

THE IMPACT OF COLLABORATION: THE VALUE OF UK MEDICAL RESEARCH TO EU SCIENCE AND HEALTH



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Technopolis Group (May 2017)

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This report together with the appendices, case studies and executive summary are available at cruk.org/UKandEUresearch

The impact of collaboration: the value of UK medical research to EU science and health

A review of existing evidence and views from the EU

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The funders of the research wrote the executive summary, which was imputed by the Technopolis group.

CONTENTS

1 EXECUTIVE SUMMARY	11
1.1 Contribution of UK expertise to EU collaborations, advisory bodies and policies	12
1.2 Development of pan-EU clinical trials	13
1.3 The role of the UK's world class medical research facilities in EU science	14
1.4 Development of new therapies and medical technologies	15
1.5 An attractive training environment for early-career researchers	16
1.6 Conclusion	17
2 BACKGROUND	18
3 CONTRIBUTION OF UK EXPERTISE TO EU COLLABORATIONS, ADVISORY BODIES AND POLICIES	19
3.1 Introduction	19
3.2 Collaboration	20
3.3 Leadership	27
4 DEVELOPMENT OF PAN-EU CLINICAL TRIALS	32
4.1 Introduction	32
4.2 Pan-EU clinical trials	33
4.3 Clinical trial methodology	37
4.4 Clinical trial infrastructure	38
5 THE ROLE OF THE UK'S WORLD CLASS MEDICAL RESEARCH FACILITIES IN EU SCIENCE	41
5.1 Introduction	41
5.2 Cohort studies	44
5.3 Bioinformatics infrastructure	44
5.4 Biorepositories	45
5.5 Research facilities	45

6 DEVELOPMENT OF NEW THERAPIES AND MEDICAL TECHNOLOGIES	47
6.1 Introduction	47
6.2 Impact on public health and patients	47
6.3 Translating research into innovative therapies	52
6.4 Patient involvement in research	54
6.5 European clinical and public health guideline	55
7 AN ATTRACTIVE TRAINING ENVIRONMENT FOR EARLY-CAREER RESEARCHERS	58
7.1 UK research institutions in the health and life sciences	58
7.2 The role of the UK in training early career researchers from other EU countries	61
7.3 Training biomedical students from other EU countries	69
8 CONCLUDING REMARKS	73
ENDNOTES	75

TABLES

Table 1	Top 10 organisations in terms of Marie Skłodowska-Curie action fellowships (FP7, 2007-2013)	16
Table 2	UK contributions as percentages of internationally co-authored papers in the biomedical field to national health advisory committee members' papers of other EU countries	27
Table 3	Use of UK research infrastructures by European researchers	43
Table 4	Number of Research Excellence Framework impact case studies reporting an impact on health	49
Table 5	Examples of UK research with health impact in EU member states	50
Table 6	UK contributions as percentages of foreign papers to the evidence base of clinical guidelines for five focus EU countries and other EU member states	56
Table 7	Top UK and EU institutions (THE World University Rankings 2016-17)	59
Table 8	Top 10 organisations in terms of Marie Skłodowska-Curie action fellowships (FP7, 2007-2013)	62
Table 9	Proportion of EU-nationals in different staff categories at four NIHR BRCs	67
Table 10	EU Higher Education institutions hosting the largest number of ERC grants in the Life Sciences domain (2007-2016)	69
Table 11	Students at UK institutions studying subjects with relevance to biomedicine in 2014/15	70

FIGURES

Figure 1	Mean Normalised Citation Scores (MNCS) for medical and health research publications	12
Figure 2	Number of clinical trials conducted by country with or without collaboration with other EU countries	14
Figure 3	Mean Normalised Citation Scores (MNCS) for medical and health research publications. Score for publications involving or not involving collaborations between EU26 and the UK. The horizontal line indicates the value for world average (MNCS=1). (a) Stratified by five focus countries (b) Stratified by three disease areas and public health	22
Figure 4	Level of participation in health-related research projects funded through the EU framework programmes, FP7 and Horizon 2020. Total number of participations in projects and EU project funding are provided for focus countries.	24
Figure 5	Level of participation in health-related research projects funded through the EU FP7 and coordinated by the UK. Total number of participations in projects and EU project funding are provided for focus countries.	25
Figure 6	Collaborative links in health-related projects for FP7 and Horizon 2020 for focus countries	26
Figure 7	Industry sponsored experimental medicine trials, European peer group	33
Figure 8	Number of clinical trials conducted by country with or without collaboration with other EU countries between 2004-2016	34
Figure 9	Number of clinical trials conducted by country with or without collaboration with other EU countries (a) Paediatric trials (b) Rare disease trials	35-36
Figure 10	Number of clinical trials by country and disease area	37
Figure 11	Destinations of researchers leaving MRC-funded projects	64
Figure 12	Destinations of researchers moving to other EU countries after leaving MRC-funded projects	64
Figure 13	Percentage of MRC-funded postdoctoral researchers and research fellows moving to advanced career positions, by destination	66
Figure 14	Proportion of EU-nationals in different staff categories at four NIHR BRCs (% of total staff)	67
Figure 15	Host countries of ERC grant holders (2007-2016), all research domains	68
Figure 16	Destination of EU-domiciled biomedical postgraduates, 6 months after completing UK studies	71
Figure 17	Destination of EU-domiciled biomedical undergraduates, 6 months after completing UK studies	72

BOXES

Box 1	Leadership in rare disease research	31
Box 2	Importance of the UK for pan-EU trials	40
Box 3	UK research on statins contributes to cardiovascular disease prevention in the EU	48
Box 4	UK researchers are leading the way in breast cancer	48
Box 5	Global impact of UK's discovery of monoclonal antibodies for treatment of rheumatoid arthritis	53
Box 6	The Person-Centred UK model of dementia care adopted throughout the EU	55
Box 7	UK research findings underpin EU policies aimed at reducing smoking	56
Box 8	Links in training and research – the Max Planck Society	60

LIST OF ACRONYMS

ABPI	Association of the British Pharmaceutical Industry
ASH	Action on Smoking and Health
BBMRI	Bio-banking and Biomolecular Resources Research Infrastructure
BDG	Bradford Dementia Group
BHF	British Heart Foundation
BMBF	Federal Ministry of Education and Research (German acronym)
BMJ	British Medical Journal
BMS	Biology and Medicine Section
BRC	Biomedical Research Centre
BRCA1	Breast Cancer-Associated 1
BRCA2	Breast Cancer-Associated 2
CAT	Cambridge Antibody Technology
CEGRD	European Commission Expert Group on Rare Diseases
CG	Clinical Guidelines
CPRD	Clinical Practice Research Datalink
CTD	Clinical Trials Directive
CTSU	Clinical Trial Service Unit
CTU	Clinical Trial Unit
CVD	Cardiovascular Disease
DALY	Disability-adjusted Life Year
DCM	Dementia Care Mapping
DLHE	Destination of Leavers from Higher Education
DMD	Duchenne Muscular Dystrophy
HPA	Health Protection Agency
EBCTCG	Early Breast Cancer Trialists' Collaborative Group
EBI	European Bioinformatics Institute
EULAR	European League Against Rheumatism
EC	European Commission
ECACC	European Collection of Authenticated Cell Cultures
ECCO	European Cancer Organisation
ECG	European Clinical Guidelines
EFPIA	European Federation of Pharmaceutical Industries and Associations
EMA	European Medicine Agency
EMBL	European Molecular Biology Laboratory
EMBO	European Molecular Biology Organisation
ERC	European Research Council
ERN	European Reference Networks
ESS	European Social Survey
EU	European Union
EU28	All 28 member states of the European Union
EU27	All member states of the European Union except the UK
EU26	All member states of the European Union except the UK and Croatia
FP7	Framework Program 7

FPE	Full Person Equivalent
H2020	Horizon 2020
HE	Higher Education
HESA	Higher Education Statistics Agency
HFSP	Human Frontier Science Program
HTA	Health Technology Assessment
IMI	Innovative Medicine Initiative
IoPPN	Institute of Psychiatry, Psychology and Neuroscience
ISBE	Infrastructure for systems biology Europe
JACS	Joint Academic Coding System
JPI	Joint Program Initiative
LDL	Low-Density Lipoprotein
LMB	Laboratory of Molecular Biology
LRI	London Research Institute
MC	Marie Skłodowska-Curie
MHRA	Medicines and Healthcare Products Regulatory Agency
MLC	Mary Lyon Centre
MNCS	Mean Normalised Citation Score
MPI	Max Planck Institute
MRC	Medical Research Council
MS	Member State
NCD	Non-Communicable Disease
NHS	National Health Service
NIBSC	National Institute for Biological Standards and Control
NICE	National Institute of Health and Care Excellence
NIH	National Institutes of Health
NIHR	National Institute for Health Research
NMD	Neuromuscular Disease
NOCRI	NIHR Office for Clinical Research Infrastructure
PCC	Person-Centred Care
RA	Rheumatoid Arthritis
RCP	Royal College of Physicians
RD	Rare Disease
RCT	Randomised Controlled Trial
REF	Research Excellence Framework
THE	Times Higher Education
SAB	Scientific Advisory Board
SEP	Standard Evaluation Protocol
SIGN	Scottish Intercollegiate Guidelines Network
SIOPE	European Society for Paediatric Oncology
SIOP WT 2001	Trial looking at treatment for children and young people with Wilms' tumour
UCL	University College London
UK	United Kingdom
WOSCOPS	West of Scotland Coronary Prevention Study
WHO	World Health Organisation

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1 EXECUTIVE SUMMARY

Scientists have greater impact when they collaborate internationally. EU programmes have helped to foster and strengthen scientific cooperation and the UK has been a major contributor to this, especially in medical research. As the UK develops a new relationship with the EU it is vital that negotiations result in the best possible outcome for science and patients across the EU. Although collaboration will continue after Brexit, any limitations on the ability of researchers and institutions to work together could diminish the impact of science both in the UK and the EU.

This report identifies some of the main ways in which UK research contributes to medical progress, it highlights the benefit this has delivered for EU science and ultimately how this has improved the health of patients and the public across the EU. The evidence shows that the UK has made key contributions in five areas:

5 KEY AREAS

- 1 Contributions to advisory bodies, networks and policies that underpin research across the EU and its member states
- 2 Participation in pan-EU clinical trials, providing notable leadership for rare disease and paediatric clinical trials
- 3 Co-ordination and hosting of some of Europe's unique large-scale infrastructures for medical research
- 4 Development of new therapies and medical technologies that benefit EU patients, backed by a thriving pharmaceutical and biotechnology sector
- 5 Training early career researchers from across the EU, to develop their skills and launch their research careers

This report was funded by eight leading UK medical research funders and charities, all actively engaged in the EU's health and research landscape. One of the strengths of the UK's medical research sector is the diversity of organisations involved in funding activity and policy dialogue, including medical research charities and patient representative organisations. The UK has a long history of patient involvement and continues to serve as a model for other EU countries in this area.

This report brings together extensive evidence from a number of disease areas, including cardiovascular diseases, musculoskeletal conditions, cancer and mental health. The research team from the independent policy research organisation, Technopolis undertook an extensive literature review, data analysis and in-depth interviews with leading European researchers and institutional stakeholders in the medical research field, as well as developed eight case studies on the UK's contribution to EU science and health.

1.1 Contribution of UK expertise to EU collaborations, advisory bodies and policies

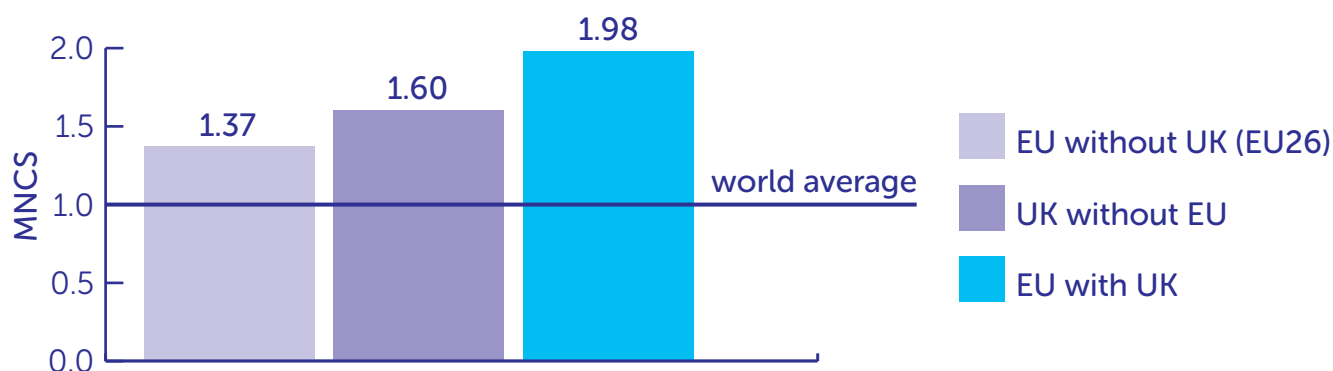
“The UK has excellent organisations and institutions, e.g. the Royal Society, the Academy of Medical Sciences, and the Royal College of Physicians. These institutions have a large arsenal of experts who can be put forward for important committees and boards. In the EU setting, we would miss the UK experts if not available, as they have a lot of quality to offer.”

Professor Jos van den Meer, Professor of Medicine, Radboud University Medical Center, The Netherlands

The UK is an important partner in the EU research landscape, contributing to almost 20% of the total research work carried out within EU health programmes between 2007 and 2016. Collaborating in research like this has mutual benefits, particularly in terms of impact. Bibliometric analysis of EU medical and health research publications shows that collaboration with the UK greatly increases the impact of EU26 publications, and vice versa (see **Figure 1**).

Both the Mean Normalised Citation Score (MNCS), and the proportion of, internationally co-authored publications in the top 10% of highly cited publications in their research field is higher for UK and other EU co-publications compared to EU26 only (without UK co-authors) or UK only (without EU26 co-authors). The EU26 already achieves a MNCS score of 1.37 without the UK, which is higher than the world average, but the MNCS score of UK+EU26 publications is 1.98, or twice the world average. Similarly, the proportion of top 10% highly-cited publications increases from 15% to 23% for the EU26 when collaborating with the UK. Increases are also observed for the UK when collaborations with the EU26 are included, albeit to a lesser extent.

Figure 1 Mean Normalised Citation Scores (MNCS) for medical and health research publications



Source: Data analysis CWTS, Leiden University; data source: Web of Science core collection Clarivate Analytics

In addition to citation impact, the UK is a strong collaborator, contributing intellectually and materially to pan-European health and life sciences. It plays a central role in the European Strategy Forum on Research Infrastructures (ESFRI) and the development of the European Bioinformatics Institute (EBI) in Cambridgeshire, one of the satellite institutions of the European Molecular Biology Laboratory (EMBL). The UK hosts the headquarters of several other important institutions, such as the European Life Science Infrastructure for Biological Information (ELIXIR), which unites Europe's leading life science organisations in managing and safeguarding the increasing volume of data being generated by publicly funded research.

The UK is active in maintaining Europe's key registries and research networks in rare diseases. The UK co-ordinates the highest number of European registries of all EU member states, including those for childhood lung diseases, Huntington's disease and familial pancreatic cancer. Specialised UK health care providers have taken a significant role in the development of the new European Reference Networks (ERNs): the UK co-ordinates a quarter of the 24 thematic networks and participates in nearly all, thereby pooling knowledge and sharing research expertise. These actions contribute significantly to accelerate innovation in medical science and deliver evidence-based treatment to patients across the EU.

UK experts also contribute to advisory boards and scientific evaluation panels across Europe. For example, the highest number of evaluation assignments were delivered by UK scientists for the European Research Council's Life Sciences panel. UK scientists also provide valuable advice to many individual research institutions, such as Germany's Max Planck Institutes. There are 48 UK members of their Scientific Advisory Boards, representing 17% of total members, more than any other EU country¹.

"The UK has always been a very constructive contributor to European science and research policies"

Magda Chlebus, Director of Science Policy at the European Federation of Pharmaceutical Industries and Associations (EFPIA)

1.2 Development of pan-EU clinical trials

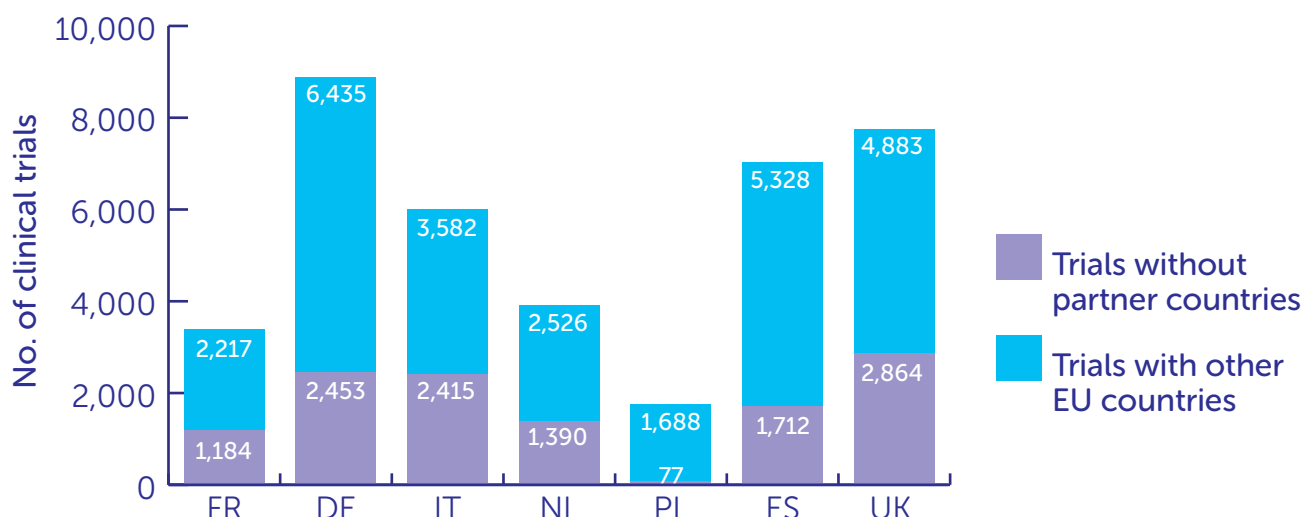
The UK has a long history of evidence-based, ground-breaking medical research – the Medical Research Council (MRC) pioneered randomised control trials in the 1940s, which have since become the gold standard of clinical trial design.

The UK undertakes a huge amount of clinical trials activity, both in national and pan-EU trials. It has the highest number of phase I trials – those testing a new drug or treatment for the first time – in the EU and the second highest number of phase II and III trials after Germany.

Pan-EU collaboration is particularly important for research on rare diseases and clinical trials for children, where there are small numbers of available trial participants in individual member states. In such circumstances, pan-EU collaboration is essential and the UK has led or participated in the largest number of pan-EU clinical trials for rare disease and paediatric treatments.

The UK is an attractive base for pan-EU clinical trials, conducting the third largest numbers of clinical trials with EU partners, after Germany and Spain. Of 200 clinical trials directly funded by Cancer Research UK, more than a quarter (28%) involve patients from at least one other EU country. This showcases the importance the UK attaches to pan-EU trials, for the advancement of research and the benefit of European patients.

Figure 2 Number of clinical trials conducted by country with or without collaboration with other EU countries



Source: Technopolis Group; European Clinical Trials Database

The UK's Medicines and Healthcare Products Regulatory Agency (MHRA) is recognised as one of the leading national authorities in the field, protecting and improving public health as well as supporting innovation through research and development. The MHRA authorises clinical trials and regulates medicines and medical devices, as well as sharing knowledge and expertise with the European Medicines Agency (EMA). Between 2008 and 2016, the MHRA acted as Scientific Advice Co-ordinator in at least 20% of centralised EMA medicine approval procedures.

The UK's regulators and advisory bodies work with international peers, sharing expertise and providing advice on clinical trials. The MHRA has been instrumental in designing and delivering a robust regulatory environment across the EU, providing an attractive and harmonised framework for clinical trials. This ultimately leads to faster access to innovative medicines for patients across Europe, a view that interviewees for this report shared.

1.3 The role of the UK's world class medical research facilities in EU science

"The UK puts a lot of energy in coordinating European research infrastructures."
Dr Edvard Beem, Co-Director, Netherlands Organisation for Health Research & Development (ZonMW)

Although many EU countries provide excellent medical research facilities, the UK offers resources which are often unique in Europe – providing access to research equipment, lab space and technical support that enables participating researchers to flourish. Four pan-European health-related research infrastructures have their headquarters in the UK, while bio-repositories like the Public Health England (PHE) Culture Collections or the Mary Lyon Centre are widely used by EU research communities, in many cases providing unique strains and cell lines.

The Wellcome Trust Sanger Institute is one of the largest bioinformatics centres in the world, hosting visitors from across Europe working on joint projects. Thousands attend advanced biomedical courses at the Institute each year and millions visit the website.

These scientific facilities are complemented by a legacy of substantial – and growing – investment in population research. The UK supports an unparalleled collection of large-scale population cohort studies, such as the 1946 birth cohort study – the longest continually running study of its kind in the world. These resources provide exceptionally rich data from across a person's lifetime, typically as an open access resource, and are used in large numbers of EU studies, as well as to inform policy on issues ranging from child poverty through to ageing populations and migration.

The quality and completeness of data routinely collected by the UK's National Health Service (NHS) is generally high; for example the English cancer registry is world-leading in its data collection, analysis and research². The NHS encompasses almost all of the UK's diverse population; creating a valuable unified resource for cross-EU epidemiological research.

1.4 Development of new therapies and medical technologies

"I think the UK is very mature in translational research, probably more mature than many other countries. There is a real urge to speed up access to the latest innovation in healthcare for the earliest possible benefit of patients"

Dr Pierre Meulien, Executive Director, Innovative Medicines Initiative (IMI)

The UK has one of the largest development pipelines globally, including 500 new biotechnology-based drugs and 600 innovative pharmaceutical product candidates. Looking at existing medicines, around 25% of the world's top 100 prescription medicines were discovered and developed in the UK and three of the five top-selling drugs globally act on a mechanism discovered by UK researchers to combat rheumatoid arthritis and other inflammatory conditions – revolutionising the treatments available. This is testimony to the strength of the UK research system and its ability to translate discoveries into real world solutions.

Experts interviewed for this report highlighted the UK's capacity to quickly translate innovative solutions into commercial products. This has meant that patients across the EU benefited from many advances in therapeutics and devices several years before the rest of the world, thanks to the enabling regulatory environment offered by the EU and the EMA, allowing such UK-rooted products to reach patients within the EU faster.

The UK's medical research community is collaborating with EU counterparts at the forefront of many innovative treatments. This includes the development of a new generation of genetically targeted personalised medicines, cancer immunotherapy treatments, and interventions for wellbeing and mental health, including dementia care mapping (DCM) to deliver more person-centered care (PCC), a model which is now widely used across the EU for people with mild to moderate dementia.

NICE, the UK's National Institute for Health and Care Excellence, is at the heart of collaborations with EU counterparts on Health Technology Assessment (HTA) methodologies and projects such as 'Harmony', the big data platform funded by the EU Innovative Medicine Initiative. The Harmony project aims to improve care for blood cancer patients across the EU.

NICE decisions are taken as an example by many countries in Europe. This has a great impact in Europe, especially in countries with a less developed structure for conducting HTAs. [...] We see the UK as providing a very efficient example and try to copy it."

Dr Frank Hulstaert, Senior Researcher, Belgian Health Care Knowledge Centre

1.5 An attractive training environment for early-career researchers

The UK contributes significantly to the global research workforce, second only to the USA in terms of the number of science graduates trained³. Around 16,000 students from other EU countries are registered on biomedical courses at UK higher education institutions, of which around 6,500 are postgraduates. Of the 5,475 biomedical students from other EU countries that graduated in 2014/15, around 18% took up positions in EU nations outside the UK.

“The UK continues to be an invaluable source of training and inspiration, especially in the life and medical sciences today, through its unique international outlook.”

Professor Werner Kühlbrandt, Director of the Max-Planck Institute of Biophysics Frankfurt

Experts interviewed for this study highlighted the quality of the UK training experience, the valuable skills and networks available and the positive impact on career progression. Global mobility is a key feature of the UK medical research community, with almost 30% of staff working on MRC grants taking up positions in other countries following the conclusion of their UK grant (11% going to EU countries and 16% going outside the EU). From 2006-2016, an estimated 650 UK-trained researchers leaving such MRC-funded projects moved to advanced positions in other EU countries, taking with them the training and expertise gained in the UK.

Interviewees for this study said that the UK education system empowers graduates with the ability to think analytically and innovatively, making it a highly attractive destination for early career researchers. The EU's Marie Skłodowska-Curie action (MSCA) fellowships support the most promising individual researchers from anywhere in the world and the UK was the top destination for fellows under FP7ⁱ (2007-2013), with five UK institutions among the top ten organisations (**Table 1**).

Table 1 Top 10 organisations in terms of Marie Skłodowska-Curie action fellowships (FP7, 2007-2013)

Institution	Country	Number of MSCA fellowships
Centre National de la Recherche Scientifique	France	514
University of Cambridge	UK	300
University of Oxford	UK	299
Imperial College London	UK	261
Max Planck Society	Germany	250
Consejo Superior de Investigaciones Científicas	Spain	250
University College London	UK	177
ETH Zürich	Switzerland	163
Copenhagen University	Denmark	163
University of Birmingham	UK	143

Source: DG EAC, Nov 2014, presented in Avramov, D. (2015) FP7 ex-post evaluation PEOPLE Specific Programme (2007-2013): Rationale, implementation and achievements, Annex 1, Table 1

i FP7 was the European Union's Research and Innovation funding programme for 2007-2013.

1.6 Conclusion

In conclusion, strong research collaboration between the UK and the EU benefits all, enabling discoveries that benefit patients everywhere. This report demonstrates that the UK makes a significant contribution to the success of medical research across the EU. It does this in many ways, from hosting European research networks, providing leadership in pan-EU trials, acting as a test bed for new discoveries and innovations, to educating and training the next generation of scientists.

The value of research collaboration between the UK and EU is further demonstrated by the higher impact of publications achieved when co-authored by UK and EU researchers. As the UK develops a new relationship with the EU, it is vital that negotiations result in the best possible outcome for science and patients across Europe. Any limitations on the ability of researchers and institutions to work together could diminish the impact of science both in the UK and the EU.

2 BACKGROUND

This report was funded by eight leading UK medical research funders and charities: the Academy of Medical Sciences (AMS), Arthritis Research UK, the Association of Medical Research Charities (AMRC), the British Heart Foundation (BHF), Cancer Research UK (CRUK), the Medical Research Council (MRC), MQ: Transforming Mental Health and Wellcome.

This report brings together evidence from a number of disease areas including cardiovascular diseases, musculoskeletal conditions, cancer, and mental health. The research team also focused on the UK's contribution to five individual EU states: France, Germany, Italy, the Netherlands and Poland. These were selected to reflect a range of geographies across the EU and their different levels of medical research activity.

The research was conducted between November 2016 and March 2017. The tight timeframe was based on a desire to provide insights to inform Brexit negotiations but this limited the scope of the study. The research team undertook an extensive literature review, data analysis and in-depth interviews with leading European researchers and institutional stakeholders in the medical research field. To illustrate the role of the UK within the EU the study includes several case studies where the UK played an important role in medical research and training. Full details on methodology, case studies and further data are available in the appendices (available at cruk.org/UKandEUresearch).

Where possible, the research looked at data available from EU countries. In other cases, data were more widely derived from European countries, including those which are not members of the EU. There is therefore a mixture of 'EU' and 'Europe' found in the report.

The research did not seek to assess the contribution of the EU to UK medical research, nor other EU member states' contributions. It also did not seek to assess the wider international impact of the UK.

3 CONTRIBUTION OF UK EXPERTISE TO EU COLLABORATIONS, ADVISORY BODIES AND POLICIES

KEY POINTS

- The UK is an important partner in the EU research landscape with a strong research community that contributes to and influences EU science and research at various levels. Bibliometric analysis of EU medical and health research publications (2005-2014) shows that collaboration between the UK and EU increases the impact of publications for both.
 - UK researchers help to shape EU medical research through membership of advisory bodies and expert groups across the EU. Through participation in cross-EU networks and engaging with EU institutions, the UK has contributed to EU research ethics, legislation and guidelines in areas such as data protection and the use of animals for research.
 - The UK's Medicines and Healthcare Products Regulatory Agency (MHRA) is the EU's leading national regulator for examining licensing applications. It collaborates with the European Medicines Agency (EMA) on matters related to the licensing, monitoring and standards for medical products, thus providing valuable support and regulatory expertise across EU.
 - Many specialised NHS providers in the UK have taken a leading role in the development of European reference networks, which aim to link up health providers from across the EU to pool knowledge and expertise. Of these, 25% of rare disease networks are being led by NHS trusts.
-

3.1 Introduction

Science in general, and medical research in particular, is enhanced by the collaboration of scientific communities across the globe where each makes a valuable contribution to the whole. EU programmes have helped to foster and strengthen scientific cooperation and the UK has been a major contributor to, and a beneficiary of, this collaborative community – especially in medical research.

The UK ecosystem of researchers, funders and policy makers is well-organised, interconnected, and efficient. It is known for its strategic approach and pragmatism, as well as a deep connectivity which includes world-leading universities, frontline NHS hospitals and a host of independent UK charities and foundations able to support innovative ideas and networks that span international borders. Patient organisations and medical journals also contribute to this unique ecosystem; journals such as the British Medical Journal and the Lancet shape the global conduct of medical research, increase openness and transparency, and campaign to reduce duplication of research.

“The UK research community is particularly strong and well set up to do research. The community thinks in an international way, and has access to long term and strategic funding which allows it to make large contributions.”

Professor Iain Mattaj, Director General, European Molecular Biology Laboratory (EMBL) Heidelberg, Germany

The UK research community has generated important scientific data and shaped emerging research fields. It also contributes to research across the EU by coordinating pan-European

research networks and serving on scientific advisory committees and panels at the European level.

"The UK is good in combining the results of good education, excellent knowledge and tradition to find new ways to evolve. This also is apparent in European programmes, organisations and institutes. If the UK participates or leads, the performance is very good."

Professor Wiek van Gilst, Head of Experimental Cardiology, University Medical Center Groningen, The Netherlands

"Today, research from the UK definitely contributes to EU knowledge in key areas. [...] The UK is among the top 5 countries that repeatedly produce interesting new data and results."

Professor Peter Naredi, President of the European Cancer Organisation (ECCO); Professor of Surgery, University of Gothenburg, Sweden

3.2 Collaboration

UK-EU collaborations help to bring some of the best medical researchers together, adding value and quality to the research as well as developing skills and outputs. These networks facilitate new discoveries, enable these discoveries to be disseminated and increase their impact on society. Collaboration allows researchers across the EU to access state-of-the-art research equipment and infrastructure in partnering member states and maximise efficiency by pooling resources⁴. The recently established Francis Crick Institute in London is a prime example of an international community collaborating to translate fundamental biology into treatments. It is the biggest biomedical research facility under a single roof in Europe, bringing together 1500 scientists from across the world.

There are high levels of UK-EU collaboration. In 2014, UK-based medical researchers (with awards from the MRC) reported that 18% of all their collaborations are with European researchers⁵.

- This is more than for any other continent⁵.
- This can be specified further, as there are hundreds of unique collaborations occurring. The highest number of unique collaborators come from Germany (1536), followed by France (382) and the Netherlands (266)⁵.
- This is also exemplified by the British Heart Foundation (BHF). For BHF lead scientists, the highest number of collaborations in other EU countries (i.e. EU28 minus UK) were with Germany (24% or 87 out of 364), the Netherlands (16%, or 57), then Italy and France (10% or 37)⁶.
- This is not unusual, as reported by the Association of Medical Research Charities (AMRC). Researchers from EU member states are by far the most frequent partners (outside the UK) for grants by AMRC members⁷.

The pan-EU collaborations also draw involvement from other funders, including the pharmaceutical industry. For instance, the UK pharmaceutical companies GlaxoSmithKline and AstraZeneca are actively participating in the EU Innovative Medicines Initiative (IMI), a partnership between European industry, academia and biotech organisations to speed up the

development of better and safer medicines for patientsⁱⁱ. The UK's scientific contribution has been further reinforced by policy outputs which inform and influence EU strategies. One such example is the Antimicrobial Resistance Reviewⁱⁱⁱ cited in the European Council's 2016 paper on "Council conclusions on the next steps under a One Health approach to combat antimicrobial resistance".

Experts across the EU, interviewed in this study, highlighted that the leading research institutions located in the UK contribute to making UK-based researchers attractive partners for EU projects. One example is the Institute of Psychiatry, Psychology and Neuroscience (IoPPN), part of King's College London, a leading centre for mental health research in Europe, and sought-after partner in many EU collaborations in that field.

"There is a strong tendency to include the Institute of Psychiatry, Psychology and Neuroscience at King's College London in research consortia to put together the best possible European grant proposal."

Professor Andreas Meyer-Lindenberg, Director of the Central Institute of Mental Health, University of Mannheim, Germany

3.2.1 Citation impact

Scientific collaboration results in a clear 'win-win situation' for medical researchers both in the UK and the EU. Analysis of publication and citation data for medical and health research^{iv} papers published between 2005 and 2014 shows that the citation impact^v of EU26 (EU28 without UK and Croatia^{vi}) publications are increased when produced in collaboration with the UK. In turn, collaboration with the EU26 increases the publication quality indicators for UK outputs as well.

Both the Mean Normalised Citation Score (MNCS) and the proportion of internationally co-authored publications in the top 10% of highly cited publications in their research field is higher for UK and other EU co-publications compared to EU26 only (without UK co-authors) or UK only (without EU26 co-authors). The EU26 already achieves a MNCS score of 1.4 without the UK, which is higher than the world average; but the MNCS score of UK + EU26 publications is 2.0, or twice the world average. Similarly, the proportion of top 10% highly-cited publications increases from 15% to 23% for the EU26 when collaborating with the UK. Increases are also observed for the UK when collaborations with the EU26 are also included, albeit to a lesser extent. (**Figure 3a**)

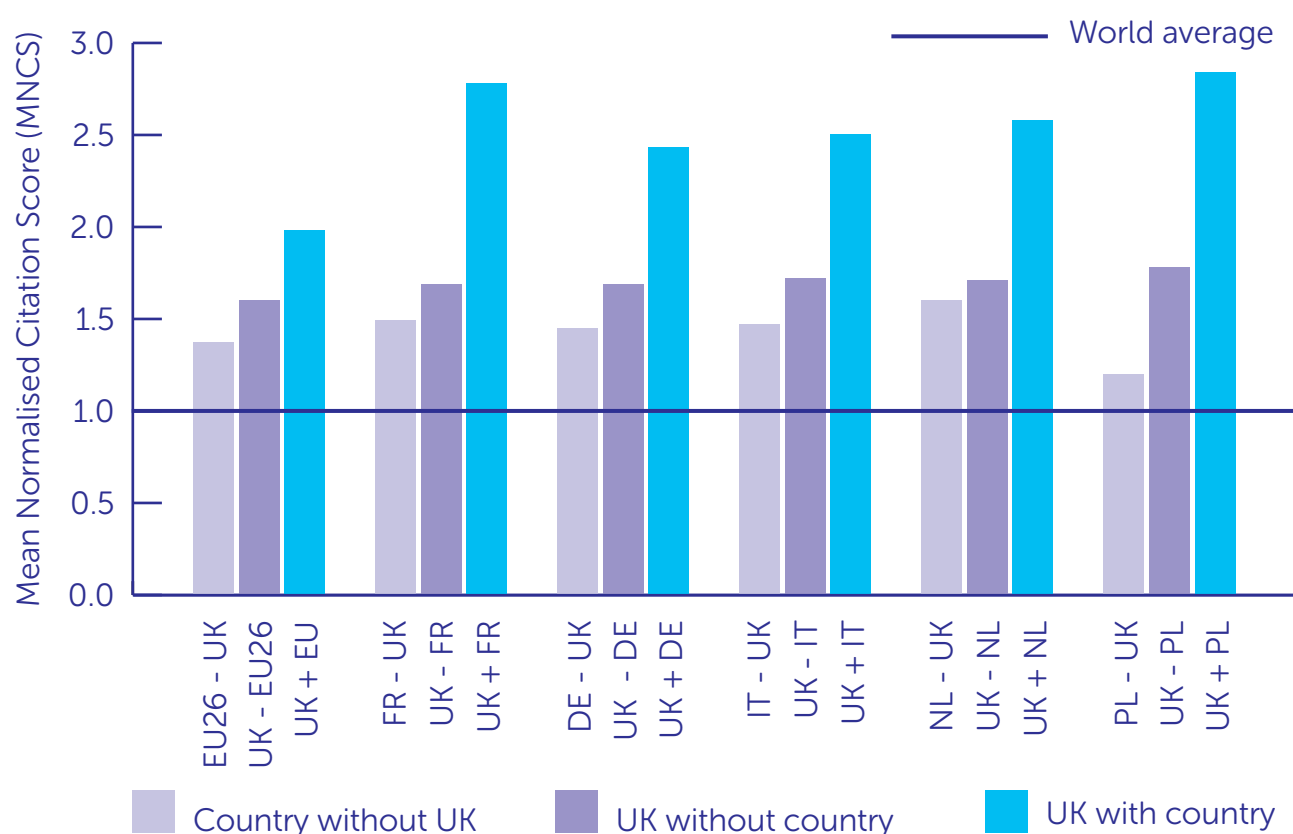
- ii The Innovative Medicines Initiative (2015). Available from: <http://www.imi.europa.eu/content/nd4bb> [Accessed 24 March 2017].
- iii Council of the EU (2016) Council conclusions on the next steps under a One Health approach to combat antimicrobial resistance. Available from: http://ec.europa.eu/dgs/health_food-safety/amr/docs/ev_20160617_mi_en.pdf [Accessed 24 March 2017].
- iv For a list of Web of Science subject categories included in the bibliometric analysis, see Appendix E at cruk.org/UKandEUresearch
- v Citation impact quantifies the citation or referencing of a scholarly work. Higher citation count for an individual article is commonly attributed to higher scientific merit and hence higher impact in the respective research field.
- vi The current study gathered citation data for articles published between 2005 and 2014. Croatia was not part of the bibliometric analysis as it only joined the European Union in July 2013 as its 28th member state. The five focus countries in this study (FR, DE, IT, NL, PL) were EU member states in the entire period. Note that publication for focus countries is defined here as having at least one author from the relevant country but not from the UK. Similarly, EU26 publications are defined as having at least one author from EU member states but not from the UK. Publications for UK is defined here as at least one author from UK but not from other EU countries.

Analysis of publications of the five focus countries, France, Germany, Italy, the Netherlands, and Poland show a largely similar trend. Collaborative papers with UK co-authors have significantly higher citation impact than those without UK co-authors, with a noticeable positive trend for all countries between 2005 and 2014. Interestingly, the strongest impact of UK collaboration was observed for one of the newer EU member states, Poland, where the MNCS value increased from 1.2 without UK collaboration to 2.8 with UK collaboration in 2005-2014, with a clear positive trend observable since 2010^{vii,viii}.

We also analysed citation impacts for four specific research fields: three disease areas (cancer, cardiovascular diseases, and musculoskeletal conditions) as well as public, environmental, and occupational health. In all cases, collaboration between researchers from the UK and EU leads to scientific publications with considerably higher citation impacts (over twice as high as the world average) than without collaboration for either parties (**Figure 3b**).

Figure 3 Mean Normalised Citation Scores (MNCS) for medical and health research publications. Score for publications involving or not involving collaborations between EU26 and the UK. The horizontal line indicates the value for world average (MNCS=1)^{ix}.

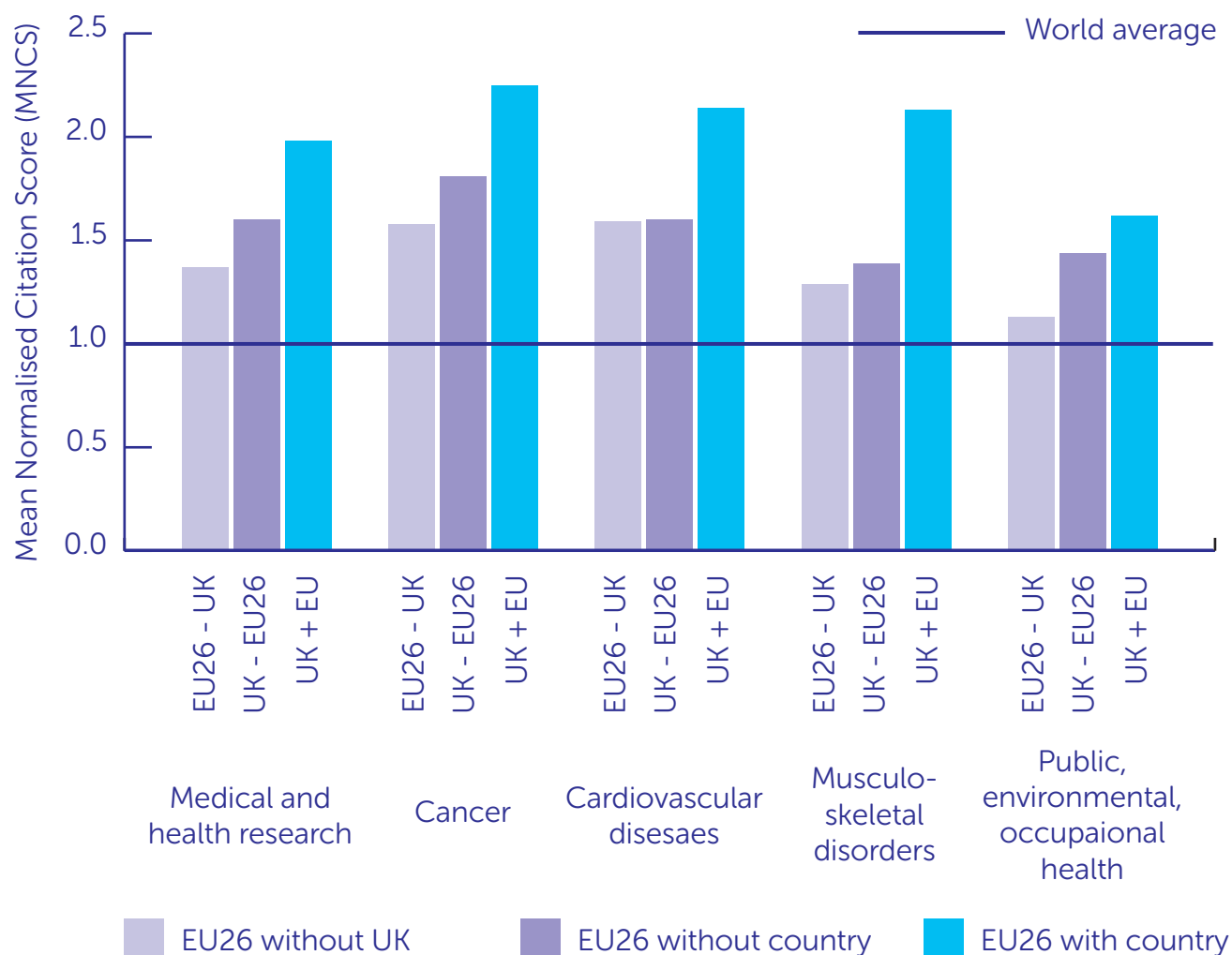
(a) Stratified by five focus countries



Source: Data analysis CWTs, Leiden University; Data source: Web of Science core collection Clarivate Analytics

- vii Longitudinal data (unpublished) analysed for three year time periods shows that the largest increase occurred in the most recent period of 2012-2014 in Poland
- viii Additional analysis is available in the appendices.
- ix The central bars in each set show the UK score minus the noted country. For example France has a score of 1.69 and this shows all the UK's internationally co-authored papers without contribution from France.

(b) Stratified by three disease areas and public health



Source: Data analysis CWTs, Leiden University; Data source: Web of Science core collection Clarivate Analytics

3.2.2 Level of collaboration with EU partners

The UK is punching above its weight as part of the combined EU research endeavour. Analysis of participation in health-related research projects^x funded through the EU research funding programmes, Framework Programme 7 (FP7) (2007-2013) and Horizon 2020 (2014-March 2017), shows that the UK has had the strongest participation among all EU28 countries in terms of number of participants in research projects and corresponding financial value. This demonstrates the quality of researchers based in the UK.

EU research funding received by the UK benefits the whole of the EU. The combined framework programmes included a total of 2,300 UK participations^{xi} in over a 1,000 health-related projects with a value of €1.2bn (18% of the research funding in health programmes). Between 2007 and March 2017, the UK delivered health-related research work worth €4.8m

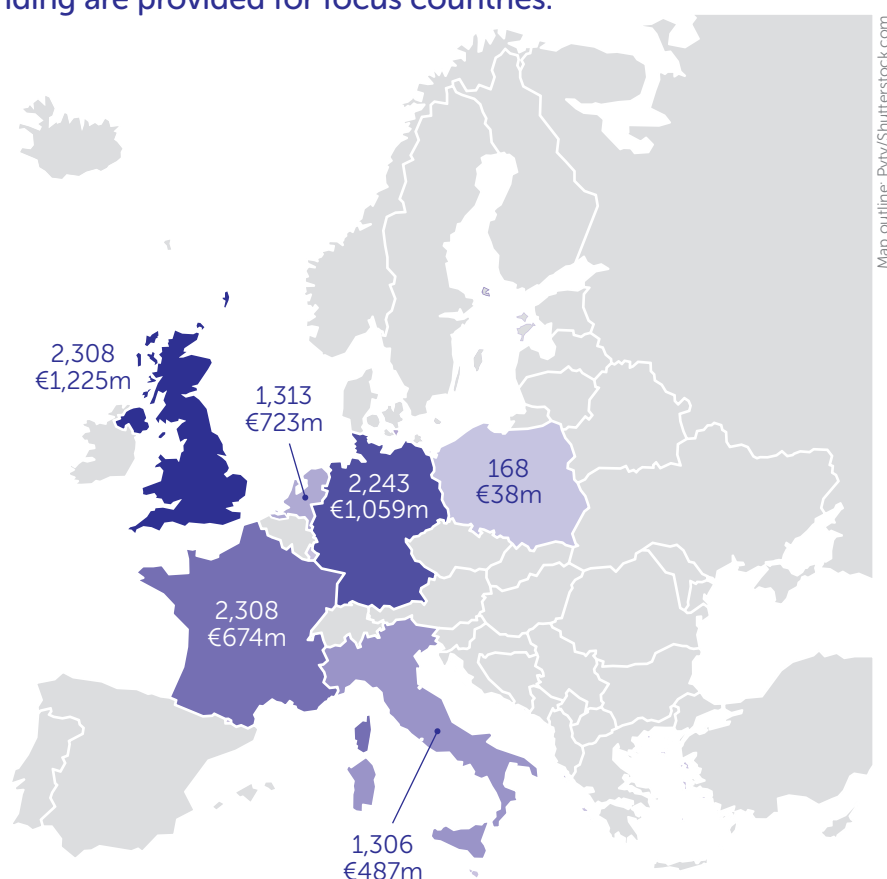
^x Data obtained using eCORDA iSearch facility by the Medical Research Council for Health programme in FP7 and Health, demographic change and wellbeing programme in Horizon 2020.

^{xi} 'Participations' means the act of involvement of a legal entity in a project. A single participant can be involved in multiple projects

per 1,000 researchers^{xii}. This performance ratio is similar to that of Italy, higher than that of Germany or France, but below that of the Netherlands (see Table 13 in Appendix F at cruk.org/UKandEUresearch).

Figure 4 shows a map illustrating the total EU project funding received by different countries for health-related research projects from the framework programmes between 2007 and March 2017. Focus countries are shaded according to the total funding they received, from light blue for the lowest level of funding to dark blue for the highest level of funding of €1bn (the UK).

Figure 4 Level of participation in health-related research projects funded through the EU framework programmes, FP7 and Horizon 2020. Total number of participations in projects and EU project funding are provided for focus countries.

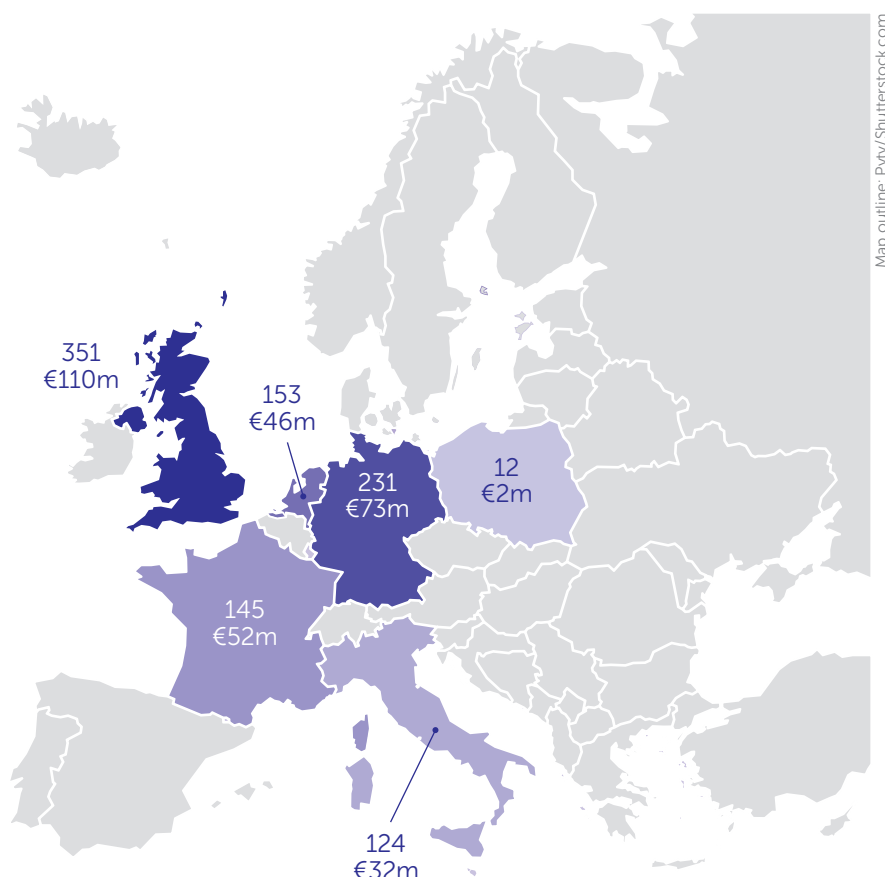


Source: Data analysis by MRC Information and Analysis Team and Technopolis; Data source: eCORDA iSearch (March 2017)

It is also possible to illustrate the level of participation and funding received by EU member states in FP7 for health-related projects that were brought about and coordinated by the UK. While the UK received €110m in EU research funding through 351 UK-coordinated participations, these projects also yielded more than €366m of funding through 1,233 participations from EU27 countries. **Figure 5** illustrates that these UK-coordinated projects resulted in large participations from Germany (231), the Netherlands (153), France (145) and Italy (124), bringing €203m of research funding to these countries.

xii Total number of full-time equivalent researchers in individual countries 2007-2014 available from Eurostat, average value was used as proxy to estimate the size of a country's medical researcher base.

Figure 5 Level of participation in health-related research projects funded through the EU FP7 and coordinated by the UK. Total number of participations in projects and EU project funding are provided for focus countries.

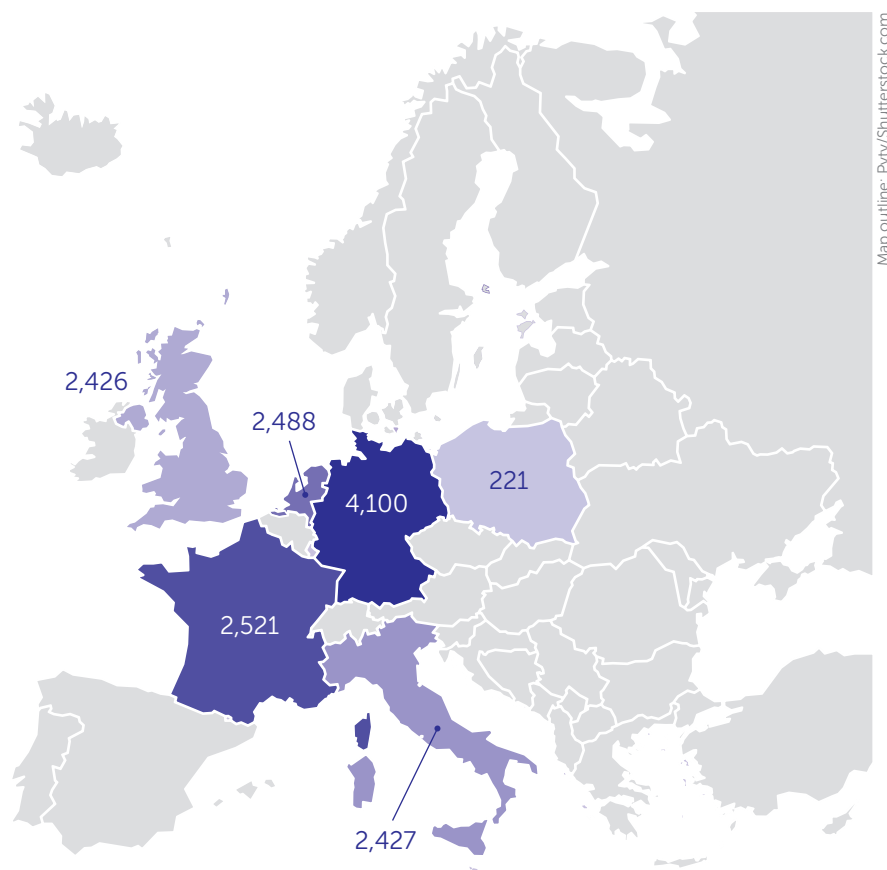


Source: Technopolis analysis based on eCORDA (October 2016).

An analysis of the collaborative links^{xiii} formed through health-related research projects under FP7 and Horizon 2020 shows the UK's most common international partners (**Figure 6**). The greatest number of links between the UK and other EU countries are with Germany (4,100), France (2,521), the Netherlands (2,488) and Italy (2,427), while internal collaborative links within the UK number 2,426. These partnerships greatly enhances the quality and breadth of medical research by both partners.

xiii A collaborative link is assumed to exist between each pair of participants in each project, based on the data provided in eCORDA iSearch.

Figure 6 Collaborative links in health-related projects for FP7 and Horizon 2020 for focus countries



Source: Data analysis by MRC Information and Analysis Team and Technopolis; Data source: eCORDA iSearch (September 2016).

3.2.3 National health advisory committees

National health advisory committees in EU member states are responsible for the development of public health guidance and advice to their respective ministries of health. The committees benefit from UK medical expertise through collaboration with UK-based researchers and clinicians. These often extensive links facilitate the dissemination of research between member states and channel its impact on policy making. The influential position of committee members makes it more likely that UK research has a wider impact in the EU and helps to bring UK experience and knowledge to bear on health issues in other EU member states.

Between 2008 and 2013, national health advisory committees produced over 12,000 papers; UK researchers contributed to a third of these^{xiv}. The highest UK contributions^{xv} were made to research papers of Dutch and French committee members; 38% and 42%, respectively (**Table 2**). The UK's contribution to committee members' research is disproportionately larger than would be expected given the level of biomedical co-authorship with those EU countries generally, suggesting that the UK is a preferred partner for health committee members. For the Netherlands, the UK contribution to committee members' papers is 40% higher than expected

xiv This analysis was based 57 committees identified in 19 other EU countries, with a membership of 1,357 researchers, Using the bibliometric data source Web of Science core collection Clarivate Analytics.

xv The figures are based on integer count of contributions to allow comparison with its overall presence in the relevant field of science; we also present fraction count in Appendix L (see cruk.org/UKandEUresearch).

(38.3% compared to 27.9%), in France it is 80% higher (42.1% compared to 23%). For all EU countries the UK's contribution to committee members' papers is far higher than the global rate of UK biomedical co-authorship, of around 10%. There is also evidence that the level of UK contribution is increasing over time (from 2009 to 2013), suggesting that the UK is playing an increasingly supportive role in the research outputs of EU national health advisory committee members.

Table 2 UK contributions as percentages of internationally co-authored papers in the biomedical field to national health advisory committee members' papers of other EU countries

	UK contribution (%) to national health advisory committee members' internationally co-authored papers	UK contribution(%) to EU country's internationally co-authored papers	UK contribution(%) to global internationally co-authored papers, without the EU country ^{xvi}
Germany	22.0	20.8	9.7
France	42.1	23.0	9.4
Italy	25.9	25.3	9.4
the Netherlands	38.3	27.9	9.3
Poland	28.6	25.7	9.1
EUR15 ^{xvii}	27.0	23.2	10.7

Source: Data analysis King's College London & Evaluametrics; Data source: Web of Science core collection Clarivate Analytics

3.3 Leadership

3.3.1 Regulation and standards

The UK's Medicines and Healthcare Products Regulatory Agency (MHRA), is recognised as one of the leading authorities in its field, both within Europe and globally⁸. As such it collaborates with other organisations, particularly with the European Medicines Agency (EMA) on matters related to the licensing, monitoring and standards for medical products.

The MHRA has been appointed by the EMA as lead agency for examining licensing applications, based on objective criteria that ensure the use of the best expertise available; it has also been chosen by EU companies as their preferred lead assessor. Between 2008 and 2016⁹, the MHRA acted as Scientific Advice Co-ordinator appointed by the EMA in at least 20% of centralised medicine approval procedures and provided data in about 50% of all decentralised medicine

xvi These figures show the 'expected' rate of UK contribution (integer count) to internationally co-authored papers in the biomedical field, when researchers of a given country choose from a random pool of international researchers.

xvii The Kings College analysis identified data for 21 countries with health advisory committees. Taking away the UK and the 5 focus countries, 15 remains. These are: Austria, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, Hungary, Ireland, Lithuania, Luxembourg, Portugal, Spain, Switzerland. The term EUR has been used rather than EU as not all countries are members of the EU.

approval procedures^{xviii}, as applicant companies commonly selected the UK as the Reference Member State^{xix}. The MHRA has also played a key role in EU negotiations addressing regulatory concerns in the revised EU Medical Devices legislation¹⁰. In addition, the National Institute for Biological Standards and Control (NIBSC), which merged with the MHRA in 2013, is responsible for developing and producing over 90% of the WHO international standards for biological medicines¹¹.

“UK bodies such as the MHRA have a very strong influence in shaping standards and industrial compliance policies. In clinical operations, they have issued guidance about how to approach risk-based monitoring, which helps pharma companies to plan and monitor their studies in a modern and effective way.”

Senior Pharmaceutical Industry representative, Poland

The UK also took the lead in setting the research agenda for the Protection of Animals used for Scientific Purposes Directive, which came into force in 2013¹². The draft proposal was subject to a significant advocacy effort from the UK and the EU life sciences sector and involved sustained engagement with EU institutions, particularly with the European Parliament. UK guidance on the use of laboratory animals was already the gold standard for the European Federation of Pharmaceutical Industries and Associations and was promoted as a good practice standard in this Directive.^{xx}

Alongside the Netherlands and Denmark, the UK continues to lead on laboratory animal ethics and has contributed significantly to the promotion of the three Rs – Replacement, Reduction, and Refinement – as the guiding principles for the use of animals in research.^{xxi}

The UK helped shape EU research policy through its participation in cross-EU consortia and networks¹³. The UK research community played an active role and contributed considerable resource towards developing the new General Data Protection Regulation (GDPR) ‘Regulation (EU) 2016/679’¹⁴ which comes into force in 2018¹⁵. UK life science organisations identified issues with the proposed legislation that would have imposed disproportionate limits on the use of health data in research. A coordinated and constructive campaign secured amendments to the Regulation that overturned the requirement for consent in the case of research, allowing life-saving medical research to continue.

Similarly, the Durham University School of Medicine, Pharmacy and Health worked closely with the WHO Regional Office for Europe, to help to design the ‘European Action Plan for Strengthening Public Health Capacities and Services’, impacting directly on international healthcare practices¹⁶.

Interviewees for this report felt that the UK has shown leadership at the European level with regards to regulation and standards, contributing to EU science policy making with a high level of competence, strategic thinking and willingness to share. In their view, the UK has been a constructive contributor to policies, particularly in relation to novel – and possibly controversial – technologies, bringing rationality and pragmatism into discussions on topics such as stem

xviii The decentralised procedure (DCP) is a European medicines authorisation route. DCP may be used if the product is not already authorised in any Member State, but the applicant does not want to use the centralised procedure, or the product is not eligible for the centralised procedure.

xix A reference member state (RMS) does an initial evaluation of the product and issues a draft assessment report to be considered by the other member states.

xx Interview with Dr Magda Chlebus, 8 February 2017.

xxi Interview with Dr Bonnie Wolff-Boenisch, 25 January 2017.

cell and animal research. Two interviewees explained that when they were developing research policies in their own countries, they first looked at “what the UK is doing”.

“The UK has always been a very constructive contributor to European science and research policies. I would be personally worried about research into sensitive technologies without UK participation. UK brings a lot of rationality and pragmatism into the discussions.”

Magda Chlebus, Director of Science Policy at the European Federation of Pharmaceutical Industries and Associations (EFPIA)

3.3.2 Committees and advisory groups

UK researchers significantly contribute to EU research excellence through their extensive membership of influential scientific committees and panels.

“The UK has excellent organisations and institutions, e.g. the Royal Society, the Academy of Medical Sciences and the Royal College of Physicians. These institutions have a large arsenal of experts who can be put forward for important committees and boards. In the EU setting, we would miss the UK experts if not available, as they have a lot of quality to offer.”

Professor Jos van den Meer, Professor of Medicine, Radboud University Medical Center, The Netherlands

It is difficult to conduct a comprehensive analysis of the exact number of UK-based researchers in advisory bodies and expert groups across Europe. However, reviewing the history of the European Molecular Biology Laboratory (EMBL) from 1971 onwards shows that 19 out of 131 (15%) scientific advisory committee members were UK-based^{xxii}, second only to US-based researchers¹⁷.

Similarly, the largest number of assignments^{xxiii} for the European Research Council (ERC) evaluation panel that reviews grant proposals in the Life Sciences domain^{xxiv} were delivered by experts based in the UK (15%, or 137)^{xxv}; 11% of assignments were delivered by expert panellists from Germany, 10% from France, 7% from Italy and 6% from the Netherlands. ERC panellists are renowned scientists and scholars from all over the world¹⁸, selected by the ERC Scientific Council based on individual scientific reputation and excellence.

UK experts also sit on review panels of national research organisations in other EU member states such as Germany’s Max Planck Institutes. Each institute is guided by a scientific advisory board (SAB) with about 8-10 expert members, totalling 277 SAB members for the 30 institutes in the Biology & Medicine section. UK-based researchers represent the biggest membership block

xxii 18 and 15 scientific advisory committee members were based in Germany and France, respectively.

xxiii This is a term that ERC use for the individual task (proposal assessment) panel members are tasked to do.

xxiv The three ERC domains are Life Sciences, Physical and Engineering Sciences, and Social Sciences and Humanities. ERC Life Sciences domain covers the following areas: Molecular and Structural Biology and Biochemistry; Genetics, Genomics, Bioinformatics and Systems Biology; Cellular and Developmental Biology; Cellular and Developmental Biology; Neurosciences and Neural Disorders; Immunity and Infection; Diagnostic Tools, Therapies and Public Health; Evolutionary, Population and Environmental Biology; Applied life Sciences and Non-Medical Biotechnology.

xxv ERC personal communication (March 2017). Figures are for ERC calls 2014-2015, Starting Grants 2016 and Consolidator Grants 2016.

of these advisory boards, contributing 48 members (17%), more than any other EU country^{xxvi}. In addition, UK-based scientific experts actively contribute to developing research excellence in new EU member states, including Poland, as explained by the Programme Officer below:

“Our current programme, International Research Agendas, which is about creating centres of research excellence in Poland, uses international expert review panels. On the first panel, the majority of European reviewers were UK-based.”

Programme Officer, Non-governmental organisation, Poland

3.3.3 Pan-European rare-disease research

The European Reference Networks (ERNs), formed in 2017, aim to link up leading specialised health care providers across the EU so they can pool knowledge and expertise. This is intended to promote evidence-based treatments and increase the speed and scale at which innovation in medical science and health technologies is incorporated into healthcare provision.

Participating clinicians will collaborate on a wide range of activities, including improving clinical guidelines and patient pathways, sharing medical information on clinical cases and agreeing on treatment options, conducting clinical research and improving medical education and training.

Specialised UK health care providers have a key role in the development of ERNs: 34 NHS Trusts participate in 22 ERNs, making the UK the most well represented country in this research and training network^{xxvii}. The UK coordinates 6 of the 24 thematic ERNs, more than any other member state, including in the key areas of epilepsies, rare auto-immune and auto inflammatory diseases, rare hepatic diseases and rare neuromuscular diseases.

The UK published its Strategy for Rare Diseases¹⁹ in 2013 which made specific commitments to improve the lives of those with rare diseases. The UK hosts and maintains a total of 84 registries that are key instruments to develop clinical research in the field of rare diseases, improving patient care and health care planning²⁰. The UK coordinates the highest number of European registries (17 out of 59) of all EU member states, including those for childhood lung diseases, Huntington’s Disease, and familial pancreatic cancer.

“The UK has very good registers for rare cancers, and clinical studies for rare indications are relatively easy to perform in the UK. The patients can be included from only a few centres, which is very good in terms of quality control, and trials not only include drugs, which is also very important.”

Professor Piotr Rutkowski, Professor of Surgical Oncology, Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology, Poland

The UK has many small charities and funders that support research on rare diseases and leads on coordinating research activity across the EU. The Ataxia-Telangiectasia Society, part of the euro-ataxia network, led the establishment of an international clinical research network and conference series, and recently obtained funding for a European Ataxia-Telangiectasia patient registry²¹. The UK patient group AKU Society²² has a central role in current clinical trials run by a consortium of 12 European partners to find a treatment for the rare disease alkaptonuria (AKU).

xxvi Germany’s Max Planck Institutes scientific advisory board members in the Biology & Medicine section include: Germany (31, 11%), France (18, 6%), and the US (114, 41%) (Personal communication, MPG office, 30 Jan 2017).

xxvii UK members of ERN. Available from: https://ec.europa.eu/unitedkingdom/news/uk-health-care-providers-join-eu-medical-networks-better-treat-rare-diseases_en [Accessed 28 February 2017].

Box 1 Leadership in rare disease research

Rare diseases are estimated to affect more than 30 million EU citizens –in other words, “rare diseases are rare, but rare disease patients are numerous”²³. The socioeconomic burden of these illnesses is therefore substantial. The annual societal cost to the EU of one such rare disease, Duchenne Muscular Dystrophy (DMD), is estimated at €2.4 billion per year. Cross-border collaboration in research and patient care is of particular importance for rare diseases, as this allows pooling of limited expertise, resources, data and patient networks.

Academic and clinical researchers in Newcastle, UK, have played a central role in many European (and international) efforts to progress rare disease research, policy, and care. Newcastle University coordinates several large-scale initiatives such as TREAT-NMD, a European network of excellence in neuromuscular disease (NMD) research and RD-CONNECT, a rare disease research infrastructure with a global platform capable of linking often disparate, data sources. By participating in two European Joint Actions, EUCERD and RD-Action, Newcastle has also supported EU policy development and helped EU member states to codify rare diseases in their national health information systems and implement interoperable data-sharing platforms in order to improve their rare disease healthcare delivery. Newcastle is also the coordinator of three European Reference Networks.

(Full case study is available at cruk.org/UKandEUresearch)

3.3.4 Medical Research Council leadership

Funders like the UK’s Medical Research Council take a major role in funding health research in the EU including offering leadership in the following projects:

- Developing the strategic research agenda of the European Joint Programme Initiative (JPI) on neurodegenerative diseases²⁴.
- Leading, on behalf of the UK, the EU Joint Programming Initiative on AMR which aims to coordinate research activity across 17 member states as well as Norway, Switzerland, Canada, Israel and Turkey²⁵.
- Leading the UK delegation on the Horizon 2020 Programme Committee for the Health, Demographic Change and Wellbeing Challenge²⁶.

“For the UK, networks not only consist of researchers but also have a dedicated team of science managers, much needed to establish and continuously support the functioning of these large pan-European networks. This well-organised infrastructure has been important for the success of the UK in bringing visibility to rare disease in Brussels.”

Professor Leena Bruckner-Tuderman, Vice President of the Deutsche Forschungsgemeinschaft (DFG); Albert-Ludwigs-University of Freiburg, Germany

4 DEVELOPMENT OF PAN-EU CLINICAL TRIALS

KEY POINTS

- The UK was the first to develop randomised clinical trials and continues to develop novel trial methodologies for use across the EU.
 - The UK, along with Germany and the Netherlands, is regarded as one of the best clinical trial markets in Europe by key stakeholder groups such as the BioPharma industry, medical device manufacturers, clinical research organisations, and clinical trial units.
 - In terms of the number of clinical trials conducted, the UK ranks first for phase I and second for phase II and III trials, according to data cited by the Association of the British Pharmaceutical Industry (ABPI) for 2015.
 - Analysis of records in the European Clinical Trials Database (EudraCT) shows that the UK
 - has the third highest number of joint trials with other EU countries, after Germany and Spain
 - has the second highest number of joint trials with other EU countries for rare diseases and paediatric patients
 - is among the five EU member states that conduct the highest number of clinical trials in cancer, cardiovascular diseases, mental health and musculoskeletal conditions.
 - The UK actively contributes to how clinical trials are conducted in EU member states through advocating for improvements to the EU Clinical Trials Directive, offering training in conducting clinical trials to new EU member states and providing a good example of an efficient and evolving clinical trial system.
 - The UK is an attractive destination for pan-EU clinical trials because of its proven track record in efficiently delivering results, and the presence of specialised clinical research centres/ clinical trial units and highly competent trial expertise.
 - Patient groups, government-funded infrastructure such as the Clinical Practice Research Datalink and a high level of awareness about clinical trials in the UK population allow efficient recruitment of patients to trials.
 - The UK regulator, the MHRA, is respected by industry and other peer institutions across Europe as a good source of knowledge and scientific advice on conducting clinical trials.
-

4.1 Introduction

The UK has a long history of conducting evidence-based research, including clinical trials. The high quality expertise and infrastructure that the UK has developed over time makes it an ideal collaborator in pan-EU trials. High calibre personnel, a network of clinical research centres linking academia and hospitals, and engaged patient groups help the UK to contribute to multi-national trials. As illustrated in the rare diseases case study in **Box 1** (page 31), this contribution is crucial in the areas of rare diseases and paediatric clinical trials where the small number of available trial participants necessitates pan-EU collaboration.

"The UK was key in initiating the evidence-based approach to medicine, and continues to be world leading in development and refinement of clinical research methodologies."

Professor Liselotte Højgaard, Chair of the Advisory Group on Health for H2020; Former Chair of the European Medical Research Council; University of Copenhagen, Denmark

"The UK is at the top level in both research quality and ethics."

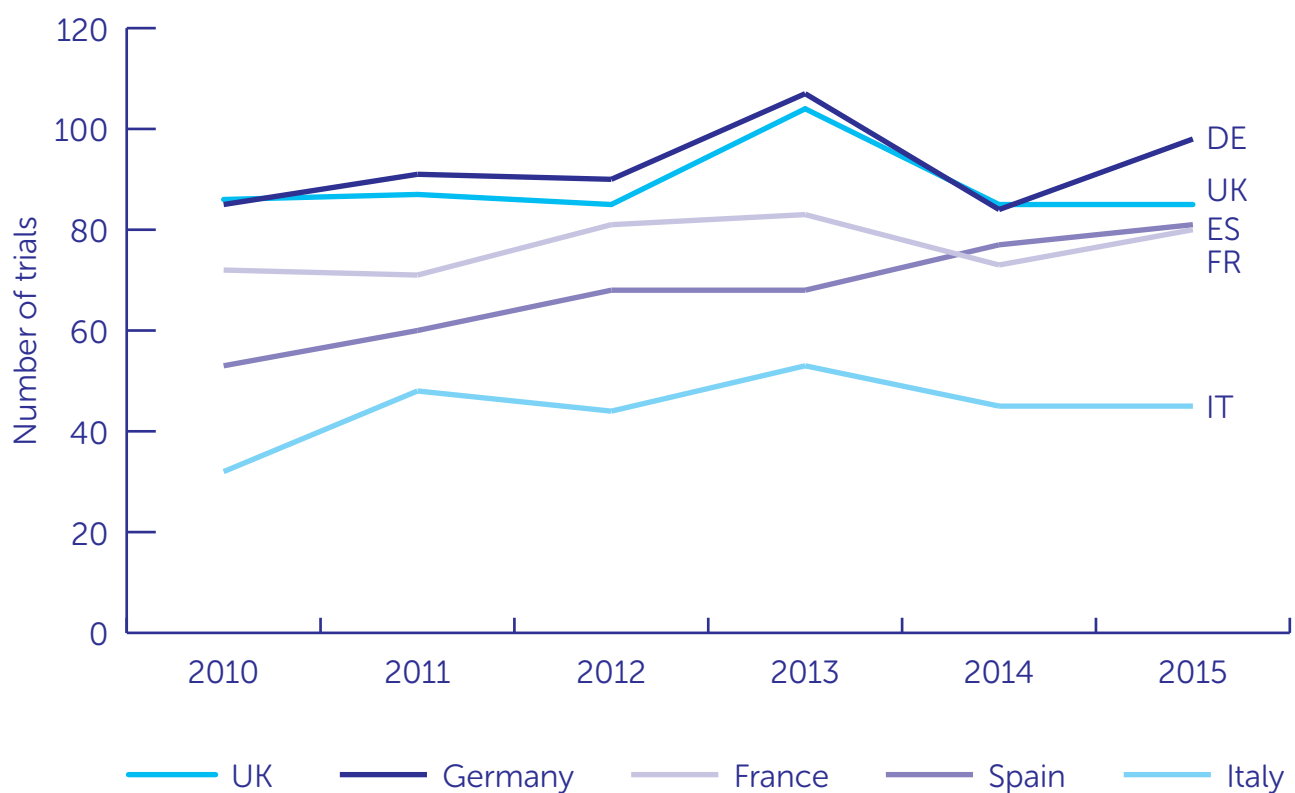
Professor Peter Naredi, President of the European Cancer Organisation (ECCO) and Professor of Surgery, University of Gothenburg, Sweden

4.2 Pan-EU clinical trials

The UK is regarded as one of the best clinical trial markets in the EU, alongside Germany and the Netherlands, by key stakeholder groups, such as the BioPharma industry, medical device manufacturers, clinical research organisations and clinical trial units²⁷. The Association of the British Pharmaceutical Industry (ABPI) recently reported that the UK conducted the highest number of phase I trials in the EU and the second highest number of phase II and III trials (after Germany) in 2015²⁸.

In addition, for industry-sponsored experimental medicine trials, the UK is second only to Germany amongst EU countries (7).

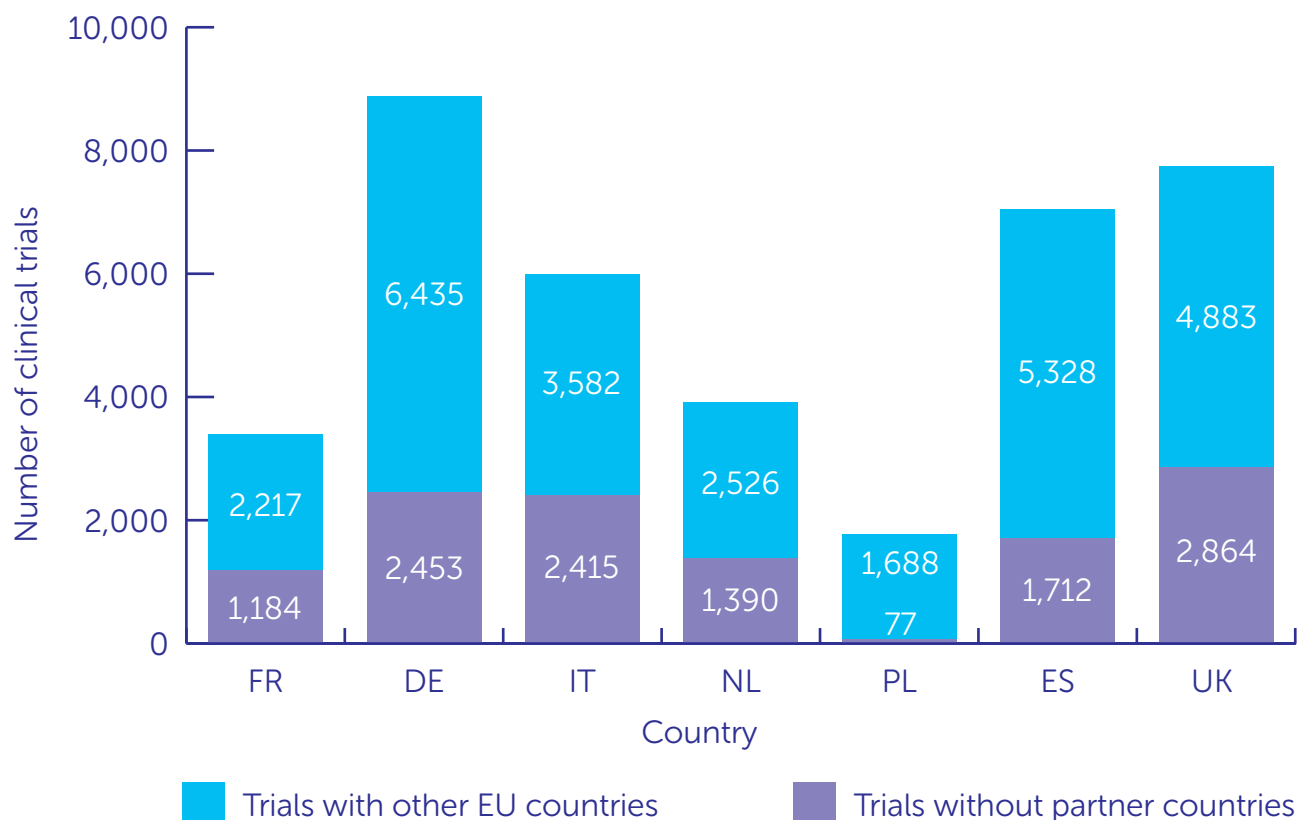
Figure 7 Industry sponsored experimental medicine trials, European peer group



Source: Clarivate Analytics. Open for innovation: UK Biopharma R&D Sourcebook (2016)

Analysis of clinical trials (both industry-led and investigator-led trials) included^{xxviii} in the European Clinical Trials Database EudraCT²⁹ shows that, in addition to the UK having the highest number of country-specific clinical trials (n=2,864) in the database, it has the third highest number of joint trials (n=4,883) with other EU countries, following Germany (n=6,435) and Spain (n=5,328) (**Figure 8**).

Figure 8 Number of clinical trials conducted by country with or without collaboration with other EU countries between 2004-2016



Source: Technopolis Group; European Clinical Trials Database

Notably, the UK participates in the highest number of clinical trials for rare diseases (n=1,349) and paediatric patients (n=1,193) within the EU, thus leading the way in the development of new treatments for these patients. The vast majority of these clinical trials involve active collaboration with EU countries (**Figure 9^{xxix}**). Low participation rates and/or small numbers of patients, especially in the case of rare diseases, means that a single country cannot recruit enough trial participants in isolation, making cross-EU partnerships necessary.

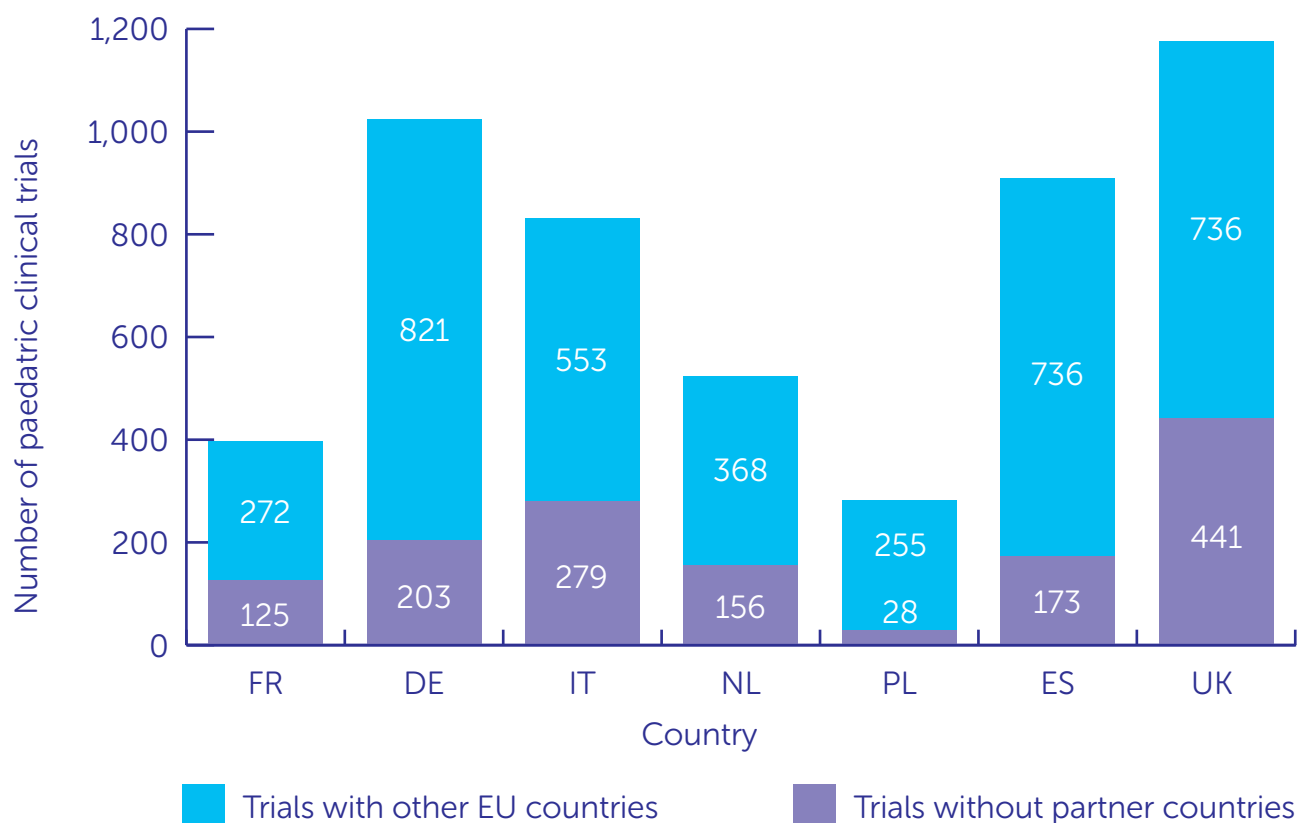
The ratio of trials involving EU collaboration to those that do not is about 3:1 for all trials, 4:1 for paediatric trials, but 6:1 for rare diseases trials. (See case study on Leadership in rare diseases research, at cruk.org/UKandEUresearch)

^{xxviii} Note that Phase I trials data may be incomplete in the database as it relies on voluntary reporting, while Phase II-IV trials registration is compulsory. In addition, only clinical trials for medicinal products are included in the database, and clinical trials for surgical procedures, medical devices or psychotherapeutic interventions are not available.

^{xxix} Note that in a small number of cases it was not possible to identify whether a trial involved EU collaboration or not based on EudraCT data.

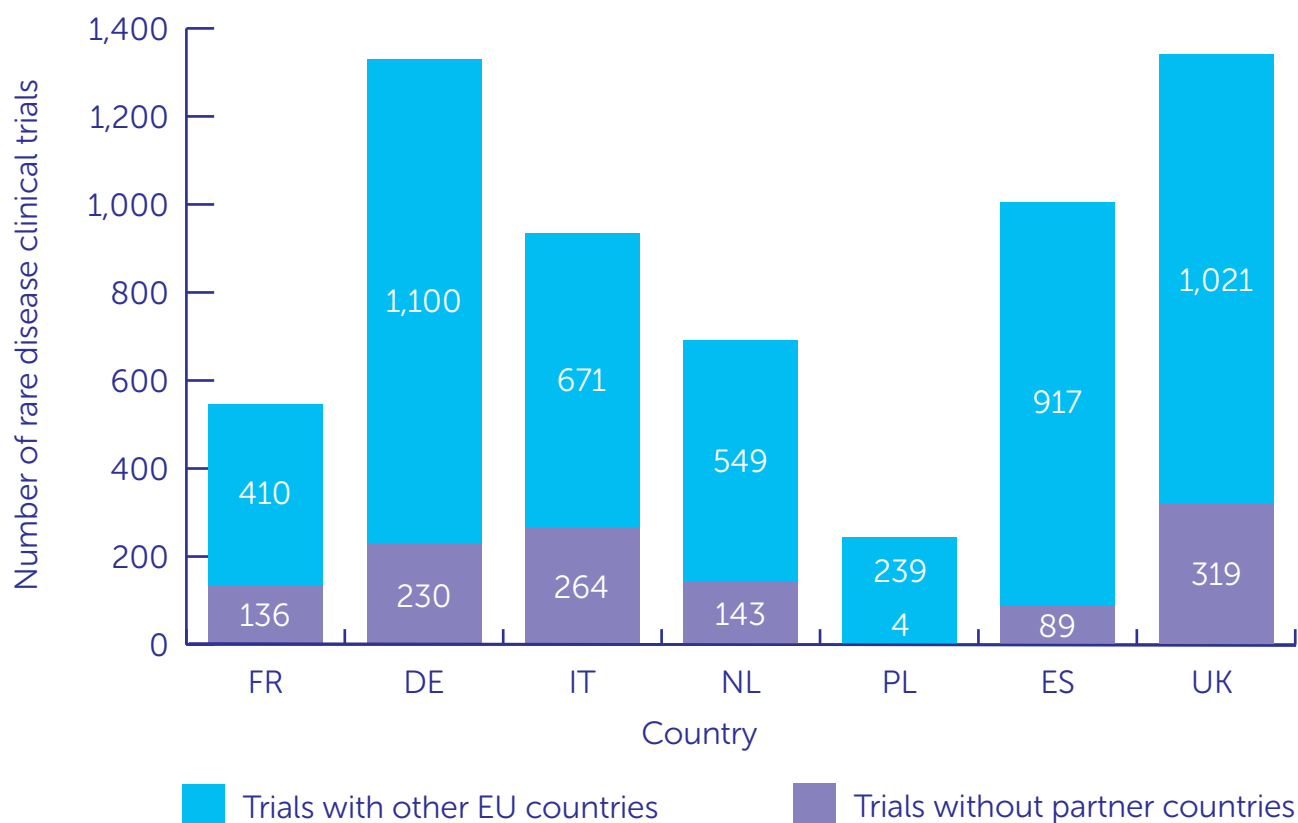
Figure 9 Number of clinical trials conducted by country with or without collaboration with other EU countries

(a) Paediatric trials



Source: Data analysis: Technopolis Group; Data source: European Clinical Trials Database (January 2017)

(b) Rare disease trials



Source: Data analysis: Technopolis Group; Data source: European Clinical Trials Database (January 2017)

Clinical trials in the UK are funded by government, industry and charities, and frequently involve collaboration with the EU. For example, of the 200 clinical trials directly funded by Cancer Research UK, 28% involve patients from at least one other EU country³⁰.

In rare diseases such as paediatric cancer, Europe-wide collaboration is essential for developing new treatment regimens. The European Society for Paediatric Oncology (SIOPE) is a pan-European organisation representing more than 1,600 members across 34 European countries, of which the UK is a key contributor. Professor Pamela Kearns, from the UK, is currently president-elect of SIOPE³¹.

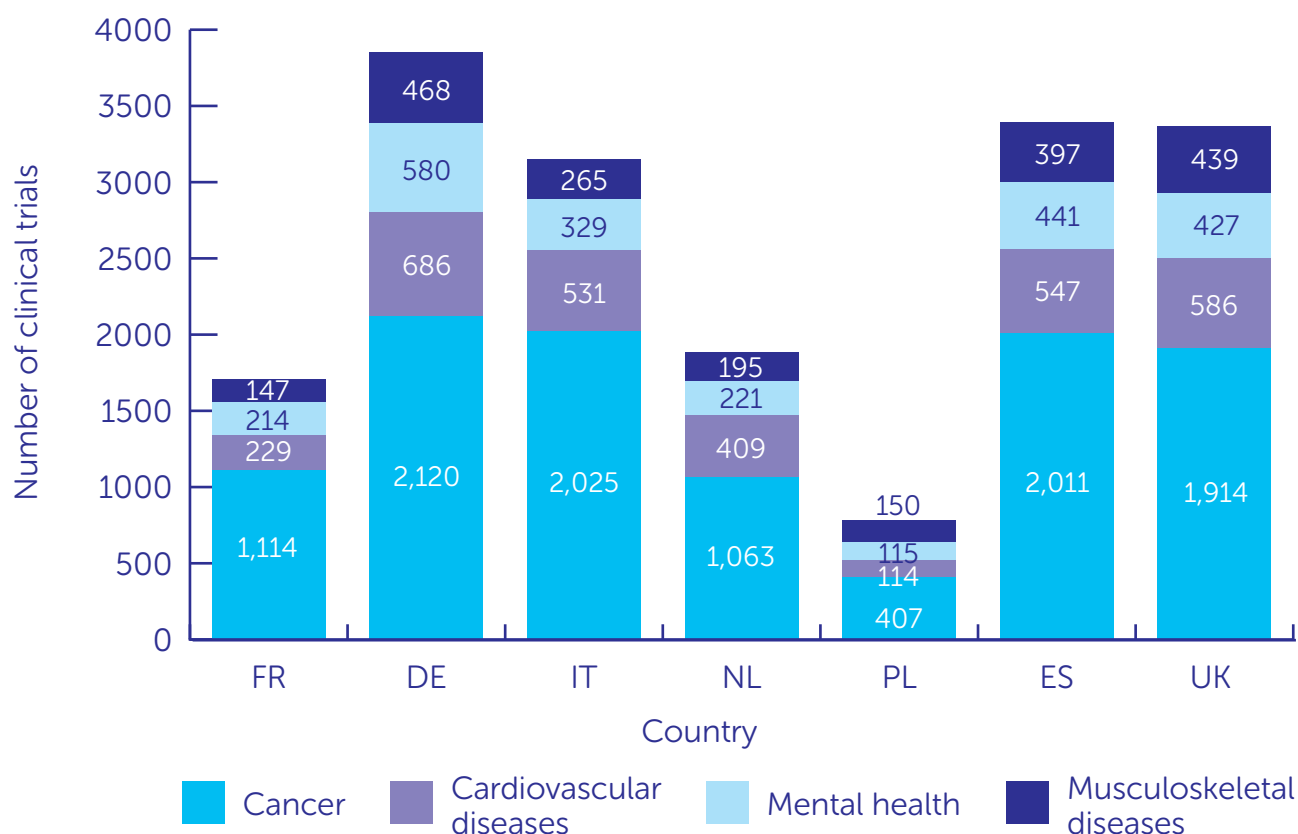
The UK has been instrumental in leading a number of European Paediatric cancer trials through SIOPE. One such example is SIOP WT 2001, a randomised controlled trial for stage II –III intermediate risk Wilms' Tumour (a type of kidney tumour) led by Professor Pritchard Jones of University College London and supported by Cancer Research UK. The trial ran for a decade due to the rarity of the patient population and was published in the *Lancet* in 2015. The results have demonstrated the safe omission of doxorubicin from the treatment regimen to reduce cardio-toxicity and this approach has now become the standard of care for patients³².

The UK was instrumental in creating the SIOPE strategic plan for childhood cancer including leadership. The need for a plan was first recognised in a framework 7 (FP7) funded project: The European Network for Cancer Research in Children and Adolescents (ENCCA)³³.

Another example is the BEACON-neuroblastoma Phase II clinical trial led by the University of Birmingham, which aims to test a novel drug treatment for childhood neuroblastoma (a form of cancer) ³⁴. The trial includes sites in six other EU member states.

When looking at clinical trials by country and disease areas, the UK ranked in the top 4 for clinical trials in cancer, cardiovascular diseases, mental health and musculoskeletal conditions (**Figure 10**). Germany, Spain and Italy also featured among the five most active EU member states in conducting trials in these disease areas, with Germany emerging as the leader in each area.

Figure 10 Number of clinical trials by country and disease area



Source: Technopolis Group; European Clinical Trials Database

4.3 Clinical trial methodology

"The UK was the first to set up clinical trials, a structured way of clinical research, which it continues to develop further."

Professor Wiek van Gilst, Head of Experimental Cardiology, University Medical Center Groningen, The Netherlands

The Medical Research Council (MRC) pioneered Randomised Controlled Trials (RCT) in the 1940s and Sir Austin Bradford Hill is credited with inventing the modern RCT, which has become the gold standard of clinical trial design ³⁵. Since then, RCTs have been used to ensure the accuracy and reliability of the results generated by research institutions worldwide. This is one of the most significant advances in modern research methodology – one that enabled the generation of much of the high-quality evidence on which modern medicine depends.

The UK continues to contribute to novel trial methodology. Examples include the AKU Society international programmes of clinical trials for alkaptonuria³⁶ and the recommendations on clinical trials for small populations³⁷.

The EU Clinical Trials Directive 2001/20/EC (CTD), implemented in 2004, aimed to harmonise authorisation of clinical trials for medicinal products across the EU to improve the generation of reliable patient data^{xxx}. However this piece of legislation was seen as unnecessarily bureaucratic by the UK medical research community. The European Commission ran several consultations on plans to revise it, during which organisations representing the medical research community in the UK persuasively set out their position. For example, Cancer Research UK played a key role in providing evidence demonstrating the negative impact the Directive was having³⁸. A new Clinical Trials Regulation informed by UK views has now been passed and is expected to come into effect in 2018. The scientific community see this as a considerable improvement on the CTD, addressing many of the previous problems.

The UK has also actively contributed to the operation of clinical trials in EU member states by providing training to new member states such as Poland and Hungary via twinning programmes under the Technical Assistance and Information Exchange instrument of the European Commission^{xxxi}. Additionally, UK clinical trial protocols and structures are also being adopted by EU countries, including Belgium and Denmark.

Interviewees for this study were impressed by the UK's rigorous approach to health technology assessment (HTA) and cost-effectiveness, benefitting from the ability to collect data through the centralised NHS. They explained that clinical guidelines developed by the National Institute of Health and Care Excellence (NICE) were widely accepted and often thought of as a reference point, shaping clinical guidelines globally for the benefit of patients. Other EU countries often model their own HTA agencies on NICE, or set up HTA research programmes guided by the NIHR's HTA programme.

"We have tried to copy some of the UK approaches, particularly those for comparative effectiveness in clinical research with public money, from the UK National Institute for Health Research (NIHR) Health Technology Assessment programme. We see the UK as a very useful example and the NIHR is providing valuable support in translating this knowledge."

Dr Frank Hulstaert, Senior Researcher, Belgian Health Care Knowledge Centre (KCE), Belgium

4.4 Clinical trial infrastructure

The UK is an attractive destination for clinical trials because of its high patient recruitment potential including the third largest population in the EU³⁹. The UK also operates with specialised clinical research centres, networks and trials expertise. Clinical trial sponsors and organisers are able to access information quickly and effectively, and there is a proven track record in efficiently delivering results.

The quality and efficiency of the UK clinical trials system was considered exceptional by several of those interviewed for this study. Other interviewees added that the MHRA acts as a respected

xxx European Parliament and Council of the European Union. Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use. Official Journal of the European Communities. 2001, L121/34.

xxxi Interview with Magda Chlebus, 8 February 2017.

source of knowledge and advice on conducting clinical trials. In 2011 the UK government acted to reduce the administration burden of setting up clinical trials without compromising on patient safety and research quality⁴⁰. Current initiatives such as the Accelerated Access Review aim to streamline clinical trial setup further, so that patients can get quicker access to new innovative treatments, diagnostics and medical technologies⁴¹.

The UK government has invested in systems to increase the efficiency of patient recruitment to clinical trials⁴². It invested £60m in a secure Clinical Practice Research Datalink (CPRD) to link primary and secondary care data at an unidentifiable patient level and to provide researchers with access to patient data for clinical trial registration and observational studies. The NIHR has developed a smartphone app that provides information about clinical trials to patients and publishes the Research Activity League Table which shows research activity across all NHS trusts in England. Consequently, the general level of awareness about clinical trials is seen to be higher in the UK than elsewhere in the EU, according to interviewees. Patient groups are often integrated into clinical trials, for example DevelopAKUre, the UK-based AKU Society and the French ALCAP patient groups are playing a major role in patient recruitment and public communication.

“The UK is one of the leading countries for pragmatic trials and new methods like electronic trials”.

Dr Frank Hulstaert, Senior Researcher, Belgian Health Care Knowledge Centre (KCE), Belgium

Several interviewees applauded the UK clinical research system as unique within Europe because of the juxtaposition of academic expertise from universities with clinical expertise from the NHS combined with sustained funding from government and charities. Facilities such as the NIHR Biomedical Research Centres (BRCs) provide early phase trials infrastructure and are embedded within NHS Trust-University partnerships⁴³.

Other NIHR facilities include 19 purpose-built Clinical Research Facilities for Experimental Medicine with specialist clinical research and support staff to speed up the translation of scientific advances for the benefit of patients and 18 adult and 11 paediatric Experimental Cancer Medicine Centres, in close partnership with Cancer Research UK and the Departments of Health in each of the devolved nations (Northern Ireland, Scotland and Wales).

Another facility – the MRC Clinical Trial Unit (CTU) – is renowned for conducting high-impact clinical trials⁴⁴. The CTU is a centre of excellence for conducting clinical trials, meta-analyses and epidemiological studies, and is committed to strengthening and expanding the evidence base for healthcare nationally and internationally. Key areas of research include cancer, infections and clinical trial methodology. The CTU has a proven track record of osteosarcoma research and has been leading clinical trials in this rare cancer for over 25 years. Hence, it was chosen as the co-ordinating data centre for the pan-EU EURAMOS-1 trial.^{xxxii} The CTU was responsible for overall trial management and analyses; it collected and quality-controlled patient data not only from the UK, but also Belgium, The Netherlands and Ireland.

Due to this unique combination of expertise and infrastructure, the UK adds significant value to pan-EU clinical trials through the recruitment of patients, high-quality clinical research expertise and a well-organised clinical research system. An example from the paediatric field includes the EU Framework Programme 7 project NEMO⁴⁵, the largest multi-centred European study of safety and efficacy of an antiepileptic medicine against seizures in newborn babies. The

xxxii Maintenance treatment with interferon-alpha following intensive multi-agent chemotherapy and surgery for high-grade osteosarcoma.

multidisciplinary group of experts from academia and industry span 13 European countries (and the USA) and the pan-EU trial was coordinated from the UK.

Box 2 Importance of the UK for pan-EU trials

The UK is a highly desirable destination for pan-EU clinical trials because of its proven track record in efficiently delivering results and the availability of specialised clinical trial units and clinical trials expertise ⁴⁶.

The UK has immense patient recruitment potential through the combination of a large population and high patient awareness of clinical trials. Well-coordinated patient groups and registries are key assets. For example, participation of the AKU Society, a UK-based patient group, was crucial for recruiting patients to pan-EU clinical trials of nitisinone, a potential treatment for the rare disease, alkaptonuria ⁴⁷. The UK's Royal Liverpool University Hospital is coordinating these trials and providing vital expertise to researchers and patients across other EU countries.

The UK, through its participation in clinical trials, contributes to improved public health in the EU by informing EU clinical practice and guidelines. The UK is a leader in paediatric and rare diseases trials. In these and other areas, UK leadership and participation in pan-EU trials continues to contribute to the identification of effective and safe therapies. International clinical trials conducted with UK participation led to the use of tocilizumab for some forms of juvenile idiopathic arthritis^{xxxiii, xxxiv}, which may improve the quality of life for many children with this disease.

There are also economic benefits for EU health systems such as when cheaper treatments are identified, international clinical trials combining UK and EU participation showed that XELOX (combination therapy of capecitabine and oxaliplatin) therapy is significantly cheaper for bowel cancer than the previously recommended treatment ⁴⁸.

(Full case study available at **cruk.org/UKandEUresearch**)

xxxiii Dueckers G, Guellac N, Arbogast M, Dannecker G, Foeldvari I, Frosch M, Ganser G, Heiligenhaus A, Horneff G, Illhardt A, Kopp I. Evidence and consensus based GKJR guidelines for the treatment of juvenile idiopathic arthritis. *Clinical immunology*. 2012;142(2):176-193.

xxxiv University College London. Tocilizumab – a new treatment for severe juvenile idiopathic arthritis in children. Webpage. Available from: **<https://www.ucl.ac.uk/impact/case-study-repository/new-treatment-for-severe-juvenile-idiopathic-arthritis-in-children>** [Accessed 2 March 2017].

5 THE ROLE OF THE UK'S WORLD CLASS MEDICAL RESEARCH FACILITIES IN EU SCIENCE

KEY POINTS

- The UK helps to support and maintain essential research infrastructure for the EU research community. UK research facilities are typically available at low or no cost to EU-based researchers. These often provide unique resources not available elsewhere in the EU and are usually funded either solely or partly by UK funders.
 - The UK provides major research assets that the EU community is able to capitalise upon. For example, the UK supports a globally unparalleled collection of large-scale population cohort studies, including the 1946 Birth Cohort and the UK Biobank (with 500,000 participants).
 - The UK hosts unique culture collections that provide valuable materials to other EU researchers. The four Public Health England (PHE) Culture Collections and the Medical Research Council's (MRC) Mary Lyon Centre provide biological strains and cultures (viruses, bacteria, fungi, cell lines, mouse strains, etc.) which are only available from these collections.
-

5.1 Introduction

The UK has a sophisticated portfolio of research infrastructure available for use by international researchers.

These include population cohorts, disease platforms, high-throughput sequencing centres, data platforms and hubs, clinical trial units and culture collections. In most instances, the research facilities or resources are available free of charge or on a cost-only basis to EU member states.

These research facilities often provide unique information or samples that are not available elsewhere in the EU, or sometimes, the world. The research infrastructure is often funded entirely or partly by the UK government or charitable funders; these include Public Health England, the MRC, Biotechnology and Biological Sciences Research Council (BBSRC), Cancer Research UK, Wellcome and other members of the Association of Medical Research Charities. In addition, a number of these facilities have also received funding from the EU to develop these resources.

The UK provides the headquarters of four pan-European health-related research infrastructures ⁴⁹:

- European Life-science Infrastructure for Biological Information (ELIXIR) in Hinxton, Cambridgeshire;
- Integrated Structural Biology Infrastructure (INSTRUCT) in Oxford;
- Infrastructure for Systems Biology-Europe (ISBE) in London (Imperial College) (in construction phase);
- European Social Survey (ESS ERIC) in London (City University).

As such, the UK plays an active role in coordinating cross-EU research networks to which it contributes valuable resources such as high-tech expertise and institutional space. These headquarters are embedded in prominent universities or intellectual hubs where relevant skills and a collaborative environment are available for them to flourish. The UK also contributes intellectually and materially to EU health infrastructures as a partner, e.g. in INFRAFRONTIER (European Research Infrastructure for the generation, phenotyping, archiving and distribution of mouse disease models) and BBMRI (Biobanking and BioMolecular resources Research Infrastructure).

“The UK puts a lot of energy in coordinating European research infrastructures. The UK has taken the lead regarding Health and Food via the European Strategy Forum on Research Infrastructures (ESFRI), which it does very well.”

Dr Edvard Beem, Co-Director, The Netherlands Organisation for Health Research and Development (ZonMW), The Netherlands

Data across a range of research facilities have been collected and **Table 3** (page 43) presents statistics on the use of these UK infrastructures by non-UK EU researchers.

Table 3 Use of UK research infrastructures by European researchers^{xxxv}

Name of research facility	Type of research facility	Use by EU27 researchers (% of total)	Total number of requests/ Downloads per year	Top three user countries (EU27)	Access charges
Health Protection Agency Culture Collections	Biorepository	48%	5,289	Germany, France, Italy	Not-for-profit (to cover running costs)
Mary Lyon Centre	Biorepository	Cryo course:31% Mouse stocks:14%	Cryo course:10 Mouse stocks:252	Cryo course: Germany, Netherlands, Finland/ Czech Republic Mouse stocks: Germany, France, Italy	Not-for-profit (to cover running costs)
European Bioinformatics Institute	Bioinformatics facility	On-site training: 35% Data:13%	On-site training: 523 Mean data requests: 9,859,319,220	Information not available	Training: approx. 100 GBP per day to cover costs Data: free
Wellcome Trust Sanger Institute	Research Institute	Courses: 25% Mouse stocks: 54% Website visits: 23%	Courses: 2,707 Mouse stocks: 2,347 Website visits: 7,781,233	Website visits: Germany, France, Italy	Not-for-profit (to cover running costs) Data: free
UK Biobank	Biorepository/ cohort	10%	53	Netherlands, Sweden, Estonia/France/Spain	£250 + VAT application fee £1,500 + VAT for access to data only additional costs for biological samples, re-contact requests, etc.
1958 cohort	Population cohort	10%	2,675	Italy, Ireland, Germany	Free
National Survey of Health and Development	Population cohort	6%	65	Denmark, France, Netherlands	Free

Data analysis: Technopolis Group; Data source: provided by individual research facilities

5.2 Cohort studies

The UK supports a globally unparalleled collection of large-scale population cohort studies which provide a wealth of data for studying health and wellbeing throughout the life course.⁵⁰

One of the oldest running cohort studies in the world is the MRC National Survey of Health and Development/1946 Birth Cohort⁵¹. This unique resource includes a variety of data about participants including on their development, childhood, IQ, socioeconomic factors, health behaviours and measures of health. The UK Biobank was established in 2007, with £62m of initial funding from a coalition of charities and government bodies.^{xxxvi} It has also been supported by the Welsh Government, British Heart Foundation, Cancer Research UK and Diabetes UK, and is hosted by the University of Manchester and supported by the NHS⁵². The UK Biobank is the most detailed study of its kind in the world with demographic, genetic and health-related data as well as biological samples and biological assay data available to researchers. It is also one of the largest biobanks with 500,000 people, and experiences a huge level of demand from across EU and is expected to grow further.^{xxxvii}

5.3 Bioinformatics infrastructure

The UK is home to resources used by geneticists and molecular biologists all over the world, including the EU. The branch of the European Molecular Biology Laboratory (EMBL) located in the UK, the EMBL-European Bioinformatics Institute (EBI), hosts the European Life-science Infrastructure for Biological Information (ELIXIR)⁵³. ELIXIR is a pan-European initiative to coordinate, sustain and integrate Europe's life science bioinformatics resources.

Sixteen countries (as well as EMBL) are members of ELIXIR; these include EU members and non-members such as Switzerland, Norway and Israel. ELIXIR also receives grants from the UK Biotechnology and Biological Sciences Research Council (BBSRC). The EMBL-EBI is funded primarily by EMBL member states which include both EU and non-EU countries⁵⁴. Some of the other major funders include the European Commission (EC), the US National Institutes of Health (NIH), Wellcome, UK Research Councils and industry programme partners.

The EBI is a three-strand mission: to train bioinformaticians, to provide data services, and to support industry to use the data on offer. The EBI makes biological data freely available through the world's most comprehensive range of molecular databases.

The Sanger Institute, in addition to core funding from Wellcome, is also supported by a number of external grants from funders including UK Research Councils, charities (including Cancer Research UK), the EC and NIH⁵⁵. The Sanger Institute is driven by imaginative scientists with a shared commitment to understanding genomes and their biological implications, but with diverse expertise in biology, genetics, medicine, pathology, technology, informatics, computational science, mathematics and statistics.

The Sanger Institute provides training courses, open access data and genetically modified mice and stem cells. Having provided advice, expertise and vision towards delivering the UK's 100,000 Genomes project which aims to sequence 100,000 genomes to revolutionise treatments in the NHS, the Sanger Institute is now advising France and Denmark on implementing similar initiatives^{xxxviii}.

xxxvi Wellcome, Medical Research Council, Department of Health, Scottish Government and the Northwest Regional Development Agency

xxxvii Personal communication, Mr Andrew Trehearne, UK Biobank, 10 January 2017.

xxxviii Personal communication, Dr Julia Wilson, The Sanger Institute, 13 December 2016.

“The UK biobanks lead the field because of infrastructures like ELIXIR, which the UK can build on. They are hence involved in important discussions about bioinformatics, big and open data, and data management.”

Dr Bonnie Wolff-Boenisch, Head of Research Affairs, Science Europe

5.4 Biorepositories

The UK hosts culture collections such as the four Public Health England (PHE) Culture Collections⁵⁶ and the Mary Lyon Centre (MLC) for mouse strains funded by the MRC, which provide biological strains and cultures to EU researchers⁵⁷. For many of the strains and cell lines, these biorepositories are the only EU based source^{xxxix} and are supplied on a not-for-profit basis to researchers all over the world, including the EU.

The MLC has over 2,800 strains of mice and is the UK archiving node for mouse strains^{xl} – each EU country has one archiving node.^{xli} The MLC and its sister institute, the Mammalian Genetics Unit have participated in many cross-EU collaborations such as the high throughput mouse phenotyping project, EUMODIC, which established the groundwork for the International Mouse Phenotyping Consortium⁵⁸. The MLC also provides training courses on specialised techniques such as phenotyping, culturing, storage and distribution on a cost-only basis to EU researchers.

The UK Stem Cell Bank is another valuable resource for international researchers. Supported by the UK’s MHRA, it supplies materials for stem cell research and works in collaboration with academia, industry and the MHRA Innovation Office to support companies and academics in navigating the regulatory process to bring innovative medicines to market⁵⁹.

5.5 Research facilities

UK national facilities offer research equipment and laboratory space as well as technical knowhow to EU researchers, thus supporting and enhancing collaborative EU research activity. One such facility is ISIS, a pulsed neutron and muon source at the Rutherford Appleton Laboratory in Oxfordshire⁶⁰. It is owned and operated by the UK Science and Technology Facilities Council and supports an international community of more than 3,000 scientists probing the microscopic structure and dynamics of matter. It is the most productive research centre of its type in the world. About 8% of ISIS beamtime is used for medical research, of which around 20% is used by researchers from other EU countries.^{xlii} Historically, ISIS has had access to funding from the EU (as part of large multi-facility EU grants) over several framework programmes. These have provided beam fees, plus travel and subsistence costs for EU researchers to use ISIS. The ISIS facility has bilateral agreements with several countries (e.g. Italy, Sweden, and The Netherlands) which provide funding for their researchers to use ISIS. The facility also runs training courses, for international scientists who come to use the instruments⁶¹.

The UK’s National Institute for Health Research (NIHR), which primarily funds and supports world-leading clinical, applied health and social care research, also maintains facilities such as Biomedical Research Centres/Units (BRCs/BRUs) that EU researchers can access. Recently, 40%

xxxix Personal communication, Dr Martin Fray, Mary Lyon Centre, Harwell, 21 December 2016 and Dr Bryan Bolton, HPA Culture Collections, 19 January 2017.

xl This is part of a network for storage and distribution of mouse strains

xli Personal communication, Dr Martin Fray, Mary Lyon Centre, 21 December 2016.

xlii Personal communication, Dr Philip King, ISIS, 3 February 2017.

of the BRCs/BRUs (n=13, total 31) that completed a questionnaire^{xliii} regarding their activities and impacts stated that EU scientists requested access to their facilities to take advantage of high-quality technical assistance. Five centres indicated that facility usage by other EU scientists was between 10-20% of overall capacity. One centre stated that EU researchers used the facilities 140 days per year (representing a value of around £50,000), while another mentioned that EU researchers had worked in their facility for approximately 50% of the time over the last year.

The NIHR also provides facilities for bioscience companies and other interested groups. The NIHR Office for Clinical Research Infrastructure (NOCRI) helps global industry, charities and national and international government agencies to navigate the clinical research environment and to set up collaborations with NIHR centres in a streamlined and efficient way, while facilitating recruitment of NHS patients for clinical trials^{62, 63}. NOCRI is able to offer a bespoke service for setting up clinical studies, along with world leading expertise and facilities which saves time, costs and de-risking investment for clinical trial sponsors.

xliii Survey results provided by NIHR for the purposes of this study

6 DEVELOPMENT OF NEW THERAPIES AND MEDICAL TECHNOLOGIES

KEY POINTS:

- The UK has the largest pipeline of therapeutic treatments in the EU, with more than 800 possible products in development in 2016⁶⁴.
 - 25% of the world's top 100 prescription medicines were discovered and developed in the UK⁶⁵.
 - The UK is an acknowledged pioneer in the development of novel technologies such as personalised medicines.
 - Experts based in other EU countries consider the UK 'very mature' in translational research, leading to accelerated access to treatments for patients, in the EU and beyond.
 - The UK has a long history of patient involvement and continues to serve as a model for other EU countries in this area.
 - UK research findings are of high relevance and value to informing clinical guidelines and hence shaping medical practice, in the EU.
-

6.1 Introduction

Research underpins the development of new or improved products and treatments, produces intellectual property for take-up by industry, and provides evidence to inform policies across the world. The pathway from research to impact on patient health involves an entire ecosystem of public and private R&D investment, health systems, and policy makers. In this global endeavour, discoveries made in one location can lead to a break-through in another, and the process is rarely linear, with each player providing an important contribution towards real world solutions.

6.2 Impact on public health and patients

As described in the preceding chapters, UK researchers make valuable contributions to the EU – and global – research and policy community. These contributions take a variety of forms, evident in the MRC's report 'Outputs, outcomes and impact of MRC research'⁶⁶. Of the 6,000 MRC awards for which data are available, 28% reported that their work had produced research tools or methods for others to use, such as in vivo models of mechanisms and symptoms, reagents, databases and biological samples, and data analysis techniques. 23% of awardees reported that they had influenced policy, through clinical guideline revisions and participation as members of advisory committees. Of these, one third had influenced policy internationally and in other EU countries^{xliv}.

Box 3 describes an example of how a UK clinical study conducted by the University of Glasgow⁶⁷ has shaped medical practice in the EU and globally: the long-term benefits of lowering cholesterol levels of people at risk of developing cardiovascular disease.

xliv 25% of influences had an international remit, i.e. including Europe, and 7% indicated that they affected Europe specifically.

Box 3 UK research on statins contributes to cardiovascular disease prevention in the EU

Cardiovascular disease (CVD) causes 37% (over 1.8 million) of all deaths in the EU each year, with an estimated economic cost of €210 billion⁶⁸. People with a high level of cholesterol in their blood are at a high risk of developing CVD. Statins, a group of medicines that can help lower the level of blood cholesterol, can help to protect healthy people with high levels of blood cholesterol from developing CVD.

Research conducted at the University of Glasgow in 1995 produced the first evidence that lowering blood cholesterol could reduce the risk of developing CVD. The West of Scotland Coronary Prevention Study (WOSCOPS), a longitudinal study involving more than 6,500 men, showed that statins reduced the risk of a heart attack in healthy individuals with high cholesterol levels by 31% after 5 years of regular intake. A follow-up study in 2007⁶⁹ demonstrated the long-term benefits of statins: taking statins over a period of five years slowed down disease progression and subsequent use continued to reduce the risk of CVD^{70, 71}.

This landmark research drove the global adoption of statins as the first-line medical option for the prevention of CVD. This preventive use of statins is now recommended by the European Society of Cardiology and the European Atherosclerosis Society.

(Full case study available in at cruk.org/UKandEUresearch)

Over the past 40 years, advances in cancer treatment have led to valuable health gains, and cancer survival rates have doubled⁷². Research conducted in the UK produced some of the crucial findings and tools that contributed to this remarkable achievement. **Box 4** outlines how UK research contributed at key points along the pathway from research to patient benefit in the area of breast cancer.

Box 4 UK researchers are leading the way in breast cancer

Breast cancer is the most common form of cancer in the EU, and the leading cause of death from cancer in women⁷³. An estimated 364,000 patients were newly diagnosed in 2012 and 92,000 women died of the disease that year in the EU. The economic cost of breast cancer in the EU has been estimated at a €15 billion for 2009⁷⁴.

UK researchers have made important contributions to the field of breast cancer research that include:

- identifying genetic faults that can cause breast cancer, such as the discovery of the “Breast Cancer-Associated” (BRCA) genes, BRCA1 and BRCA2
- discovering new drugs with potential to treat breast (and other) cancers, such as the PARP inhibitors
- developing models that healthcare providers can use to identify women with elevated risk of developing breast cancer, such as the BOADICEA online tool
- optimising breast cancer treatments, e.g. by coordinating the work of a large global collaboration, the EBCTCG, which combines and analyses data from all relevant clinical trials

This body of work has supported substantial progress in the fight against breast cancer: Today, women with breast cancer have a 78% chance of surviving at least 10 years, compared to only 40% in the 1970s⁷⁵.

(Full case study available in at cruk.org/UKandEUresearch)

Research Excellence Framework (REF) case studies

The UK's Research Excellence Framework (REF) is a system for assessing the quality and impact of research in UK higher education institutions⁷⁶, coordinated by the UK's four Higher Education Funding Councils⁷⁷. The latest REF assessed UK research during the period 2008–2013, with expert panels carrying out their assessment in 2014. Universities across the UK submitted information on the research carried out at their institutions, including impact case studies which are publically available online⁷⁸. Each of the case studies provides (self-reported) evidence of UK contributions, often over many years, along the pathway from research to impact on society.

An analysis of the REF2014 impact case studies shows that research in the UK has improved health and clinical outcomes in countries across Europe and globally (**Table 4**). More than a third of case studies from the medical and health sciences reported an impact on health worldwide (823 of 2200)^{xlv}. Of these 85 reported an impact specifically in the Netherlands, and 72 in Germany. The largest number of impacts was reported in the area of mental health (264), followed by cardiovascular diseases (233). **Table 5** provides examples of REF case studies that report impacts in other EU member states, across a broad range of research fields.

Table 4 Number of Research Excellence Framework impact case studies reporting an impact on health

Health impact location	Total	Cancer	Cardiovascular diseases	Mental health	Musculoskeletal conditions
Worldwide	823	200	233	264	146
Europe (incl. UK)	648	166	189	219	124
France	47	12	11	13	6
Germany	72	14	15	24	14
Italy	58	14	12	21	5
Netherlands	85	16	16	36	17
Poland	15	4	2	4	3
UK	562	158	176	184	118

Only submissions in the research subject area 'Medical and Health Sciences' are included in the table. Disease areas were defined through key word searches. One or more impact locations were assigned to each case study.

Source: Data analysis: Technopolis Group; Data source: REF2014 impact case studies database, Available from: <http://impact.ref.ac.uk/CaseStudies>

xlv REF 2014 assigns submitted case studies to a single 'Summary Impact Type' and one or more global locations on the basis of text analysis of the first section of the impact case study template ('Summary of the Impact'). See <http://impact.ref.ac.uk/CaseStudies/FAQ.aspx> [Accessed 27 March 2017]

Table 5 Examples of UK research with health impact in EU member states

Country of impact	Funder	UK institution	Underpinning research	Summary of impact
Germany	Astra Zeneca, Da Costa, Cancer Research UK	Queen Mary, University of London	First and largest double-blind randomised trial to compare the efficacy and safety of anastrozole, tamoxifen or both as treatment for oestrogen receptor positive breast cancer in postmenopausal women (ATAC study)	Change in the standard recommended treatment for oestrogen receptor-positive breast cancer, from tamoxifen to anastrozole (an aromatase inhibitor)
France, Italy, Finland, Sweden	MRC, British Heart Foundation, Wellcome Trust, Leducq Transatlantic Network	King's College London	Identification and characterisation of titin mutations and their link to genetic muscle disease	Screening for titin mutations is now routinely performed in national prenatal genetic diagnosis clinics, resulting in better detection and care for individuals with genetic muscle disease. This research has also informed European clinical guidelines for the diagnosis of muscle disease.
Germany, Netherlands	UK Department of Health; National Institute for Health Research; BUPA Foundation	University of Nottingham	Developed evidence-based treatment pathways for children with eczema by first systematically reviewing all existing evidence to identify research gaps, prioritising those gaps with patients, and then addressing them through national randomised controlled trials; also led development and validation of international diagnostic criteria for eczema	Diagnostic criteria for eczema widely used criteria worldwide; findings informed European guidelines; research into nurse-led clinics led dermatologists in the UK, Germany and the Netherlands to set up similar clinics from 2005 to 2012, which have been shown to be cost saving.
Europe-wide, Mainly Germany and Italy	Medtronic	University of Hull	Led the key trial demonstrating that cardiac resynchronization therapy (CRT), a specialised type of pacemaker, significantly reduces morbidity and mortality and improves the quality of life of selected patients with heart failure (CARE-HF study)	European Society guidelines endorse recommendations based on the CARE-HF study; about 21 more patients alive after 5 years out of 100 patients treated; CRT devices implanted in over 60 000 individuals in EU27 in 2015 of which almost half in Germany (21 139) and Italy (12 815) – so approximately 12 600 EU27 individuals will extend their lifespans each year

Country of impact	Funder	UK institution	Underpinning research	Summary of impact
Poland	National Institute for Health Research; New Zealand Ministry of Research Science and Technology	University of Dundee	Brought the Hall Technique (placing preformed metal crowns over decaying teeth) to the dental profession's attention; demonstrated increased treatment acceptability for children, parents and dentists; showed improved outcomes over standard fillings, economic viability and reduced general anaesthesia requirement	Hall Technique formally adopted as best practice in Poland; improved clinical outcomes in children
Germany, Netherlands, Italy, Ireland, Portugal	National Health Service; National Institute for Health Research	University College London	Developed and evaluated Cognitive Stimulation Therapy (CST), an evidence-based, brief, group therapy for people with mild to moderate dementia; clinical trials showed significant benefits in cognition and quality of life plus cost-effectiveness	World Alzheimer's Report (2011) advocated routine use of CST in early stage dementia patients as a low-cost and effective intervention; since 2008 being used in European countries
EU member states	UK Department of Health, National Institute for Health Research	Centre for Suicide Research, University of Oxford	Over 1m people die by suicide each year, and in the UK it is the leading cause of death for men from 16 to 35. It was discovered that reducing the size of packs of painkillers and changing type of painkiller could save many lives: it was decided that co-proxamol should be withdrawn and between 2005 and 2007 its use was gradually phased out with no new patients being prescribed the drug. By 2008 it had been completely withdrawn. Keith Hawton's team found that not only did suicides using co-proxamol reduce, but also there was no accompanying switch to overdoses involving other drugs.	As a result of this line of research titled 'Stopping suicide and self-harm: changing painkillers on our shelves', The European Medicines Agency (EMA) recommended that dextropropoxyphene, the toxic component of co-proxamol, should not be prescribed within the EU.

Source: Data analysis: Technopolis Group; Data source: REF2014 impact case studies database, Available from: <http://impact.ref.ac.uk/CaseStudies>

6.3 Translating research into innovative therapies

The UK has the largest pipeline of therapeutic treatments in Europe, developing more than 800 product candidates in 2016, compared to around 600 in Germany and 550 in France⁷⁹. 25% of the world's top 100 prescription medicines were discovered and developed in the UK⁸⁰; testimony to the strength of the UK R&D ecosystem and its ability to translate research into real world solutions, with impact in the EU and beyond.

There was a general view among interviewees that the UK is forward-thinking in setting its innovation policies and, as cited below, has a mature translational research landscape leading to accelerated access to treatments for patients in the EU and beyond.

"I think the UK is very mature in translational research, probably more mature than many other countries. There is a real urge to speed up access to the latest innovation in healthcare for the earliest possible benefit of patients"

Dr Pierre Meulien, Executive Director, Innovative Medicines Initiative (IMI)^{xlvi}

The UK is an acknowledged pioneer in the development of several novel technologies. The UK is central to the development of a new generation of personalised medicines – those tailored to an individual's genetic makeup. The NHS fosters new genomic technologies and the development of an integrated informatics capacity, sets up infrastructures such as the Genomic Medicine Centres and pioneers personalised medicine approaches across the health system⁸¹. Similarly, the UK is at the forefront of cancer immunotherapy treatments, working on developing genetically engineered viruses to target cancer cells, new immunotherapy drugs, and pioneering clinical trials in this field⁸².

The UK government was credited with making an effort to strengthen the connections between industry and academia.

"The UK government was among the first to make a large strategic effort to strengthen industry, and the connections between industry and academia. These connections are now no longer something academics need to be ashamed of."

Professor Liselotte Højgaard, Chair of the Advisory Group on Health for H2020; Former Chair of the European Medical Research Council; University of Copenhagen, Denmark

Interviewees considered the UK's innovation policy to be advanced compared to other countries. The translational research interface between pure research settings, hospitals and industry was well established, helping to speed up innovation and patients' access to the latest healthcare developments. In particular, the unique ability to gather data from 140 NHS hospitals and the alignment of hospital trusts with academic institutions were highlighted by a number of interviewees.

xlvi The Innovative Medicines Initiative (2015). Available from: <http://www.imi.europa.eu/content/nd4bb> [Accessed 24 March 2017].

"In my opinion, the main strength of the UK lies in its capability to transfer innovative technology to the market. It has built a great track-record and can obviously organise each step from the research lab to the product. [...] Italy welcomes this innovative technology coming from the UK: Patients have been able to benefit from improvements brought about by new products earlier than patients in other parts of the world."

Dr Giovanni Leonardi, Director General of Research and Innovation in Healthcare, Ministry of Health, Italy

Box 5 provides one example of how UK discoveries in basic science successfully led to broad impact on the pharmaceutical industry delivering benefits for patients in the EU and worldwide: the use of monoclonal antibodies to treat inflammatory diseases such as rheumatoid arthritis.

Box 5 Global impact of UK's discovery of monoclonal antibodies for treatment of rheumatoid arthritis

Rheumatoid arthritis (RA) causes severe inflammation of the joints. In the EU RA affects around 5 in 1000 adults⁸³ and represent a significant economic cost – estimated at €45 billion each year (2008)⁸⁴, and a total annual social cost of RA of €3.5 billion per year in Italy alone (2014)⁸⁵.

In the 1970s and 80s, scientists at the University of Cambridge were instrumental in driving forward research into the production of monoclonal antibodies suitable for treating human patients⁸⁶. Researchers from the Kennedy Institute of Rheumatology (at the time part of Imperial College London) went on to demonstrate unprecedented improvement in RA patients treated with antibodies directed against TNF, a molecule which occurs naturally in the body and plays a key role in inflammation^{87, 88}. The introduction of this new class of therapies in the early 2000s has revolutionised the treatment of RA and other inflammatory diseases.

These key discoveries continue to have broad impact on the pharmaceutical industry: In 2015, three of the five top-selling drugs globally were biological molecules blocking the action of TNF (Humira®, Enbrel® and Remicade®)⁸⁹, and Remicade has been used to treat over 2.6 million patients worldwide with inflammatory conditions such as RA, Crohn's disease, and plaque psoriasis⁹⁰. These therapies represent a new therapeutic option to alleviate the suffering of RA patients in the EU⁹¹.

Today, these therapies are being used, or are in development, for treatment of a broad spectrum of diseases including autoimmune diseases, cancer, multiple sclerosis and Alzheimer's disease.

(Full case study available in at cruk.org/UKandEUresearch)

"UK charities, such as Arthritis Research UK, are very strong and are very important for funding Rheumatoid Arthritis (RA) research. It is the UK that pioneered the treatment of RA with biologicals, and researchers from the UK are involved in almost all RA programmes at EU level".

Professor Francis Berenbaum, Chair of Rheumatology, Faculty of Medicine, University Pierre and Marie Curie, Paris, France.

6.4 Patient involvement in research

To ensure that the 'right' research questions are tackled, the 'consumers' of this research – patients, carers, and others affected need to be able to inform funders and policy makers about their needs and be involved in steering research strategies and investments.

The UK has a long and deep history of patient involvement. The UK National Cancer Research Institute (NCRI), a partnership of 19 organisations who collectively spend more than £490 million per year on cancer research, involves consumers in all of its activities^{xlvi}. The NCRI Consumer Forum is a UK-wide network of cancer patients and carers who are involved in all aspects of cancer research in the UK: from identifying topics, commissioning and undertaking research, to analysing results and evaluating projects.

NCRI Consumers are also involved at the EU-level and have presented to the European Parliament and the Commission on privacy and data usage for medical research, and on the importance and patient-focused uses of cancer registration. They have authored guidance on Plain English summaries, in advance of the EU regulations requiring such summaries, speak at European conferences and meetings, and have founded or co-founded European patient groups such as EuroSarcoma and Unite2Cure.

Experts consulted as part of this study emphasised the UK's flagship role in patient involvement, and the active, well-informed role patient groups play within the UK research ecosystem. Its strong history of including patients in the planning, implementation, and evaluation stages of research programmes were mentioned, with structures such as the NIHR's James Lind Alliance recognised for stimulating this bottom-up approach. Interviewees explained that other EU countries, many of which started to involve patients only recently, have looked to the UK as a model in this area^{xlvi}.

"The UK is without a doubt leading the pack in terms of patient involvement."
Dr Frank Hulstaert, Senior Researcher, Belgian Health Care Knowledge Centre (KCE), Belgium

"This [patient involvement] is where Europeans are drawing on the UK's example, as there is a much stronger focus on patient involvement in the UK."
Dr Hubert Misslisch, Coordinator 'International Cooperations', DLR Project Management Agency, Health Research, on behalf of the Federal Ministry of Education and Research, Germany

"The patient organisations in the UK are really strong and patient participation is well developed. This has impact on EU research and education."
Professor Francis Berenbaum, Chair of Rheumatology, Faculty of Medicine, University Pierre and Marie Curie, France

An example of UK research using a patient-centred approach is work done by the University of Bradford Dementia Group on the development of the Person-Centred Care model (**Box 6**).

xlvi Personal Communication, Mr Richard Stephens, Chair of NCRI Consumer Forum, 23 March 2017.

xlvi Scandinavian countries and the Netherlands were also highlighted as strong in patient involvement.

Box 6 The Person-Centred UK model of dementia care adopted throughout the EU

In 1997, the Bradford Dementia Group, a research group at Bradford University, created a new model of Dementia Care: the Person-Centred Care (PCC) model⁹². PCC is based on a deeper understanding of the experience of living with dementia. Previously, care for people with dementia focused solely on minimising the symptoms of disease. PCC, on the other hand, focuses on the person's well-being. The Bradford Dementia Group also developed a unique tool for monitoring the interaction between carers and people living with dementia, called Dementia Care Mapping (DCM)⁹³.

The use of PCC in conjunction with DCM has transformed policy and practice in dementia care in Europe and beyond. PCC has been shown to enhance the well-being of people with dementia, from diagnosis to end of life. In care homes where the PCC model is fully implemented, everyone who comes into contact with a person living with dementia is PCC-trained and interactions are assessed through DCM. This ensures a fully protected environment for people living with dementia and provides a better level of care^{xlix}.

Over the past twenty years, PCC has spread beyond the UK. Germany was one of the first European countries to adopt the PCC in the early 2000s, followed by others, such as Denmark, the Netherlands, Spain, Portugal, Italy, France, and Sweden⁹⁴. In Sweden, The Netherlands and Norway, PCC and DCM have been incorporated into national strategy⁹⁵; the model was also included in European psycho-social intervention guidelines⁹⁶. Across Europe, an estimated 12,000 practitioners have been trained in DCM since the early 1990s⁹⁴.

(Full case study available in at cruk.org/UKandEUresearch)

6.5 European clinical and public health guidelines

Clinical guidelines recommend how healthcare professionals should care for people with specific conditions⁹⁷. They may offer concise instructions on any aspect of a condition, including recommendations about providing information and advice, prevention, diagnosis, treatment and longer-term management. Guidelines serve as an important tool for making care more consistent and efficient, and for closing the gap between what clinicians do and those practices supported by scientific evidence⁹⁸. A citation in clinical guidelines indicates that a research finding can inform and change real world practice.

Of a total of nearly 6,000 MRC awards that reported on outcomes and impacts, 472 (or 8%) indicated that their research had been cited in clinical guidelines^l.

In this study, an analysis of clinical guidelines of EU member states published between 2002-2013 in the areas of oncology, cardiovascular diseases and mental health demonstrates that UK research papers have contributed significantly to the evidence base which other EU countries draw on when developing their clinical guidelines. UK publications are cited more often in clinical guidelines than in research publications^{li} of their respective global fields.

xlix Personal Communication Dr Silvia Vettor, Geriatric Psychologist in the Veneto region, Italy, 13 Feb 2017.

l Medical Research Council. Outputs, outcomes and impact of MRC research: 2014/15 report. Available from: <https://www.mrc.ac.uk/successes/outputs-report/> [Accessed 27 March 2017] Note that the report does not provide a break-down by location of impact.

li UK contribution on a fractional count basis (%) to global internationally co-authored papers, without the EU country. These figures show the 'expected' rate of UK contribution to internationally co-authored papers in the research of the respective disease area, when guideline developers of a given country choose from a random pool of international papers.

This indicates that UK research was seen as highly relevant to EU national guideline developers and helped to shape medical practice in EU countries. In the area of oncology, German and Dutch guidelines cited UK research papers over twice as frequently than expected, based on the presence of UK research papers in oncology.

In the area of cardiovascular diseases, the citation rate in clinical guidelines was particularly high – more than twice as high than citation rates in research papers in Germany, France, and Poland, and more than five times as high in Italy. The UK contribution to mental health clinical guidelines was about twice as high for France and Poland as expected based on UK contribution to the world.

Table 6 UK contributions as percentages of foreign papers to the evidence base of clinical guidelines for five focus EU countries and other EU member states

	Oncology			Cardiovascular diseases			Mental health conditions		
Country	Clinical guidelines	Cancer Research	Ratio	Clinical guidelines	CVD Research	Ratio	Clinical guidelines	MH Research	Ratio
Germany	11.2	5.3	2.1	15.2	6.3	2.4	14	8.6	1.6
France	6.5	5.2	1.2	13.7	6.1	2.3	15.9	8.3	1.9
Italy	7.8	5.3	1.5	32.3	6.2	5.3	10.3	8.3	1.2
Netherlands	11.1	5.1	2.2	n/a	6.0	n/a	12.5	8.3	1.5
Poland	4.9	5.1	1.0	14.1	5.9	2.4	18	8.1	2.2
Other EU	11.7	5.6	2.1	13.2	6.7	2.0	14.3	9.1	1.6

Source: Data analysis King's College London & Evaluametrics; Data source: national clinical guidelines, Web of Science core collection Clarivate Analytics

Evidence and insights from research also inform public health policies and guidelines, such as public health policies aimed at reducing the number of individuals who smoke cigarettes. UK research on the negative effects of cigarette smoking on health contributed to the large body of evidence that underpins wide-ranging changes in smoking policies across the EU – and a concurrent drop in smoking rates Europe from 40% in the 1970s to 28% today (**Box 7**).

Box 7 UK research findings underpin EU policies aimed at reducing smoking

Tobacco consumption is the single largest avoidable health risk in the European Union⁹⁹. Smoking tobacco causes cancer, cardiovascular disease and other illnesses. More than a quarter of Europeans smoke tobacco¹⁰⁰ and 700,000 adults aged 30-69 die from smoking-related causes every year¹⁰¹. Around 50% of smokers die prematurely – on average 14 years earlier – and smokers have more life years in poor health⁹⁹.

The economic burden of smoking has been estimated at more than €500 billion¹⁰². While this situation is serious, it has markedly improved over the past decades. Between 1979 and 2010, smoking rates in the EU dropped by around 35%, supported by policies aimed at reducing tobacco consumption¹⁰³. UK researchers provided some of the key evidence on which these policies are based.

From the 1950s onwards, research by Sir Richard Doll and Sir Austin Bradford Hill (funded by the UK Medical Research Council) provided definitive proof of a link between smoking

and lung cancer, heart attacks, lung disease and other illnesses¹⁰⁴. Following these studies, doctors in the UK were the first globally to call for concerted action such as supporting smokers in quitting and national health education campaigns¹⁰⁵. This early adoption by the UK medical profession may have been helped by the fact that Doll and Hill's study participants were 40,000 UK doctors – two thirds of all doctors in the country at the time¹⁰⁴.

More recently, a 2012 review conducted by the University of Stirling (the 'Stirling Review') found strong evidence that plain packaging would reduce the attractiveness and appeal of tobacco products¹⁰⁶. The review's findings informed consultations on tobacco product packaging in the EU and member states. In May 2016, a revised EU Tobacco Products Directive tightened the rules on cigarette packaging and labelling¹⁰⁷, and France and Ireland (along with the UK) banned branded packaging¹⁰⁸. A similar EU-wide ban on branded packaging, which is currently under discussion, would be estimated to reduce the number of smokers by 2.4 over a five-year period, resulting in annual healthcare savings of €506 million.¹⁰⁹

7 AN ATTRACTIVE TRAINING ENVIRONMENT FOR EARLY-CAREER RESEARCHERS

KEY POINTS

- The UK trains many high-profile researchers from the EU: it is the top destination for Marie Skłodowska-Curie fellows, hosts the second highest number of Human Frontier Science Program fellows, and hosts the largest number of ERC grant holders.
 - UK universities are among the top institutions in the world for health and life science subjects, and train the second highest number of science graduates in the world, after the USA (2015).
 - Four UK universities are consistently among the top ten institutions, in terms of global ranking and in terms of hosting EU research fellows and ERC grant holders: the University of Oxford, the University of Cambridge, Imperial College London, and University College London.
 - Early career EU researchers move to other EU countries after working in the UK. An estimated 650 UK-trained researchers leaving MRC-funded projects moved to senior roles in other EU countries over the 2006–2016 period. (data from MRC, Researchfish)
-

7.1 UK research institutions in the health and life sciences

The UK has a very strong reputation for the quality of its education and research in the life sciences, medicine and healthcare, attracting many EU scientists and students to UK's institutions.

7.1.1 World University rankings

Students and researchers from the EU benefit from access to education and training at UK universities, among the top institutions in the world for health and life science subjects. The UK scores highly in the Times Higher Education (THE) World University Rankings^{lii}, second only to the USA¹¹⁰. Four UK institutions are consistently among the top ten, both overall and in the areas of “clinical, pre-clinical and health” and “life sciences^{liii}”: the University of Oxford (U Oxford), the University of Cambridge (U Cambridge), Imperial College London, and University College London (UCL).

Other UK institutions, Queen Mary University London and the University of Edinburgh (U Edinburgh), also hold top positions based on their citation score, i.e. the number of times their published work is cited by scholars globally (an indication of the level of influence scholarly work has on the global research community). The only other EU institution that features among the top ten in the “clinical, pre-clinical and health” subject area is the Karolinska Institute in Sweden. **Table 7** summarises the position of these institutions in the rankings. These rankings align with the top institutions hosting EU researchers with competitive grants and fellowships (Marie Skłodowska-Curie Fellowships and ERC grants, see sections 7.2.1 and 7.2.4)

lii The Times Higher Education (THE) World University Rankings are the only global university performance rankings that look at universities across teaching, research, citations, industry income and international outlook

liii Full lists of subjects included in the THE's definition of “clinical, pre-clinical and health” and “life sciences”. Available from https://www.timeshighereducation.com/world-university-rankings/2016/subject-ranking/clinical-pre-clinical-health-0#!/page/0/length/25/sort_by/rank/sort_order/asc/cols/stats; https://www.timeshighereducation.com/world-university-rankings/2016/subject-ranking/life-sciences-0#!/page/0/length/25/sort_by/rank/sort_order/asc/cols/stats. [Accessed 8 Feb 2017]

"The UK is attractive for young people from Germany to move to and get research experience. It is a good training ground for young researchers, with universities of great visibility and reputation."

Professor Detlev Ganten, German National Academy of Sciences Leopoldina;
President, World Health Summit, Charité – Universitätsmedizin Berlin, Germany

Table 7 Top UK and EU institutions (THE World University Rankings 2016-17)

Ranking by subject area	UK institutions	Other EU institutions
All	U Oxford – rank 1 U Cambridge – rank 4 Imperial College London – rank 8	No other EU institutions in top 10 ^{liv}
Clinical, pre-clinical and health	U Oxford – rank 1 U Cambridge – rank 3 Imperial College London – rank 4 UCL – rank 6	Karolinska Institute, Sweden – rank 10
Research score ^{lv}	U Oxford – rank 1 U Cambridge – rank 2 UCL – rank 3	Karolinska Institute, Sweden – rank 6
Citation score	U Oxford – rank 1 Queen Mary University London – rank 3 U Cambridge – rank 4 U Edinburgh – rank 7 Imperial College London – rank 9	No other EU institutions in top 10
Teaching environment score	U Oxford – rank 7 Imperial College London – rank 10	No other EU institutions in top 10
Life Sciences	U Cambridge – rank 2 U Oxford – rank 3 Imperial College London – rank 9	No other EU institutions in top 10
Research score	U Oxford – rank 2 U Cambridge – rank 3 Imperial College London – rank 4 UCL – rank 5	Karolinska Institute, Sweden – rank 9
Teaching environment score	U Cambridge – rank 2 U Oxford – rank 4	No other EU institutions in top 10

Source: Times Higher Education World University Rankings 2016-17

^{liv} Note that ETH Zurich – Swiss Federal Institute of Technology Zurich is rank 9.

^{lv} Times Higher Education World University Rankings methodology. Available from <https://www.timeshighereducation.com/world-university-rankings/methodology-world-university-rankings-2016-2017>. [Accessed 7 Feb 2017].

7.1.2 Perceptions of the strengths of UK education and training and its value to the EU

Interviews conducted as part of a study on the UK's contribution to global health highlighted a number of key strengths of UK universities in teaching¹¹¹. These included: a culture of scientific rigour and understanding the theoretical underpinnings of the subject; training constantly being updated to reflect the latest research and evidence, and the depth and range of skills being taught.

A consequence was that the UK education system was viewed as producing graduates with strong analytical and innovative thinking skills, ultimately leading to patient benefits and health.

"The UK continues to be an invaluable source of training and inspiration, especially in the life and medical sciences today, through its unique international outlook."

**Professor Werner Kühlbrandt, Director of the Max-Planck-Institute of Biophysics
Frankfurt, Germany**

Several interviewees for this study felt the UK is "an attractive training ground for young researchers" and that a research period in the UK increased career opportunities in their home countries.

An exceptional aspect of the UK was that students were encouraged to challenge and question more established researchers, helped by a relatively 'flat hierarchy' where senior faculty engage directly with junior researchers (see also Max Planck Society case study at cruk.org/UKandEUresearch) helping to produce graduates and researchers with strong skills in critical thinking.

Interviewees also pointed out that the UK is a key part of a global education and training system in the medical sciences and that the English language, as the global language of research and business, has made the UK a more attractive destination.

"The UK offers good quality education and it trains EU students and researchers to be critical. Many of these students and researchers go home and take their experiences and networks with them."

Programme Officer, Non-governmental organisation, Poland

Box 8 Links in training and research – the Max Planck Society

The Max Planck Society in Germany is a world-renowned research association located in Germany¹¹². The Society's Biology and Medicine Section (BMS) comprises 27 institutes which work across the entire breadth of the life sciences. The Society defines itself as a person-centred research organisation, focused solely on attracting the world's leading talent.

Professor Bill Hansson, who heads the BMS section, commented that the UK's strong educational system makes a significant contribution to the training of excellent scientists. The Society continues to draw on this excellence, with many of its top researchers spending some time working in the UK.

Two directors of Max Planck Institutes, Professor Dr Werner Kühlbrandt and Professor Dr Ralf Adams, spent several years at UK institutions. Reflecting on their experience in the UK, they highlighted the scientific excellence, buzzing research atmosphere, and open international

outlook. To this day, both researchers continue to benefit from the skills they acquired in this unique environment and apply them to their work:

"I acquired knowledge and skills in my area of science that at the time were not available anywhere in Germany, or indeed in the world. I was most impressed with the scintillating scientific atmosphere at the MRC LMB, which has been, and continues to be, the most important hub of innovation and one of the most successful research laboratories anywhere, ever. I still profit daily from my time in the UK and am in close contact with colleagues at the LMB and other institutions on a regular basis."

Professor Werner Kühlbrandt, Director of the Department of Structural Biology at the Max Planck Institute of Biophysics in Frankfurt

"It was fantastic to work in a cutting edge scientific environment at the Cancer Research UK London Research Institute. It is fair to say that I would not be the same person and scientist today without the positive influence of my time working in the UK. I learned to appreciate the benefits of a flat hierarchy, an open-minded attitude and tolerance. It has greatly influenced my career afterwards."

Professor Ralf Adams, Director of the Max Planck Institute for Molecular Biomedicine in Münster

7.2 The role of the UK in training early career researchers from other EU countries

7.2.1 Research fellowships – Marie Skłodowska-Curie Actions and HFSP Fellows

The European Commission's Marie Skłodowska-Curie (MSCA) fellowships support the most promising individual researchers from anywhere in the world¹¹³. These highly prestigious, competitive awards are typically two years in duration and successful applicants have complete flexibility in choosing where to conduct their research¹¹⁴.

The UK is the top destination for MSCA fellows¹¹⁵. Of the approximately 50,000 MSCA fellowships awarded under FP7, around 5,700 (or 11%) chose to work in the UK, approximately 4,000 of which were from other EU countries^{lvi}. This can be compared with 2,200 MSCA fellows from other EU countries working in Germany, and 1,500 in Spain and France. Five UK institutions were among the top 10 in terms of the number of MSCA fellowships^{lvii} under FP7 (2007-2013): the University of Cambridge, University of Oxford, Imperial College London, University College London, and the University of Birmingham.

lvi Of these, the largest number of fellows were of Italian nationality (around 700), followed by Spain (550), Germany (500), France (350), Poland (250), and the Netherlands (200).

lvii An individual can have held more than one fellowship between 2007 and 2013.

Table 8 Top 10 organisations in terms of Marie Skłodowska-Curie action fellowships (FP7, 2007-2013)

Institution	Country	Number of MSCA fellowships
Centre National de la Recherche Scientifique	France	514
University of Cambridge	UK	300
University of Oxford	UK	299
Imperial College London	UK	261
Max Planck Society	Germany	250
Consejo Superior de Investigaciones Científicas	Spain	250
University College London	UK	177
ETH Zürich	Switzerland	163
Copenhagen University	Denmark	163
University of Birmingham	UK	143

Source: DG EAC, Nov 2014, presented in Avramov, D. (2015) FP7 ex-post evaluation PEOPLE Specific Programme (2007-2013): Rationale, implementation and achievements Annex 1, Table 1

“The UK is a strong influence in the training of medical researchers and, within Europe, is the number one preferred country for early postdocs going by far – for example through the Marie Curie actions.”

Dr Hubert Misslisch, Coordinator ‘International Cooperations’, DLR Project Management Agency, Health Research, on behalf of the Federal Ministry of Education and Research, Germany

Compared with other EU countries, the UK trains the most incoming fellows from other EU countries relative to the number of UK nationals that move to another country for training: The UK receives 3,000 more EU research fellows than UK nationals moving to another EU country^{lviii}.

A 2014 survey^{lix} shows that there is a net outflow of trained researchers in the longer term: Of the 1,755 MC fellows who responded to the survey¹¹⁶, across all disciplines, a quarter had been hosted in the UK (25%) but only 11% of respondents were still employed in the UK.

The trend was similar for the Netherlands: while it had hosted 6% of survey respondents, only 3% were employed in the country at the time of the survey. By contrast, other EU countries employed the same number of former MC fellows as they had hosted (15% in France, 10% in Germany, and 8 % in Italy), and Spain had ‘gained’ former MC fellows: Having hosted 8% of the survey respondents, it now employed 13%.

lviii However, data on the mobility of MC fellows after completion of their fellowships is not systematically collected, and hence we do not know how many of these researchers ultimately return to their home countries, seek longer-term positions in their host countries, or move to a different country altogether.

lix Most respondents had between 6 and 25 years of research experience, and continued to work in research as a main part of their occupational activities (94% or 1,324).

“The UK is influential in terms of training EU researchers who then return to their own countries. [...] Marie Curie grants hosted in the UK are of great value to pre- and postdoctoral researchers in the EU. The UK is a very attractive destination for Marie Curie Fellows, perhaps because of the leadership, excellent research centres and language.”

Professor Celso Arango, President of the European College of Neuropsychopharmacology (ECNP); Universidad Complutense, Spain

The UK's attractiveness as a 'training ground' for research is also evident in the choice of host country of another highly competitive fellowship programme, the Human Frontier Science Program (HFSP)^{lx}. The HFSP supports novel and interdisciplinary research in the biosciences, with emphasis on intercontinental collaboration and support for young investigators¹¹⁷. HFSP fellowships are prestigious 3-year awards which enable the successful applicants to conduct research at institutions abroad. The UK was the host for 12%, or 8-9 fellows of 75 HFSP fellowships awarded in 2014, 2015, and 2016¹¹⁸. This is the second highest proportion after the US (59-73%) and ahead of Germany (3-7%).

7.2.2 Researchers funded by the UK Medical Research Council

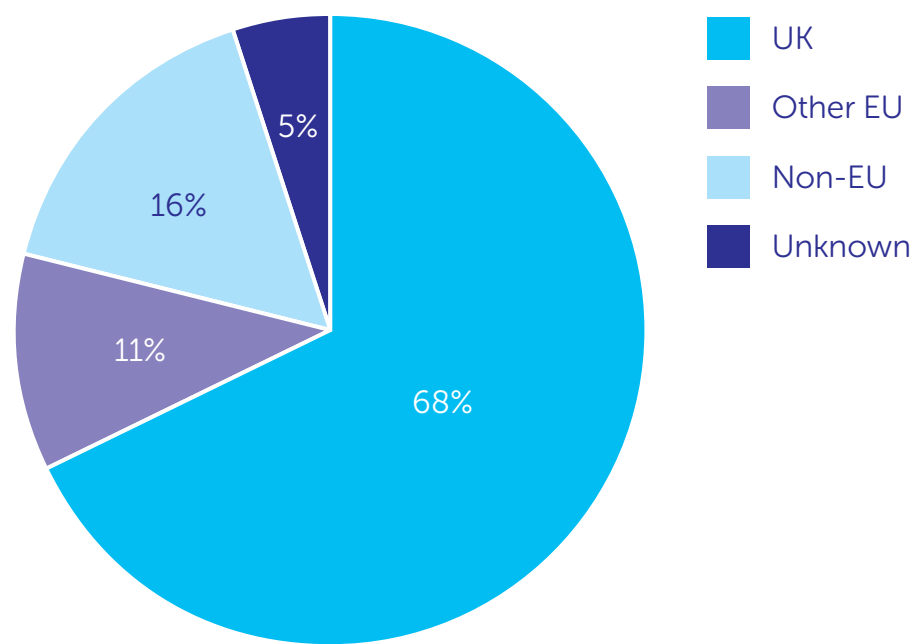
Researchfish^{® 119} is an online system used by the UK's Medical Research Council (MRC) and other funding agencies to capture information about the research they fund. This includes information on the destinations of staff after their MRC awards expires.

Researchfish data tracks nearly 11,000 researchers funded by the MRC at some point in their career, over the ten years from 2006-2016^{lxi}. After leaving MRC-funded projects, 68% (7352) of researchers remained in the UK, 11% (1222) moved to other EU countries, and 16% (1683) moved to non-EU countries as shown in **Figure 11**. Of those moving to other EU countries, the majority, 23% (279), moved to Germany, followed by France (225, 18%), Spain (140, 11%), Italy (80, 7%), Sweden (61, 5%) and the Netherlands (58, 5%) (see **Figure 12**). 1%, or 18 researchers, moved to Poland. The remaining 30% (361) moved to EU countries other than those named above.

lx The Human Frontier Science Program (HFSP) is an international program of research support, funding frontier research on the complex mechanisms of living organisms.

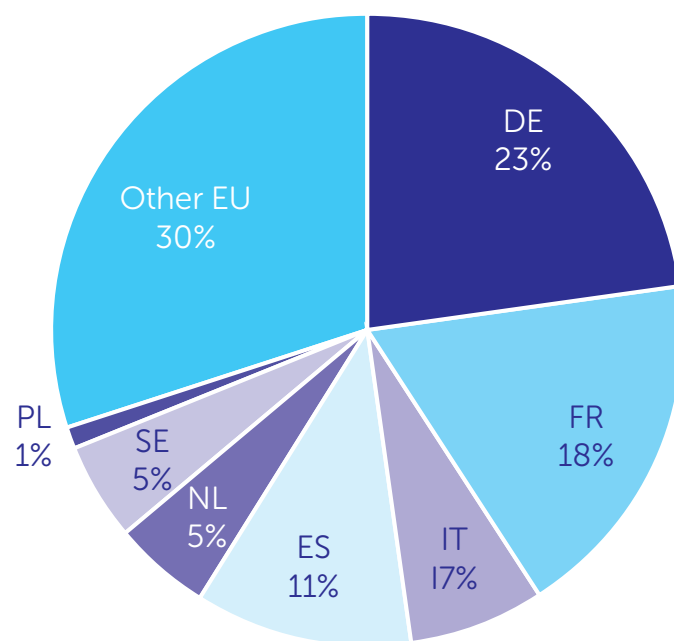
lxi This figure includes all MRC-funded researchers irrespective of nationality or domicile prior to taking up the MRC position. Researchfish does not capture this data; an analysis of researcher 'flows' is hence not possible.

Figure 11 Destinations of researchers leaving MRC-funded projects



Data analysis by MRC Information and Analysis Team and Technopolis; Data source: Researchfish® MRC data

Figure 12 Destinations of researchers moving to other EU countries after leaving MRC-funded projects



Data analysis by MRC Information and Analysis Team and Technopolis; Data source: Researchfish® MRC data

Researchfish also collects data on the employment sector and the type of role researchers take up after they leave MRC-funded projects. 61% (6,550) of researchers remained in academia, whereas 10% (1,122) moved to the private sector.

The data is generally consistent with researchers' career progression. For example, those previously described as students tended to gain roles as postdoctoral researchers and some researchers previously described as postdoctoral researchers or research fellows gained more advanced career positions^{lxii}.

Postdoctoral researchers and research fellows who trained in the UK may base their decision to move to other EU countries on opportunities for career progression: The proportion of 'movers' to advanced career positions is higher for those who moved to other EU countries (33%, 260 of 793) than for those who remain in the UK (24%, 799 of 3,298^{lxiii}) (see **Figure 13**).

These figures differ between individual EU countries, for example 35% of those who move to France (62 of 177) and 14% of those who move to the Netherlands (5 of 36) take up advanced career positions. While we do not have data that allows us to assess whether UK-trained researchers are more successful in securing these positions than applicants from other countries, the data suggests that they are of a high calibre and able to progress their careers.

"A research period in the UK provides EU researchers with an increased chance for a good career in their home countries."

Professor Leena Bruckner-Tuderman, Vice President of the Deutsche Forschungsgemeinschaft (DFG); Albert-Ludwigs-University of Freiburg, Germany

As approximately 40% of MRC principal investigators have provided feedback on where their colleagues went next via Researchfish® over the 2006-2016 period, we can extrapolate that 650 MRC-trained researchers moved to advanced positions in other EU countries.

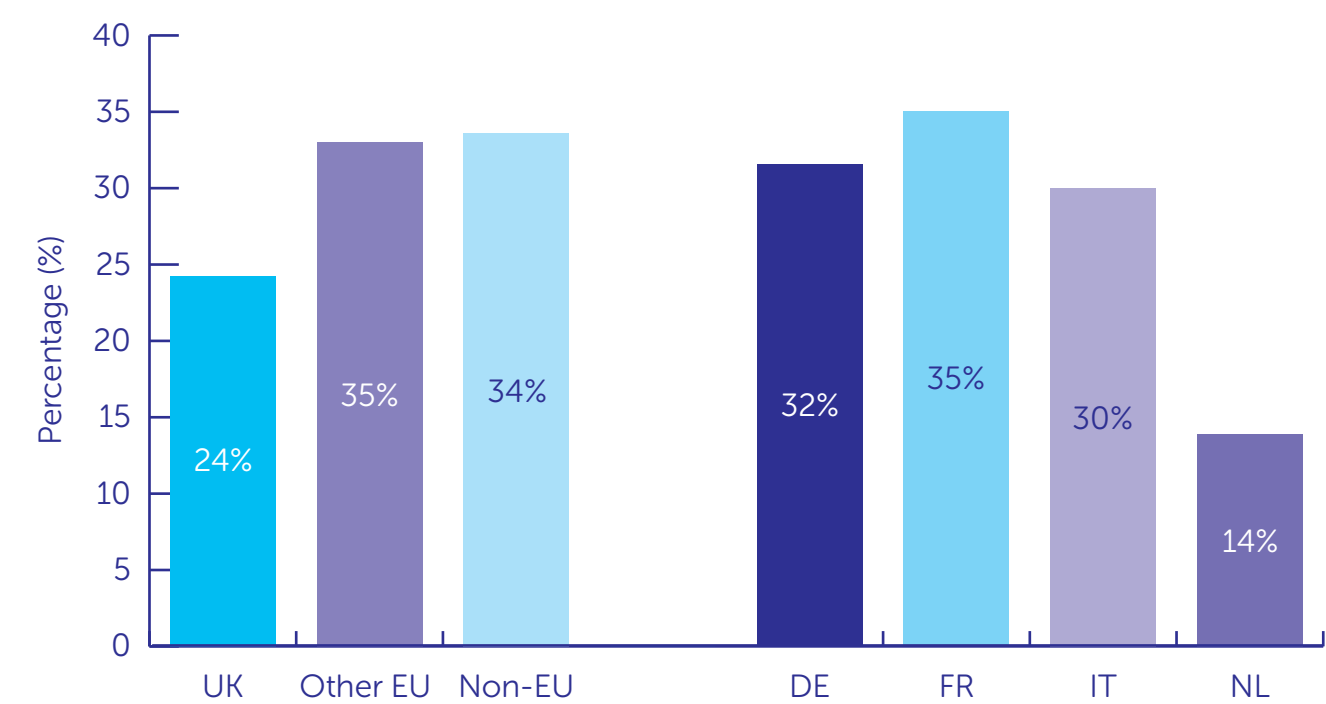
The actual figure for all 'movers' to other EU countries will be much higher, since biomedical researchers supported by other funding sources, such as other UK research councils and UK foundations and charities, are not included.^{lxiv}

lxii Advanced career positions were defined as: lecturer, research project leader, or research fellow.

lxiii This excludes individuals who moved to positions within healthcare and hospitals, as this constitutes a much larger proportion in the UK than other countries and would hence skew the proportion of advanced career positions moves further.

lxiv For research funders other than the MRC, it is hard to separate out biomedical researchers from all funded researchers.

Figure 13 Percentage of MRC-funded postdoctoral researchers and research fellows moving to advanced career positions, by destination



Data analysis by MRC Information and Analysis Team and Technopolis; Data source: Researchfish® MRC data

7.2.3 Researchers working at the UK Biomedical Research Centres

Biomedical Research Centres (BRC), funded by the UK’s National Institute for Health Research (NIHR), are partnerships between an academic partner, usually a research university or similar specialised-institution, and an ‘NHS Host’, typically in a hospital trust. The 11 BRCs focus on translational research, with the aim of turning basic research discoveries into medical applications and then to apply them into daily clinical practice^{lxv}.

Estimates from four large BRCs, each with more than 80 researchers from EU countries, indicate that EU researchers may return to their home countries following a training period in the UK, taking their research skills and networks with them. Across the four BRCs, the proportion of EU nationals was lower in the established researcher group than the early career researcher group.^{lxv}

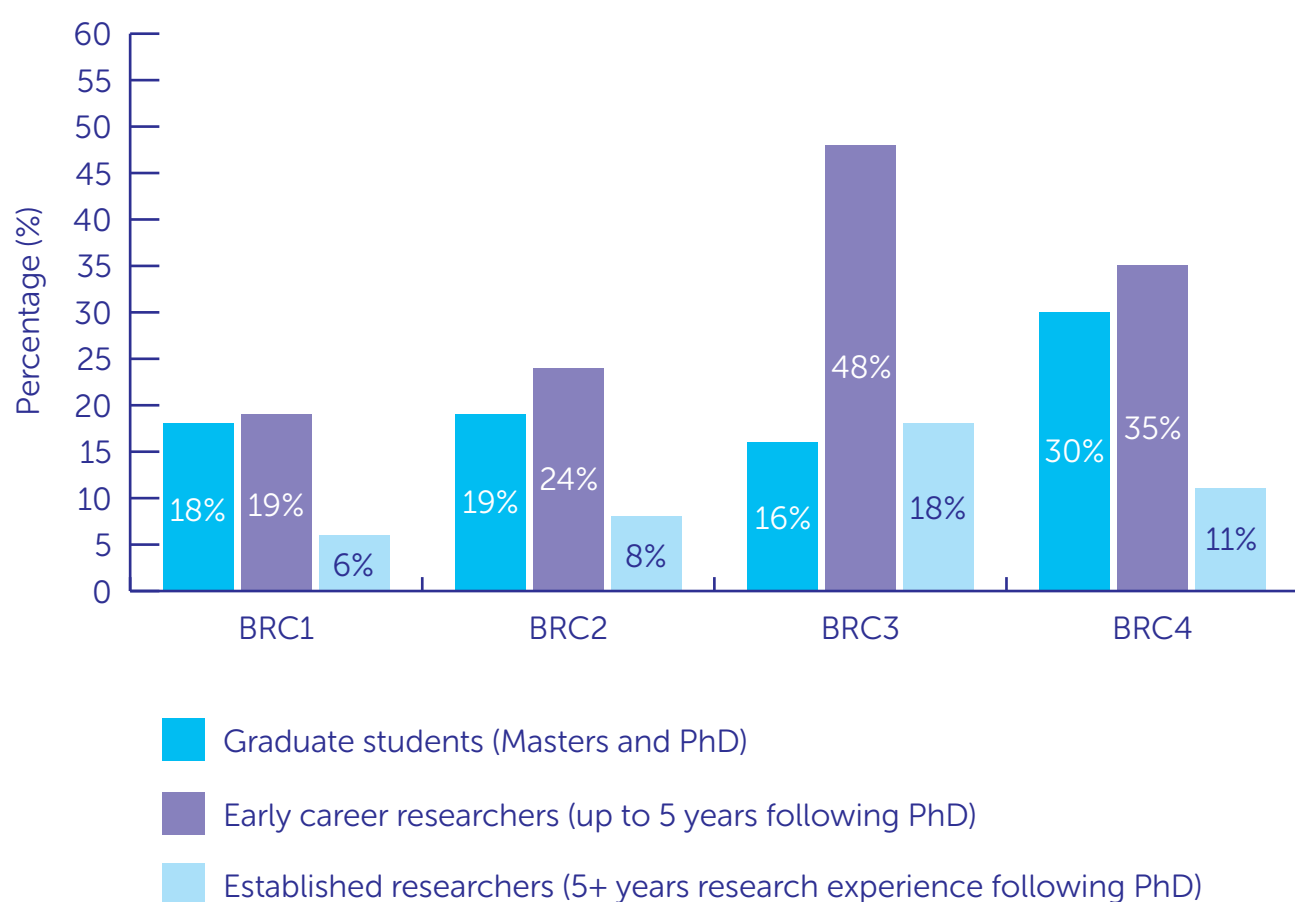
lxv We cannot draw definitive conclusions, as the BRCs do not have comprehensive information on their researchers’ next destinations.

Table 9 Proportion of EU-nationals in different staff categories at four NIHR BRCs

	BRC1	BRC2	BRC3	BRC4	Total staff number
Graduate students (Masters and PhD)	18%	19%	16%	30%	1,310
Early career researchers (up to 5 years following PhD)	19%	24%	48%	35%	1,696
Established researchers (5+ years research experience following PhD)	6%	8%	18%	11%	484

Data source: NIHR survey of BRC/BRUs, January 2017

Figure 14 Proportion of EU-nationals in different staff categories at four NIHR BRCs (% of total staff)



Data source: NIHR survey of BRC/BRUs, January 2017

7.2.4 European Research Council grants

The ERC encourages high quality research in Europe by supporting top researchers through competitive funding calls^{lxvi}. Its grant schemes are open to researchers of any nationality, age and gender, from anywhere in the world, to perform research in Europe.

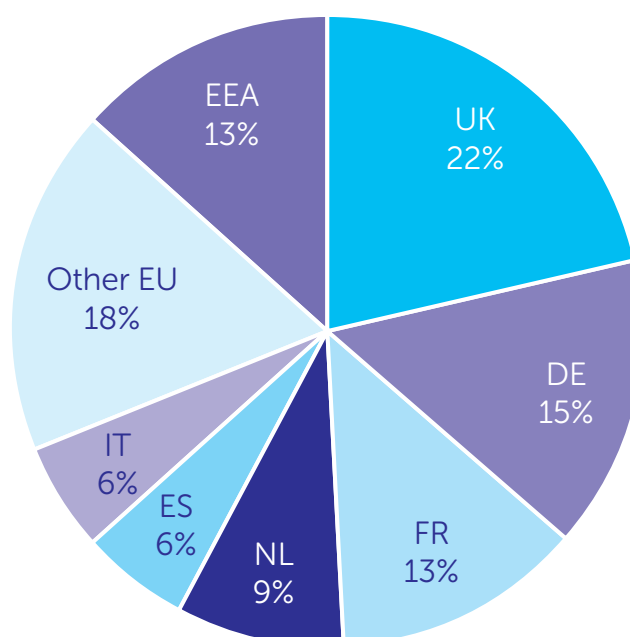
Between 2007 and 2016, more than one in five (22%) ERC grant holders chose to work in the UK (**Figure 15**), followed by Germany (15%) and France (13%).

"The capacity of the UK to attract leading researchers and thus ERC grantees is significant. [...] It shows that the system is attractive, because the working conditions are good, people feel that they get support from the institutions [...] The UK's contribution to all fields of science is remarkable, the contribution it makes is significant, including in the health sciences."

Professor Jean-Pierre Bourguignon, President of the European Research Council

The UK was also the most popular destination for researchers who move to another country to take up their ERC grant. While the majority of grantees (6,208 of 6,907) remained in the countries they were based when they took up ERC grants, 20% of those researchers who move countries came to the UK (140 of 699). In comparison, 17% of researchers move to Germany (119), 10% to France (73), 8% to the Netherlands (58), and 6% to Italy (40).

Figure 15 Host countries of ERC grant holders (2007-2016), all research domains



Source: European Research Council (ERC) Office. Data as of 14/12/2016, includes: Starting Grants 2007-2016, Consolidator Grants 2013-2016, Advanced Grants 2008-2015 in all research domains (Life Sciences; Physical and Engineering Sciences; Social Sciences and Humanities). Current signatories of the grant agreement taken into account.

lxvi European Research Council. Available from <https://erc.europa.eu> [Accessed 28 Feb 2017]

Five UK universities are among the top 10 universities located in EU member states that were selected by ERC grantees between 2007 and 2016 in the Life Sciences domain as well as across all research domains^{lxvii} (**Table 10**).

Table 10 EU Higher Education institutions hosting the largest number of ERC grants in the Life Sciences domain (2007-2016)

Name of Higher Education institutions	Total number of ERC grants
University of Cambridge	66
University College London	53
University of Oxford	52
Karolinska Institute	42
Flanders Institute for Biotechnology	32
University of Helsinki	32
Imperial College	30
University of Copenhagen	29
University of Edinburgh	28
Uppsala University	26

Source: European Research Council (ERC) Office. Data as of 14/12/2016, includes: Starting Grants 2007-2016, Consolidator Grants 2013-2016, Advanced Grants 2008-2015. Current signatories of the grant agreement taken into account.

7.3 Training biomedical students from other EU countries

The UK contributes strongly to the global pool of skilled scientists, training the 2nd highest number of science graduates after the USA (2015)¹²¹. UK universities also train a broad range of health professionals, with 31 medical schools which provide education for 41,000 students¹²². More than 70 universities provide nursing education, over 80 universities offer training for allied health professionals, and more than 140 universities and colleges offer health management courses¹²³.

7.3.1 Undergraduate and postgraduate training in the UK – official statistics

The Higher Education Statistics Agency (HESA) produces official statistics on higher education in the UK^{lxviii}. In 2014/15, the total student population captured by HESA was 2.27 million; 124,600 (5%) of these students, were residents of EU member states other than the UK, immediately prior to taking up their studies ('other EU-domiciled'). Students domiciled in non-EU countries made up 14% of the student population.

lxvii Figures include three types of grant, over different time periods: Starting Grants (2007-2016), Consolidator Grants (2013-2016), and Advanced Grants (2008-2015).

lxviii Higher education data in the UK is collected by the Higher Education Statistics Agency (HESA). HESA student data was accessed and analysed via the HEIDI portal by the Medical Research Council's (MRC) Information and Analysis team. Full person equivalent (FPE) counts were chosen for all data extracted. Figures are rounded by each UK institution and so aggregates will be over-stated. A description of the data captured by HESA, definition of FPE, nationality and domicile is available from <https://www.hesa.ac.uk/support/definitions/students>. [Accessed 8 Feb 2017]

Approximately 15% of all students at UK higher education institutions study subjects relevant to biomedicine^{lxix} ('biomedical students') – around 325,000 students in 2014/15. Roughly two thirds are undergraduates studying for their first degree and a quarter are postgraduates (research)^{lxx}. 4% of these undergraduate students (9,410) and 8% of the postgraduate students (6,590) were domiciled in other EU member states. This is also comparable to the General Medical Council's analysis, stating that around 3% of medical students in the UK were from European countries (1,200)¹²⁴. Some of the key figures from HESA are summarised in **Table 11**.

Table 11 Students at UK institutions studying subjects with relevance to biomedicine in 2014/15

	Number of students	
HESA student population, all subjects	2,270,000	Total student population in the UK
Students in subjects relevant to biomedicine ('biomedical students')	325,000	15% of HESA student population
Biomedical students domiciled in other EU countries	16,000	5% of biomedical students
• Undergraduate	9,410	4% of all biomedical undergraduate students
• Postgraduate	6,590	8% of all biomedical postgraduate students

Data source: HESA

Higher education statistics from other EU member states, Germany, France and the Netherlands were compared to the UK's 'other EU-domiciled' biomedical student population in context (16,000, 5%). While the subject categories are defined differently in the various countries, these statistics suggest that Germany, France and the Netherlands each hosts about 2-4% of its undergraduate 'biomedical' student population from other EU countries (separate figures for postgraduate study were not available).

HESA also conducts a survey of students six months after they leave the UK higher education institution. In 2014/15, 1,500 biomedical postgraduate students who had been domiciled in other EU countries prior to taking up their studies in the UK responded to this leavers survey^{lxxi}. Of students, 40% (595) had gained employment, just under one third (415) indicated that they

lxix For further explanation, see Appendix G at cruk.org/UKandEUresearch. HESA uses the Joint Academic Coding System (JACS) system to classify academic subjects; of the 164 JACS principal subject codes, 24 were selected as relevant to biomedical research.

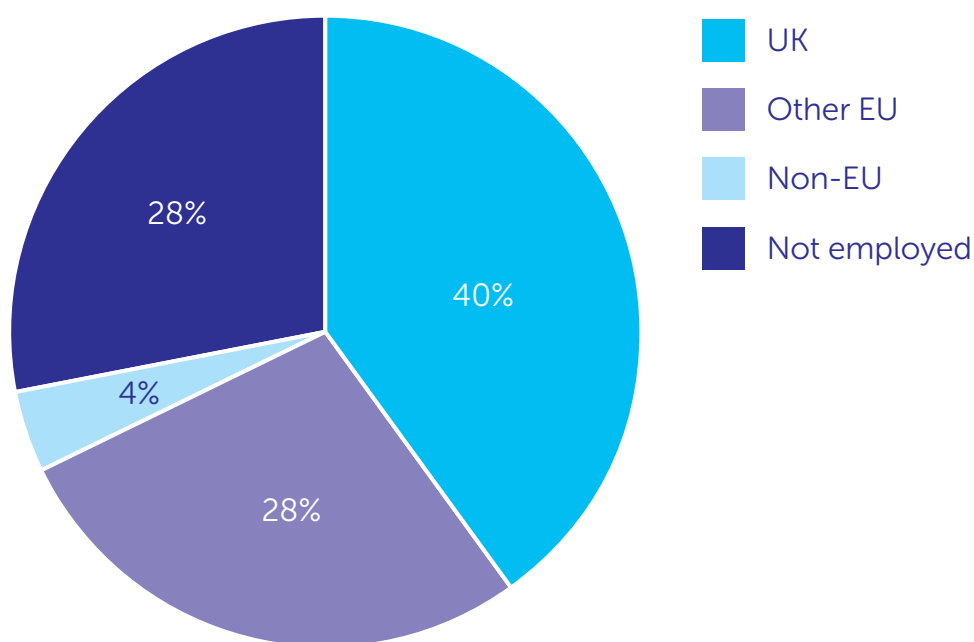
lxx The remainder is split across several categories (postgraduate taught, undergraduate other etc.). Definitions available from <https://www.hesa.ac.uk/data-and-analysis/publications/destinations-2012-13/definitions>. [Accessed 8 Feb 2017]

lxxi The number of qualifiers contacted by HESA is lower than the total in previous tables – this is referred to as the "target" population. Data is available for approximately 60% of the population of qualifiers with studies relevant to biomedicine. The approach to the destination of leavers from survey is explained at <https://www.hesa.ac.uk/data-and-analysis/publications/destinations-2012-13/introduction>. [Accessed 8 Feb 2017]

had moved to employment in the EU and 55 (4%) students are either employed outside of the EU, 420 (28%) were not employed and for 15 (1%) the status is not known (see figure 16)^{lxxii}.

For biomedical undergraduate students^{lxxiii}, 1,520 leavers from other EU countries responded. Just under half of these students gained employment in the UK (685, 45%), 155 (10%) returned to employment in the EU, and 670 (44%) were not employed. 10 (1%) moved to employment outside the EU (see **Figure 17**).

Figure 16 Destination of EU-domiciled biomedical postgraduates, 6 months after completing UK studies

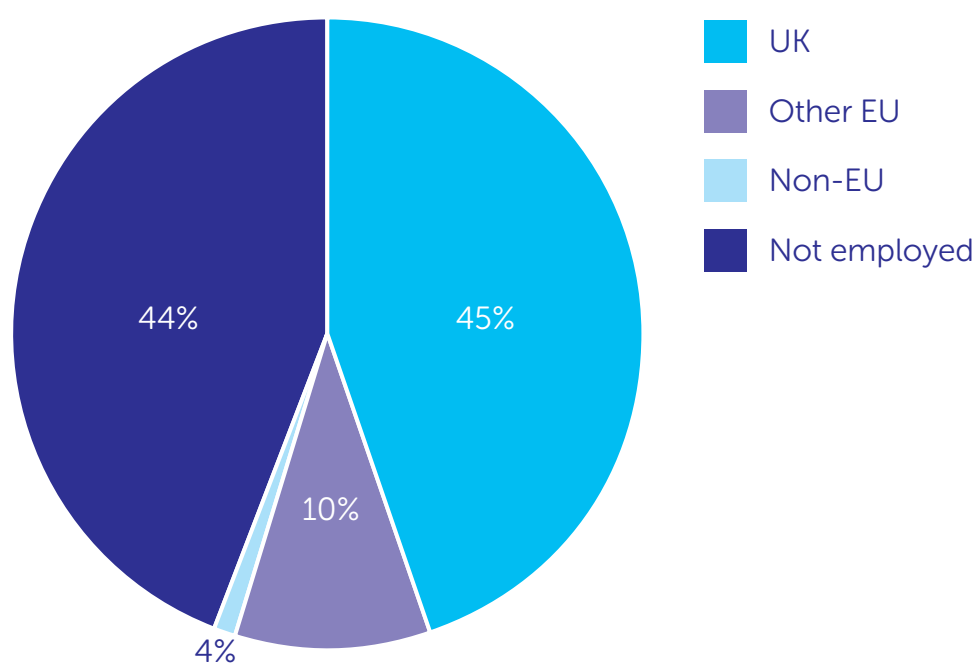


Data Analysis by MRC Information and Analysis Team and Technopolis; Data source: HESA

^{lxxii} Since DHLE survey respondents account for only around 60% of students who leave UK higher education, the actual number of leavers moving to employment in 'other' EU countries is thus proportionately higher. Therefore, in each year, about 1,400 students leave the UK to contribute to the EU labour force with the biomedical skills obtained in the UK.

^{lxxiii} Undergraduates include those obtaining a first degree, the numbers obtaining other graduate qualifications are very small.

Figure 17 Destination of EU-domiciled biomedical undergraduates, 6 months after completing UK studies



Data Analysis by MRC Information and Analysis Team and Technopolis; Data source: HESA

8 CONCLUDING REMARKS

High quality, successful medical research relies heavily on collaboration. The strength of the EU lies in its ability to foster such collaboration and inspire each nation to play to its strengths and lead on specific areas of medical research. The UK contributes significantly to this joint European research effort in a number of ways.

UK contributions to advisory bodies, collaborations, networks and policies help underpin research across the EU and its member states

- As a partner in the European research landscape, the UK contributes almost 20% of the total research work carried out within EU health programmes between 2007 and 2016.
- The Mean Normalised Citation Score (MNCS) for co-publications of UK and EU researchers is almost double the world average^{lxxiv}, delivering a higher impact compared to UK publications without a EU26 co-author or EU26 publications without a UK co-author.
- The UK is a strong collaborator in pan-European health and life sciences initiatives, playing a central role in Europe's key research networks and hosting headquarters for several important European institutions.
- Furthermore, UK experts provide valuable input to many individual research institutions, such as Germany's Max Planck Institutes through their scientific advisory boards (SABs) with more SAB members based in the UK than in any other EU country.

Participation in pan-EU clinical trials, with the UK providing notable leadership for rare disease and paediatric clinical trials

- The UK undertakes a huge amount of clinical trial activity, including in pan-EU trials. The UK has the highest number of phase I trials in the EU and the second highest number of phase II and III trials, after Germany.
- When it comes to trials in rare diseases and paediatric conditions, the UK has led or participated in the largest number of pan-EU trials – international collaboration is particularly important for these trials. After Germany and Spain, the UK is the third most frequent partner in pan-EU trials.
- The UK's Medicines and Healthcare Products Regulatory Agency (MHRA) is recognised as one of the leading national authorities for the regulation of clinical trials, medicines and medical devices. As well as this, it has a strong history of sharing knowledge and expertise with the European Medicines Agency (EMA), and has acted as Scientific Advice Co-ordinator in at least 20% of centralised EMA medicine approvals.
- The UK has helped to establish networks of patients and professionals for rare diseases, making it easier to recruit patients for clinical trials

The UK co-ordinates and hosts of some of Europe's unique large-scale infrastructures for medical research

- The UK provides major research assets that the EU capitalises upon, such as the Wellcome Trust Sanger Institute, one of the largest bioinformatics centres in the world, bio-repositories

lxxiv For internationally co-authored publications

like the Public Health England Culture Collection and the Mary Lyon Centre. In addition, four pan-European health related research infrastructures have their headquarters in the UK.

- The UK supports an unparalleled collection of large-scale population cohort studies, including the 1946 Birth Cohort and the UK Biobank, that are used in a large number of EU studies as well as informing policy across the member states.
- The quality and completeness of data collected by the UK's NHS is very high, for example the English cancer registry, creating a valuable unified resource for cross-EU epidemiological research.

The UK plays a leading role in the development of new therapies and medical technologies that benefit EU patients, backed by a thriving pharmaceutical and biotechnology sector

- Around 25% of the world's top 100 prescription medicines were discovered and developed in the UK and three of the five top-selling drugs globally act on a mechanism discovered by UK researchers.
- Experts interviewed highlight the UK's capacity to quickly translate innovative solutions into commercial products, meaning that patients from across Europe benefitted from advances several years before the rest of the world.
- 500 new biotechnology-based drugs are under development and 600 innovative pharmaceutical product candidates are in the pipeline in the UK.
- The UK medical research community is collaborating with EU counterparts at the forefront of many innovative treatments, including the development of new genetically targeted, personalised medicines and cancer immunotherapy treatments.

The UK is an attractive training environment for early career researchers from across the EU, developing their skills and launching their research careers

- The UK contributes significantly to the global research workforce, training the second highest number of science graduates after the USA.
- Experts interviewed highlighted the quality of the UK training experience, noting that it empowers graduates with to think analytically and innovatively.
- Students from EU member states make up 8% of all postgraduate and 4% of all undergraduate students in the UK studying subjects relevant to biomedicine.
- More than 5,700 Marie Curie fellows from other EU countries moved to the UK under FP7 – making the UK the top destination for these researchers.

Strong collaboration between the UK and the EU benefits all and is something the UK medical research funders highly value. Not only does collaboration produce higher impact in terms of publications, it enables discoveries that benefit patients everywhere.

The evidence highlighted in this report demonstrates that the UK makes a significant contribution to the success of European medical research. As the UK develops a new relationship with the EU, it is vital that all partners strive for an outcome that is in the best interest of science and patients across Europe.

ENDNOTES

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