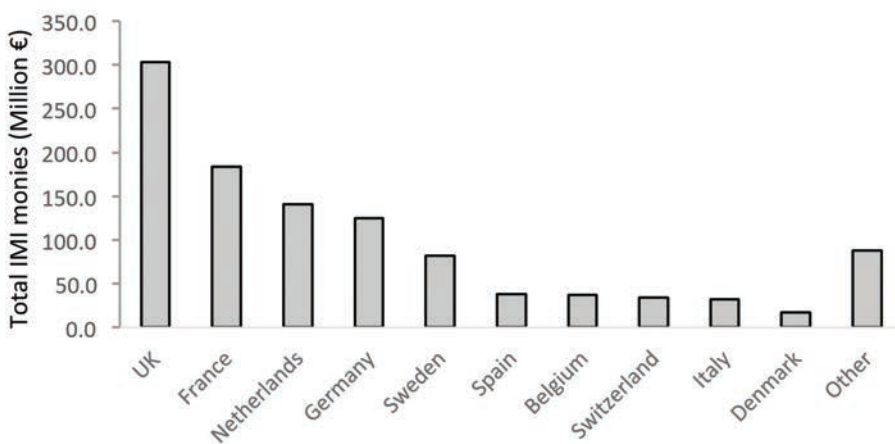
NOTES: Percentage of initiator organisations conducting work for customers in each way, n=44.

6.7 One important framework for collaboration in Europe has been the **Innovative Medicines Initiative (IMI)**, which is one of the world's largest collaborative medical research initiatives. This Public Private Partnership brings together the pharmaceutical industry with academia, small and medium sized enterprises (SMEs), and others, to accelerate medicines discovery and development. It has a **total budget of over €5 billion between 2008 and 2024**, provided jointly by European Commission research funding, and in-kind contribution from pharmaceutical companies, and more recently, other industrial sectors.

The ABPI undertook research this year to assess the patterns of collaboration in IMI, and this publication is available to read in full on our website (link below). The **UK has received 28% of total IMI funding from the EU Commission, the largest amount of any country**. This totals €302.8 million to date. Both UK academic institutions and SMEs receive the highest levels of IMI funding of any country; 30% of all funding received by UK academic institutions and 22% of all funding received by UK SMEs. The UK also has the highest number of participants in both academia and SMEs (each with 21% of participants in their category), indicating that the high proportion of funding received by the UK is not due to attracting a few large projects, but reflects high levels of participation by UK institutions across the IMI.

The UK has attracted funding in IMI projects across a **wide range of research fields and therapeutic areas**. The UK has leveraged particularly high proportions of funding in **respiratory diseases, vaccine development, infectious diseases**, and diabetes. Proportionally less-well funded areas include training, antimicrobial resistance and oncology. To some extent this reflects strengths of the UK's scientific base.

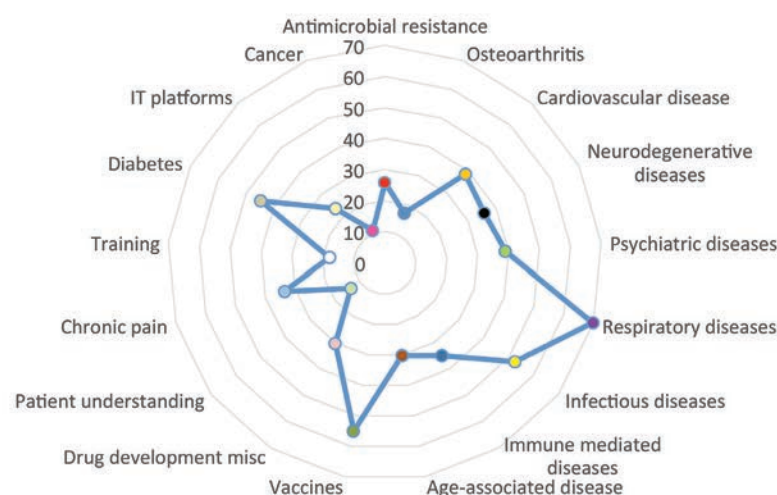
Total IMI funding per country



SOURCE: 2016 UK Participation in the Innovative Medicines Initiative. http://www.abpi.org.uk/our-work/library/industry/Documents/UK_Participation_in_IMI.pdf

NOTES: IMI funding (from EU Commission) for top 10 country recipients, with all other participating countries collated in "other". Data provided directly by EFPIA for all participating IMI countries.

IMI funded UK research areas as a percentage of IMI total



SOURCE: 2016 UK Participation in the Innovative Medicines Initiative. http://www.abpi.org.uk/our-work/library/industry/Documents/UK_Participation_in_IMI.pdf

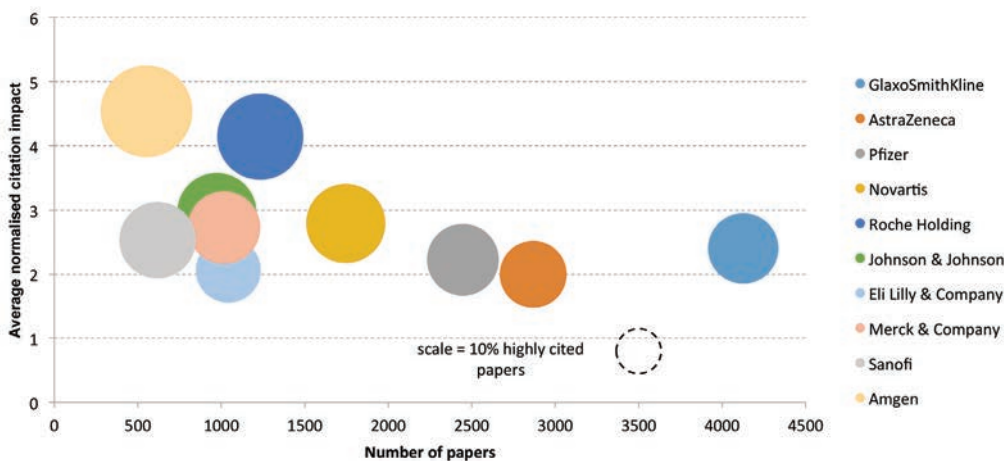
NOTES: Proportion of IMI monies received by the UK split by research area. IMI projects were allocated a therapeutic/research area, and data were calculated using UK and total project data.

6.8 An important way of mapping scientific collaborations is through the study of their published papers. We have worked with Clarivate Analytics this year to map the current collaboration patterns between the pharmaceutical industry and academia in the UK for the life sciences, using this important technique. The analysis that follows further illustrates the **strength of academic-industry collaboration in the life sciences in the UK**.

The following figures show that pharmaceutical companies **co-authored over 16,000 papers** with UK organisations **between 2006 and 2015**, and were acknowledged as providing funding for research on over 38,000 papers. These include companies with little or no in-house R&D footprint in the UK, as well as those with significant in-house work in the UK.

Both papers co-authored by pharmaceutical companies and those acknowledging company funding were **on average more highly cited than the global average**, suggesting they have a higher than average impact.

Pharmaceutical companies with highest number of co-authored UK papers, by number of papers and citation impact



SOURCE: Data provided by Clarivate Analytics

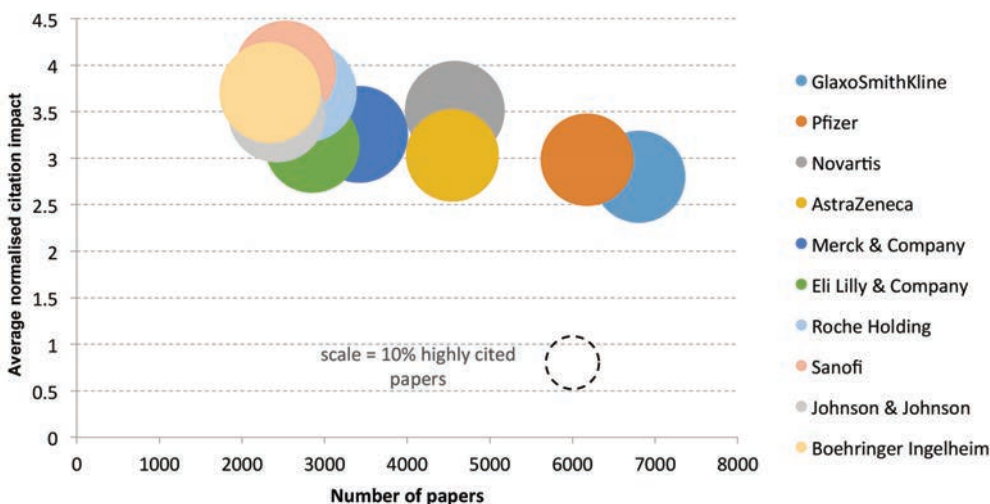
NOTES: Number of papers, normalised citation impact, and % highly cited papers, produced by UK organisations and either co-authored by pharmaceutical companies (top) or acknowledging funding from pharmaceutical companies (bottom) between 2006 and 2015. Only the 10 pharmaceutical companies with the highest number of collaborative papers are shown.

UK co-authored publications were selected by using Web of Science address data. Funding information comes from the Web of Science funding acknowledgement data. Some automatic and manual unification was done on organisation names.

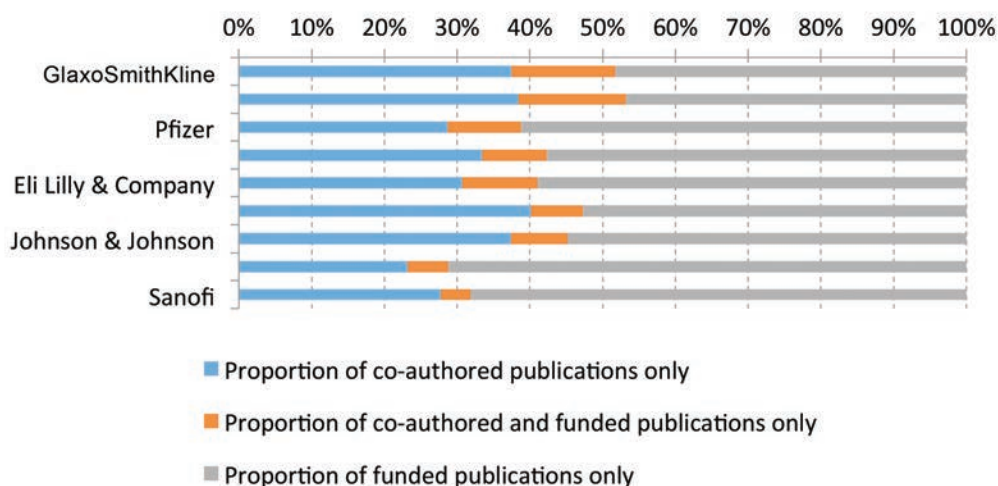
Normalised citation impact: citation rates vary between research fields and with time, consequently, analyses must take both field and year into account. In addition, the type of publication will influence the citation count. The standard normalisation factor is the world average citations per paper for the year and journal category in which the paper was published.

Highly cited papers: highly cited work is recognised as having a greater impact; the high citation rates are correlated with other qualitative evaluations of research performance, such as peer review. Papers that are in the top 10% in terms of citation frequency, taking into account year of publication and field, are considered to be highly cited.

Pharmaceutical companies with highest number of funded UK papers, by number of papers and citation impact



Top pharmaceutical collaborators of UK research split by type of collaborative activity



SOURCE: Data provided by Clarivate Analytics

NOTES: Proportion of publications (which includes papers, meeting abstracts, book reviews, editorial material, and other publications recorded in Web of Science) both co-authored and funded, co-authored, or funded, by the pharmaceutical companies collaborating on the highest number of publications with UK organisations, 2006-2015.

UK co-authored publications were selected by using Web of Science address data. Funding information comes from the Web of Science funding acknowledgement data. Some automatic and manual unification was done on organisation names.

Only the pharmaceutical companies with the highest number of collaborative papers are shown.

6.9 The table and map below show the location of pharmaceutical companies collaborating with UK organisations between 2011 and 2015, as indicated through co-authorship of publications. These show that UK organisations **collaborate with pharmaceutical industry researchers located not only in the UK, but across the world**, particularly in Europe, North America, and Asia. Only four of the top ten cities for industry location were based in the UK, with five of the ten in the USA.

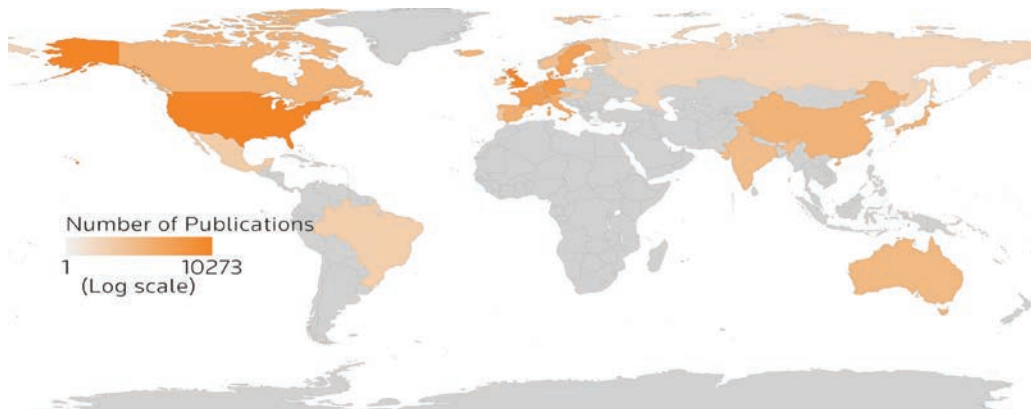
Top 10 cities for location of pharmaceutical companies collaborating with UK organisations

Rank	City	Country	Number of publications
1	Basel	Switzerland	1,575
2	Macclesfield	UK	1,083
3	Stevenage	UK	846
4	San Francisco	USA	676
5	Indianapolis	USA	662
6	Cambridge	USA	627
7	Cambridge	UK	606
8	Uxbridge	UK	584
9	Res Triangle Pk	USA	562
10	E Hanover	USA	561

SOURCE: Data provided by Clarivate Analytics

NOTES: Top 10 most frequently occurring city names in the addresses of top 25 pharmaceutical companies - collaborators of UK research, between 2011 and 2015.

Global locations of pharmaceutical companies collaborating with UK organisations



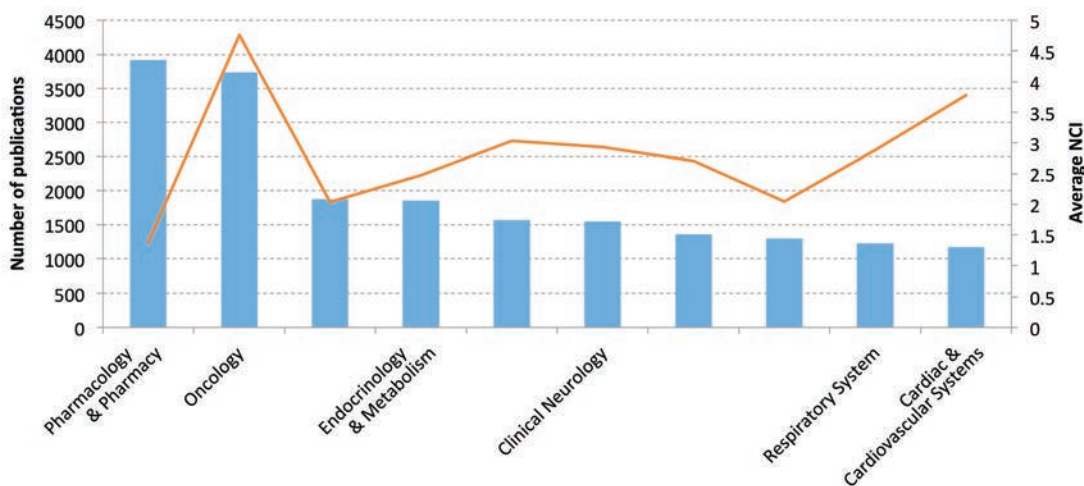
SOURCE: Data provided by Clarivate Analytics

NOTES: Map of countries from addresses of the authors from top 25 pharmaceutical companies within the publications from collaboration with UK authors between 2011 and 2015. Countries with 10 or more publications are shown.

6.10 The pharmaceutical industry collaborates with UK organisations on a broad range of research fields, echoing the strength shown above of the UK in attracting collaborative funding from the IMI across broad research topics (figure 6.7). The most common collaborations between 2006 and 2015 were in **pharmacology & pharmacy, oncology, neurosciences, and endocrinology & metabolism.**

Collaborative research between the industry and UK organisations showed **a higher than average citation impact across all research fields**, but this was **particularly high in oncology and rheumatology**, which may reflect academic strength of the UK in these fields.

Research fields with highest number of collaborative publications between UK organisations and pharmaceutical industry



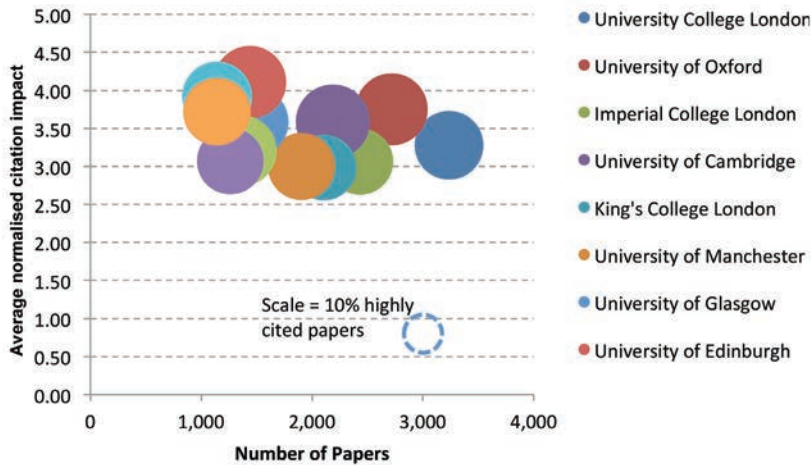
SOURCE: Data provided by Clarivate Analytics, NCI = Average normalised citation impact

NOTES: Number of publications produced by top 25 pharmaceutical companies in collaboration with UK research by biomedical research field. There are 254 Web of Science journal categories. Journals are assigned to one or more categories, and every article within that journal is subsequently assigned to that category. Papers from prestigious, 'multidisciplinary' and general medical journals are assigned to specific categories based on the journal categories of the references cited in the article. 36 Web of Science subject categories were chosen to represent biomedical research field and publications within these categories were included in analysis.

6.11 The pharmaceutical industry **collaborates with a broad range of institutions in the UK**, including universities, hospitals, and public research institutions. The graph below shows the number of papers, and average normalised citation impact, for **UK organisations publishing more than 1000 collaborative papers** between 2006 and 2015. For each of these organisations, papers published in collaboration with industry were **on average much more highly cited** than the global average.

Universities published the highest number of papers in collaboration with industry, but on average hospitals and other public research institutes published a slightly higher proportion of highly cited papers.

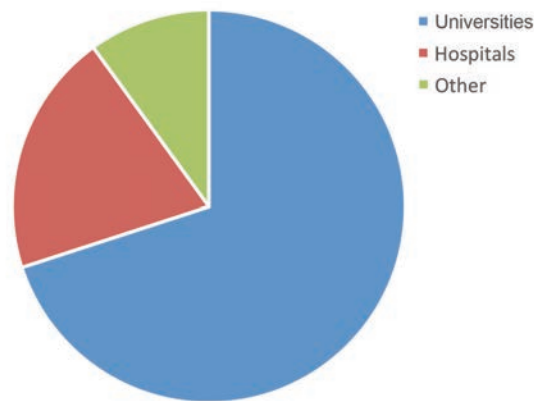
UK organisations with highest number of collaborative papers with the pharmaceutical industry



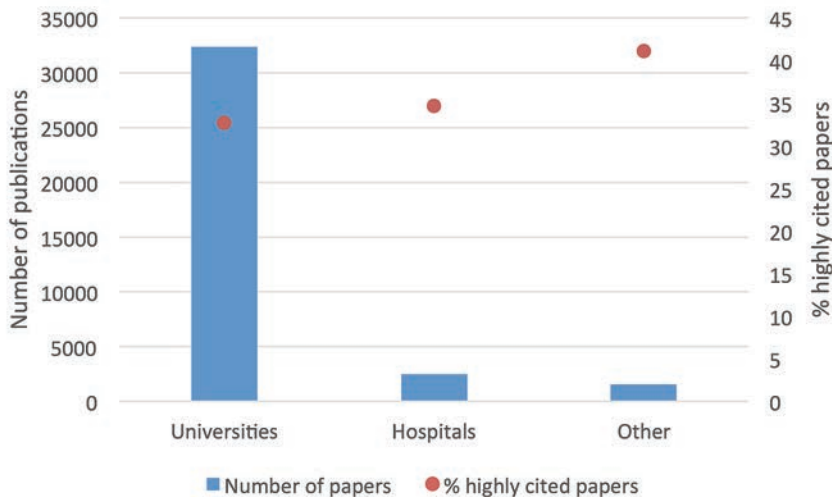
SOURCE: Data provided by Clarivate Analytics

NOTES: Number of papers, normalised citation impact, and % highly cited papers, produced by UK organisations acknowledging funding from the pharmaceutical industry, for the top 25 pharmaceutical company collaboration funders, 2006-2015. Only UK organisations with more than 1000 papers published in this period are shown. See previous notes on citation impact and % highly cited papers.

Types of organisation in the top 50 UK organisations collaborating with the pharmaceutical industry



Number of collaborative papers and highly cited papers by organisation type



SOURCE: Data provided by Clarivate Analytics

NOTES: Top 50 UK organisations by number of publications acknowledging funding from the pharmaceutical industry, for the top 25 pharmaceutical company collaboration funders, 2006-2015. Organisations were allocated as universities, hospitals, or other organisations (mostly charity or public research institutes). See previous notes on % highly cited papers.

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