



# The National Institute for Health Research at 10 years

## An impact synthesis

100 Impact Case Studies

RAND Europe and the Policy Institute at King's



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100 Impact Case Studies

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The Policy Research in Science and Medicine (PRiSM) unit brings together research expertise from RAND Europe and the Policy Institute at King's College London.

The PRiSM unit delivers research-based evidence to the UK's National Institute for Health Research (NIHR) to support NIHR's research strategy, *Best Research for Best Health*, and contributes to the science of science policy field in the UK, Europe and internationally.

This is an independent report by the PRiSM unit, commissioned and funded by the Policy Research Programme in the Department of Health. The views expressed are not necessarily those of the Department of Health.

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# Preface

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To mark its tenth anniversary, the National Institute for Health Research (NIHR) commissioned the Policy Research in Science and Medicine (PRiSM) unit to examine ways in which its investments in clinical, applied health and social care research, as well as support of research infrastructure, have benefitted the health research landscape.

This report identifies 100 examples of positive change and impact, based on available evidence, resulting from NIHR's support of research over the last 10 years. It provides an overview of more detailed case studies, published separately in a full report, grouped under 10 thematic headings. It concludes with a reflection of what the evidence suggests about NIHR's wider impacts. This report is supported by a *Summary Report* which provides an overview of all of the examples contained in this document.

Drawing together – for the first time – examples of the breadth of NIHR's impacts in a single resource, the report will be of interest to healthcare professionals involved in research, academics working in health and social care, and members of the public wishing to understand the value of research in the NHS.

The PRiSM unit brings together research expertise from RAND Europe and the Policy Institute at King's College London. It delivers research-based evidence to support NIHR's research strategy, Best Research for Best Health, and contributes to the science of science policy field in the UK, Europe and internationally.

RAND Europe is a not-for-profit organisation whose mission is to help improve policy and decisionmaking through research and analysis.

The Policy Institute at King's College London acts as a hub, linking insightful research with rapid, relevant policy analysis to stimulate debate, inform and shape future policy agendas.

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# 1. Introduction to the report

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## 1.1. Introduction

The National Institute for Health Research (NIHR) funds and supports world-leading clinical and applied health and social care research.

Providing £1 billion of funding per annum to support research and the research infrastructure in the NHS, NIHR aims to: drive faster translation of new treatments, technologies and diagnostics to improve outcomes for health and care services; promote the wealth of the nation, including via inward investment from the health research community; pull basic science discoveries through into tangible benefits for patients and the public; and provide research evidence to support more effective and cost-effective NHS delivery.

NIHR looks to achieve these aims through strategic partnerships, including with charities, industry, other government funders and academia, and it does so with patients and the public at the heart. It supports centres, units, facilities and expert research teams within the NHS, as well as programmes and systems to deliver high-quality research. This enables NIHR to respond rapidly to research priorities and opportunities identified by commissioners, front line staff, service users/patients and the health research community. By connecting academia, the NHS and other parts of the health and care system, NIHR funding supports research that is improving lives, reducing costs and advancing science for national and international benefit.

NIHR celebrates its tenth anniversary in 2016. It is an appropriate time to step back and consider how NIHR has changed the wider health research landscape. In light of this, the Department of Health commissioned the Policy Research in Science and Medicine (PRiSM) unit to consider the question ‘*What are the ways in which NIHR has benefited the health research landscape in the past 10 years?*’ The objective was to identify and celebrate examples where benefits to and wider impacts on the health research landscape have occurred and to synthesise this evidence in one report.<sup>1</sup>

## 1.2. Background

NIHR was created in April 2006 under the government’s health research strategy, *Best Research for Best Health*, and is funded by the Department of Health. This strategy outlined the direction that NHS research and development should take in order to deliver NIHR’s vision ‘to improve the health and

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<sup>1</sup> This report was not commissioned as an evaluation. A full list of caveats and limitations is provided below.



wealth of the nation through research'. At the time, the perception was that there were weaknesses in NHS R&D funding; it was thought that the funding too often resulted in poor-quality research. There was also significant concern about the funding being diverted to support service delivery, rather than research, and about a decline in the number of clinical academics. The ambition of NIHR, led by the then-incoming Director of R&D and now Chief Medical Officer in England, Professor Dame Sally Davies, was to turn this around and create an environment that valued clinical research as highly as basic research<sup>2</sup> and that maximised opportunities for patient benefit. The strategy *Best Research for Best Health* set out the roadmap for how to get there. At its core were five strategic goals through which it would transform the research landscape:

- Establish the NHS as an internationally recognised centre of research excellence;
- Attract, develop and retain the best research professionals to conduct people-based research;
- Commission research focused on improving health and social care;
- Manage our knowledge resources; and
- Act as sound custodians of public money for public good.<sup>3</sup>

Today NIHR organises its activities around four main areas of work:

- Infrastructure – providing facilities and people to the research enterprise
- Faculty – supporting and developing individuals to lead, support and carry out research
- Research – commissioning and funding research
- Systems – creating systems to manage and support research and its outputs

As an impact synthesis, and not an evaluation, the report aims to provide an analytical understanding, based on available evidence, of the ways in which the activities of the NIHR have led to positive change within the health research landscape. A full list of related caveats and limitations is provided below, along with the full details of the methodology used in the report.

### 1.3. Methodology

The 100 case studies identified in this report were selected on the following basis:

- An initial set of more than 200 examples which broadly reflected the original five goals of *Best Research for Best Health* were identified in consultation with senior managers from the Department of Health and the NIHR, from a review of annual reports, and from the list of more than 200 impact case studies submitted to the 2014 Research Excellence Framework (REF) which cited NIHR-funded research.
- This long list was reviewed and examples were subsequently clustered to arrive at 10 thematic areas.

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<sup>2</sup> This was implied in a statement in the so-called 'Cooksey Report', which was released in December 2006, that there were, at the time, 'perverse incentives that value basic science more highly than applied research'. (Cooksey D. 2006. *A review of UK health funding*. London: Stationery Office. p. 1)

<sup>3</sup> Research and Development Directorate, Department of Health. 2006. *Best Research for Best Health: A new national health research strategy*. London: Stationery Office.

- Individual case study examples were explored further, and those where only limited evidence of benefit was readily available were discarded.
- A final short list of just over 100 case studies was agreed with senior Department of Health and NIHR managers.
- Finally, evidence of impacts and other benefits was synthesised from a variety of sources, including published reports, peer-reviewed articles, and short interviews with relevant researchers or individuals associated with the research and its benefits. No primary research was done to generate new evidence of impacts or other benefits. Where evidence was limited to NIHR publications, this is noted in the case studies.

In order to generate the illustrative activities under each theme we followed a six-step process:

1. *Generating a long list:* A long list of over 200 activities was developed as described above.
2. *First round of theme allocation:* Each activity was independently coded to a theme for which there was greatest alignment by two researchers. During this process, brief research was conducted around each example and similar examples were grouped together.
3. *First allocation workshop:* The research team met to agree the initial theme allocations and to resolve discrepancies. Themes were allocated to researchers for a more intensive review of each activity.
4. *Second round of coding and allocation:* Activities were further researched and coded according to the following characteristics: Health Research Classification Scheme (HRCS) codes to ensure representation across disease areas; socio-demographics (ethnic minorities, women, children, etc.); region (where applicable); area of NIHR structure (Faculty, Research, Systems, Infrastructure); NIHR funding stream; and availability of evidence about impact.
5. *Second allocation workshop, including cross-checking for representation:* Themes with too many activities were reviewed and activities were re-assigned where possible in order to ensure a balance of activities across themes and characteristics. At this stage, activities were discarded from themes if there was a lack of evidence about impact.

Evidence of impacts and other benefits was synthesised from a variety of sources, including published reports, peer-reviewed articles and short interviews with relevant researchers or individuals associated with the research and its benefits. No primary research was done to generate new evidence of impacts or other benefits. Wherever possible we tried to source peer-reviewed and other independent sources of information which demonstrated the impact of the activity, though as noted below in the caveats this was not always possible.

## 1.4. Caveats and Limitations

There are several caveats and limitations to synthesis of impacts presented in this report:

There are several caveats and limitations to this report:

- This study was commissioned as a synthesis of impacts and benefits, not an evaluation. Its aim was not to generate new evidence of NIHR's impact, nor to evaluate it against a set of aims and objectives. Rather, we set out to identify and synthesise existing evidence about NIHR's impacts over the past 10 years, as demonstrated through a series of case study examples.
- One of the primary criteria in selecting case studies was availability of data and evidence of impact. Generation of primary data was outside the scope of this report, so where there was little or no readily available evidence of impact, a case study was not included.
- Over 60 per cent of the examples draw on impact case studies submitted to the 2014 REF exercise, and the limitations of those case studies are also applicable to our report.<sup>4</sup>
- Few case studies are based on research solely supported by NIHR. Although our aim is to highlight NIHR's contribution to the health and care system, we note that many of these contributions have happened in partnership with other funders.
- Where possible, we identified independent sources of evidence to confirm impacts and benefits; however, in many cases this was not possible, and hence we relied on evidence supplied by those directly involved in the case studies.
- In summarising the evidence across each of the 10 thematic areas, we are mindful that the evidence we are drawing upon is limited to the 10 case studies within that theme. We acknowledge that the parts may not (necessarily) be representative of the whole and may only present part of a larger picture.
- Although we tried to ensure representation across NIHR's activities, funding streams, infrastructure and geographical reach, we could not, and do not claim to, touch on every part of the NIHR system.
- Research is inevitably speculative – it is aimed at addressing unknowns; therefore, not all NIHR-funded activities will have demonstrable benefit in the way shown by the case studies.

In compiling the 100 case studies in this report we have, necessarily, needed to strike a balance between breadth and depth. The case studies provide an initial snapshot into the activities undertaken and the impacts and benefits which may have been realised. There are, inevitably, levels of detail and depth which we have not been able to include due to the time and resource constraints. However, in capturing the breadth, rather than depth, across 100 examples, we hope to provide some sense of the many ways in which NIHR has had a demonstrable impact on the wider health and care system in the past ten years.

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<sup>4</sup> The Research Excellence Framework is the system for assessing the quality of research in UK higher education institutions ([www.ref.ac.uk](http://www.ref.ac.uk)). In the REF, impact case studies were submitted by all participating higher education institutions, which provided summaries of the wider impacts, defined as any effect on, change to or benefit beyond academia to the economy, society, culture, public policy or services, health, the environment, or quality of life. The full database of impact case studies submitted in the last REF is available at <http://impact.ref.ac.uk/CaseStudies/>. See also King's College London and Digital Science. 2015. The nature, scale and beneficiaries of research impact: An initial analysis of Research Excellence Framework (REF) 2014 impact case studies. London: King's College London and Digital Science. As of 9 May 2016: <http://www.kcl.ac.uk/sspp/policy-institute/publications/Analysis-of-REF-impact.pdf>

## 1.5. Structure of this report

The remainder of this report is structured around the 10 themes of positive change which have been identified through our synthesis. These are:

- Bringing breakthroughs to patients
- Supporting the nation to deliver world-leading research with global impact
- Making the nation's health and care system the best it can be
- Working with charities and the third sector on common agendas
- Supporting public health delivery
- Putting patients and the public at the heart of all stages of research
- Creating opportunities for economic and social returns
- Enabling clinical research excellence
- Supporting, training and developing a diverse workforce in the NHS and academia
- Investing across the nation

Each theme begins with a theme summary, highlighting how the evidence from each of the case studies fits together under each theme. There are then 10 individual case studies within each theme demonstrating the different ways impacts and other benefits that have been realised. The case studies are short and are intended to provide a snapshot of the impacts or benefits. They are not detailed accounts of the underpinning research, the pathways to impact, nor the impacts themselves. Each case study has a narrative section and then a supporting evidence section. Each piece of evidence has a short description indicating its nature and the information about the impacts it contains. Each case study as presented here can be used as a starting point for finding out more information about the activity by either using the evidence sources and/or contacting any of the individuals identified.

## 2. Bringing breakthroughs to patients

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### 2.1. Summary

**Innovative. Transformational. Accessible.**

*NIHR drives the development of the evidence base needed to bring innovative treatments and other interventions into practice and improve the lives of patients. This research evidence informs new clinical guidelines and facilitates the translation of innovations into clinical practice.*

NIHR-funded research on new and existing drugs, devices and diagnostics provides an evidence base for changes to treatments, policies and guidelines where existing treatments are unsatisfactory or where more evidence is needed to support new approaches. To this end, NIHR supports both novel trials and scale-ups of trials, building on existing studies.

Findings from NIHR-funded research are changing guidelines for clinical practice at both the national and international levels. These guidelines support improvements to commissioning practices, medical education and clinical communication. All three types of improvement are crucial if new treatments are to translate into patient benefits. For example<sup>5</sup>:

- Safer methods of screening for Down's syndrome, using non-invasive prenatal genetic testing, stand to reduce the number of women needing diagnostic tests that carry a risk of the woman losing her baby. This research is now feeding in to UK national screening policy.
- Fewer patients with Bell's palsy face hospitalisation, following research to demonstrate the benefits of treating this form of facial paralysis with steroids rather than antivirals. This work has informed the first definitive treatment guidelines for this condition in the UK, India, Spain and Ireland.
- A trial demonstrating the effectiveness of mindfulness-based cognitive behavioural therapy led a local Primary Care Trust to commission a clinic providing this therapy for patients with treatment-resistant depression. The findings generated considerable media interest, helping to raise patients' awareness of treatment options available to them.

By filling gaps in evidence of clinical effectiveness, NIHR-funded research helps to develop treatments that are safer, less invasive and more focused on patients' quality of life. Further evidence of the cost- and

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<sup>5</sup> As will be the case for each theme summary, the examples presented here are fully expanded upon below in each theme.

time-efficiency of treatments helps to ensure that a greater number of patients have access to healthcare resources. This is illustrated by the following:

- An intelligent knife (or ‘iKnife’) uses real-time information on the molecular profile of cancerous tissue as it cuts. This knife is now in trials to determine whether it can improve cancer surgery by identifying the boundaries between healthy and diseased tissue.
- Risk-adapted radiotherapy for breast cancer is a less toxic form of radiotherapy shown to be as effective as conventional whole breast radiotherapy in preventing recurrence of cancer, while requiring far fewer hospital visits.
- The Hall technique is a less painful and minimally invasive treatment for child tooth decay that is now included in dental guidelines and clinical education curricula following findings that it is more acceptable to both patients and clinicians.
- Challenging ‘breakthrough’ status in new antipsychotic drugs has shown that older classes of drugs for schizophrenia can be just as effective as new drugs, and at a fraction of the price. This is resulting in cost savings to local NHS Trusts.

Moreover, by supporting research across multiple disease areas, from rare diseases to cancer, NIHR ensures that the benefits of novel research reach a diverse range of patients. For example:

- Dramatic improvements in survival rates for patients with chronic granulomatous disease, a rare immunodeficiency disease which affects around 100 people in the UK, are the result of research to determine the long-term effectiveness of bone marrow transplantation.
- The world’s first ever implant of a fully synthetic trachea was possible after NIHR-supported research led to ground-breaking uses of nanocomposite materials for rejection-free tissue transplants.

Finally, NIHR-funded work aimed at revolutionising the way clinical data is collected and utilised is helping to ensure that England remains at the forefront of the types of novel research described above. An example of this is:

- The 100,000 Genomes Project – which is funded as a partnership with NIHR, Public Health England, NHS England and Health Education England – is combining genomic sequence data with medical records in order to better understand causes and potential treatments of cancer and rare diseases, and is facilitating future research.

### *2.1.1. Applying medical advances for the benefit of the few: improving treatments for a rare blood disorder (chronic granulomatous disease)*

Rare diseases present a difficult picture when it comes to weighing up the value of different medical approaches, particularly so when the disease is severe and present from birth. Originally termed ‘a fatal granulomatous disease of childhood’ when first described in the 1950s [1], chronic granulomatous disease (CGD) affects around 100 people in the UK [2]. The disease arises due to a defect in patients’ white blood cells, meaning that they are unable to fight infection. While the prognosis for babies born with CGD has improved, estimates in 2008 placed mortality by the age of 30 as high as 45 per cent [3]. With

only four babies born with CGD in the UK each year, data on the long-term implications and impact of the disease on patients' lives are understandably scarce [4].

In 2009, a team in Newcastle reported results of their having treated 20 patients with bone marrow transplantation – specifically, using tissue from either matched siblings, or matched unrelated individuals, for which there is a wider pool of potential donors [5]. The technique proved successful, with 18 patients cured, although a number of them later developed complications, some of which were severe [5]. In order to progress clinicians' understanding, and evaluate the effects of different treatments – including newer, gene-based therapies – on patients' quality of life, in 2010 the NIHR supported the Newcastle team to carry out a longer-term study.

Funded under the NIHR Research for Patient Benefit scheme, this study investigated which treatments offered the best patient outcomes, not only in terms of admissions to hospital and the need for surgery and multiple medications, but also in terms of patients' wellbeing, mental health, and intelligence [2].

Drawing on clinical data from a national CGD patient registry [3], the research team identified 73 children living with CGD in the UK, and it recruited 59 of them to the study [6]. The team found that children who had not undergone bone marrow transplantation had poorer outcomes across a range of measures, including physical, emotional and social wellbeing. Whereas patients who had not had a transplant were admitted to hospital with a serious infection on average once every 3.5 years, post-transplant patients had no serious infections [6].

The study influenced practice by shaping international guidelines, with the European Society for Immunodeficiencies and European Group for Blood and Marrow Transplantation noting in 2011 the excellent outcomes after transplantation. Practice in the UK has also shifted to incorporate the findings of the research, with Great Ormond Street Hospital (the second of two specialist centres in the UK equipped to treat patients with CGD) also adopting a strategy of bone marrow transplantation [4].

Of the 36 children who received a transplant between 2008 and 2013, 32 are alive and cured of the disease. Based on the study results, the team have produced information and engagement materials, promoted via the UK CGD Society [4]. Through its support of research, the NIHR has contributed to impacts for the patients themselves and their families, both in the UK and globally, by advancing understanding and best practice in treating this rare but challenging disease.

## Evidence

[1] Bridges RA, Berendes H, Good RA. 1959. A fatal granulomatous disease of childhood: The clinical, pathological, and laboratory features of a new syndrome. *AMA Journal of Diseases of Children* 97 (4): 387-408. As of 29 April 2016: <http://www.ncbi.nlm.nih.gov/pubmed/13636694>

Original clinical description of what is now termed chronic granulomatous disease, highlighting its near-ubiquitous fatality when first encountered in the 1950s.

[2] National Institute for Health Research. n.d. Chronic granulomatous disease: Clinical course, quality of life, cognitive outcome and cost benefit with conservative or curative treatment. As of 29 April 2016: <http://www.nihr.ac.uk/funding/funded-research/funded-research.htm?postid=1741>

A description of the NIHR's funding of CGD research via its Research for Patient Benefit scheme, including information on CGD's prevalence in the UK population.

[3] Jones LB, McGrogan P, Flood TJ, Gennery AR, Morton L, Thrasher A, Goldblatt D, Parker L, Cant AJ. Special article: Chronic granulomatous disease in the United Kingdom and Ireland: A comprehensive national patient-based registry. *Clinical and Experimental Immunology* 152 (2): 211-18. doi:10.1111/j.1365-2249.2008.03644.x

Descriptive epidemiological analysis of clinical features and outcomes of patients in the UK and Ireland with CGD enrolled in a patient registry that was established in 2000.

[4] Research Excellence Framework. 2014. Curing chronic granulomatous disease in children through early bone marrow transplant. [Case study 21717.] As of 29 April 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=21717>

Research Excellence Framework case study detailing the wider impacts of the NIHR's investment in CGD research.

[5] Soncini E, Slatter MA, Jones LBKR, Hughes S, Hodges S, Flood TJ, Barge D, Spickett GP, Jackson GH, Collin MP, Abinun M, Cant, AJ, Gennery AR. 2009. Unrelated donor and HLA-identical sibling haematopoietic stem cell transplantation cure chronic granulomatous disease with good long-term outcome and growth. *British Journal of Haematology* 145 (1): 73-83. doi:10.1111/j.1365-2141.2009.07614.x. As of 30 March 2016: <http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2141.2009.07614.x/abstract>

The results of a retrospective case series analysis of 20 patients with CGD undergoing bone marrow transplantation at Northern Supra Regional HSCT (hematopoietic stem cell transplantation) Unit for Primary Immunodeficiency, Newcastle upon Tyne, between 1998 and 2007. The paper describes the success of the procedure in a majority of patients, as well as complications associated with transplants, and makes the case for early transplantation in patients with CGD.

[6] Cole T, Pearce MS, Cant AJ, Cale CM, Goldblatt D, Gennery AR. 2013. Clinical outcome in children with chronic granulomatous disease managed conservatively or with hematopoietic stem cell transplantation. *Journal of Allergy and Clinical Immunology* 132 (5): 1150-5. doi:10.1016/j.jaci.2013.05.031

The results of the NIHR-supported Research for Patient Benefit study, a retrospective case series analysis comparing outcomes in patients with CGD who received bone marrow transplants with outcomes in patients managed conservatively.



### *2.1.2. Providing better outcomes for patients with Bell's Palsy through trials of steroids*

#### Case study

In 2007, an NIHR-funded multicentre study led by the University of Dundee demonstrated that early treatment with steroids provides better outcomes for patients with Bell's palsy (BP) than does treatment with antivirals. The study also showed the former to be more cost effective. These findings led to changes to guidelines on the treatment of BP and to prescribing practices, and impacted the wider body of research on BP.

Bell's palsy is a form of temporary facial paralysis which can lead to persistent facial nerve malfunction and deformity. It affects between 12,400 and 24,800 people per year in the UK [1]. Prior to this study, which was funded by the NIHR Health Technology Assessment (HTA) programme using the Clinical Practice Research Datalink (CPRD) (which, in turn, is partially funded by the NIHR), the aetiology of BP was unknown, and no best treatment was defined. Cochrane reviews published in 2002 [2] and 2004 [3] identified a need for more high-quality evidence to determine whether the condition should be managed through early treatment with steroids and/or antivirals, the latter of which are more expensive and had increasingly been prescribed in the absence of definitive guidance on treating BP.

This HTA-funded study was a national, acute, primary care trial which involved GPs from half of all Scottish practices. Other key design features included a primary outcome measure (complete recovery from BP at three and nine months) of relevance to policymakers as well as patients and clinicians, the reporting of adverse events, and the use of an intention-to-treat analysis.

The study found that early treatment with the steroid prednisolone led to significantly increased likelihood of full recovery at both three and nine months, while treatment with the antiviral aciclovir had little or no effect [4]. The study rejected the hypothesis that BP is caused by the effect of the herpes simplex virus on the facial nerve.

The study had a significant impact on clinical practice for the treatment of BP, as well as policy, health and economic impacts. Findings from the study have been incorporated into guidelines from clinicians produced by the NHS and in other countries including India, Spain and Ireland. These included guidance on avoiding unnecessary medication.

Actual changes in clinical decision-making were measured through an analysis of prescribing behaviour in 14,460 BP cases between 2001 and 2012 [5], using the CPRD database. The analysis showed that, following the publication of the trial in October 2007, there were increases of up to 70 per cent in prescription of prednisolone and reductions of up to 41 per cent in prescription of antivirals for BP patients. This impact on practice was associated with positive impacts on health, with a 36 per cent reduction in referrals to hospital of BP patients. The study found that 83 per cent of patients treated with prednisolone recovered normal facial function within three months, compared with 64 per cent of patients not treated with prednisolone [4]. Regarding economic impact, whereas treatment with antivirals involves the prescription of a relatively expensive drug or combination of drugs, treatment with steroids requires a GP to prescribe only a single, relatively inexpensive drug [6]. Hernández et al found that

treatment with prednisolone cost 6.5 per cent less than treatment without prednisolone, and that 12.8 per cent more patients were cured at nine months when treated with prednisolone [6].

The study also had an impact on the wider body of research on BP. The paper resulting from the study has featured in commentaries in major journals such as the *Lancet*, and as of October 2013 it had been cited 270 times [7]. Furthermore, based on the findings of the study, the Cochrane Collaboration identified a need for previous reviews of steroids and antivirals for BP to be updated, and the group responsible for the study is collaborating with colleagues in Chile to carry out this update [8][9]. The group has also been commissioned by the Cochrane Neuromuscular review group at King's College London to produce a review of all interventions for BP [7]. Finally, the study has been recognised by the Royal College of General Practitioners, Academy of Medical Royal Colleges and Sense About Science as a 'game changer in evidence based medicine' due to its evidence-based approach to general practice [10].

## Evidence

[1] Facial Palsy UK. 2016. What is Bell's palsy? As of 29 April 2016: <http://www.facialpalsy.org.uk/about-facial-palsy/causes-diagnoses/bells-palsy/37>

Webpage describing symptoms, causes and diagnosis of Bell's Palsy.

[2] Salinas RA, Alvarez G, Daly F, Ferreira J. 2004. Corticosteroids for Bell's palsy (idiopathic facial paralysis). *Cochrane Database of Systematic Reviews* 2:CD001942. doi:10.1002/14651858.CD001942.pub2

Results of a systematic review of the evidence of the effect of steroid therapy in the recovery of patients with Bell's Palsy.

[3] Allen D, Dunn L. 2004. Aciclovir or valaciclovir for Bell's palsy (idiopathic facial paralysis). *Cochrane Database of Systematic Reviews* 1:CD001869. doi:10.1002/14651858.CD001869.pub2

Results of a literature review of the evidence of the effect of Aciclovir or similar agents for the treatment of Bell's Palsy.

[4] Sullivan F, Swan I, Donnan P, Morrison J, Smith B, McKinstry B, Davenport R, Vale L, Clarkson J, Hernández R, Stewart K, Hammersley V, Hayavi S, McAteer A, Gray D, Daly F. 2009. A randomised controlled trial of the use of aciclovir and/or prednisolone for the early treatment of Bell's palsy: The BELLS study. *Health Technology Assessment* 13 (47). doi:10.3310/hta13470

Results of a randomised controlled trial testing the effects of aciclovir used in combination or separately with oral prednisolone for the early treatment of Bell's Palsy.

[5] Morales D, Donnan PT, Daly F, Staa TV, Sullivan FM. 2013. Impact of clinical trial findings on Bell's palsy management in general practice in the UK 2001–2012: Interrupted time series regression analysis. *BMJ Open* 16 (3): e003121. doi:10.1136/bmjopen-2013-003121

Results of a study measuring the incidence of Bell's Palsy in the UK and the impact of clinical trials on the management of Bell's Palsy.

[6] Hernández R, Sullivan F, Donnan P, Swan I, Vale L. [for the BELLS trial group] 2009. Economic evaluation of early administration of prednisolone and/or aciclovir for the treatment of Bell's palsy. *Family Practice* 26: 137-44. doi:10.1093/fampra/cmn107

The results of a randomised controlled trial-based economic evaluation of early administration of prednisolone in combination or separately to acyclovir for the treatment of Bell's Palsy.

[7] Research Excellence Framework. 2014. Changing clinical practice in Bell's palsy: The impact of a clinical trial highlighting the impact of evidence for primary care. [Case study 39367.] As of 29 April 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=39367>

Research Excellence Framework case study detailing the impact of early treatment with Predisolone.

[8] Lockhart P, Daly F, Pitkethly M, Comerford N, Sullivan F. 2009. Antiviral treatment for Bell's palsy (idiopathic facial paralysis). *Cochrane Database of Systematic Reviews* 4:CD001869. doi:10.1002/14651858.CD001869.pub4

Results of a systematic review of the evidence assessing the efficacy of aciclovir or similar agents for treating Bell's palsy.

[9] Salinas RA, Alvarez G, Daly F, Ferreira J. 2010. Corticosteroids for Bell's palsy (idiopathic facial paralysis). *Cochrane Database of Systematic Reviews* 3: CD001942. doi:10.1002/14651858.CD001942.pub4

Findings of a systematic review of the evidence assessing the effect of corticosteroids in the treatment of Bell's Palsy.

[10] Academy of Medical Royal Colleges. 2013. Evidence Based Medicine Matters. London: Sense About Science. : Academy of Medical Royal Colleges. As of 29 April 2016: <http://www.senseaboutscience.org/data/files/resources/124/Evidence-Based-Medicine-Matters.pdf>

Report by the Academy of Medical Royal Colleges summarising the evidence to provide an evidence based for practicing evidence-based medicine for the treatment of Bell's Palsy.

### *2.1.3. Bringing more acceptable treatments into practice to treat child tooth cavities*

#### **Case study**

NIHR-funded research has brought into dental practice certain treatments which are more acceptable to patients and clinicians than those already in use, as well as being more effective. A study conducted by the University of Dundee established the clinical effectiveness and acceptability (to both patients and clinicians) of the Hall technique, which provides for non-invasive treatment of decayed baby teeth. This study is also an example of NIHR-funded research overcoming barriers to generalisability and translation, as it conducted clinical trials in a primary care setting which had previously proved challenging.

Childhood experience of dental treatment is a significant factor in the development of dental anxiety [1], which can lead to avoidance of necessary dental treatment in later life [2]. The Hall technique enables minimally invasive management of dental decay in children by placing preformed metal crowns over teeth, thus avoiding injections and drilling. Prior to this study, challenges in conducting research in

primary care presented barriers to the generalisability and translation of research on treatments such as the Hall Technique [3]. The study, funded through the NIHR Health Technology Assessment (HTA) programme, consisted of a split-mouth-designed trial, in which children were treated using both the Hall Technique and standard dental care.

The study produced positive findings in relation to both the effectiveness of the Hall technique and its acceptability to patients and clinicians [4]. Regarding the former, at two-year follow-up, the study found the Hall technique to be more effective than conventional dental fillings in preventing dental pain and infection in children [4]. This was confirmed at five-year follow-up, which found that the Hall technique was associated with reductions in pain, infection and the need for extractions under general anaesthetic compared to standard treatment [5]. The five-year follow-up also showed that the frequency of 'major failures' (irreversible pulpitis, loss of vitality, abscess or tooth unrestorable) was lower in the Hall Technique arm (2 per cent) than in the control arm (17 per cent) [5]. With regard to acceptability, the study found that the Hall technique was preferred to standard treatment by 72 per cent of children, 63 per cent of parents and 73 per cent of dentists [4]. Findings on both effectiveness and acceptability have been corroborated by two clinical audits of the Hall technique [6][7].

Findings from the study have had a significant impact in the UK and abroad - in clinical practice, in policy, in teaching and training, and on the body of research related to the Hall Technique. The Hall technique has been included in Scottish guidelines on the prevention and management of tooth decay in children [8], and in national guidelines for countries including New Zealand and Poland [3]. The trial's results and the Hall technique's inclusion in guidelines have been accompanied by an increase in uptake by clinicians. A survey of Scottish specialists following the trial found that 75 per cent were using the Hall technique, with 65 per cent identifying it as their preferred treatment for children with significant tooth decay [9]. A further study showed that the use of preformed metal crowns in Scotland increased from less than 600 in 2000-01 to more than 7,000 in 2011-12 [10]. Moreover, the fact that the Hall technique is now included in undergraduate curricula suggests that its uptake is likely to be sustained. Starting in 2008, the Technique is being taught in 15 out of 16 undergraduate dental schools in the UK and in all 18 dental therapy schools [11], and has been incorporated into a postgraduate training module as part of the NHS e-Den Project [12]. The impact of this change to dental training was demonstrated by a survey published in 2012, which found that half of postgraduate students identified the Hall technique as their preferred treatment of decay in children with dental anxiety [13].

The study's impact on the body of research around the management of decay is evidenced by the Hall technique's inclusion in an updated Cochrane review, which found significant advantages to the use of less invasive treatments such as the Hall technique [14]. An independent commentary on the Hall technique drew similar conclusions [11], while senior clinical teachers and clinical directors from outside the UK have visited Dundee Dental School to investigate the effects of adopting the technique [3]. The study has also contributed to driving research around minimally invasive dental treatments for children, some of which has been supported by the NIHR. The NIHR Health Technology Assessment programme provided funding for the original researchers to conduct further research on the Hall technique as part of the Fillings in Children's Teeth; Indicated Or Not (FiCTION) project, which seeks to inform further best practice and shape policy on child dental care in the UK [15].

## Evidence

[1] Diercke K, Ollinger I, Bermejo JL, Stucke K, Lux CJ, Brunner M. 2012. Dental fear in children and adolescents: A comparison of forms of anxiety management practised by general and paediatric dentists. *International Journal of Paediatric Dentistry* 22: 60-7. doi:10.1111/j.1365-263X2011.01158.x

Findings of a study examining different methods of anxiety management practised by general and paediatric dentists,

[2] Milgrom P, Weinstein P. 1993. Dental fears in general practice: New guidelines for assessment and treatment. *International Dental Journal* 43: 288-93.

Published guidelines for the assessment of dental fear in general practice.

[3] Research Excellence Framework. 2014. The Hall technique as a non-invasive method for managing caries in children's primary teeth. [Case study 35824.] As of 29 April 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=35824>

Research Excellence Framework case study which provides an evidence base for the Hall technique (a non-invasive treatment for decayed baby teeth).

[4] Innes NPT, Evans DJP, Stirrups DR. 2007. The Hall technique: A randomized controlled clinical trial of a novel method of managing carious primary molars in general dental practice: Acceptability of the technique and outcomes at 23 months. *BMC Oral Health* 7: 18. doi:10.1186/1472-6831-7-18

Results of a randomised controlled trial on the acceptability and outcomes of the Hall technique, 23 months after treatment.

[5] Innes NPT, Evans DJP, Stirrups DR. 2011. Sealing caries in primary molars: Randomized control trial, 5-year results. *Journal of Dental Research* 90: 1405-10. doi:10.1177/0022034511422064

Results from a randomised controlled trial examining the results of the Hall technique five years after treatment, compared with T clinical/radiographic failure rate of general dental practitioners.

[6] Morgan AG, Gilchrist F, Cowlam J, Rodd HD. 2012. Comparative outcomes for Hall vs conventionally placed preformed metal crowns. *International Journal of Paediatric Dentistry* 22 (Suppl. 2): 10-21. Abstract P29. doi:10.1111/j.1365-263X2011.01255.x

Results of a study comparing outcomes of the Hall technique comparing with conventionally placed preformed metal crowns.

[7] McKinney A, Britton KFM, Innes NPT, Cairns A. 2011. The success of Hall technique crowns on a student outreach clinic. *International Journal of Paediatric Dentistry* 21 (Suppl. 2): 8-9. Abstract PP4. doi:10.1111/j.1365-263X2011.01167\_4.x

The findings of a study examining childhood awareness of rationale and acceptability of the use of fluoride varnish in the prevention of caries.

[8] Scottish Dental Clinical Effectiveness Programme. 2010. Prevention and management of dental caries in children. As of 29 April 2016: [http://www.sdcep.org.uk/wp-content/uploads/2013/03/SDCEP\\_PM\\_Dental\\_Caries\\_Full\\_Guidance1.pdf](http://www.sdcep.org.uk/wp-content/uploads/2013/03/SDCEP_PM_Dental_Caries_Full_Guidance1.pdf)

Report by the Scottish Dental Clinical Effectiveness Programme on the prevention and management of dental caries in children.

[9] Bark JE, Dean AA, Cairns AM. 2009. Opinion and usage of the 'Hall technique' amongst paediatric dental specialists in Scotland. *International Journal of Paediatric Dentistry* 19 (Suppl. 2): 9-18. Abstract P10. doi:10.1111/j.1365-263X2009.01009\_5.x

Results of a qualitative study examining the opinion and usage of the Hall technique amongst paediatric dental specialists based in Scotland.

[10] Information Services Division Scotland. n.d. General Dental Service: Registrations and participation analysis 2000–2012. As of 29 April 2016: <http://www.isdscotland.scot.nhs.uk/Health-Topics/Dental-Care/General-Dental-Service/dental-informatics-programme.asp?Co=Y>

Webpage detailing the Dental Informatics Programme, including programme summary and contact details.

[11] Rosenblatt A. 2008. The Hall technique is an effective treatment option for carious primary molar teeth. *Evidence Based Dentistry* 9 (2): 44-5. doi:10.1038/sj.ebd.6400579

Results of a randomised control trial investigating whether the use of the Hall techniques is an effective treatment option for children, compared to usual care, measured in terms of success, minor failure, or major failure.

[12] e-Learning for Healthcare. 2016. e-Den. As of 29 April 2016: <http://www.e-lfh.org.uk/projects/dentistry/>

Webpage describing the e-Den project.

[13] Foley JI. 2012. Short communication: A pan-European comparison of the management of carious primary molar teeth by postgraduates in paediatric dentistry. *European Journal of Paediatric Dentistry* 13: 41-6. doi:10.1007/BF03262840

A study by postgraduates in paediatric dentistry, of European Paediatric dentists, using an online questionnaire, comparing the management of carious primary molar teeth.

[14] Ricketts D, Lamont T, Innes NPT, Kidd E, Clarkson JE. 2013. Operative caries management in adults and children. *Cochrane Database of Systematic Reviews* 2013 3:CD003808. doi:10.1002/14651858.CD003808.pub3

Findings of a systematic review examining the evidence of partial or no dentinal caries removal compared with complete caries removal for the management of dentinal in both adults and children.[15] Innes NPT, Clarkson JE, Speed C, Douglas GVA, Maguire A. 2013. The FiCTION dental trial protocol – Filling children's teeth: Indicated or not? *BMC Oral Health* 13: 25. doi:10.1186/1472-6831-13-25

The findings of a National Institute for Health Research (NIHR) Health Technology Assessment (HTA) commissioned study, examining the clinical and cost-effectiveness of restoration caries in primary teeth compared with no treatment.

#### *2.1.4. Changing the use of genomic information in healthcare systems: the 100,000 Genomes Project*

##### Case study

The 100,000 Genomes Project is a landmark commitment to harness the power of genetic information (one's genome being the complete set of DNA contained within a cell's nucleus) to enable more precise diagnoses of disease, more targeted and personalised treatments and new therapeutics and cures. Managed through a company wholly owned by the Department of Health, namely Genomics England Ltd, the 100,000 Genomes Project is an ambitious effort to change how the NHS delivers medicine in the 21<sup>st</sup> century [1]. Given the potential of the project to deliver new scientific insights, the NIHR has been a primary partner from its inception [2].

Seeking to involve participants who are most likely to benefit, the project set out to sequence the genomes of individuals from two principal groups: patients with rare inherited diseases, and those with cancer. The NIHR was involved in pilot projects to pump-prime activity in both of these areas [2].

For the rare disease pilot, the NIHR BioResource - Rare Diseases worked in partnership with Genomics England to recruit 2,000 people. The pilot aimed to obtain samples from family 'triads' – two parents and one affected child – to identify the genetic causes of rare disease [2]. In March 2015, the Centre for Life in Newcastle announced that two families had received a diagnosis that would not have been possible were it not for this project. One patient was found to have a rare genetic variant identified as the cause of a severe kidney condition. The discovery enabled his family members to be tested and, in the case of those carrying a similar variant, offered treatment to prevent or delay kidney damage. The other discovery – involving two brothers – identified a mutation as the cause of a muscle wasting disease [3]. In one of a number of news reports covering the announcement, one of the brothers said:

'I wanted to be part of the 100,000 Genomes Project as it will help future generations in the long-term. It is great that research schemes such as this are being undertaken as it will enable experts to further understand rare diseases better' [4].

In parallel, one of two cancer pilots involved a partnership with a series of six NIHR Biomedical Research Centres (BRCs) – the other being a partnership with Cancer Research UK. Its aim was to develop new standards for collecting the clinical and digital data that would underpin genomic studies of both cancerous and non-cancerous cells and tissues [2]. In August 2015, the NIHR BRC at the University of Oxford and Oxford University Hospitals NHS Trust was the first to open recruitment to patients with cancer [5]. Less than two months later, Genomics England announced that they had sequenced over 5,000 genomes [6].

The 100,000 Genomes Project is currently well underway, sequencing around 100 genomes a day. With committed partnerships from the NIHR and other UK organisations at the cutting edge of modern biomedicine, this transformative programme stands to dramatically shift how genomic information is used in healthcare systems both in the UK and around the world.

##### Evidence

[1] Genomics England. 2015. The 100,000 Genomes Project. As of 29 April 2016: <http://www.genomicsengland.co.uk/the-100000-genomes-project/>

Summary information on the aims and supporting narrative underpinning the 100,000 Genomes Project, as well as its scope.

[2] Genomics England. 2015. The 100,000 Genomes Project protocol. London: Genomics England. As of 29 April 2016: [http://www.genomicsengland.co.uk/wp-content/uploads/2015/03/GenomicEnglandProtocol\\_030315\\_v8.pdf](http://www.genomicsengland.co.uk/wp-content/uploads/2015/03/GenomicEnglandProtocol_030315_v8.pdf)

Full protocol detailing the three phases of the 100,000 Genomes Project planned to 2017, including information on how data will be used and shared, how participants will be involved, and aspects of the project's governance and management.

[3] Genomics Education Programme. 2015. Step Closer to Mainstream Precision Medicine. As of 13 May 2016: <https://www.genomicseducation.hee.nhs.uk/news/item/24-step-closer-to-mainstream-precision-medicine>

Announcement of the first two diagnoses that the 100,000 Genomes Project enabled through its sequencing of families with rare diseases.

[4] Press Association. 2015. Genomes project produces first diagnoses of rare diseases. The Guardian [11 March 2015.] As of 29 April 2016: <https://www.theguardian.com/science/2015/mar/11/genomes-project-diagnoses-rare-diseases>

News coverage of the three men and their families who received a diagnosis of their disease, having volunteered for the 100,000 Genomes Project.

[5] Hamblin A. 2015. 100,000 Genomes Project will help people for generations to come. As of 29 April 2016: <https://www.england.nhs.uk/2015/08/angela-hamblin/>

Announcement of the first cancer patients to be recruited to the 100,000 Genomes Project.

[6] Genomics England. 2015. 5,000 whole genome sequences. As of 29 April 2016: [www.genomicsengland.co.uk/5000-whole-genome-sequences/](http://www.genomicsengland.co.uk/5000-whole-genome-sequences/)

Announcement of progress in sequencing more than 5,000 genomes, with links to patient stories and a discussion of challenges encountered in the project thus far.

### *2.1.5. Ensuring that advanced methods of antenatal genetic testing are introduced with patients' best interests at heart*

#### Case study

Implementing a 'breakthrough' technology from the realm of experimentation into routine clinical practice requires clinicians to tread a careful path: guided not merely by what they can do, but what they ought to do, in the best interests of patients. Medical advances in understanding and manipulating the makeup of the human genome – as exemplified by the transformative nature of initiatives such as the 100,000 Genomes Project – are helping the NHS to usher in a new era of genomic medicine. However, to ensure an appropriate and acceptable use of genomic information in medical decision-making requires



a specific kind of patient-focussed research. With funding from the NIHR's Programme Grants for Applied Research, Professor Lyn Chitty at the University College London Institute of Child Health – via the Reliable Accurate Prenatal non-Invasive Diagnosis (RAPID) study – has established how clinicians ought best to use advanced genetic screening methods, to improve the safety of antenatal testing [1].

Professor Chitty's work focuses on the use of genetic tests capable of detecting tiny quantities of fetal DNA present in a mother's bloodstream, as a means to establish the presence or absence of disease in the unborn child. Importantly, non-invasive genetic testing of this kind poses no risk to the fetus – in contrast to amniocentesis, which is associated with a 1 in 100 chance of inducing miscarriage [2].

The NIHR's funding enabled Professor Chitty and her team at UCL to establish stringent laboratory and clinical standards for two main types of non-invasive prenatal testing. The first looked at sex-linked disorders, such as Duchenne muscular dystrophy, and other single gene disorders such as certain causes of dwarfism [3]. As well as demonstrating the effectiveness of these new methods of testing, the research examined benefits and disadvantages as perceived by the patients themselves – both practical (such as avoiding miscarriage) and psychological (such as providing peace of mind) [4]. By ensuring both the feasibility and acceptability of the tests, Professor Chitty's team was able to establish itself as the UK's – and one of the world's – first public service laboratories offering non-invasive testing of this kind in a routine clinical setting [2].

The second focus of Professor Chitty's NIHR-funded work has been to determine whether non-invasive prenatal testing can be introduced as a method of screening for Down's syndrome. In June 2015, she presented results from more than 2,500 women who had taken the test. Her team's findings showed that non-invasive testing reduced the need for follow-on invasive tests, with women being positive about its potential. One woman classified as having a 'high risk' pregnancy said:

'You get told 1 in 30 and although that sounds relatively high... we probably wouldn't have done [invasive testing] because there's a risk of miscarriage.... I think that we were very lucky. It's enabled us to make an informed choice about what happens for the rest of our lives' [5].

This research fed into a report for the UK National Screening Committee to support the introduction of non-invasive prenatal testing into the NHS pathway for Down's syndrome [6] In January 2016, the committee recommended that these tests be introduced as a result of their ability to reduce the numbers of women needing unnecessary diagnostic tests that carry a risk of losing their baby [7].

Through its funding of careful, sensitive and compassionate programmes of research such as this, the NIHR is helping to ensure that breakthroughs in biomedical science are deployed appropriately for the benefit of patients throughout the NHS, and beyond.

## Evidence

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Details of the NIHR's programme grant awarded to Professor Chitty's research to develop non-invasive methods of prenatal diagnosis.

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<http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=21969>

REF impact case study detailing the course of Professor Chitty's research and wider impacts of the NIHR's funding.

[3] Hill M, Finning K, Martin P, Hogg J, Meaney C, Norbury G, Daniels G, Chitty LS. 2010. Non-invasive prenatal determination of fetal sex: Translating research into clinical practice. As of 16 May 2016:

<http://onlinelibrary.wiley.com/doi/10.1111/j.1399-0004.2010.01533.x/full>

Results of research examining fetal sex as determined by non-invasive methods in over 500 pregnancies, confirming its accuracy and efficiency.

[4] Lewis C, Hill M, Skirton H, Chitty LS. 2012. Non-invasive prenatal diagnosis for fetal sex determination: Benefits and disadvantages from the service users' perspective. *European Journal of Human Genetics* 20: 1127-33. doi:10.1038/ejhg.2012.50

Patients' perceptions of non-invasive prenatal testing obtained via interviews with 38 women who had undergone such tests for determining the sex of their foetus.

[5] European Society of Human Genetics. 2015. ESHG 2015 conference press release: Non-invasive prenatal testing: Effective, safe, preferred by parents, and applicable in a range of disorders. As of 29 April 2016: <https://www.eshg.org/13.0.html>

Announcement of the results of Professor Chitty's NIHR-funded programme grant to explore appropriate methods of introducing non-invasive prenatal diagnosis into the NHS.

[6] Chitty L, Cameron L, Daley R, Fisher J, Hill M, Jenkins L, Kroese M, McEwan A, McKay F, Morris S, Verhoef T, Wright D. 2015. RAPID non-invasive prenatal testing (NIPT) evaluation study: a report for the UK National Screening Committee. Executive summary. As of 29 April 2016: [http://legacy.screening.nhs.uk/policydb\\_download.php?doc=551](http://legacy.screening.nhs.uk/policydb_download.php?doc=551)

Report for the UK National Screening Committee synthesising findings of the NIHR-funded RAPID programme grant.

[7] Public Health England. 2016. UK NSC recommendations include new bowel cancer screening test. As of 29 April 2016: <https://www.gov.uk/government/news/uk-nsc-recommendations-include-new-bowel-cancer-screening-test>

Recommendations of the UK National Screening Committee, including the phased introduction of non-invasive prenatal testing for fetal anomalies, such as Down's syndrome.

### *2.1.6. Reducing the toxicity of treatments for patients with breast cancer with risk-adapted radiotherapy (TARGIT) following lumpectomy*

#### Case Study

The NIHR's Health Technology Assessment (HTA) programme supports research that brings innovative treatments into a clinical setting. The HTA-funded TARGIT-A and TARGIT-B trials build on existing studies (supported by funders including University College London Hospitals Trust and the Photoelectron Corporation) to demonstrate the effectiveness of more targeted radiotherapy to reduce the number of sessions and time required, provide safer treatment and deliver cost savings.

Following breast-conserving surgery, many patients are unable to attend clinics daily for 3 to 6 weeks to receive post-operative whole-breast radiotherapy. Without the option of radiotherapy to reduce the risk of recurrence of cancer, many patients (most commonly in developing countries, but also in Europe and the USA) often opt for mastectomy. Previous studies by a team at University College London developed the hypothesis that radiotherapy could be limited in select cases to the tumour bed where the majority of recurrences appear, leading to the development of TARGeted Intraoperative radioTherapy (TARGIT) technology [1][2].

Building on the initial research, the HTA programme provided funding to the UCL team to conduct clinical trials of the treatment. The HTA-funded TARGIT-A randomised controlled trial (RCT) compared single-dose TARGIT with the standard three- to six-week course of radiotherapy, finding TARGIT to be as effective as whole-breast radiotherapy in preventing recurrence of cancer [3]. The RCT also found non-breast cancer deaths (mainly from cardiovascular causes) to be significantly less frequent in TARGIT patients than in whole-breast radiotherapy patients [3]. The TARGIT-B trial has been launched with HTA funding to test the effect of TARGIT in young and high-risk patients.

The TARGIT-A trial was the first proof of principle of this type of treatment [4]. It has had a significant impact on clinical practice, accompanied by health, policy and economic impacts. Resulting changes to clinical practice mean that more than 200 breast cancer teams now use TARGIT and over 8,000 patients have received the treatment [4]. TARGIT's worldwide uptake is evidenced by its inclusion in guidelines by the European Society of Breast Cancer Specialists [5], and the European Society of Medical Oncology (whose guidelines are also endorsed by the Japanese Society for Medical Oncology) [6] and in German national guidelines [7]. In the UK, the National Institute for Health and Care Excellence (NICE) is considering recommending the introduction of TARGIT in routine practice [8].

These guidelines are backed by a body of expert opinion supporting TARGIT. The Marmot committee, commissioned by the UK Department of Health and Cancer Research UK to report on the benefits and harms of breast cancer screening, reported that, in selected patients, the use of TARGIT instead of whole-breast radiotherapy has the potential to minimise side effects due to over-diagnosis and resultant overtreatment associated with mammographic screening [9]. In addition, in 2011, 52 experts at the St. Gallen International Breast Cancer Conference voted in favour of using intraoperative radiation in selected patients [10].

The adoption of TARGIT has resulted in improved patient outcomes As well as providing an alternative to mastectomy, the lower degree of toxicity of TARGIT compared with whole-breast radiotherapy means

that it results in fewer deaths; mortality from cardiovascular diseases and cancer among the 1,140 patients receiving TARGIT was 3.9 per cent, compared with 5.3 per cent among the 1,158 receiving whole-breast radiotherapy [4]. TARGIT has also received higher ratings than conventional radiotherapy for patient satisfaction and quality of life [4].

In addition to being an effective treatment, TARGIT has proved to be time- and cost-efficient due to the lower number of radiotherapy sessions required compared with conventional radiotherapy. TARGIT can be completed within 4 routine radiotherapy sessions, whereas conventional radiotherapy requires 30 sessions. Based on staff hours alone it is estimated that the NHS will save around £60 million per year [4].

## Evidence

[1] Vaidya JS, Baum M, Tobias JS, D'Souza DP, Naidu SV, Morgan S, Metaxas M, Harte KJ, Sliski AP, Thomson E. 2001. Targeted intra-operative radiotherapy (Targit): An innovative method of treatment for early breast cancer. *Annals of Oncology* 12 (8): 1075-80. As of 29 April 2016: <http://annonc.oxfordjournals.org/content/12/8/1075.long>

Pilot study with 25 patients followed up over 24 months reporting the findings of targeted intra-operative radiotherapy versus post-operative tumour bed-boost for the treatment of early breast cancer.

[2] Vaidya JS, Baum M, Tobias JS, Morgan S, D'Souza D. 2002. The novel technique of delivering targeted intraoperative radiotherapy (Targit) for early breast cancer. *European Journal of Surgical Oncology* 28 (4): 447-54. doi:10.1053/ejso.2002.1275

Peer-reviewed journal article describing the Targit study and the intraoperative technique to be tested with early breast cancer patients in a randomised control trial.

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Results of the TARGIT trial which compared targeted intraoperative radiotherapy with the conventional policy of whole breast external beam radiotherapy for the treatment of breast cancer.

[4] Research Excellence Framework. 2014. Targeted intraoperative radiotherapy at the time of lumpectomy for patients with early breast cancer as an alternative to conventional 3–6 weeks of postoperative radiotherapy. [Case study 38117.] As of 29 April 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=38117>

Research Excellence Framework case study reporting the results of targeted intraoperative radiotherapy for patients with early breast cancer, up to six weeks postoperative radiotherapy.

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European Society of Breast Cancer Specialists (EUSOMA). *The Lancet. Oncology* 13 (4): e148-60. doi: 10.1016/S1470-2045(11)70383-7

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Clinical practice guidelines published by the European Society for Medical Oncology (ESMO) for the treatment and ongoing management of primary breast cancer.

[7] German National Guidelines. 2012. Interdisciplinary guidelines for the diagnosis, therapies and aftercare of breast cancer.

National Guidelines for Germany recommending best practice for the diagnosis, treatment and aftercare of breast cancer, published for multiple disciplines.

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[9] Marmot M, Altman G, Cameron DA, Dewar JA, Thompson SG, Wilcox M. 2013. Independent UK Panel on Breast Cancer Screening replies to Michael Baum. *BMJ* 346: f873. doi: <http://dx.doi.org/10.1136/bmj.f873>

Letter from the Independent UK panel on Breast Cancer Screening in response to publication by Michael Baum justifying details published in an early report by the Panel.

[10] Goldhirsch A, Wood WC, Coates AS, Gelber RD, Thürlimann B, Senn HJ. 2011. Strategies for subtypes – Dealing with the diversity of breast cancer: Highlights of the St. Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer. *Annals of Oncology* 22 (8): 1736-47. doi: 10.1093/annonc/mdr304

Publication highlighting the key findings, evidence, and arguments from the St. Gallen International Expert Consensus, on how to treat early breast cancer.

### 2.1.7. Increasing the availability of psychological support for depression

#### Case study

NIHR funding has supported research into evidence-based approaches and improved access to mental health care. The Mood Disorders Centre (MDC) is a joint venture between the NHS and the University of Exeter and that has received funding from the NIHR, as well as from the Wellcome Trust, the Brain and Behaviour Research Foundation, and the Medical Research Council [1]. Three studies funded by the NIHR Health Technology Assessment (HTA) programme have formed part of the MDC's contribution to developing an evidence base for approaches to treating depression, and translating that evidence into interventions and changes in practice.

Depression is the most frequent cause of disability worldwide [2]. NIHR-funded research by the MDC has had impact in 1) targeting treatment-resistant depression; 2) reducing vulnerability; and 3) improving access to effective psychological interventions. In the area of treatment-resistant depression, NIHR funding supported a large-scale randomised controlled trial (RCT) which confirmed the value of cognitive behavioural therapy (CBT) as a supplement to pharmacotherapy for treatment-resistant depression in primary care [3]. With the goal of reducing vulnerability, an HTA grant to the MDC funded the largest ever RCT of mindfulness-based CBT (MBCT), which uses meditational approaches to increase resilience. For the final objective (improving access), NIHR funding supported the Cost and Outcome of Behavioural Activation (COBRA) RCT which compares the efficacy and cost-effectiveness of two therapies namely, behavioural activation and CBT. This trial aims to determine whether behavioural activation offers a means of overcoming the limited availability of treatment for many patients due because it is delivered by less expensive healthcare professionals than CBT.

The MDC's NIHR-funded research, both in itself and as part of the centre's overall body of research, has had significant impacts on policy and practice, as well as societal impacts [1]. The ongoing COBRA trial addresses a call from the National Institute for Health and Care Excellence (NICE) for research into behavioural activation, and it is therefore expected to follow previous MDC studies in shaping NICE guidance on MBCT [1]. The MBCT research demonstrating the value of the treatment, including the NIHR funded RCT, has brought about changes to practice, through service provision, including the local Primary Care Trust's commissioning of a treatment clinic providing MBCT in Exeter [1]. The same research has also informed the implementation of MBCT through the resultant guidance resources [1], which were downloaded 700 times in the first three months following their publication online [1].

The MDC's MBCT work has also been incorporated into evidence-based training for healthcare professionals, including MSc training in MBCT at the University of Exeter [1]. By driving these evidence-based changes into practice, service provision and training, the MDC's work (including its NIHR HTA-funded studies) has led to improved care for patients. More than 2,400 patients in Devon have been treated by the MDC, of whom half were treated at the MDC clinic and half were treated as part of trials [1].

In addition to clinical impacts, the MDC's overall body of work has achieved a broader societal impact and choice for patients by raising awareness of treatment options for depression through coverage in mainstream media. These media sources include *The Daily Telegraph*, *Daily Mail*, *The Herald*, the *BBC*

*News website, Radio 4, the BBC World Service, Metro, Irish Independent, New Scientist, and The Guardian* [1].

## Evidence

[1] Research Excellence Framework. 2014. Mood Disorders Centre – Improving psychological treatments for depression. [Case study 37318.] As of 29 April 2016:  
<http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=37318>

Research Excellence Framework Study: Mood Disorders Centre.

[2] World Health Organization. 2000. Depression: A global crisis. Geneva: World Health Organization. As of 29 April 2016:

[http://www.who.int/mental\\_health/management/depression/wfmh\\_paper\\_depression\\_wmhd\\_2012.pdf](http://www.who.int/mental_health/management/depression/wfmh_paper_depression_wmhd_2012.pdf)

World Federation for Mental Health document on depression.

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<https://www.nice.org.uk/guidance/cg90/evidence/full-guidance-243833293>

NICE guidelines on the treatment and management of depression in adults.

### *2.1.8. Harnessing advances in nanotechnology to produce nanocomposite materials for 'smart' organ scaffolds*

#### Case study

The NIHR funds research that translates novel technologies into innovative treatments. Researchers at University College London's Centre for Nanotechnology and Regenerative Medicine, funded in part by the NIHR's New and Emerging Applications of Technology (NEAT) programme, have developed nanocomposite biomaterials and used them to manufacture fully synthetic human organs, leading to improved patient outcomes from transplants [1][2]. This study is also an example of NIHR-supported research being commercialised, as two spinout companies have been created to market the technology (for further examples of this, see chapter 8).

Conventional organ transplant methods are associated with a number of difficulties, such as a lack of available donor organs and undesirable patient outcomes including the need for immunosuppressive drugs to prevent rejection [3]. Research led by Professor Alexander Seifalian, and funded in part by the NIHR, was driven by the development of two novel non-biodegradable and bioabsorbable nanocomposite polymers, which further research showed to be suitable materials for organ regeneration scaffolds that can be used to grow new tissue [1][4]. The research team built on these findings to manufacture scaffolds from the nanocomposite polymer, which were functionalised with proteins and peptides and/or seeded

with stem cells. Further research led to the development of ‘smart’ scaffolds to regenerate a variety of organs and tissues, including in paediatric patients. The combined result of this research was the capability to manufacture synthetic organs tailored to individual patients using CT scans of their native organs.

This research has had an impact on clinical practice, along with associated health and commercial impacts. Most notably, the research brought the first fully synthetic organ into a clinical setting, providing the world’s first synthetic trachea to be implanted into a patient in 2011 [2]. The implant procedure was made easier by the use of CT scans to model the synthetic organ on the patient’s own trachea. Moreover, the use of the patient’s own stem cells for the implant removed the need for the patient to take immunosuppressive drugs as would have been required with a conventional transplant. The success of the implant has had an impact on longer-term patient outcomes, with the implanted trachea functioning well more than two years after the procedure [3]. A professor of laryngology at the Royal Throat, Nose and Ear Hospital reported that ‘This is the first time that a trachea made from a synthetic scaffold (here repopulated using stem cells), has preserved life and quality of life for longer than a few months’ [3]. The successful implant addresses a clear clinical need: because tracheal tumours are generally too large to be surgically resected by the time of diagnosis, there is a requirement for effective alternatives.

Furthermore, this research has implications for the development of synthetic organs more broadly, which have the potential to have a significant positive impact on a number of areas where current treatments are inadequate. One example is Professor Seifalian’s team using its platform nanotechnology in the development of the first synthetic tear ducts, now implanted into five patients. This has important consequences for patient outcomes, as patients whose tear ducts have been removed (for example due to cancer) would suffer from constantly watering eyes if not treated, and previous treatments had poor clinical outcomes. In contrast, the surgeon who implanted the tear ducts developed by Professor Seifalian’s team reported positive results following the procedure [5].

This positive impact on outcomes reflects the wider impact of this research. The development of fully synthetic organs and tissue allows clinical practice to overcome a number of the difficulties associated with conventional treatments, including the issue of availability of donor organs [3]. The use of patients’ own stem cells addresses the risk in conventional transplants of a harmful immune system response in the recipient due to donor cells not being completely removed from the organ [3].

The UCL team’s research has also had commercial impact, having led to more than 10 patents. Two spinout companies have been established to commercialise the use of the nanomaterials developed. Belsize Polymer (listed as dissolved as of 2015 [6]) was set up in 2013 to take forward clinical trials and commercialisation of synthetic organs, and SmartTech, a joint venture with Pharmidex and Flexicare Medical, was established in 2013 to commercialise the use of the UCL team’s nanomaterials for nerve regeneration and stents [3].

## Evidence

[1] Raghunath J, Zhang H, Edirisinghe MJ, Darbyshire A, Butler PE, Seifalian AM. 2009. A new biodegradable nanocomposite based on polyhedral oligomeric silsesquioxane nanocages:



Cytocompatibility and investigation into electrohydrodynamic jet fabrication techniques for tissue-engineered scaffolds. *Biotechnology and Applied Biochemistry* 52 (1): 1-8. doi: 10.1042/BA20070256

An article about the development of nanocomposite biomaterials.

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An academic article about the application of the material in a health context (synthetic trachea).

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[4] Kannan RY, Salacinski HJ, Butler PE, Seifalian AM. 2005. Polyhedral oligomeric silsesquioxane nanocomposites: The next generation material for biomedical applications. *Accounts of Chemical Research* 38 (11): 879-84. doi: 10.1021/ar050055b

[5] Chaloupka K. 2012. Nanotechnology meets lacrimal duct system. In: 150 Jahre Universitäts-Augenklinik Zürich, edited by K Landau, 153-5. Luzern: U. Novotny Fachverlag. doi:10.5167/uzh-66647. As of 16 May 2016: <http://www.zora.uzh.ch/66647/>

Article that corroborates the use of POSS-PCU in synthetic lacrimal duct surgery and the benefits to patients.

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Details on Companies House webpage describing Belsize Polymer company details (now dissolved.)

### *2.1.9. Improving the precision of real-time diagnoses by using advanced technologies*

#### Case study

The MRC-NIHR National Phenome Centre which is a partnership between the NIHR, the Medical Research Council (MRC), and academic partners Imperial College London and King's College London, is opening a new chapter in analytical chemistry. Adapting cutting-edge technology for use in a hospital environment, the Phenome Centre is developing advanced ways to detect the hallmarks of disease [1].

The advanced equipment that makes up the Phenome Centre's state-of-the-art analytical laboratory, a suite of mass spectrometry and nuclear magnetic spectroscopy machines, was initially acquired to carry out rapid drug testing of athletes at the 2012 Olympic Games. Alongside funding from a number of industry partners and the EU, funding from the MRC/NIHR provided the means to repurpose this equipment to test blood and other human samples for signature biochemical markers. In this way, the centre provides a population-wide phenotyping service (one's 'phenome' being the sum of observable

characteristics of a cell, tissue, or individual) able to analyse up to 100,000 samples per year, and ten tests per sample [1].

An example of one of the areas in which the Phenome Centre is breaking new ground comes from its pilot of an intelligent knife – or ‘iKnife’ – that can provide near-real-time information on the biological makeup of tissue, as it cuts. The NIHR Biomedical Research Centre (BRC) at Imperial had originally funded Professor Jeremy Nicholson, the centre’s director, and Lord Ara Darzi, to work on a prototype iKnife device.

They recruited Professor Zoltan Takáts to the Imperial team and the collaboration proved productive. In 2013, they published results of their efforts to use the iKnife as a means to improve cancer surgery. Their aim was to identify whether tissue was cancerous by using the signature molecules given off by the electrosurgical scalpel, in real time, while patients underwent surgery to have a solid tumour removed. When compared with the results of traditional pathology tissue testing, the iKnife correctly identified the histological diagnosis in 100 per cent of samples from 81 patients. By analysing the unique molecular profiles of the different tissues, the iKnife also provided additional biochemical information on the types of cancer present [3].

Applying this technology, the team are conducting further trials to develop the iKnife as a means to improve the accuracy of surgery [4]. In the case of cancer surgery, their ambition would be to circumvent the need either to remove excess healthy tissue surrounding the tumour, or send tissue samples for pathology testing to identify the persistence of cancerous cells while patients remain under anaesthetic [5].

By integrating analytical specialists within facilities that house the latest technological equipment, and bringing this to within the access of leading clinical facilities, the NIHR is helping to drive advances in diagnostics, and better inform treatment decisions, at the cutting edge of modern medicine.

## Evidence

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[4] Wong S. 2014. Waters Corporation acquires iKnife technology. Life-Sciences-UK.com. As of 29 April 2016: <http://www.life-sciences-uk.com/news/imperial-college-waters-acquires-london-corporation-nyse-wat-2001-104606.html>

News of the Waters Corporation's acquisition of iKnife to develop the technology for clinical use.

[5] National Institute for Health Research and Imperial Biomedical Research Centre. 2016. An 'intelligent knife' that tells the surgeon where to cut. As of 29 April 2016: <http://imperialbrc.org/our-impact/case-studies/intelligent-knife-surgery>

News of the Imperial team's initial testing of the iKnife in 81 patients undergoing cancer surgery.

### *2.1.10. Challenging 'breakthrough' status to determine the most cost-effective drugs to treat schizophrenia*

#### Case study

Breakthroughs in medical healthcare do not only take place through a process of developing new and better drugs, devices and diagnostics. There are times when it is equally, if not more, important to evaluate whether existing therapies would be better applied or made more readily available to patients, as medical knowledge advances. The largest of the NIHR's research funding streams, its Health Technology Assessment (HTA) programme, plays an important role in gathering and making available evidence on the cost-effectiveness of different therapies. In a landmark trial supported by this programme, researchers at the University of Manchester helped to demonstrate that a new generation of antipsychotic drugs to treat schizophrenia were not as effective under 'real life' clinical conditions as practitioners had been informed.

The history of this trial dates back to the introduction of a class of antipsychotic drugs in the 1990s, hailed at the time as the first major advance in therapeutics for schizophrenia in 40 years. Limited evidence underpinning a number of the claims of these drugs' superiority – in particular given their significantly higher price – had placed healthcare policymakers, who were working in a climate of ever-increasing mental healthcare costs, in a difficult position [3].

The Manchester team therefore set about to test whether the use of the newer 'second-generation' antipsychotic drugs was associated with improved quality of life, when compared with the older 'first generation' therapies. The team did this via a pragmatic trial – one mimicking routine clinical practice as far as practical under controlled conditions.

The trial concluded that the older drugs were as clinically effective as the newer drugs, with comparable side effects [2]. Patients reported no preference for either class of drug [2]. Importantly, the team found the older drugs to be far more cost-effective, priced at between 20 to 30 times cheaper than their more recent counterparts [1].

The findings surprised even the trial team themselves, who were quoted on the front page of the Washington Post as saying they were *'so certain they would find exactly the opposite that they went back to make sure the research data had not been recorded backward.'* Nevertheless, the team's conclusions proved valid and have since been incorporated into treatment guidelines in the UK, United States, and Canada – where audits of prescribing practices showed a measurable impact on the rates of clinicians prescribing second generation vs. first generation antipsychotics [4].

With further support from the NIHR under its Research for Patient Benefit (RfPB) programme, the Manchester team went on to demonstrate real savings of approximately £200,000 from encouraging clinicians in Bury Primary Care Trust to change their prescribing practices in line with the revised guideline recommendations [4].

While the nuances of applying evidence-based medicine are complex and the application is highly specialised, the NIHR's support of this kind of pragmatic cost-effectiveness research plays a vital role in providing evidence for the allocation of increasingly scarce resources in the NHS. By appropriately and methodically challenging the claims of 'breakthrough' status in the case of second-generation antipsychotics – asking, as one researcher put it, 'how an entire medical field could have been misled' – this work has brought about significant cost savings, reducing the burden of paying for expensive and questionably effective drugs in a resource-constrained healthcare system [4].

## Evidence

[1] Davies LM, Lewis S, Jones PB, Barnes TRE, Gaughran F, Hayhurst K, Markwick A, Lloyd H. 2008. Cost-effectiveness of first- v. second-generation antipsychotic drugs: results from a randomised controlled trial in schizophrenia responding poorly to previous therapy. *British Journal of Psychiatry* 191 (1): 14-22. doi:10.1192/bjp.bp.106.028654

Results of a cost-effectiveness analysis, subsequent to the principal publication of the CUtLASS trial results by the Manchester team.

[2] Jones PB, Barnes TRE, Davies L, Dunn G, Lloyd H, Hayhurst, KP, Murray, RM, Markwick A, Lewis SW. 2006. Randomized controlled trial of effect on quality of life of second generation versus first generation antipsychotic drugs in schizophrenia. *Archives of General Psychiatry* 63: 1079-87. doi:10.1001/archpsyc.63.10.1079

Results of the pragmatic CUtLASS randomised controlled trial, undertaken by the Manchester team to compare the effectiveness of first- versus second-generation antipsychotics.

[3] Lewis S, Lieberman J. 2008. CATIE and CUtLASS: Can we handle the truth? *British Journal of Psychiatry* 192 (3): 161-3. doi:10.1192/bjp.bp.107.037218. As of 30 March 2016: <http://bjp.rcpsych.org/content/192/3/161>

An editorial providing further historical context for, and implications of, the CUtLASS trial.

[4] Research Excellence Framework. 2014. CUtLASS: Changing attitudes and prescribing practice: Cost effectiveness of first versus second generation antipsychotic drugs in people with schizophrenia. [Case study 28074.] As of 29 April 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=28074>

REF case study detailing the wider impacts of the CUtLASS trial on policy and practice.

[5] Vedantam S. 2006. In antipsychotics, newer isn't better. The Washington Post (3 October). As of 29 April 2016: <http://www.washingtonpost.com/wp-dyn/content/article/2006/10/02/AR2006100201378.html>

Media commentary around the time of publication of the CUtLASS trial, providing reactions from the medical and pharmaceutical communities.

## 3. Supporting the nation to deliver world-leading research with global impact

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### 3.1. Summary

**Global. Exemplary. Pioneering.**

*NIHR sets a standard for high-quality research that improves global healthcare. The evidence that it generates drives international advances, establishes medical best practice and ensures global preparedness against disease.*

NIHR contributes to breakthrough discoveries with international impact. For example:

- More than 1 million people worldwide who would otherwise die each year from traumatic injury stand to benefit from NIHR-funded research into the novel, off-label use of a drug, tranexamic acid, that has been shown to significantly reduce the risk of bleeding to death if administered within the first three hours of trauma.
- More than 1,700 healthcare organisations worldwide are using the WHO's Surgical Safety Checklist, a tool that significantly reduces post-operative complications and that was developed from a series of indicators informed by NIHR-funded research into patient safety.
- Hundreds fewer people are at risk of fatal poisoning following the withdrawal of co-proxamol in the UK, other EU member states and a number of other countries on the basis of findings from NIHR-backed studies.

NIHR provides researchers with the means to draw together and apply evidence of international best practice. NIHR-funded programmes of patient, and patient-focused, research are improving lives and patient safety worldwide:

- The 1 in 600 babies born each year in the UK with cleft lip and palate will benefit from more equitable and better quality surgery, following NIHR's investment in research on centralising cleft services in fewer specialist centres. As a result, the clinical infrastructure is now in place to support national and international trials of new approaches in order to improve cleft care.
- Children with eczema now receive therapies based on internationally validated guidelines, with standardised methods to self-report their responses to treatment feeding in to a global resource of clinical trials.
- Stroke survivors have access to advanced assistive technologies to support one-to-one rehabilitation, which are being put into practice as part of an internationally relevant programme of research that has trained more than 2,500 therapists.

- Elderly people with dementia will receive a more personalised approach to their care, via an NIHR programme on the impact of behavioural – as opposed to solely pharmacological – interventions.
- Artificial knee joints produced by foreign manufacturers are being tested to strict quality standards, using advanced bioengineering simulators. These devices are being manufactured and trialled as part of a collaboration involving the Leeds NIHR Musculoskeletal Biomedical Research Unit.

NIHR also undertakes research which impacts on global health, for example, within its Biomedical Research Centres and within NIHR centres dedicated to patient safety research, as shown by the following examples:

- NIHR is protecting patients' and communities' rights, working to safeguard all participants in research by improving international ethical standards designed to ensure appropriate consent mechanisms and minimise the risk of creating inequalities.
- NIHR is playing a part in trials of candidate vaccines for Ebola through its support of the Oxford Biomedical Research Centre, which is part of a study enrolling more than 500 participants in vaccine trials in Europe and Africa.

### *3.1.1. Minimising human factor errors with a surgical checklist to improve the safety of operations*

#### Case study

NIHR research has played a pivotal role in efforts to try to understand and adapt to human factors that affect clinical performance and patient safety. To drive improvements in this area, in 2007, the NIHR provided funding for two centres that would be dedicated to a process of delivering real benefits for patients, via research into such safety issues such as prescription errors, misdiagnoses and accidents during surgery [3].

One of these two NIHR-funded Patient Safety Translational Research Centres is based at Imperial College London. Led by Professor Lord Ara Darzi, the centre has received over £12.5 million in funding from the NIHR, and has pioneered an intervention that has led to significant impacts on global health. The Imperial team investigated factors relating to human behaviour, team skills, and the surgical environment in the operating theatre, in order to determine their contribution to errors in surgical performance and procedures. Feeding in their findings via their participation in the World Health Organisation (WHO)'s Safe Surgery Saves Lives working group, the team developed a series of evidence based indicators which forms the basis of the WHO Surgical Safety Checklist [1].

The team went on to lead an international pilot evaluation of the checklist, which demonstrated a reduction in patient mortality following major operations (1.5% to 0.8%) and inpatient complications (11% to 7%) when the checklist was in use. Further benefits included higher teamwork and surgical teams' improved compliance with standard care processes [1]. The NIHR-funded Imperial centre played a key role in these and further evaluations, providing an academic base and facilities for multidisciplinary research and innovations for safer healthcare.

In 2009, use of the checklist was mandated throughout the NHS [5]. As part of a national ‘Patient Safety First’ campaign to determine its effectiveness, the NIHR supported a survey of 19 hospitals and 3,000 NHS personnel [2]. Collecting data from nearly 7,000 patients, the study found significant reductions in post-operative complications associated with use of the checklist, in particular when all three sections of the checklist were completed in full [4]. The checklist was used in over 96 per cent of operations, with a rising majority of operating staff both wanting to use the checklist and believing that it made surgery safer [4].

The NIHR’s support of research to develop and implement use of the checklist across the NHS is having an impact on 4.6 million patients undergoing surgery annually in England alone. Worldwide, these figures scale up to an estimated quarter of a billion patients undergoing surgery each year. With the checklist in use in more than 1,700 healthcare organisations around the globe (a number still rising), the international impacts of the NIHR’s efforts to improve patient safety are having a significant effect on patients’ lives [1].

## Evidence

[1] Research Excellence Framework. 2014. Making surgery safer: The WHO Surgical Safety Checklist. [Case study 42204.] As of 2 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=42204>

REF case study describing research at the Imperial Patient Safety Translational Research Centre and its contribution to the WHO Surgical Safety Checklist, with information on the checklist’s uptake and global impacts.

[2] National Institute for Health Research. 2013. Annual Report 2011/12. London: NIHR. As of 2 May 2016: [http://www.nihr.ac.uk/documents/about-NIHR/NIHR-Publications/NIHR-Annual-Reports/NIHR%20Annual%20Report%202011\\_2012.pdf](http://www.nihr.ac.uk/documents/about-NIHR/NIHR-Publications/NIHR-Annual-Reports/NIHR%20Annual%20Report%202011_2012.pdf)

Report including data from the NIHR-supported evaluation of the checklist, specifically views from NHS personnel around its use.

[3] National Institute for Health Research. 2015. Patient Safety Translational Research Centres. As of 2 May 2016: <http://www.nihr.ac.uk/about/patient-safety-translational-research-centres.htm>

Information on the two Patient Safety Translational Research Centres supported by the NIHR, with an overview of their remit and funding agreed from August 2012.

[4] Mayer EK, Sevdalis N, Rout S, Caris J, Russ S, Mansell J, Davies R, Skapinakis P, Vincent C, Athanasiou T, Moorthy K, Darzi A. 2016. Surgical checklist implementation project: The impact of variable WHO checklist compliance on risk-adjusted clinical outcomes after national implementation: A longitudinal study. *Annals of Surgery* 263 (1): 58-63. doi:10.1097/SLA.0000000000001185

Results of a longitudinal study of 6,714 patients at 5 academic and community hospitals, to evaluate how use of the checklist impacted on clinical outcomes.

[5] NHS. 2009. WHO Surgical Safety Checklist. As of 2 May 2016: <http://www.nrls.npsa.nhs.uk/alerts/?entryid45=59860>

Patient safety alert to healthcare organisations, requiring use of checklist in any operating theatre environment, along with materials to encourage its effective implementation.



### *3.1.2. Making the best of an old drug: how tranexamic acid is saving lives around the world*

#### Case study

Identifying gaps in the evidence base underpinning medical treatments can sometimes lead to significant breakthroughs that go on to have profound global impacts. As part of its remit to evaluate both the effectiveness and the affordability of drugs being used in the NHS, the NIHR's Health Technology Assessment programme supported a trial based around a question of how an existing blood clotting agent might be used to help blood loss from trauma, which is a major cause of death around the world.

The Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage (CRASH-2) trial was a randomised controlled trial undertaken in 274 hospitals in 40 countries, bringing together commercial, charitable and public funding to investigate the role of an out-of-patent ('generic') drug, tranexamic acid, in preventing uncontrolled bleeding in trauma patients. The trial was designed to make use of an existing network of researchers and doctors with an interest in trauma, specifically following a Cochrane review of the use of drugs such as tranexamic acid, which found limited evidence to support their use in such circumstances [1].

With the support and early involvement of patient and practitioner groups across the globe, the trial recruited more than 20,000 participants [1]. It demonstrated that tranexamic acid significantly reduced the risk of patients bleeding to death (by 14%) if administered within the first three hours of trauma [2].

The trial team went to significant efforts to engage practitioners around the results of their work. As part of an independent evaluation of the trial process, they noted the challenges of having only limited resources available for engagement, given the lack of an obvious industry partner as a result of the drug being out of patent and therefore on the market in an inexpensive form [1]. That said, the team deployed novel communications channels, including a cartoon, songs and a comic, and the study's results went on to receive widespread coverage, including pickup from international media [3].

In part due to their involvement in the trial itself, the UK military swiftly began using tranexamic acid to treat wounded soldiers in the field [4]. In parallel, evidence of the drug's cost-effectiveness [5] was deemed sufficiently compelling that in 2010 the World Health Organisation (WHO) included it on their essential medicines list [6]. Shortly after this in 2011, British Armed Forces protocols [7] and Cochrane Review guidelines [8] incorporated the use of tranexamic acid as a means to reduce trauma mortality rates. In 2012, the UK's National Institute for Health and Care Excellence released its first ever evidence summary for an off-label drug to encourage wider use of tranexamic acid following trauma [9].

As a result of its significant investment in the novel use of an old drug, and its efforts to implement its use in acute settings – such as by ambulance crews and emergency departments in the south west of England [10] – the NIHR supported deployment of a therapy that stands to benefit over a million people worldwide each year who would otherwise die from traumatic bleeding [2]. Current uses of tranexamic acid now range from parachute regiments, [11] through to paramedics [12] and paediatricians [13]. Over 75 per cent of trauma victims in the UK receive treatment with tranexamic acid [4]. With the capacity to save 100,000 lives a year, the worldwide net health benefit of the global use of tranexamic acid is estimated to be worth £26 billion [14].

## Evidence

[1] Guthrie S, Bienkowska-Gibbs T, Manville C, Pollitt A, Kirtley A, Wooding S. 2015. The impact of the National Institute for Health Research Health Technology Assessment programme, 2003–13: A multimethod evaluation. *Health Technology Assessment* 19 (67): 1-291. doi:10.3310/hta19670

RAND Europe's independent evaluation of the impacts of the Health Technology Assessment programme, with detailed case study write-ups of specific HTA-funded initiatives, including the CRASH-2 trial.

[2] CRASH-2 trial collaborators. 2010. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): A randomised, placebo-controlled trial. *Lancet* 376 (9734): 23-32. doi:10.1016/S0140-6736(10)60835-5

Findings of the CRASH-2 trial, conducted across 40 countries, noting the effectiveness of tranexamic acid in reducing the risk of death by bleeding in trauma patients.

[3] Research Excellence Framework. 2014. Identifying and promoting a new trauma treatment which could save over 100,000 lives a year. [Case study 41458.] As of 5 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=41458>

REF case study detailing impacts of the CRASH-2 trial, in particular. Evidence of the trial team's efforts to undertake innovative engagement activities to promote the study's findings.

[4] Guthrie S, Hafner M, Bienkowska-Gibbs T, Wooding S. 2015. Returns on research funded under the NIHR Health Technology Assessment programme. Santa Monica, Calif.: RAND Corporation. As of 5 May 2016: [http://www.rand.org/pubs/research\\_reports/RR666.html](http://www.rand.org/pubs/research_reports/RR666.html)

PRiSM's independent evaluation of the economic returns from the HTA programme, with case study write-ups of specific HTA-funded initiatives, including the CRASH-2 trial.

[5] Guerriero C, Cairns J, Perel P, Shakur H, Roberts I. 2011. Cost-effectiveness analysis of administering tranexamic acid to bleeding trauma patients using evidence from the CRASH-2 trial. *PLoS One* 6(5):e18987. doi:10.1371/journal.pone.001898

Sub-analysis of the CRASH-2 trial results, demonstrating the cost-effectiveness of tranexamic acid when used to treat trauma in low-, middle and high-income settings.

[6] Roberts I, Kawahara T. 2010. Proposal for the inclusion of tranexamic acid (anti-fibrinolytic – lysine analogue) in the WHO Model List of Essential Medicines. Geneva: WHO. As of 5 May 2016: [http://www.who.int/selection\\_medicines/committees/expert/18/applications/TRANEXAMIC\\_ACID\\_10\\_2.pdf?ua=1](http://www.who.int/selection_medicines/committees/expert/18/applications/TRANEXAMIC_ACID_10_2.pdf?ua=1)

Application on the use of tranexamic acid in trauma, prepared for the WHO's 18th Expert Committee on the Selection and Use of Essential Medicines.

[7] British Armed Forces. 2011. Tranexamic acid (TXA) in tactical combat: Casualty Care Guideline Revision Recommendation Committee on Tactical Combat Casualty Care. As of 5 May 2016: [http://www.medicalsci.com/files/tranexamic\\_acid\\_\\_txa\\_\\_in\\_tactical\\_combat\\_casualty\\_care.pdf](http://www.medicalsci.com/files/tranexamic_acid__txa__in_tactical_combat_casualty_care.pdf)

Proposal for a revision of Tactical Field Care and Tactical Evaluation Care guideline to incorporate use of tranexamic acid for trauma.

[8] Roberts I, Shakur H, Ker K, Coats T. 2012. Antifibrinolytic drugs for acute traumatic injury. *Cochrane Database of Systematic Reviews* 12:CD004896. doi:10.1002/14651858.CD004896.pub3

Cochrane collaboration systematic review quantifying the effects of antifibrinolytic drugs on mortality, vascular occlusive events, surgical intervention and receipt of blood transfusion after acute traumatic injury. This review recommended use of tranexamic acid to reduce mortality in bleeding trauma patients without increasing the risk of adverse events.

[9] National Institute for Health and Care Excellence. 2012. Significant haemorrhage following trauma: Tranexamic acid. [ESUOM1.] AS of 3 May 2016: <http://www.nice.org.uk/advice/esuom1/chapter/Key-points-from-the-evidence>

First evidence summary of an unlicensed or off-label use of a medicine considered of significance to the NHS, to support the use of tranexamic acid for trauma, in the absence of a licensed alternative.

[10] National Institute for Health Research Collaboration for Leadership in Applied Health Research South West Peninsula. 2015–16. TXA in trauma. As of 3 May 2016: <http://clahrc-peninsula.nihr.ac.uk/research/txa-in-trauma>

The NIHR's Collaboration for Leadership in Applied Health Research South West Peninsula's role in implementing the use of tranexamic acid in acute care settings in partnership with local NHS teams and the South Western Ambulance Service NHS Foundation Trust.

[11] Morrison JJ, Ross JD, Dubose JJ, Jansen JO, Midwinter MJ, Rasmussen TE. 2012. Association of cryoprecipitate and tranexamic acid with improved survival following wartime injury. *JAMA Surgery* 148 (3): 218-225. doi: 10.1001/jamasurg.2013.764.

Results of a retrospective observational study investigating the effects of different clotting agents on the survival in combat-injured patients, conducted by a research group including members of the NIHR New Queen Elizabeth Hospital in Birmingham and 144 Parachute Medical Squadron, 16 (Air Assault) Medical Regiment, Colchester.

[12] Joint Royal Colleges Ambulance Liaison Committee. 2012. Guidelines. As of 5 May 2016: <http://www.classprofessional.co.uk/books/uk-ambulance-services-clinical-practice-guidelines-2013-pocket-book-digital-edition-5848>

National clinical practice guidelines based on current best evidence for the provision of ambulance services.

[13] Royal College of Paediatrics and Child Health. 2012. Major trauma and the use of tranexamic acid in children. London: RCPCH. As of 5 May 2016: <http://www.rcpch.ac.uk/system/files/protected/page/Major%20Trauma%20and%20the%20Use%20of%20Tranexamic%20Acid%20in%20Children%20-%20Evidence%20Statement%202012-11.pdf>

Guidelines from the Royal College of Paediatrics and Child Health on the use of tranexamic acid.

[14] Research Excellence Framework. 2014. A new use for an old drug: Administration of tranexamic acid to prevent trauma deaths from bleeding. [Case study 34476.] As of 5 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=34476>

Research Excellence Framework case study detailing wider impacts on policy and practice following from the CRASH-2 trial.

### *3.1.3. Expediting trials of Ebola vaccines through the early stages of research*

#### Case study

The Ebola virus epidemic that emerged in Guinea in December 2013 has, to date, infected more than 28,000 people and killed more than 11,000 [1]. Although the World Health Organisation (WHO) declared a number of the worst-affected countries virus-free by the end of 2015, flare-ups continue to occur. In these cases, having an effective Ebola vaccine is crucial to confine the spread of the virus and protect those who have come into contact with infected people [2]. Research can aid in efforts to speed up the development of new vaccines and prevent the devastating impact of this current epidemic and future outbreaks of Ebola virus [3].

This most recent Ebola outbreak posed an unprecedented challenge for patients and healthcare systems around the globe. Reviewing the UK's preparedness for such emergencies, a recent report from the UK House of Commons Science and Technology Select Committee spoke of 'a long-term market failure to invest in interventions for rare but potentially catastrophic epidemics' [4]. Despite this, there remains no approved vaccine for Ebola virus, and global experts are still calling for intensified research to prevent the next epidemic [5]. In November 2014, the Innovative Medicines Initiative (IMI), Europe's largest public-private collaboration for the development of medicines for patients, launched a €280 million programme to speed up the progress of research around a vaccine for Ebola [6].

One project to receive funding from the IMI was a collaborative group led by the French Institute of Health and Medical Research (INSERM) who are project coordinators, and including doctors and scientists in the Oxford Vaccine Group, as well as London School of Hygiene and Tropical Medicine, Le Centre Muraz, Inserm Transfert (IT), and the Janssen Pharmaceutical Companies of Johnson & Johnson [3]. The Oxford site of the study will aim to recruit healthy volunteers from across the UK. The Oxford study is supported by the NIHR Oxford Biomedical Research Centre (BRC), a partnership between the University of Oxford and Oxford University Hospitals NHS Trust [3].

Within six months of IMI's funding announcement, the EBOVAC programme had begun recruiting patients to one of a series of trials to test a new 'prime boost' vaccine. This method of vaccination, using the vaccine Ad26.ZEBO, is designed to offer long-lasting immunity to the virus [3]. To speed up the research process, constituent studies within the EBOVAC programme are running in parallel – with phase 1, 2 and 3 trials all planned concurrently [7]. As of March 2016, more than 350 subjects had been recruited to the trial in Europe, with a further 130 of more than 1,000 intended subjects have been recruited in Africa [8].

It is clear that in order for health workers in affected areas to mobilise an appropriate response to the next Ebola outbreak, trials of candidate vaccines must have progressed to a point where they can be deployed without delay in the event of an epidemic [5]. Encouraging evidence of the success of this unorthodox parallel trials approach comes from a WHO-sponsored multilateral effort to trial a different vaccine

(rVSV-ZEBOV) in August 2015. That trial reported 100 per cent efficacy amongst more than 7,600 people in Guinea [9].

Through its provision of infrastructure to support these trials, the NIHR is helping to ensure that important research into Ebola continues at a pace that will ensure greater preparedness for this lethal disease.

## Evidence

[1] WHO. 2016. Ebola Situation Report – 30 March 2016. As of 3 May 2016: <http://apps.who.int/ebola/current-situation/ebola-situation-report-30-march-2016>

The World Health Organization's situation report detailing numbers of confirmed, probable and suspected cases of Ebola virus disease worldwide.

[2] WHO. 2016. WHO coordinating vaccination of contacts to contain Ebola flare-up in Guinea. As of 3 May 2016: <http://www.who.int/features/2016/ebola-contacts-vaccination/en/>

News article describing the WHO's ongoing role in containing outbreaks of Ebola virus and the role of vaccines in preventing its spread.

[3] University of Oxford. 2015. Oxford Ebola vaccine study moves to next phase. As of 3 May 2016: <http://www.ox.ac.uk/news/2015-07-15-oxford-ebola-vaccine-study-moves-next-phase>

Press release from the University of Oxford noting the NIHR's role in fast-tracking trials of a vaccine for Ebola virus.

[4] House of Commons Science and Technology Committee. 2016. Science in emergencies: UK lessons from Ebola. [HC 469.] As of 3 May 2016:

<http://www.publications.parliament.uk/pa/cm201516/cmselect/cmsstech/469/469.pdf>

Report reviewing the UK's response to the Ebola crisis, providing recommendations for improved future responses to epidemics, such as calls for the government to publish an emerging infectious disease strategy to maximise the impact of public and private investment in research and development in this area.

[5] Piot P, Stoffels P. 2015. Ebola will always return unless we develop the tools to end it. The Guardian. As of 3 May 2016: <http://www.theguardian.com/global-development/2015/nov/24/ebola-develop-tools-to-end-it-vaccine-sierra-leone-virus-epidemic>

Article by Professor Peter Piot, who co-discovered the Ebola virus in 1976, describing the continuing urgency of challenges posed by the most recent outbreak in West Africa.

[6] Innovative Medicines Initiative. n.d. Innovative Medicines Initiative launches Ebola+ programme (press release). As of 3 May 2016: <http://www.imi.europa.eu/content/ebola-programme-launch>

Press release detailing aims and ambitions of IMI's multimillion-Euro call for proposals in Ebola research.

[7] Thiebaut R, Douoguih M, Pollard AJ, Watson-Jones D, Snape M. n.d. Development of a prophylactic Ebola vaccine using an heterologous prime-boost regimen. As of 3 May 2016: [http://www.ebovac2.com/images/EBOVAC\\_Targeting%20Ebola.pdf](http://www.ebovac2.com/images/EBOVAC_Targeting%20Ebola.pdf)

Information from the EBOVAC team on the series of trials currently underway to develop the Ad26.ZEBOV 'prime boost' Ebola vaccine.

[8] EBOVAC2. 2016. 1st EBOVAC2 e-newsletter. As of 3 May 2016: [http://www.ebovac2.com/images/EBOVAC2\\_newsletter\\_no.\\_1\\_March\\_2016.pdf](http://www.ebovac2.com/images/EBOVAC2_newsletter_no._1_March_2016.pdf)

e-Newsletter from the EBOVAC2 trial, updating on progress with patient recruitment and other milestones, as one of a series of constituent trials in the EBOVAC programme.

[9] Henao-Restrepo AM, Longini IM, Egger M, Dean NE, Edmunds WJ, Camacho A, Carroll MW, Doumbia M, Draguez B, Duraffour S, Enwere G, Grais R, Gunther S, Hossmann S, Kader Kondé M, Kone S, Kuisma E, Levine MM, Mandal S, Norheim G. 2015. Efficacy and effectiveness of an rVSV-vectored vaccine expressing Ebola surface glycoprotein: Interim results from the Guinea ring vaccination cluster-randomised trial. *The Lancet* 386 (9996): 857-66. doi: 10.1016/S0140-6736(15)61117-5

Results of a cluster-randomised, ‘ring vaccination’ trial of the rVSV-ZEBOV vaccine among 7,651 subjects in Guinea.

### *3.1.4. Protecting patients’ and communities’ rights when taking part in research trials*

#### Case study

Over the past five years, more than three million people in the UK took part in high quality research, with support from the NIHR’s Clinical Research Networks [1]. Ensuring that research subjects are afforded appropriate practical and ethical protections, while maintaining their participation throughout the duration of a trial, is a major challenge [2]. Since 2008, the NIHR Biomedical Research Centre (BRC) at University College London (UCL)/UCL Hospitals (UCLH) has been supporting Dr Sarah Edwards’s work into research ethics and governance. This work has fed into important international consensus statements regarding research subjects’ rights to withdraw from trials, as well as the ethics of conducting particular forms of trials increasingly deployed in resource-poor contexts [3].

An early strand of Dr Edwards’s NIHR-funded research examined the concept of introducing a contract for participants taking part in studies. This put forward the notion of subjects consenting to explicit terms that would qualify the consequences of their withdrawing from a study, as a means to improve both retention rates and the mutual responsibility between researchers and participants [4]. Based on this and further studies of participants’ views around withdrawing from trials [5], Dr Edwards was invited to draft a number of clauses for a revision of the Declaration of Helsinki [3]. This statement acts as the most authoritative international guidance for human research ethics, and forms part of EU and UK regulations for trials involving medicinal products [6].

Dr Edwards’s research also investigated the ethical issues surrounding cluster randomised controlled trials (RCTs) – where groups of subjects, as opposed to individuals, are randomly assigned to receive interventions. The research argued that researchers conducting cluster RCTs ought to employ modified design strategies to minimise the risk of creating inequalities (health, economic or social) among different groups participating in the trial [7]. Later work set out the cases – such as epidemics or other public health emergencies – where cluster RCTs could provide a way to gather meaningful scientific data, while managing the spread of disease [8].

This work fed directly into international recommendations on the ethics of conducting cluster RCTs known as the Ottawa Statement [9]. Subsequent policy impacts of this work include impacts on the Food and Drug Administration and the Department of Health and Human Sciences in the USA, who incorporated these guidelines into their regulations for how to conduct cluster RCTs. In addition, the World Health Organisation cited Dr Edwards's recommendations in support of their guidelines on patient safety research, noting the particular vulnerability of patients in resource-poor settings to increased risks of inequalities, when considering cluster trial designs [3].

Dr Edwards's work has gone on to directly impact resource-poor communities, feeding into the design of a model strategy to improve women's and children's health, as part of a cluster RCT carried out in the slums in Mumbai, India [10]. In supporting Dr Edwards's leadership role, the NIHR is contributing to work that is safeguarding the design of research, to benefit both participants in and the wider beneficiaries of trials taking place across the UK, and around the world.

## Evidence

[1] National Institute for Health Research. n.d. The NIHR Clinical Research Network is funded by the Department of Health to deliver a portfolio of high-quality clinical research in the NHS in England. Here are the key statistics for 2014/15. As of 3 May 2016: <https://www.crn.nihr.ac.uk/about-crn/our-performance/key-statistics-2/>

Information on the NIHR Clinical Research Network's support of clinical research within the UK.

[2] Alexander W. 2013. The Uphill Path to Successful Clinical Trials. Keeping Patients Enrolled. *Pharmacy and Therapeutics* 38 (4): 225-227. As of 3 May 2016: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3684189/>

Paper examining the consequences of participants dropping out of clinical trials and the impact of this on data collection and the progress of research.

[3] Research Excellence Framework. 2014. Limits to individual choice in health research involving human subjects. [Case study 40440.] As of 3 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=40440>

Research Excellence Framework impact case study describing Dr Edwards's research into the ethics of clinical trials, with details of how international bodies have adopted this work into research governance standards to protect patients' interests.

[4] Edwards SJ. 2011. Assessing the remedy: the case for contracts in clinical trials. *The American Journal of Bioethics* 11 (4): 3-12. doi:10.1080/15265161.2011.560340

Article proposing the concept of 'informed withdrawal' as means to improve clinical trial retention rates.

[5] Bidad N, MacDonald L, Winters ZE, Edwards SJL, Horne R. 2014. Views on the right to withdraw from randomised controlled trials assessing quality of life after mastectomy and breast reconstruction (QUEST): findings from the QUEST perspectives study (QPS). *Research Ethics* 10 (1): 47-57. doi: 10.1177/1747016114524503

Study of the importance of patients' views around the right to withdraw from a trial of reconstructive breast surgery, and the circumstances under which they would exercise that right.

[6] World Medical Association. n.d. WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects. As of 3 May 2016:  
<http://www.wma.net/en/30publications/10policies/b3/>

Statement of internationally adopted principles of medical ethics.

[7] Conrad E, Edwards S. 2011. Inequalities and fairness in cluster trials. *Research Ethics* 7(2): 58-65. doi: 10.1177/174701611100700205

Paper proposing that researchers carrying out cluster RCTs consider using modified research design strategies in cases where there is a high risk of generating inequalities among groups.

[8] Edwards S. 2013. Ethics of clinical science in a public health emergency: drug discovery at the bedside. *The American Journal of Bioethics* 13 (9): 3-14. doi:10.1080/15265161.2013.813597

Paper examining the rationale of restricting new medicines via clinical trials in the context of public health emergencies, and how cluster trials – when fairly conducted – can provide a balance between therapeutic access and coordinating observations via experimental approaches.

[9] Weijer C, Grimshaw JM, Eccles MP, McRae, AD, White A, Brehaut JC, Taljaard M, the Ottawa Ethics of Cluster Randomized Trials Consensus Group. 2012. The Ottawa Statement on the Ethical Design and Conduct of Cluster Randomized Trials. *PLoS Medicine* 9(11): e1001346. doi:10.1371/journal.pmed.1001346

Consensus statement providing researchers and research ethics committees with detailed guidance on the ethical design of cluster RCTs.

[10] Lignou S, Das S, Mistry J, Alcock G, Shah More N, Osrin D, Edwards S. 2016. Reconstructing communities in cluster trials? *Trials* 17: 166. doi: 10.1186/s13063-016-1284-6

Views of participants in a cluster RCT of 600 households situated in informal communities (slums) in Mumbai, which trialled community resource centres as an intervention to improve the health and nutrition of women and children.

### *3.1.5. Placing people at the heart of more effective interventions for dementia*

#### Case study

Dementia is a rapidly growing international problem, with the Global Observatory for Ageing and Dementia Care predicting that the number of people with dementia worldwide will rise from 36 million in 2010 to 115 million in 2050 [1]. When compared to research into cancer or heart disease, dementia research has received a less than proportionate share of public investment, given the increasing burden of this disease [1]. Referring to a growing ‘national crisis’, in 2012, UK Prime Minister David Cameron launched the National Dementia Challenge [2]. The NIHR is playing a leading role in addressing this challenge, by investing in dedicated efforts such as the Dementia Translational Research Collaboration, and with the appointment of Martin Rosser as the National Director for Dementia Research [2]. The NIHR’s investments in specific areas of dementia research – in particular the challenge of basing dementia care around the experiences and needs of patients themselves – are providing a model for international best practice in this complex and urgent area.



Since 2007, the NIHR has funded a series of research studies at the School of Dementia Studies at the University of Bradford (formerly the Bradford Dementia Group), the University of Hull, and other collaborating NHS partners in the Yorkshire and Humber region [3]. Much of this group's work builds on the concept of 'person-centred care', initially developed by Bradford Professor Tom Kitwood, which aims: 'to ensure well-being, achieved by affirming personhood, meeting people's psychological needs and understanding their perspective' [3].

Part of the challenge of re-aligning dementia care away from a focus on 'the disease', and towards a focus on 'the person', was having a means to understand and record dementia patients' experiences of their own care. The Bradford team and its collaborators developed a method called dementia care mapping (DCM) – that provides a common framework to assess and improve upon the quality of person-centred care. This in turn has acted as a catalyst to improve the quality of life for people with dementia [3].

Through its wide-ranging funding, the NIHR is contributing to an internationally-relevant evidence base that supports carers using such methods as DCM. Since 2008, the Bradford team have trained more than 3,000 practitioners internationally in person-centred care approaches, contracting with more than 10 international organisations in a number of countries [3]. A randomised controlled trial of this approach in Australia demonstrated decreased falls and agitation amongst care home residents [4]. Similar trials are taking place in Netherlands [5] and, with further NIHR funding, in the UK [6].

A recent evaluation of the dementia research landscape, conducted by RAND Europe, highlighted the UK's global strength in person-centred approaches to dementia care. One interviewee noted:

... 'in psychosocial research that's been talked about at the current initiative of the World Dementia Research Council, the UK has been very much in the lead' [1].

By drawing together experts including physicians, mental health specialists, therapists, and care home staff, and placing the person at the centre of behavioural, rather than solely pharmacological, interventions, the NIHR and its commitment to dementia research is setting a leading example for practitioners and researchers around the globe.

## Evidence

[1] Marjanovic S, Robin E, Lichten C, Harte E, MacLure C, Parks S, Horvath V, Côté G, Roberge G, Rashid M. 2015. A Review of the Dementia Research Landscape and Workforce Capacity in the United Kingdom. Santa Monica, Calif.: RAND Corporation. As of 3 May 2016: [http://www.rand.org/pubs/research\\_reports/RR1186.html](http://www.rand.org/pubs/research_reports/RR1186.html)

Evaluation commissioned by the Alzheimer's Society to analyse the UK's dementia research landscape and workforce capacity and inform funding and capacity-building efforts in dementia research.

[2] Prime Minister's Office. 2012. 'Dementia challenge' launched. As of 3 May 2016: <https://www.gov.uk/government/news/dementia-challenge-launched>

Government announcement of measures aimed at making the UK a world leader in dementia care and research.

[3] Research Excellence Framework. 2014. Improving care for people with dementia. [Case study 43368.] As of 3 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=43368>

Research Excellence Framework case study detailing the NIHR's support of research into person-centred care at the University of Bradford and collaborating partners, providing details of the international relevance and impact of this work.

[4] Chenoweth L, King M, Jeon Y, Brodaty H, Stein-Parbury J, Norman R, Haas M, Luscombe G. 2009. Caring for Aged Dementia Care Resident Study (CADRES) of person-centred care, dementia-care mapping, and usual care in dementia: a cluster-randomised trial. *The Lancet Neurology* 8 (4): 317-325. doi: 10.1016/S1474-4422(09)70045-6

Australian RCT of person-centred care and dementia care mapping in 15 care sites with 289 residents, demonstrating its capacity to reduce agitation in people with dementia.

[5] Van de Ven G, Draskovic I, Adang E, Donders R, Post A, Zuidema S, Koopmans R, Vernooij-Dassen M. 2012. Improving person-centred care in nursing homes through dementia-care mapping: design of a cluster-randomised controlled trial. *BioMed Central Geriatrics* 12:1. doi: 10.1186/1471-2318-12-1

Design of a cluster RCT of dementia care mapping as a means to improve person-centred care in the Netherlands.

[6] National Institute for Health Research. n.d. HTA - 11/15/13: Evaluating the effectiveness and cost effectiveness of Dementia Care Mapping (DCM) to enable person-centred Care for people with dementia and their carers: A UK cluster randomised controlled trial in care homes (DCM EPIC trial) As of 3 May 2016: <http://www.nets.nihr.ac.uk/projects/hta/111513>

Ongoing NIHR-funded cluster RCT examining the effectiveness of dementia care mapping among 750 residents of 30 care homes.

### *3.1.6. Restoring lost limb function in stroke patients through assistive technologies*

#### Case study

Stroke affects approximately 150,000 people in the UK each year, with one third of patients requiring costly and labour-intensive rehabilitative care to restore lost movement. Researchers at the University of Southampton have developed innovative technologies to stimulate patients' muscles and support their rehabilitation, without requiring such intensive one-to-one practitioner-led care. Funding from the NIHR is generating the evidence to promote these technologies into widespread use, and ensure that the UK remains at the forefront of international best practice [1].

Functional electrical stimulation (FES) – the use of electrical pulses delivered directly to the nerves – as a means to facilitate movement in patients with nerve damage and paralysis, has been in use since the 1960s [2]. Led by Professor Jane Burridge, the Southampton team's early research demonstrated that implantable FES devices, which placed micro-stimulators into the limbs of stroke patients to restore movement, could be safe and effective [3], and improved users' quality of life [4].

In 2009, the NIHR funded a programme grant to examine the opportunities and barriers that would affect how FES, as well as other forms of assistive technology, might best translate into clinical practice to benefit stroke patients. The work involved searching the international literature for evidence of promising

treatments and consulting with stroke patients, their carers, health professionals and commissioners to understand the hurdles to the use of these technologies in the NHS [5]. The research provided a detailed picture of different users' views on the different factors – such as the design of devices', the types of clinical trials, and the provision of services – that could contribute to more effective stroke rehabilitation [6]. It also surveyed stroke interventions currently in practice in the UK, and assessed these in the context of both national and international guidelines, to determine a 'core' series of component treatments for limb rehabilitation following stroke, from the use of movement therapy through to assistive technologies [7].

Drawing on findings from this research, the Southampton team secured partnership funding to develop a multidisciplinary International MSc in Advanced Rehabilitation Technologies. This collaborative venture is coordinating different partners' use of new technologies to inform learning, harmonising educational methods and techniques, and linking education and research across Europe with industry partners [8].

There have also been efforts in training therapists worldwide. As president of the International Functional Electrical Stimulation Society (IFESS), Professor Burridge has hosted workshops to train therapists and both clinical and non-clinical specialists in the use of this technology. Overall, the Southampton team have trained more than 2,500 therapists in the use of FES, in 14 countries [1].

With further funding from the NIHR's Research for Patient Benefit programme, the team also developed and trialled web-based programmes, to help patients overcome habitual non-use of the arm or hand affected by stroke [9] By funding research into these assistive approaches, the NIHR is widening the therapeutic options available for patients with stroke, while reducing the need for costly one-to-one rehabilitative interventions [1].

## Evidence

[1] Research Excellence Framework. 2014. Innovative Technologies for Stroke Rehabilitation. [Case study 43853.] As of 3 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=43853>

Research Excellence Framework impact case study from the University of Southampton, detailing research to improve the effectiveness of technologies to aid patients' recovery of movement and independence, and the international impacts of this work.

[2] Liberson WT, Holmquest HJ, Scot D, Dow M. 1961. Functional electrotherapy: stimulation of the peroneal nerve synchronized with the swing phase of the gait of hemiplegic patients. *Archives of physical medicine and rehabilitation*. As of 3 May 2016: <http://www.ncbi.nlm.nih.gov/pubmed/13761879>

Paper detailing original use of electrotherapy as a means to stimulate movement in patients with paralysis.

[3] Burridge J, Haugland M, Larsen B, Pickering RM, Svaneborg N, Iversen HK, Brøgger Christensen P, Haase J, Brennum J, Sinkjaer T. 2007. Phase II trial to evaluate the ActiGait implanted drop-foot stimulator in established hemiplegia. *Journal of Rehabilitation Medicine* 39 (3): 212-218. doi:10.2340/16501977-0039

Results of a phase 2 trial of an implantable FES device, ActiGait, to improve walking in 15 participants who had suffered a stroke.

[4] BurrIDGE JH, Haugland M, Larsen B, Svaneborg N, Iversen HK, Brøgger Christensen P, Pickering RM, Sinkjaer T. 2008. Patients' perceptions of the benefits and problems of using the ActiGait implanted drop-foot stimulator. *Journal of Rehabilitation Medicine* 40 (10): 873-875. doi:10.2340/16501977-0268

Participants' views on the ActiGait device, indicating improvements in their quality of life and ease of use compared with 'surface' systems.

[5] National Institute for Health Research. 2009-2012. Development of an integrated service model incorporating innovative technology for rehabilitation of the upper limb following stroke. As of 3 May 2016: <http://www.nihr.ac.uk/funding/funded-research/funded-research.htm?postid=2213>

Details of the NIHR's programme grant to explore the use of assistive technologies and their delivery within the NHS.

[6] Hughes A, BurrIDGE JH, Holtum Demain S, Ellis-Hill C, Meagher C, Tedesco-Triccas L, Turk R, Swain I. 2014. Translation of evidence-based Assistive Technologies into stroke rehabilitation: users' perceptions of the barriers and opportunities. *BioMed Central Health Services Research* 14: 124. doi: 10.1186/1472-6963-14-124

Study of the views of patients, carers and healthcare professionals on barriers to the use of assistive technologies for stroke rehabilitation.

[7] McHugh G, Swain ID, Jenkinson D. 2014. Treatment components for upper limb rehabilitation after stroke: a survey of UK national practice. *Disability and rehabilitation* 36 (11): 925-931. doi:10.3109/09638288.2013.824034

Study of the types of treatment most commonly provided to treat patients with mild, moderate and severe impairment following stroke.

[8] Advanced Rehabilitation Technologies. Developing a trans-disciplinary European MSc. (homepage). As of 3 May 2016: <http://www.rehabtech.soton.ac.uk/>

Website of the Southampton team's MSc programme, providing a shared learning environment for students across a number of disciplines to study the use of rehabilitative technologies.

[9] Meagher C, Hughes A, Pollet S, Yardley L, BurrIDGE J. 2011. Development and pilot evaluation of a web-supported programme of Constraint Induced Therapy following stroke (LifeCIT). (At 6th UK Stroke Forum, Glasgow, GB, 29 Nov - 01 Dec 2011). As of 3 May 2016: <http://eprints.soton.ac.uk/272682/>

Further NIHR funding of a trial of intensive exercise of stroke-affected limbs, through the use of a mitt on patients' unaffected hands.

### *3.1.7. Informing the setup of health services to ensure equity of care for children born with cleft lip and palate*

#### **Case study**

Cleft lip and palate is a common malformation affecting one in every 600 babies. Estimates suggest that approximately every two minutes somewhere in the world a child is born with a cleft lip or palate [1].

Treatment for babies born with clefts is highly variable, with resource-poor countries at a greater risk of not repairing cleft palates, resulting in higher infant mortality rates for those affected [2]. In the UK, discrepancies in the quality of care for children born with cleft lip and palate identified in the 1990s resulted in a policy to centralise services to fewer numbers of specialist centres. To establish the impact of this reconfiguration, the NIHR funded a programme grant at the University of Bristol. Results of this research are prompting other international cleft service providers to adopt similar centralisation strategies to ensure the quality and equity of care in their countries [3].

Earlier work by the Bristol group had identified that outcomes for children born with a cleft lip and palate in the UK varied and were often suboptimal. It revealed, for example, that UK children were far more likely than their European counterparts to require multiple operations during the early years of their life, to correct for discrepancies in the growth of their upper and lower jaw – 40 per cent in the UK compared with just 4 per cent in the other European comparators. At the time, 57 centres across the country provided care for children with clefts. The aim of reconfiguring services, and basing them around a multidisciplinary model (where patients would receive care from surgeons, speech and language therapists and other specialists), was to improve outcomes for children, by treating them in fewer centres, with more highly trained staff [3].

With funding from the NIHR's Programme Grants for Applied Research, the Bristol team set out to evaluate and draw together the most effective ways of working across the newly reconfigured cleft lip and palate services. Their challenge was how to move cleft care from a predominantly audit-based (i.e. locally reflective) service, to one that applied evidence of national and international best practice [4].

The research showed that over the fifteen-year period evaluated, centralisation from 57 down to 11 more specialised multidisciplinary cleft lip and palate services in the UK improved outcomes for children. Surgeons had harmonised their surgical procedures, with half the numbers of children requiring corrective surgery to their upper jaw due to poor bone growth, compared with figures prior to centralisation of services. Speech outcomes were also better in significantly more children, with improvements in their self-confidence [5].

The Bristol team's NIHR-funded work collected sufficiently detailed data, from a large enough number of participating centres, to underpin future randomised controlled trials and observation studies, as part of an international data platform, such as in New Zealand, to ensure that patients receive care delivered to a consistent standard [6]. The NIHR's support of patient-focussed research, combined with an ongoing process of centralisation, has helped to reverse a situation where cleft lip and palate clinical care in children was based on low levels of evidence. This has ensured that the required clinical research infrastructure is now in place to run larger studies as part of a nationally and, increasingly, internationally-coordinated response [7].

## Evidence

[1] Mossey P, Little J. 2009. Addressing the challenges of cleft lip and palate research in India. *Indian Journal of Plastic Surgery* 42: S9-S18. doi: 10.4103/0970-0358.57182

Article exploring inequalities in healthcare coverage for children born with clefts in India, which also provides information on the global incidence of the disease.

[2] Cubitt J, Hodges A, Van Lierde K, Swan M. 2014. Global Variation in Cleft Palate Repairs: An Analysis of 352,191 Primary Cleft Repairs in Low- to Higher-Middle-Income Countries. *The Cleft Palate-Craniofacial Journal* 51 (5): 553-556. doi:10.1597/12-270

Results of a global survey of more than 350,000 cleft operations performed over a three-year period from 2008.

[3] Research Excellence Framework. 2014. Improving care for children born with cleft lip and palate in the UK and beyond. [Case study 40173.] As of 3 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=40173>

Research Excellence Framework impact case study detailing initial surveys of cleft services in the UK and more recent NIHR-funded efforts to establish the impact of policies to centralise services.

[4] National Institute for Health Research. 2009-2014. Evidence based health care for major congenital and acquired problems of the head and neck. As of 3 May 2016: <http://www.nihr.ac.uk/funding/funded-research/funded-research.htm?postid=2215>

Information on the NIHR's programme grant funding work by the Bristol team to examine the provision and quality of care of patients with cleft lip and palate and head and neck cancer.

[5] Ness AR, Wills AK, Waylen A, Al-Ghatam R, Jones TEM, Preston R, Ireland AJ, Persson M, Smallridge J, Hall AJ, Sell D, Sandy JR. 2015. Centralization of cleft care in the UK. Part 6: a tale of two studies. *Orthodontics & Craniofacial Research* 18 (Supplement S2): 56-62. doi: doi/10.1111/ocr.12111/epdf

Summary of findings of the NIHR-funded Bristol team's research to evaluate the impact of cleft care centralisation, collecting data from children born with a cleft lip and palate between April 2005 and March 2007.

[6] Health Research Council of New Zealand. n.d. Dr John Thompson. As of 3 May 2016: <http://www.hrc.govt.nz/funding-opportunities/recipients/dr-john-thompson>

Information on the first study to consistently collect outcome data in relation to cleft lip and palate in New Zealand, drawing on data from the NIHR-funded work of the Bristol team.

[7] Sandy J, Rumsey N, Persson M, Waylen A, Kilpatrick N, Ireland T, Ness A. 2012. Using service rationalisation to build a research network: lessons from the centralisation of UK services for children with cleft lip and palate. *British Dental Journal* 212: 553-555. doi: 10.1038/sj.bdj.2012.470

Paper evaluating how service reconfiguration in cleft lip and palate care in the UK has created opportunities for research.

### *3.1.8. Discontinuing the sale of co-proxamol as a policy measure to lower the risk of suicide*

#### Case study

Co-proxamol is an analgesic used to treat mild to moderate pain. It is a combination of two active ingredients: paracetamol and dextropropoxyphene. This was the most frequently used drug for suicide in

England and Wales leading to 766 deaths between 1997 and 1999 [1]. Following a 2005 Medicines and Healthcare Products Regulatory Agency (MHRA) review of co-proxamol's safety and efficacy profile, it was announced that the product would be withdrawn from use in the UK by 31 December 2007 [2]. Between 2005 and 2007, doctors were asked not to prescribe this pain killer to any new patients and to switch to other analgesics in the case of patients who were already being medicated with co-proxamol [1]. Between 2007 and 2011, the NIHR funded a research programme in support of the National Suicide Prevention Strategy for England. This programme brought together leading researchers in self-harm and suicide from the Universities of Bristol, Oxford and Manchester. Professor Keith Hawton, who led the team on co-proxamol studies in Oxford, benefited from an NIHR Senior Investigator Award (2009-14) that further supported his work in this field. The teams evaluated the impact of the MHRA decision on analgesic prescribing and poisoning mortality [3]. The findings have informed European and UK medicine regulatory activity on co-proxamol. Following the UK and European decisions, other countries have also discontinued the use of co-proxamol [3].

The team investigated two types of impact: (1) the impact of the initial withdrawal phase (2005–07) and (2) the overall impact of this decision including data from the three subsequent years of full withdrawal [3]. Withdrawal of co-proxamol in the UK was found to have had important consequences in reducing the number of poisoning deaths involving this drug, namely an estimated 295 fewer suicides and 349 fewer deaths, including accidental poisonings. This amounts to more than 600 fewer deaths within the six-year period. Despite an increase in prescribing of other analgesics 20 per cent for co-codamol, 13 per cent for paracetamol, 12 per cent for co-dydramol and 8 per cent for codeine there was no evidence of significant substitution of poisoning with these medicines [4]. The research on co-proxamol is one of most important cited contributions to the National Suicide Prevention Strategy for England [1][5].

These findings were presented to the European Medicines Agency and influenced its decision to recommend, to the European Union, the ending of dextropropoxyphene prescribing in June 2010 [6]. The UK and European Union actions prompted the US Food and Drug Administration to withdraw dextropropoxyphene in the USA in 2010. Similarly in 2010, Health Canada announced dextropropoxyphene withdrawal. These withdrawals were followed by action in New Zealand, Singapore, Taiwan and India.

This NIHR funded research has enlarged the evidence base and contributed to further policy changes to lower suicide risk, including the withdrawal of dextropropoxyphene from countries in the European Union and from other countries.

## Evidence

[1] Research Excellence Framework. 2014. Withdrawal of co-proxamol: A successful international suicide prevention initiative. [Case study 4882.] As of 2 May 2016:  
<http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=4882>

The case study offers an overview of the research performed by the team led by Professor Keith Hawton in Oxford, highlighting the research that informed the MHRA decision to discontinue co-proxamol, as well as the subsequent international impact.

[2] Medicines and Healthcare Products Regulatory Agency. 2004. Withdrawal of co-proxamol products and interim updated prescribing information. [CEM/CMO/2005/2.] London: Medicines and Healthcare products Regulatory Agency. As of 2 May 2016: <https://assets.digital.cabinet-office.gov.uk/media/547307ede5274a1303000023/con019461.pdf>

[3] Gunnell D, Hawton K, Bennewith O, Cooper J, Simkin S, Donovan J, Evans J, Longson D, O'Connor S, Kapur N. 2013. A multicentre programme of clinical and public health research in support of the National Suicide Prevention Strategy for England. Programme Grants for Applied Research 1 (1). doi: 10.3310/pgfar01010

This is the programme grant for applied research report, describing in detail all the research undertaken as part of the research programme.

[4] Department of Health. 2011. Preventing suicide in England – A cross-government outcomes strategy to save lives. London: Department of Health. As of 2 May 2016: [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/430720/Preventing-Suicide-.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/430720/Preventing-Suicide-.pdf)

This is the 2012 strategy for preventing suicide in England. It references several publications that resulted from the multicentre programme.

[5] Hawton K, Bergen H, Simkin S, Wells C, Kapur N, Gunnell D. 2012. Six-year follow-up of impact of co-proxamol withdrawal in England and Wales on prescribing and deaths: Time-series study. PLoS Medicine 9 (5): e1001213. doi: 10.1371/journal.pmed.1001213

The article concludes that during the six years following the withdrawal of co-proxamol in the UK, there was a significant reduction in poisoning deaths involving this medicine. The article is also cited in reference [4].

[6] European Medicines Agency. 2009. European Medicines Agency recommends withdrawal of dextropropoxyphene-containing medicines. [Press release EMEA/401062/2009.] London: EMEA. As of 2 May 2016: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Press\\_release/2009/11/WC500010365.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2009/11/WC500010365.pdf)

Press release from the European Medicines Agency on the 25<sup>th</sup> June 2009, recommending the withdrawal of dextropropoxyphene-containing medicines.

### *3.1.9. Establishing a globally-relevant evidence base to underpin trials of new therapies for childhood eczema*

#### Case study

Eczema affects up to a fifth of children worldwide, with the numbers of cases steadily rising [1]. Professor Hywel Williams, an NIHR Senior Investigator based at the University of Nottingham's Centre of Evidence-Based Dermatology, has led international efforts to improve the quality and relevance of research into this and other skin diseases.

Prior to the NIHR's establishment, the Health Technology Assessment programme had funded Professor Williams and his team to conduct a systematic review of trials of eczema treatment [2]. The review helped



to identify treatments that worked – for example topical corticosteroids – and set priorities for further research [1].

In 2008, the NIHR funded Professor Williams to lead a programme grant focused on improving treatments for four skin diseases, including eczema [3]. This enabled Professor Williams and his team to consolidate their previous work, building on and updating their initial systematic review to create a Global Resource of Eczema Trials, known as the ‘GREAT’ database [4]. GREAT streamlined the process of finding relevant evidence for clinicians, and sought to shorten the duration and costs of other clinical eczema studies by pooling the existing literature on eczema research, in order to prevent unnecessary international duplication [5]. Professor Williams also contributed to ongoing work to map the global prevalence of eczema, as part of the world’s largest epidemiological study, the International Study of Asthma and Allergies in Childhood (ISAAC) [6]. The ISAAC criteria remain the most widely used method to diagnose eczema worldwide [1].

Professor Williams and his team’s work has provided evidence for clinical guidelines on treating eczema in children, aimed at dermatologists, paediatricians and general practitioners in the UK and internationally in South Africa, Europe, New Zealand and Japan [1]. The work has also underpinned further NIHR-funded clinical studies. For example, Health Technology Assessment programme funding enabled the team to carry out a randomised controlled trial of water softeners as an effective treatment option. The trial found that installing a water softener for three months brought about no additional relief to children with eczema [7]. If even only 10 per cent of the 400,000 UK families who had children with eczema did not buy a water softener, the team estimated they would save around £4 million over a three year period [1].

The team’s work also developed validated scales for patients to rate the severity of their disease – so-called ‘patient-reported outcome measures’ (PROMs). These are helping to capture patients’ own perceptions of their responses to the treatment they receive [1]. An eczema-specific PROM is recommended in both the UK, via the National Institute for Clinical Excellence (NICE), and the US, with an internationally-focused initiative, ‘HOME’ (which Professor Williams co-founded), recommending it as a means to compare data across clinical trials databases [8].

With the NIHR’s support, Professor Williams and his team have conducted research of direct relevance to patients and clinicians around the world. Their focus on generating and synthesising clinically relevant evidence underpins, and improves methods to treat a common condition that causes suffering to large numbers of children in the UK and internationally.

## Evidence

[1] Research Excellence Framework. 2014. Reducing treatment uncertainties for childhood eczema. [Case study 41001.] As of 2 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=41001>

Research Excellence Framework impact case study noting the NIHR’s – and, before its establishment, the NHS R&D programme’s – investment in research at the Centre of Evidence Based Dermatology at the University of Nottingham and the contribution of this work towards internationally relevant changes in policy and practice.

[2] Hoare C, Li Wan Po A, Williams H. 2001. Systematic review of treatments for atopic eczema. *Health Technology Assessment* 4 (37). doi: 10.3310/hta4370

Health Technology Assessment–funded systematic review to produce a map of randomised controlled trials of eczema treatments and summarise the available evidence.

[3] National Institute for Health Research. 2008-2013. Setting priorities and reducing uncertainties in the prevention and treatment of people with skin diseases. As of 3 May 2016:

<http://www.nihr.ac.uk/funding/fundingdetails.htm?postid=2130>

Programme grant outlining a strategy and topics for improving the treatment of patients with eczema, as well as three other common skin diseases.

[4] Global Resource for Eczema Trials. n.d. Background. As of 2 May 2016:

<http://www.greatdatabase.org.uk/GD4/Home/Background.php>

Information on the purpose and funding of the GREAT database as a resource to reduce duplication in eczema clinical research.

[5] Nankervis H, Maplethorpe A, Williams HC. 2011. Mapping randomized controlled trials of treatments for eczema - The GREAT database (The Global Resource of Eczema Trials: a collection of key data on randomized controlled trials of treatments for eczema from 2000 to 2010). *BioMed Central Dermatology* 11: 10. doi: 10.1186/1471-5945-11-10

Article summarising the purpose and methods behind the GREAT database, outlining its role as a publically available and comprehensive map of clinical research into eczema.

[6] Odhiambo JA, William HC, Clayton TO, Robertson CF, Asher MI, ISAAC Phase Three Study Group. 2009. Global variations in prevalence of eczema symptoms in children from ISAAC Phase Three. *Journal of Allergy and Clinical Immunology* 124 (6): 1251-1258. doi:10.1016/j.jaci.2009.10.009

Results of the third phase of the world's largest epidemiological study to map the prevalence of eczema.

[7] Thomas KS, Dean T, O'Leary C, Sach TH, Koller K, Frost A, William HC, the SWET Trial Team. 2011. A Randomised Controlled Trial of Ion-Exchange Water Softeners for the Treatment of Eczema in Children. *PLoS Medicine* 8(2): e1000395. doi:10.1371/journal.pmed.1000395

Health Technology Assessment–funded randomised controlled trial involving 336 children aged 6 months to 16 years old to determine whether water softeners provide relief from the symptoms of eczema.

[8] Centre of Evidence Based Dermatology. n.d. POEM – Patient Oriented Eczema Measure. AS of 3 May 2016: <https://www.nottingham.ac.uk/research/groups/cebd/resources/poem.aspx>

Page noting use of the Nottingham team's eczema-specific PROM in UK clinical guidelines and the internationally focussed HOME initiative.

### 3.1.10. *Transforming the safety and longevity of replacement knee joints through simulations*

#### Case study

Building on a commercial partnership spanning more than two decades, a collaboration among the NIHR-funded Leeds Musculoskeletal Biomedical Research Unit (LMBRU), the University of Leeds Institute of Medical and Biological Engineering (iMBE), and Simulation Solutions is setting international standards for testing artificial joints. The research is contributing to global efforts to design and test better implants for patients needing knee replacements, by developing artificial joints designed to last longer in an ageing population. Professor John Fisher, an NIHR Senior Investigator and co-director of the LMBRU, sums up the challenge facing those working in the field of medical engineering and artificial joints:

‘It’s estimated that by 2030 there’ll be five times more knee replacements in the world than there are currently. So what we’ve got to do is produce interventions that will last for 50 years. This could mean that an artificial knee joint would undergo over a hundred million steps in the patient’s lifetime’ [1].

This challenge forms the basis of the ‘50 active years after 50’ initiative, which brings together such groups as the NIHR-funded LMBRU to drive innovation in musculoskeletal research [1].

One goal of the initiative is to improve artificial joint performance to meet the demands of younger and more active patients. This work draws on the Leeds group’s long-standing collaboration with Simulation Solutions, a Manchester-based company that produces bioengineering simulators to test the design of replacement joints. Based out of an academic testing facility at the iMBE, the Leeds group has developed advanced computational and experimental methods to assess how well different joint replacement designs perform under a range of simulated clinical conditions [2].

Working together, the LMBRU, the iMBE and Simulation Solutions identified a global need for growing markets – such as those in China and Japan – to have access to simulators capable of testing artificial joints to higher standards than the current industry requirement [1]. Drawing on a vast databank of simulation tests, more than 5 billion cycles of reference data, the group co-developed standard operating procedures (SOPs) that would allow other joint replacement manufacturers to test their devices under equivalent conditions. These SOPs ensure that other academic or commercial organisations can generate reliable and robust pre-clinical data when using the simulators, in spite of their complexity [2].

The partnership is generating international impacts through its licensing of the simulation technology to organisations in China, India, Australia and elsewhere in Europe. For example, in response to an increasingly rigorous regulatory environment in China, the group has entered into an agreement with one of nine Chinese outposts of the US Food and Drug Administration (in Tianjin) to install simulators in its laboratories. This is helping to build local capacity to test devices manufactured in China, and to allow local authorities to gain more meaningful safety data, prior to obtaining regulatory approval [3].

The NIHR’s funding of research at the LMBRU is ensuring that the technology underpinning replacement joints keeps in step with patients’ needs, both in the UK, and around the world.

## Evidence

[1] The National Institute for Health Research Office for Clinical Research Infrastructure. n.d. NIHR Clinical Research Infrastructure Collaborations: Medical device and diagnostics industry partnerships. As of 9 May 2016: <http://www.nihr.ac.uk/documents/industry/Brochures/Medical-device-and-diagnostics-industry-partnerships.pdf>

NIHR brochure highlighting a series of successful research partnerships with manufacturers of medical device and diagnostics.

[2] Research Excellence Framework. 2014. Lower wearing, longer lasting joint replacements in the hip and knee. [Case study 6341.] As of 9 May 2016:

<http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=6341>

REF impact case study detailing underpinning research into joint simulation research at the University of Leeds, charting the collaboration with Simulation Solutions and describing international impacts arising from this work.

[3] Institute of Medical and Biological Engineering. 2013; 13 January. Leeds expertise helps company reach worldwide markets. As of 9 May 2016:

[http://www.imbe.leeds.ac.uk/news/Leeds\\_expertise\\_helps\\_company\\_reach\\_worldwide\\_markets\\_January2013.shtml](http://www.imbe.leeds.ac.uk/news/Leeds_expertise_helps_company_reach_worldwide_markets_January2013.shtml)

News release announcing international licensing of the Leeds group's simulation technology, with training of local staff in foreign outposts of the US Food and Drug Administration in Tianjin, China.

## 4. Making the nation's health and care system the best it can be

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### 4.1. Summary

**High-quality. Efficient. Deliverable.**

*NIHR funds research to inform, support and improve the quality, accessibility and organisation of health services. By making better use of information and resources, the evidence that this research generates offers options for sustaining and improving the NHS.*

The NHS is committed to providing high-quality healthcare for all, irrespective of age, health, race, social status or ability to pay. To do this, the NHS must continue to adapt to take advantage of new opportunities offered by science and technology.

At the disease level, numerous studies about the cost-effectiveness of specific treatments contribute to improved accessibility and better coverage of targeted populations. NIHR funds research aimed at providing higher-quality, safer and more effective and cost-effective products and solutions. Examples include the following:

- Studies into continuous subcutaneous insulin infusion for patients with diabetes are helping to educate and empower patients, improving their quality of life and likely minimising the burden on the health system by reducing their reliance on other services.
- Research into methods of expediting treatment for patients suspected of having a transient ischaemic attack ('mini-stroke') has provided a route to preventing 10,000 strokes per year, potentially saving £624 per patient and up to £200 million annually in acute care costs in the NHS.
- Research into cognitive stimulation therapy has shown it can improve memory and language functions for people with mild and moderate dementia. This therapy could save the NHS an estimated £54.9 million a year as a result of decreased use of antipsychotic medication.

NIHR funding is directly impacting on the quality of patient care through workforce interventions and knowledge sharing, as exemplified by the following:

- The Radiotherapy Trials Quality Assurance Team ensures that medical staff respect the highest standards when it comes to clinical research that has a radiotherapy component, helping professionals to transfer research knowledge to regular care through a continuous exchange of ideas.
- The Hyper-Acute Stroke Research Centres offer stroke patients the option to participate in trials of the latest 'clot-busting' therapies and have led to efforts to capture data that enhance the

quality of emergency care and improve stroke care organisation and delivery. NIHR's funding facilitated research that is difficult to conduct in traditional settings due to tight time constraints.

- The Enabling Research in Care Homes programme is helping to develop and sustain a network of 'research-ready' care homes so that residents, especially those with dementia, can take part in appropriate studies and trials. NIHR invested over £10 million in 2013 in care home research, contributing to a more inclusive health and social care system.

By financing research into service organisation and delivery, NIHR also contributes to a health and social care system which makes better use of information and resources. Examples of such research include the following:

- Studies to advance the European EQ-5D framework have allowed further development of measurement instruments that capture the health preferences of the general public. The framework fosters a culture of health system monitoring, providing accountability and transparency in healthcare decisions.
- The findings of the Birthplace in England study are providing evidence for services that offer women a choice of birth setting and are steering the healthcare system towards safer and more cost-effective births in England.
- The Clinical Record Interactive Search and the Clinical Practice Research Datalink – systems that capture and link medical data from different sources for use in research – promote the development of more efficient and resilient information systems. Both are helping to inform changes in clinical practice, for example, by identifying appropriate services for people with severe mental health illnesses on the basis of the severity of their symptoms.
- NIHR has put systems in place to improve the efficient and prompt set-up and delivery of clinical research itself, such as the introduction of contracts between the Department of Health and Local Clinical Research Networks and the initial introduction of a 'research passport' to streamline permissions to undertake research across multiple clinical locations, now managed by the Health Research Authority.

#### *4.1.1. Judging the cost-effectiveness of medicines to inform healthcare decisions and valuations*

Measuring and monitoring patient health is central to making evidence-informed decisions on health and healthcare. These assessments rely on such measurement instruments as European Quality of Life 5-Dimensions (EQ-5D), which is a standardised tool developed in Europe and used worldwide[1] to capture the self-reported health preferences of the general public. Professor Nancy Devlin's work on methods for valuing quality of life, in order to advance the way EQ-5D can be used, has been supported through many funding streams including the NIHR [2][3][4].

EQ-5D uses are particularly important because results from these analyses inform a variety of decision-making processes within the healthcare system, including: National Institute for Health and Care Excellence (NICE) decisions about reimbursement and pricing of new technologies; NHS 'need-based' allocations of budgets across regions; assessments of provider performance; and analyses of the value for money of health care services. The EQ-5D is also used in the NHS Patient Reported Outcome Measures

(PROMs) survey which captures patients' experiences of the access to and quality of healthcare they receive [5]. This, in turn, leads to a healthcare system that can monitor and improve the performance of healthcare providers, quality of services and patient health [6]. In other words, it allows for an in-depth analysis based on the public's values to inform the allocation of taxpayer contributions. This continuously refined methodology also reflects the importance of capturing patients' views and values when it comes to their own health, fostering a 'patient-centred' approach.

Professor Devlin's research is influential worldwide, fostering a culture of health system monitoring and providing accountability and transparency for healthcare decisions. The research has made significant methodological contributions to the use of EQ-5D contributions which have been widely adopted throughout the health system and which translate into the use of PROMs in economic evaluations and clinical trials. These are the foundations for a health care system that can continuously measure progress and identify areas of improvement.

## Evidence

[1] Gusi N, Olivares PR, Rajendram R. 2010. The EQ-5D Health-Related Quality of Life Questionnaire. In: Preedy VR, Watson RR (eds.) Handbook of Disease Burdens and Quality of Life Measures. New York: Springer.

This chapter explains the EuroQoL five dimensions questionnaire (EQ-5D). The authors highlight that the conceptual basis of the EQ-5D is the holistic view of health, capturing both the clinical and the psychological aspects. The chapter also details the structure and purpose of the EQ-5D – a questionnaire and a visual analogue scale (known as EQ-VAS). The EQ-VAS captures the respondents' perceptions of their own current overall health on a scale, while the self-assessment questionnaire is self-reported description of their health state in five dimensions, i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each health state can be transformed into a score, which is an expression of the quality-adjusted life years. This is commonly used in cost-effectiveness analysis.

[2] Devlin N, Parkin D, Browne J. 2010. Patient reported outcome measures in the NHS: New methods for analyzing and reporting EQ-5D data. *Health Economics* 19 (8): 886-905. doi:10.1002/hec.1608

The article reports an analysis of the EQ-5D data generated from a pilot study commissioned by the Department of Health aimed at investigating the implications for the use of EQ-5D data in performance indicators and measures of patient benefit. The research presents two new methods that had been developed for analysing and displaying EQ-5D profile data.

[3] Devlin N, Buckingham K, Tsuchiya A, Shah K, Tilling C, Wilkinson G, Van Hout B. 2013. A comparison of alternative variants of the lead and lag time TTO. *Health Economics* 22 (5): 517-32. doi:10.1002/hec.2819

The methods used to value EQ-5D include Time Trade Off (TTO), Discrete Choice Experiments, Visual Analogue Scale and Standard Gamble. The concept behind the TTO method is to find out how much time people are willing to trade off, with more time expected to be traded off with the worsening of the health state. This research presents a methodological contribution of replacing TTO with 'Lead Time' TTO. This improves upon conventional TTO by providing a uniform method for eliciting positive and

negative values. The values are sensitive to the ratio of lead time to duration of poor health and to the order in which these appear (lead vs lag).

[4] Oppe M, Devlin NJ, Van Hout B, Krabbe PFM, De Charro F. 2014. A program of methodological research to arrive at the new international EQ-5D-5L valuation protocol. *Value in Health* 17: 445-53. doi: 10.1016/j.jval.2014.04.002

The research reports on the methods used to develop the EQ-5D-5L value set for England. It also mentions that the value set to be produced will be used by healthcare decisionmakers, such as the English Department of Health and NICE. The paper explores several methodological issues relating to the analysis of valuation data, including how different data – Time Trade Off and Discrete Choice – can be used in modelling health state values.

[5] Devlin NJ, Krabbe PFM. 2013. The development of new research methods for the valuation of EQ-5D-5L. *European Journal of Health Economics* 14 (Suppl 1): 1-3. doi:10.1007/s10198-013-0502-3

The article describes the advancement of the methods for health-state valuation for the newly developed EQ-5D-5L. The piece stresses that for the first time, the European Quality of Life (EuroQol) group has a fully documented research protocol that will ensure that studies are undertaken to a high standard, using a consistent study design and methods for collecting health-state values. The potential of this approach is, among others, that it would allow international comparisons of values for EQ-5D-5L.

[6] Research Excellence Framework. 2014. International impact on the measurement of patient health and its use in health care decision-making. [Case study 44370.] As of 2 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=44370>

The case study highlights Professor Devlin's significant contributions to the refining of the European Quality of Life 5-Dimensions. The piece offers an overview of the milestones in her research, stressing her scientific leadership at the EuroQol group. The impact of all her research is worldwide and highly significant in improving health and healthcare decisionmaking.

#### *4.1.2. Implementing evidence-based brief group therapy (cognitive stimulation therapy) for people with mild to moderate dementia*

##### Case study

The Alzheimer's Society estimated that in 2015 there were 850,000 people living with dementia and predicted that this number will rise to more than 2 million by 2051 [1]. In addition to personal suffering for the patients and their families, this disease also triggers high societal costs; currently dementia costs the UK £26.3 billion a year. The development and adoption of cognitive stimulation therapy (CST) has led to important patient benefits and health system savings.

In 2003, a team at University College London, in collaboration with Bangor University, developed CST, an evidence-based, brief treatment for people with mild to moderate dementia [2]. The NIHR has supported the development of CST through several awards [2]. This programme consists of structured sessions for small groups that involve physical exercises and activities aimed to stimulate and engage



patients cognitively. The group facilitator is a trained person who works with patients with dementia. Usually the CST sessions take place in hospitals, residential homes, care homes, or day centres.

While the main beneficiaries of the CST are the patients, this therapy also has important impacts on the health system itself. CST was shown to lead to improved cognitive functioning; for example improved memory and orientation capacities, as well as improved language skills in the areas of naming, word-finding and comprehension [3]. In addition to contributing to patients improved cognition and communication, CST contributes to better social interaction, well-being and quality of life [4][5]. The benefit of CST is similar to that obtained using anti-dementia drugs [6]. Research has shown that weekly CST sessions can lead to cognitive function improvement for a six-month period from the initial programme. CST has been shown to be cost-effective [7], and the NHS Institute for Innovations [8] stated that CST can save the NHS £54.9 million a year as a result of decreased use of antipsychotic medication. This represents important cost savings for the health system as a whole.

In order to enable the benefits of CST at the health system level, the Bangor research team produced manuals and training programmes to encourage international practitioners to adopt the team's findings. These efforts have been a success, with wide international adoption of the therapy in Australia, as well as in countries located in Africa, the Americas, Asia and Europe [9].

The National Institute for Health and Care Excellence (NICE) [10] recommended CST for people with mild/moderate dementia and the 2011 World Alzheimer Report [11] states that people with early-stage dementia should receive CST. The Memory Services National Accreditation Programme now offers CST routinely in 66 per cent of UK memory services [2], highlighting the uptake of this beneficial therapy into health services and the healthcare system as a whole.

## Evidence

[1] Alzheimer's Society. 2016. Dementia 2014 infographic. As of 2 May 2016:  
<https://www.alzheimers.org.uk/infographic>

The infographic offering prevalence and cost data on dementia.

[2] Research Excellence Framework. 2014. Cognitive Stimulation Therapy – A new therapy for dementia. [Case study 36382.] As of 2 May 2016:  
<http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=36382>

The case study tracks the development and impact of CST, offering details on the underpinning research and impact of this therapy.

[3] Spector A, Orrell M, Woods B. 2010. Cognitive Stimulation Therapy (CST): Effects on different areas of cognitive function for people with dementia. *International Journal of Geriatric Psychiatry* 25 (12): 1253-8. doi: 10.1002/gps.2464.

Based on the results from a multicentre, single-blind, randomised controlled trial, the research concludes that CST has particular effects in promoting language function, which is expected to lead to generalised benefits.

[4] Aguirre E, Woods RT, Spector A, Orrell M. 2013. Cognitive stimulation for dementia: A systematic review of the evidence of effectiveness from randomised controlled trials. *Ageing Research Reviews* 12 (1): 253-62. doi: 10.1016/j.arr.2012.07.001

This systematic review identified a consistent significant benefit to cognitive function following CST treatment. The identified benefits appeared to be over and above any medication effects and remained evident at follow-up up to three months after the end of treatment. Benefits were also noted for quality of life and well-being and on staff ratings of communication and social interaction. The review recommends that CST should be made more widely available in dementia care.

[5] Woods B, Aguirre E, Spector AE, Orrell M. 2012. Cognitive stimulation to improve cognitive functioning in people with dementia. *Cochrane Database of Systematic Reviews* 2012 2:CD005562. doi: 10.1002/14651858.CD005562.pub2.

The research is a systematic review on cognitive stimulation to identify its effectiveness. The findings are that CST benefits cognition in people with mild to moderate dementia over and above any medication effects. Although the included trials were found to be of variable quality, improvements in self-reported quality of life and well-being were promising.

[6] Cognitive Stimulation Therapy. 2016. International CST groups. As of 2 May 2016: <http://www.cstdementia.com/page/international-cst-groups>

The page lists the worldwide established CST groups.

[7] Knapp M, Thorgrimsen L, Patel A, Spector A, Hallam A, Woods B, Orrell M. 2005. Cognitive Stimulation Therapy for people with dementia: Cost effectiveness analysis. *British Journal of Psychiatry* 188: 574-80. doi: 10.1192/bjp.bp.105.010561

The research is a randomised control trial that concludes that, under reasonable assumptions, there is a high probability that CST is more cost effective than treatment as usual, with regard to both outcome measures.

[8] NHS Institute for Innovation and Improvement. 2011. An economic evaluation of alternatives to antipsychotic drugs for individuals living with dementia. Coventry: NHS Institute for Innovation and Improvement, University of Warwick.

The economic evaluation explains that, combining healthcare cost savings and quality of life improvements, behavioural interventions generate a net benefit of nearly £54.9 million per year.

[9] Cognitive Stimulation Therapy. 2016. The evidence-base. As of 2 May 2016: <http://www.cstdementia.com/page/the-evidence-base>

The page offers a selection of available research conducted in relation to CST.

[10] National Institute for Health and Care Excellence. 2006. Dementia: Supporting people with dementia and their carers in health and social care. [CG42.] As of 2 May 2016: <https://www.nice.org.uk/guidance/cg42>

The guideline recommends that 'people with mild/moderate dementia of all types should participate in group Cognitive Stimulation which should be commissioned and provided by a range of health and social

care workers with training and supervision. This should be delivered irrespective of any anti-dementia drug received by the person with dementia’.

[11] Alzheimer’s Disease International. 2011. World Alzheimer report 2011. London: Alzheimer’s Disease International. As of 2 May 2016: <http://www.alz.co.uk/research/WorldAlzheimerReport2011.pdf>

The report states that there is strong evidence that cognitive stimulation (for cognitive function) is an effective intervention in mild dementia.

#### *4.1.3. Structuring self-education programme and studies into continuous subcutaneous insulin infusion therapy (CSII) for patients with diabetes*

##### Case study

Type 1 diabetes mellitus (T1DM) is a chronic disease that often first presents at a young age. The patient requires lifelong medication and monitoring. In 2015 the estimated prevalence of type 1 diabetes in children and young people under the age of 15 in England and Wales was 187.7 per 100,000. This is considered to be a high number and yet, is likely to be an underestimate as not all children over the age of 15 are seen in paediatric care [1]. The NIHR has supported a number of research projects aimed at empowering patients to better manage their T1DM, with the ultimate impact of the improving quality of life of individuals with the condition and bringing consistent savings to the health system.

Despite being a manageable clinical condition, diabetes brings with it increased risks of heart attack, stroke, sight loss, kidney failure or foot problems that can lead to amputation. These complications can occur as a result of poor management of diabetes leading to incorrect levels of insulin in the blood. When insulin levels are too high and the level of glucose in the blood falls, hypoglycaemia can set in, which in severe cases could lead to convulsions or death.

The management of diabetes requires testing and monitoring, and therefore can lead to additional costs to the health system for medical procedures and hospitalisations resulting from diabetes complications, as described above [2].

An example of NIHR-supported research aimed at educating T1DM patients to better manage their condition is the Dose Adjustment For Normal Eating (DAFNE) programme. This is a structured five-day patient education program on how to adjust insulin therapy to take account of food and exercise by effectively monitoring one’s blood glucose levels. Research has found that the DAFNE programme led to better glycaemic control, as shown by measurements of glycated haemoglobin, significant improvement in psychological well-being, and satisfaction with treatment, as well as significant decrease in perceived frequency of hyperglycaemia [3]. Following this success, the programme has been rolled out in health centres across the UK, impacting on education of patients nationwide. Approximately 900 UK healthcare professionals and 27,983 UK adults with T1DM enrolled in 4,045 courses had been trained by the middle of 2013 [4].

As anticipated, educating patients has translated into positive outcomes at the health system level. Research validated the positive effect of DAFNE on glycaemic control and also showed the benefits that the programme has had for the health system. They found that emergency call-outs for severe

hypoglycaemia fell from 10 episodes in 7 patients to 1 episode in 1 patient in the course of a year [5]. DAFNE courses were also found to reduce psychological distress and improve perceived well-being [6].

However, there are still cases where diabetes control remains problematic despite benefiting from the DAFNE approach. For example, achieving a good control of blood glucose via multiple daily injections can be difficult during the night-time. Building on the success of DAFNE, the NIHR has also funded research into continuous subcutaneous insulin infusion (CSII) via pump therapy. This therapy tries to mimic the release of insulin that would be done by a normal pancreas. In order for this therapy to be used within the healthcare system, it was appraised by the National Institute for Health and Care Excellence (NICE) in 2008 and recommended for children younger than 12 years with T1DM where multiple daily injections are impractical or inappropriate [7]. CSII is also recommended for type 1 diabetes patients older than 12 for whom multiple daily insulin therapy has not worked. In 2010, an evidence synthesis funded by the NIHR's Health Technology Assessment (HTA) programme reinforced this recommendation and showed that continuous subcutaneous insulin infusion has some advantages over multiple daily insulin injections for both adults and children who have T1DM [8]. These appraisals have relied on several studies that demonstrated the effectiveness of CSII [9][10] and has led to wider adoption across the UK.

The work on CSII has had policy impact by informing several UK guidelines, such as the NHS Technology Adoption Centre's 'How to Why to' guide, which furthered the diffusion and adoption of insulin pump therapy across the UK. This led to a 4 per cent increase in usage among affected adults between 2008 and 2012 [4]. In 2013, more than 13,400 adults and 5,000 children were using CSII pumps, resulting in improved blood glucose control and a better quality of life [11]. Among the quality of life benefits, NICE mentions flexibility of lifestyle, autonomy, and improved sleep and socialisation [7]. These positive psychological outcomes would suggest future impacts at the health system level are possible by reducing the usage of other services, in particular those aimed at improving mental health, although we do not have evidence for these as yet.

In summary, NIHR-funded research into the structured self-education programme and continuous subcutaneous insulin infusion therapy for patients with type 1 diabetes has translated into direct clinical and psychological benefits for patients at risk of hypoglycaemia. It has led to educated and empowered patients who can better manage their condition, thus optimising health services by making use of innovation and bringing savings to the health system by reducing usage of emergency call-out services.

## Evidence

[1] Alzheimer's Society. 2016. Dementia 2014 infographic. As of 2 May 2016:

<https://www.alzheimers.org.uk/infographic>

The infographic offering prevalence and cost data on dementia.

[2] Research Excellence Framework. 2014. Cognitive Stimulation Therapy – A new therapy for dementia. [Case study 36382.] As of 2 May 2016:

<http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=36382>

The case study tracks the development and impact of CST, offering details on the underpinning research and impact of this therapy.

[3] Spector A, Orrell M, Woods B. 2010. Cognitive Stimulation Therapy (CST): Effects on different areas of cognitive function for people with dementia. *International Journal of Geriatric Psychiatry* 25 (12): 1253-8. doi: 10.1002/gps.2464.

Based on the results from a multicentre, single-blind, randomised controlled trial, the research concludes that CST has particular effects in promoting language function, which is expected to lead to generalised benefits.

[4] Aguirre E, Woods RT, Spector A, Orrell M. 2013. Cognitive stimulation for dementia: A systematic review of the evidence of effectiveness from randomised controlled trials. *Ageing Research Reviews* 12 (1): 253-62. doi: 10.1016/j.arr.2012.07.001

This systematic review identified a consistent significant benefit to cognitive function following CST treatment. The identified benefits appeared to be over and above any medication effects and remained evident at follow-up up to three months after the end of treatment. Benefits were also noted for quality of life and well-being and on staff ratings of communication and social interaction. The review recommends that CST should be made more widely available in dementia care.

[5] Woods B, Aguirre E, Spector AE, Orrell M. 2012. Cognitive stimulation to improve cognitive functioning in people with dementia. *Cochrane Database of Systematic Reviews* 2012 2:CD005562. doi: 10.1002/14651858.CD005562.pub2.

The research is a systematic review on cognitive stimulation to identify its effectiveness. The findings are that CST benefits cognition in people with mild to moderate dementia over and above any medication effects. Although the included trials were found to be of variable quality, improvements in self-reported quality of life and well-being were promising.

[6] Cognitive Stimulation Therapy. 2016. International CST groups. As of 2 May 2016: <http://www.cstdementia.com/page/international-cst-groups>

The page lists the worldwide established CST groups.

[7] Knapp M, Thorgrimsen L, Patel A, Spector A, Hallam A, Woods B, Orrell M. 2005. Cognitive Stimulation Therapy for people with dementia: Cost effectiveness analysis. *British Journal of Psychiatry* 188: 574-80. doi: 10.1192/bjp.bp.105.010561

The research is a randomised control trial that concludes that, under reasonable assumptions, there is a high probability that CST is more cost effective than treatment as usual, with regard to both outcome measures.

[8] NHS Institute for Innovation and Improvement. 2011. An economic evaluation of alternatives to antipsychotic drugs for individuals living with dementia. Coventry: NHS Institute for Innovation and Improvement, University of Warwick.

The economic evaluation explains that, combining healthcare cost savings and quality of life improvements, behavioural interventions generate a net benefit of nearly £54.9 million per year.

[9] Cognitive Stimulation Therapy. 2016. The evidence-base. As of 2 May 2016: <http://www.cstdementia.com/page/the-evidence-base>

The page offers a selection of available research conducted in relation to CST.

[10] National Institute for Health and Care Excellence. 2006. Dementia: Supporting people with dementia and their carers in health and social care. [CG42.] As of 2 May 2016: <https://www.nice.org.uk/guidance/cg42>

The guideline recommends that ‘people with mild/moderate dementia of all types should participate in group Cognitive Stimulation which should be commissioned and provided by a range of health and social care workers with training and supervision. This should be delivered irrespective of any anti-dementia drug received by the person with dementia’.

[11] Alzheimer’s Disease International. 2011. World Alzheimer report 2011. London: Alzheimer’s Disease International. As of 2 May 2016: <http://www.alz.co.uk/research/WorldAlzheimerReport2011.pdf>

The report states that there is strong evidence that cognitive stimulation (for cognitive function) is an effective intervention in mild dementia.

#### *4.1.4. Delivering complex interventions quickly through Hyper-acute Stroke Research Centres*

##### **Case study**

Stroke is the largest cause of severe disability and the third biggest cause of death in the UK, with approximately 150,000 strokes occurring every year [1]. Treatment of stroke and associated productivity loss, amount to £8.9 billion a year in societal costs, with stroke treatment costs making up approximately 5 per cent of total UK NHS costs [2]. In 2013, the NIHR spent over £4.5 million on stroke research [1].

In the case of strokes, timely interventions determine the full scale of recovery. The faster treatment is initiated, the higher the chances of better health outcomes. The NIHR, in line with its vision to improve the health and wealth of the nation through research, has provided research support funding for eight Hyper-acute Stroke Research Centres (HASRC) across England to enable access to cutting-edge stroke treatment through increasing capacity and capability in the system. The idea behind the centres is that when a person has suffered a stroke, that person should be offered the possibility to participate in research studies and therefore access the latest clinical advancements in the field. In order to do this, there was a need to facilitate research team availability 24/7, which the HASRCs have achieved [3][4].

The HASRCs were launched in June 2010 with an annual £1.6 million budget and were meant to build on service reconfiguration of hyper-acute stroke services across England [5]. Dr Jonathan Sheffield, CEO at the NIHR Clinical Research Network stated that ‘Thanks to facilities like the Hyper-acute Stroke Research Centres, England has the infrastructure to lead the way in stroke research and offer more effective treatments to stroke patients across the country’[1]. This translates into opportunities for patients to access breakthrough stroke treatments, such as ‘clot busting’ therapies, immediately after having a stroke.

The impact of the HASRCs can be demonstrated by the number of patients that have taken part in clinical studies. The investment in the eight Centres has led to an overall doubling of patient recruitment into acute stroke studies as compared with recruitment prior to the NIHR investment. Specifically, the Manchester Hyper-acute Stroke Research Centre quadrupled recruitment in 7 months from 3 patients per month (2012) to 11.2 patients per month (2013). Similarly at the Nottingham Hyper-acute Stroke

Research Centre, the overall recruitment rate in 2010-11 had increased by 34 per cent in comparison with the previous year [4].

There have also been benefits for associated clinical staff. The research teams working at HASRCs are multidisciplinary and consist of clinical stroke specialists, research nurses, radiographers and interventional neuroradiologists. The establishment of the HASRCs has led to positive impacts on associated clinical staff, as highlighted by a manager of a HASRC who noted that the staff had elevated confidence and felt that research has become embedded into care rather than a separate task. Patients are also pleased with the opportunity to participate in trials at HASRCs. As mentioned by one patient

‘I was so grateful for the speed of treatment and care that I received [...] It’s only by doing research like this that we can hope to improve treatments for other stroke patients in the future’ [4].

The NIHR-funded HASRCs are increasing research capability and capacity in the field of stroke, benefiting patients as well as clinical professionals and making the UK a world-leader in hyper-acute stroke research [4].

## Evidence

[1] Focus on Stroke. 2014. Launch of the Focus on Stroke portal. As of 2 May 2016: [http://www.medicalresearchplymouth.org.uk/documents/Focus\\_on\\_Stroke.pdf](http://www.medicalresearchplymouth.org.uk/documents/Focus_on_Stroke.pdf)

This is presentation material for the new Focus on Stroke portal also provides data on Hyper Acute Stroke Research Centres.

[2] Saka Ö, McGuire A, Wolfe C, 2009. Cost of stroke in the United Kingdom. *Age and Ageing* 38 (1): 27-32. doi:10.1093/ageing/afn281

Study reporting the estimated annual costs of stroke to the UK economy using direct and indirect cost measures.

[3] National Institute for Health Research Clinical Research Network. 2015. Interview with Professor Gary Ford CBE and Dr Barry Moynihan about the Hyperacute Stroke Research Centres and their effectiveness and successes to date. As of 2 May 2016: <https://www.youtube.com/watch?v=-3-JIC2-tlc>

A video showing interview footage with Professor Gary Ford CBE and Dr Barry Moynihan about the effectiveness and success of the Hyperacute Stroke Research Centres.

[4] National Institute for Health Research Clinical Research Network. 2014. Not just hype. London: NIHR. As of 2 May 2016: <https://www.crn.nihr.ac.uk/wp-content/uploads//stroke/Not%20just%20hype.pdf>

This is a case study discussing the progress achieved by the Hyper Acute Stroke Research Centres one year after their launching.

[5] Ford GA. 2013. The UK Stroke Research Network. As of 2 May 2016: [http://www.eso-stroke.org/fileadmin/files/2013/eso-stroke/Ford\\_G.\\_UK\\_Stroke\\_Research\\_Network.pdf](http://www.eso-stroke.org/fileadmin/files/2013/eso-stroke/Ford_G._UK_Stroke_Research_Network.pdf)

Presentation of Professor Gary A Ford, Director, NIHR Stroke Research Network.

#### *4.1.5. Assuring high quality standards in radiotherapy trials*

Cancer is the leading cause of death in the UK [1], with 300,000 new cases occurring each year [2]. Radiotherapy is one of the most cost-effective curative treatments for cancer [3]. Following a 2008 review, the National Cancer Research Institute (NCRI) board established the Clinical and Translational Radiotherapy Research Working Group (CTRad) in 2009. The aim of the group is to support the design and conduct of radiotherapy trials, enable quality assurance for these trials and develop an academic radiotherapy environment in the UK [4]. With a view to achieving robust quality assurance, the Radiotherapy Trials Quality Assurance Team (RTTQA), funded by the NIHR, has been established. The RTTQA makes certain that the highest standards, which guarantee respecting subjects rights in clinical trials, are met, and has ensured delivery of high-quality data in more than 28 studies to date [5].

Recent RTTQA findings have shed light on crucial aspects in preclinical radiotherapy quality assurance, which in turn have triggered initiatives to provide all preclinical laboratories with access to standardised quality assurance procedures. This has broadened the work of the RTTQA [4] and demonstrates the breadth of its reach.

The RTTQA designs and implements quality assurance programmes for all UK Clinical Research Network Portfolio trials that contain a radiotherapy component. In 2015, the team had been involved in 10 completed studies, 18 recruiting trials and 20 newly funded ones [5]. The RTTQA provides advice and support throughout the trial process. The team is initially contacted for a preliminary assessment of the level of quality assurance that the trial would entail. After the funding has been secured and before finalisation of the protocol, the RTTQA is consulted for the development of the quality assurance guideline document, in the form of a quality assurance programme that sits alongside the trial protocol. The quality assurance programme is implemented throughout the study [6]. The programme helps improve the trial because it establishes best practices with respect to radiotherapy. It ensures 1) a consistent approach across all centres; 2) protocol adherence by the on-site research team; and 3) treatment accuracy [6]. Combined, all of these factors enable good clinical practices to be pursued, ultimately allowing the compilation of high-quality clinical data from participating subjects.

The contribution of the RTTQA to the quality of radiotherapy trials is growing in significance, in line with the number of complex radiotherapy trials, which have almost doubled between 2010 and 2014 [4]. RTTQA input in these cases rose from approximately five studies in 2010 that required complex quality assurance input, to 15 such studies in 2014 [5]. This reflects the value that RTTQA is considered to offer as a tool in clinical research [5].

The programme also has an educational component for professionals involved in radiotherapy clinical research; it provides ongoing support and fosters regular reviews of trial protocols, which allows for the introduction of new findings [7].

Documents from the RTTQA programme highlight that the benefits arising from high-quality clinical trials might also be seen in the context of a healthcare system perspective [6]. The demonstrated increase in adoption of quality assurance programmes could add to the perceived confidence in the safety and quality of new therapeutic solutions being tested, as well as in the research teams. The higher confidence in the research teams' capacities could attract more funding in the area, as demonstrated by the increased



number of clinical trials. This in turn could translate into engaging a larger number of participating subjects. While we do not have evidence of these impacts, it is the case that the NIHR-funded RTTQA exemplifies how improving the quality of radiotherapy clinical trials is leading to improved clinical practice.

## Evidence

[1] Office for National Statistics. 2015. Deaths registered in England and Wales (Series DR): 2014. As of 2 May 2016:

<http://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/death-registered-in-england-and-wales-series-dr/2015-11-09>

Webpage to a link for a Statistical Bulletin by the Office for National Statistics for the numbers of deaths registered in England and Wales for 2014, showing registered deaths by age, sex, selected underlying causes of death, and the 10 leading causes of death for both males and females.

[2] Cancer Research UK. 2014. Cancer incidence statistics. As of 2 May 2016: <http://www.cancerresearchuk.org/health-professional/cancer-statistics/incidence>

Webpage showing the cancer incidence statistics for the UK, including common cancer types.

[3] Bentzen SM, Herren G, Cottier B, Slotman B, Glimelius B, Lievens Y, Van den Bogaert W. 2005. Towards evidence-based guidelines for radiotherapy infrastructure and staffing needs in Europe: ESTRO QUARTS project. *Radiotherapy and Oncology: Journal of the European society for Therapeutic Radiology and Oncology* 75: 355-65.

Study estimating the radiotherapy infrastructure required across the 25 European countries based on best available evidence for indication of radiotherapy and national epidemiological data.

[4] National Cancer Research Institute. 2014. CTRad: National leadership in radiotherapy research. London: NCRI. As of 2 May 2016: <http://www.ncri.org.uk/wp-content/uploads/2014/10/2014-CTRad-Achievements-and-vision-WEB.pdf>

This is an evaluation of the CTRad, presenting the main outputs and achievements. It also discusses the radiotherapy quality assurance endeavours taken through the RTQA.

[5] Radiotherapy Trials Quality Assurance Team. 2015. Current and new trials 2015. As of 2 May 2016: [http://www.rtttrialsqa.org.uk/rttqa/?q=system/files/current\\_and\\_new\\_trials\\_2015.pdf](http://www.rtttrialsqa.org.uk/rttqa/?q=system/files/current_and_new_trials_2015.pdf)

PowerPoint presentation detailing recently closed or current trials and newly-funded trials in radiotherapy.

[6] Miles E. 2014. NCR Radiotherapy Trials QA Group: Our role and when to engage. As of 2 May 2016: <http://ctrad.ncri.org.uk/wp-content/uploads/2014/01/RTTQA-role-and-when-to-engage-Oct-2014.pdf>

PowerPoint presentation by Elizabeth Miles in October 2014, describing the role of the National Cancer Research Institute (NCRI) Radiotherapy Trials QA group.

#### *4.1.6. Capturing detailed patient information in a ground-breaking database to advance mental health research*

##### **Case study**

The Clinical Record Interactive Search (CRIS) system was developed in 2008 through the NIHR Biomedical Research Centre (BRC) for Mental Health at the South London and Maudsley NHS Foundation Trust (SLAM) and King's College London [1][2]. Containing records of more than 250,000 individual cases from South London, with approximately 20,000 new cases added each year [2], it is considered the largest regional register in Europe [3]. The NIHR has funded the development of CRIS (£1 million) [4], which now facilitates research in mental health using these records. This enables the identification of patterns and trends that are valuable when assessing what works and in which populations. The programme is also being developed in four other trusts, in the form of the D-CRIS programme, which aims to advance dementia research using the CRIS system [1]. CRIS is being rolled out now across the country in the form of UK-CRIS, with further external funding (Innovative Medicines Initiative grant).

CRIS captures de-identified psychiatric information (excluding name, date of birth, and address), which protects patient anonymity. The patients are informed about this and have the option to opt-out of their data being used as part of CRIS [1]. The trust's researchers have access only to the de-identified information, and the system is tightly monitored and evaluated. CRIS has been linked with numerous other databases, including databases in primary care (Lambeth DataNet), the Department for Education National Pupil Database, Hospital Episode Statistics, and databases on mortality and cancer [1]. By linking these databases, associations that otherwise would require complex and lengthy research are now able to be explored in a more cost-effective manner. The system is also technically advanced, and its natural language processing applications have facilitated the use of data on cognitive function, education, social care receipt, smoking, diagnostic statements and pharmacotherapy [1].

The high volume of data, the technical capabilities of the system, and the numerous data linkages, have led to important research outputs. One example is the discovery of a pattern suggesting that people with severe mental illnesses have a higher mortality risk than others [5]. Calculations using the CRIS data revealed, in 2010, that people with severe mental illness were two times more likely to die in comparison with those without severe mental illnesses. The research also found that people with substance-use disorders had a four-fold higher risk of mortality [5]. Calculations from 2010 concluded that this amounted to 12 life years lost for people with severe mental illnesses and 14 life years lost for those with substance-use disorders [5]. More analysis revealed more precisely which groups of persons are at risk among these populations. For the substance-use disorder group, these were women with opioid-use disorder and younger people with alcohol-use disorder [5]. Analysis using CRIS data also showed that for severe mental illnesses, such as schizophrenia and bipolar disorder, the severity of symptoms (e.g. hallucinations) was less important when predicting mortality than were difficulties carrying out regular daily activities [5]. It was also concluded that the risk of self-neglect was a better predictor of mortality than was the risk of suicide or violence assessed by health professionals. Professor Rob Stewart, head of the

epidemiology section at King's College London's Institute of Psychiatry and Honorary Consultant in Liaison Old Age Psychiatry at SLAM, who led the development of CRIS stated:

'Research of this kind illustrates the enormous value of information that can be found in health records. The studies described here would not have been possible without the CRIS data resource' [5].

These type of findings have the potential to reconfigure healthcare in the case of severe mental illnesses, as they highlight the opportunity to have more targeted services for a group of people who receive a particular diagnosis but are still predisposed to different levels of risks for some outcomes (such as death).

Other examples of research using CRIS are investigating the risks and benefits of psychotropic drugs in pregnancy [6] or exploring the service use patterns in young people with psychosis during the time of transition between child and adolescent mental health services and adult services. The latter exemplifies the way in which CRIS can be used to perform health economic analyses [7]. This will facilitate a greater understanding of the costs and consequences of mental health services and treatments, which will inform better provisions of healthcare services.

Finally, it is important to note that, in accordance with the NIHR's commitment to involving the patients in research that concerns them, CRIS was developed with significant patient/service user involvement. For example, the chair of the oversight committee has been a user of mental health services [8]. This brings the research in line with the patients' needs and facilitates diffusion of findings arising from research.

CRIS represents a new way of conducting research that has already produced important scientific outputs. The impact CRIS could have is considerable: contributing to faster personalised diagnosis and treatment benefiting patients both nationally and worldwide [4]. The programme is already receiving wide recognition, including from Prime Minister David Cameron, who highlighted CRIS as exemplar in one of his speeches announcing plans for the government's Life Sciences Strategy to advance healthcare research in the UK [8].

## Evidence

[1] Clinical Record Interactive Search (homepage). 2016. As of 2 May 2016:

<http://www.nihr.ac.uk/about/CRIS.htm>

Page detailing the Clinical Record Interactive Search tool.

[2] Perera G, Broadbent M, Callard F, Chang<sup>1</sup> C, Downs<sup>1</sup> J, Dutta<sup>1</sup> R, Fernandes A, Hayes RD, Henderson M, Jackson R, Jewell A, Kadra<sup>1</sup> G, Little R, Pritchard M, Shetty H, Tulloch A, Stewart R. 2016. Cohort profile of the South London and Maudsley NHS Foundation Trust Biomedical Research Centre (SLaM BRC) Case Register: Current status and recent enhancement of an electronic mental health record-derived data resource. *British Medical Journal Open* 6: e008721. doi:10.1136/bmjopen-2015-008721

The article highlights some of the most important technical developments in the SLaM BRC Case Register which are: the introduction of natural language processing to extract structured data from open-text fields, linkages to external sources of data, and the addition of a parallel relational database

(Structured Query Language) output. Natural language processing applications to date have facilitated usage of data on cognitive function, education, social care receipt, smoking, diagnostic statements and pharmacotherapy. Through external data linkages, large volumes of supplementary information have been accessed.

[3] Stewart R, Soremekun M, Perera G, Broadbent M, Callard F, Denis M, Hotopf M, Thornicroft G, Lovestone S. 2009. The South London and Maudsley 2009: NHS Foundation Trust Biomedical Research Centre (SLAM BRC) Case Register: Development and descriptive data. *BioMed Central Psychiatry* 9 (August): 51. doi:10.1186/1471-244X-9-51

The article follows the development of CRIS and finds that it represents a ‘new generation’ in research design, allowing in-depth secondary analysis of both numerical, string and free-text data, while preserving anonymity through technical and procedural safeguards.

[4] Kings College London. 2009. BRC for mental health gets cash for CRIS. As of 2 May 2016: <http://www.kcl.ac.uk/ioppn/news/records/2009/10October/BRCforMentalHealthgetscashforCRIS.aspx>

Webpage announcing that Kings College London was awarded £1 million in funding to support the development of the BRC’s Case Register Interactive Search (CRIS) system.

[5] Kings College London. 2012. Mental health record database reaches 200,000 patients. As of 2 May 2016: <http://www.kcl.ac.uk/ioppn/news/records/2012/October/Mental-health-record-database-reaches-200,000-patients.aspx>

Webpage announcing that the BRC’s Case Register Interactive Search (CRIS) system has reached 200,000 fully detailed, electronic mental health records.

[6] Kings College London. 2016. Antipsychotics in pregnancy. As of 2 May 2016: <http://www.kcl.ac.uk/ioppn/depts/hspr/research/CEPH/wmh/projects/A-Z/antipsychotics.aspx>

King’s College London webpage

[7] Kings College London Institute of Psychiatry. 2014. Using CRIS to increase health economics capability in South London. London: Insider Centre for the Economics of Mental and Physical Health. As of 2 May 2016: <https://www.kcl.ac.uk/ioppn/depts/hspr/research/khe/Insider/INSIDER-Summer-2014.pdf>

Insider Newsletter: The newsletter of Centre for the Economics of Mental and Physical Health revealing plans to use the BRC’s Case Register Interactive Search (CRIS) system to significantly aid health economic analyses.

[8] Kings College London. 2011. CRIS highlighted as exemplar in PM speech. As of 2 May 2016: <http://www.kcl.ac.uk/ioppn/news/records/2011/December2011/CRIS.aspx>

Link to a news report published by Kings College London, highlighting a news story in which the prime minister, David Cameron, made particular reference to the BRC’s Case Register Interactive Search (CRIS) system as an exemplar.

#### *4.1.7. Steering the health care system towards safer births in England*

##### Case study

Establishing the proper care required by women to experience safe childbirth is important because it directly translates into better health outcomes for both the child and the mother. From a health and care system perspective, striving to ensure that the right setting for childbirth is matched with the needs of the mother leads to effective use of resources by perinatal health services. The Birthplace in England Research Programme, a multidisciplinary research programme at the University of Oxford jointly funded by the NIHR Service Delivery and Organisation programme and the Department of Health Policy Research Programme [1], was set up in 2007. It aims to compare the outcomes of births planned in these four different settings, looking at safety, cost-effectiveness and women's experiences.

There are four main settings for births: home, freestanding midwifery units (FMUs), alongside midwifery units (AMUs) and obstetric units (OUs). The main differences among these settings are in the people who have clinical responsibility (midwives or obstetricians) and whether or not the unit is situated in a hospital with availability of obstetric, neonatal and anaesthetic care.

The first part of the Birthplace in England study mapped maternity care in NHS trusts and revealed that, while there were noticeable improvements in options for place of birth, there was still a substantial proportion of women unlikely to have a broad range of options available locally [2]. Furthermore, while the number of maternity units had increased in England, with an overall 11 per cent increase between 2007 and 2010 and with twice as many AMUs as in 2007 (53 compared with 26), there were regional differences when it came to availability and capacity. This led to most women giving birth in an obstetric unit [2]. These findings were important in the later update of policy recommendations that aimed to maximise the use of existing resources, such as AMUs.

The national forward-looking study of planned place of birth achieved an exceptionally high level of coverage across UK hospitals. It involved over 97 per cent of NHS trusts providing home birth services and almost 90 per cent of all midwifery units in England. One main finding was that for 'low-risk' women, defined as those who experience a straightforward pregnancy and are in good health without any serious health conditions (pregnancy-related or otherwise), the likelihood of poor health outcomes was low in all birth settings [4]. In addition, a cost-effectiveness analysis revealed that for low-risk women the cost to the NHS for birth and related postnatal care, including costs from clinical complications, was lower for births planned at home, in a FMU and in an AMU compared with births planned in an OU. The costs varied from £1,066 for home birth to £1,631 for birth in an OU [5]. This means that the option for low-risk women to give birth at home or in a midwifery unit is safe for baby and mother and saves the NHS money.

The evidence from this first part of the Birthplace in England programme has been widely discussed and disseminated in various media, from academic journals to TV, radio and national newspapers [3]. It has been cited by the Royal College of Midwives, the Royal College of Obstetricians and Gynaecologists and the National Childbirth Trust. In 2012, the UK government's White Paper *Liberating the NHS: No Decision About Me, Without Me* cited the research in support of the policy of choice of care setting [6]. The 2012 NHS Commissioning Board's Commissioning Maternity Services also mentioned this research

in support of service improvement that would offer healthy women with low-risk pregnancies a choice of birth setting [7]. In 2014, the National Institute for Health and Care Excellence (NICE) updated its guidance on care during labour and childbirth, relying heavily on findings from the Birthplace in England programme. The guidance recommends planned birth in a midwifery unit for healthy women having a first baby and planned birth in a midwifery unit or at home for healthy women having a second baby [8]. This research has also had an international impact in Brazil, where the Rede Cegonha (which translates as the stork network) has been set up to improve maternity care across the country, including the development and roll-out of 180 midwifery units nationally [3]. In Australia, an analysis of similar data also found that women who planned to give birth at a birth centre or at home were significantly more likely to have a normal labour and birth compared with women in the labour ward group [9].

Identifying the need to further explore factors that influence interventions, transfers and other outcomes in different settings and to also inform further the discussion on the organisation and delivery of services, the NIHR funded a 'follow-on' project in the form of the second part of the Birthplace in England study, which started in 2012. A 2015 report [10] of the follow-on study brought additional evidence to inform the development of care services that offer women a choice of birth setting and provide information that would help women choose their planned birth setting.

This programme has changed, through policy recommendations, the advice given to pregnant women and practice, and the research continues to produce findings that will likely translate into quantifiable safer and cost-effective births in England.

## Evidence

[1] National Perinatal Epidemiology Unit. 2016. Birthplace in England research programme. As of 2 May 2016: <https://www.npeu.ox.ac.uk/birthplace>

The webpage compiles the publications arising from the study and the latest news on the evolution of the research.

[2] Redshaw M. 2011. Birthplace in England research programme and mapping group: Mapping maternity care facilities in England. *Evidence Based Midwifery* 9: 46-52. As of 2 May 2016: <https://www.rcm.org.uk/learning-and-career/learning-and-research/ebm-articles/mapping-maternity-care-facilities-in-england>

Paper published by Evidence-Based Midwifery describing the organisation of maternity care at trust and unit level in England.

[3] Research Excellence Framework. 2014. *Where to Be Born? Evidence about the quality and safety of birth in different settings to support optimal outcomes and women's choice about place of birth.* [Case study 44342.] As of 2 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=44342>

The case study provides an overview on the major studies conducted by academic staff at City University London. Part of the research team here previously worked on the Birthplace England study, and the research is also mentioned in this Research Excellence Framework.

[4] Birthplace in England Collaborative Group, Brocklehurst P, Hardy P, Hollowell J, Linsell L, Macfarlane A, Mccourt C, Marlow N, Miller A, Newburn M, Petrou S, Puddicombe D, Redshaw M,

Rowe R, Sandall J, Silverton L, Stewart M. 2011. Perinatal and maternal outcomes by planned place of birth for healthy women with low risk pregnancies: The Birthplace in England national prospective cohort study. *British Medical Journal* 343: d7400. doi:10.1136/bmj.d7400

Results of the Birthplace Study showing the perinatal and maternal outcomes by planned place of birth for low risk pregnancies in England from a prospective cohort of approximately 65,000 women.

[5] Schroeder E, Petrou S, Patel N, Hollowell J, Puddicombe D, Redshaw M, Brocklehurst P. 2012 Cost effectiveness of alternative planned places of birth in woman at low risk of complications: Evidence from the Birthplace in England national prospective cohort study. *British Medical Journal* 344: e2292. doi:10.1136/bmj.e2292

Evidence from the Birthplace study showing the cost effectiveness of planned births either at home, in freestanding midwifery units, in alongside midwifery units, and in obstetric units for women with low risk pregnancies,

[6] Department of Health. 2012. Liberating the NHS: No decision about me, without me – Further consultation on proposals to secure shared decision-making. As of 2 May 2016: <http://docplayer.net/14386044-Liberating-the-nhs-no-decision-about-me-without-me-further-consultation-on-proposals-to-secure-shared-decision-making.html>

Subsequent publication from the Department of Health following on from the White Paper: Liberating the NHS, calling for responses to a further consultation.

[7] NHS Commissioning Board. 2012. Commissioning maternity services: A resource pack to support Clinical Commissioning Groups. London: NHS Commissioning Board. As of 2 May 2016: <https://www.england.nhs.uk/wp-content/uploads/2012/07/comm-maternity-services.pdf>

Resource pack setting out a framework to support Clinical Commissioning Groups in the commissioning of maternity services.

[8] National Institute for Health and Care Excellence. 2014. Update of intrapartum care for healthy women and babies. [CG190.] As of 2 May 2016: <https://www.nice.org.uk/guidance/cg190/chapter/1-recommendations>

National Institute for Health and Care Excellence (NICE) guidelines for delivering intrapartum care for health women and babies.

[9] Homer C, Thornton C, Scarf V, Ellwood D, Oats J, Foureur M, Sibbritt D, McLachlan H, Forster D, Dahlen H. 2014. Birthplace in New South Wales, Australia: An analysis of perinatal outcomes using routinely collected data. *BMC Pregnancy and Childbirth* 14: 206. doi: 10.1186/1471-2393-14-206

Results of a study reporting findings using routinely collected data on planned birthplace and on perinatal and maternal outcomes, and interventions in labour.

[10] Hollowell J, Rowe R, Townend J, Knight M, Li Y, Linsell L, Redshaw M, Brocklehurst P, Macfarlane A, Marlow N, McCourt C, Newburn M, Sandall J, Silverton L. 2015. The Birthplace in England national prospective cohort study: Further analyses to enhance policy and service delivery decision-making for planned place of birth. *Health Services and Delivery Research Programme* 3 (36).

doi: 10.3310/hsdr03360. As of 2 May 2016:

[http://www.journalslibrary.nihr.ac.uk/\\_\\_data/assets/pdf\\_file/0017/151253/FullReport-hsdr03360.pdf](http://www.journalslibrary.nihr.ac.uk/__data/assets/pdf_file/0017/151253/FullReport-hsdr03360.pdf)

This report summarises the findings from the follow-on study which was aimed to provide further evidence to support the development and delivery of maternity services and inform women's choice of birth setting, specifically, to explore maternal and organisational factors associated with intervention, transfer and other outcomes in each birth setting in 'low-risk' and 'higher-risk' women. The report concludes that expansion in the capacity of non-obstetric unit intrapartum care could reduce intervention rates in low-risk women and that the benefits of midwifery-led intrapartum care apply to all low-risk women irrespective of age, ethnicity or area deprivation score. The report also mentions that no change in the guidance on planning place of birth for higher-risk women is recommended.

#### *4.1.8. Initiating urgent assessment and treatment for patients following mini-strokes*

##### Case study

Costs arising from the treatment of stroke and costs incurred due to productivity loss of the UK population have been calculated to amount to approximately £8.9 billion a year [1]. Stroke treatment costs represent about 5 per cent of total UK NHS costs [1]. Research resulting from the Oxford Vascular Study (OXVASC), which is partly funded by the NIHR, has had significant impact on stroke prevention and the way minor strokes and transient ischaemic attacks (TIAs, or 'mini strokes') are managed, by informing clinical guidelines.

The OXVASC study started in 2002 and provides data on the incidence and outcome of all acute vascular events occurring in the population in Oxfordshire [2]. The NIHR has contributed to the research in different ways, such as: funding specific research on cost savings arising from early detection of TIA and stroke, in phase 2 of the OXVASC study, and providing an NIHR Senior Investigator Award to one of the principal investigators [3].

The first phase of the OXVASC study showed that the risk of stroke after a TIA is greater than originally considered, that there is a narrow time-window for prevention, and that individuals who are at highest risk of having a stroke can be identified with a simple clinical score – the ABCD [2]. It also showed that the requirement for appointments could lead to a delay in referrals for patients with a suspected TIA or minor stroke.

Based on learning from phase 1, the second phase of the research led to impacts on emergency treatment of TIA and minor stroke in primary care [2]. In this second phase, primary-care physicians were asked to send the patients immediately to the clinic, without any appointment, where treatment was initiated immediately if the diagnosis was confirmed. This led to an 80 per cent decrease in the 90-day risk of recurrent stroke in patients referred to the phase 2 clinic compared with those referred to the phase 1 clinic. In addition, clinic hospital admissions for recurrent stroke were lower when the requirement for appointments was removed, which translated to a savings of £624 per patient [4]. The Early use of eXisting PREventive Strategies for Stroke (EXPRESS) study, nested within OXVASC, determined the



effect of more rapid treatment after a TIA and minor stroke in patients who are not admitted directly to hospital [4][5].

These findings have had an impact on service provision and professional education about TIA and minor stroke. This is demonstrated by the changes the research has produced in clinical guidelines. Findings from the EXPRESS study have informed the 2007 National Stroke Strategy; the 2008 National Institute for Health and Care Excellence guidelines *Stroke: National Clinical Guideline for Diagnosis and Initial Management of Acute Stroke and Transient Ischemic Attack (TIA)*; and the 2012 Royal College of Physicians Intercollegiate Stroke Working Party's *National Clinical Guideline for Stroke* [3]. The recommendations in these documents reflect the findings from the EXPRESS study that there is a need for identification of patients at high risk of subsequent stroke and early specialist intervention, including commencement of appropriate secondary prevention treatments.

Based on the estimations from the EXPRESS study, it was calculated that emergency treatment of TIA and minor stroke in primary care would prevent about 10,000 strokes per year, adding up to savings of up to £200 million annually in acute care costs alone in the NHS [3]. Overall, the health and care system has benefited from improved stroke prevention as a result of determining the resource costs, health outcomes and cost-effectiveness in stroke care using evidence from the Oxford Vascular Study.

## Evidence

[1] Saka Ö, McGuire A, Wolfe C. 2009. Cost of stroke in the United Kingdom. *Age and Ageing* 38 (1): 27-32. doi:10.1093/ageing/afn281

Study reporting the annual cost of stroke to the UK economy using a combination of direct and indirect cost measures.

[2] National Institute for Health Research. 2016. Improving stroke prevention in routine clinical practice: Phase 2 of the Oxford Vascular Study (OXVASC) programme. As of 2 May 2016: <http://www.nihr.ac.uk/funding/funded-research/funded-research.htm?postid=2164>

Link to a project page on the National Institute for Health Research website, describing the OXVASC Study programme.

[3] Research Excellence Framework. 2014. Reduction of stroke risk by risk stratification and urgent intervention after a transient ischaemic attack (TIA) or minor stroke. [Case study 14720.] As of 2 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=14720>

The case study summarises the achievements of the team from the Stroke Prevention Research Unit in Oxford from early 2000 to 2013.

[4] Luengo-Fernandez R, Gray AM, Rothwell PM. 2009. Effect of urgent treatment for transient ischaemic attack and minor stroke on disability and hospital costs (EXPRESS study): A prospective population-based sequential comparison. *The Lancet. Neurology*. 8: 235-43. doi: 10.1016/S1474-4422(09)70019-5

This paper summarises the findings on the cost-effectiveness of the phase 2 intervention. It concludes that urgent assessment and treatment of patients with a TIA or minor stroke who were referred to a specialist outpatient clinic reduced subsequent hospital bed-days, acute costs and six-month disability.

[5] Health Economics Research Centre. 2016. Resource costs, health outcomes and cost-effectiveness in stroke care: Evidence from the Oxford Vascular Study. Nuffield Department of Population Health. As of 2 May 2016: <http://herc.medsci.ox.ac.uk/research/disease-cost-studies/studies-4/resource-costs-health-outcomes-and-cost-effectiveness-in-stroke-care-evidence-from-the-oxford-vascular-study>

The page offers a comprehensive account of this part of the research of the Oxford Vascular Study, including the publications resulting from it. This project aimed to: 1) estimate the size and predictors of immediate and long-term (i.e. five years after the event) National Health Service resource use and healthcare costs of stroke and transient ischaemic attacks; 2) estimate the size and predictors of immediate and long-term health outcomes, including five-year life expectancy, patient disability, quality of life, and quality-adjusted life expectancy; and 3) assess if urgent clinical assessment and treatment of non-hospitalised patients with a minor stroke or TIA was cost effective.

#### *4.1.9. Simplifying and streamlining clinical research initiation and delivery*

##### Case Study

One of the key objectives of the NIHR is to enable faster and easier clinical research so that the NHS and other parts of the health and social care system can take full advantage of the opportunities that science and technology offer patients, carers and those who serve them. As part of this commitment, the NIHR has established a number of processes to simplify and streamline administrative and regulatory processes. Key activities include working actively to make the performance of NHS providers in more transparent and accountable while they are starting and delivering research; providing support to help the NHS improve research performance; and simplifying approval processes for ethical research through working with the Health Research Authority (HRA) [1].

To make the performance of NHS providers in starting and delivering research more transparent and accountable, the NIHR has undertaken a number of actions to improve the timeliness under which clinical trials are undertaken. For example, it ensures that all new NIHR contracts with NHS services include requirements on the timelines under which all clinical trials by the contractors are undertaken. Since April 2014, similar requirements have been included in contracts between Department of Health and hosts of NIHR Local Clinical Research Networks (LCRNs), as well as in contracts or other forms of agreement between LCRN hosts and significant research-active providers in their patch [1].

In parallel, the NIHR played an instrumental role in setting up the Research Passport system, allowing higher education institution (HEI) researchers to undertake their research within and across NHS organisations more easily. The Research Passport introduced standardised procedures for issuing Honorary Research Contracts and Letters of Access to HEI researchers. As a result, it has streamlined processes for confirming details of the pre-engagement checks undertaken on the researcher in line with NHS Employment Check Standards [2]. There is anecdotal evidence from universities that it has sped up the process from weeks to hours [3]. The NIHR was also crucial in establishing the Champions for Research support initiative. These champions disseminate messages throughout the NHS and act as advocates for effective research management and delivery to promote the outcomes of faster and easier

clinical research [4]. From January 2015, the responsibility for supporting this initiative was transferred from the NIHR to the HRA.

To help the NHS achieve faster clinical research, the NIHR adopted the Research Support Services (RSS) framework in 2011. The RSS is a set of tools and guidelines such as the *Operational Capability Statement*, that support a consistent and streamlined approach to managing health research studies in the NHS [5]. As of December 2014, 151 NHS Trusts published their R&D Operational Capability Statements. The RSS Framework has helped the NHS service providers to meet a 70 day benchmark in new NHS contracts for recruiting the first patient to clinical trials. The framework has also helped provides to organise their capacity for managing trials from end to end, helping them deliver to time and target. Based on the adjusted data it was established that the percentage of trials meeting the 70 day benchmark increased from 47 per cent in 2013 to 75 per cent in 2015. Working with the NHS service providers has also reduced the median time from receipt of a valid research application to recruitment of the study's first patient from 105 days in the summer of 2012 to 50 days in the summer of 2015.

The NIHR has set up a number of other measures, including the NIHR Coordinated System for gaining NHS Permission (NIHR CSP) and standardised research agreements to aid efficient and effective study set-up and delivery. The CSP streamlines local NHS permission so that clinical research studies on the NIHR research portfolio can be approved more quickly [6]. As a result of the CSP, the median time for a study to gain all NHS permissions has decreased to 19 days from 28 days in 2013. Similarly, the median time for individual site NHS permissions is 6 days, an improvement on 13 days in 2013 [7]. The standardised research agreements include a model Clinical Trials Agreements (mCTA) and a model Industry Collaborative Research Agreement (mICRA). These agreements support clinical research collaborations involving the pharmaceutical and biotechnology industries, academia and NHS organisations across the UK [8].

The NIHR has also worked closely with HRA since its inception in 2015 as a new non-departmental public body, tasked with promoting the interests of patients in health research and streamlining the regulation of research. The NIHR supported the HRA's plans to create a unified approval process for research and to promote consistent and proportionate standards for compliance and inspection, including improving the processes of the National Research Ethics Service, and thus providing an efficient and robust ethics review service, which have recently been changed to the HRA Approval processes [9].

In sum, the NIHR is supporting a range of measures aimed at improving research processes and making clinical research faster and easier in the UK. This includes, among others, changing NIHR contracts to make NHS providers' research performance more transparent and accountable, developing the NIHR RSS Framework to support NHS performance improvements, and working with the HRA to simplify approvals processes for ethical research.

## Evidence

[1] National Institute for Health Research. 2015; July. Faster, easier clinical research. (version 9). As of 9 May 2016: <http://www.nihr.ac.uk/documents/about-NIHR/Briefing-Documents/5.1-Faster-Easier-Clinical-Research.pdf>

This briefing document describes the NIHR activities aimed at facilitating faster and easier clinical research.

[2] National Institute for Health Research. 2015; 22 December. Research Passports. As of 9 May 2016: <http://www.nihr.ac.uk/policy-and-standards/research-passports.htm>

This webpage provides details on the Research Passport and Streamlined Human Resources Arrangements.

[3] UK Clinical Research Collaboration. 2009; November. The changing regulatory and governance environment for health research across the UK: A guide for researchers (version 1). London: UK Clinical Research Collaboration. As of 9 May 2016: [http://www.ukcrc.org/wp-content/uploads/2014/03/R+G\\_Environment+Leaflet+FINAL.pdf](http://www.ukcrc.org/wp-content/uploads/2014/03/R+G_Environment+Leaflet+FINAL.pdf)

This document provides an overview of the changing regulatory and governance landscape for research and of the different initiatives in place.

[4] National Institute for Health Research. 2015; 7 April. Champions for Research Support. As of 9 May 2016: <http://www.nihr.ac.uk/policy-and-standards/champions-for-research-support.htm>

This webpage describes the NIHR's involvement in the Champions for Research Support initiative and includes the dissemination notes from meetings in 2014.

[5] National Institute for Health Research. 2015; 8 September. Framework for research support services. As of 9 May 2016: <http://www.nihr.ac.uk/policy-and-standards/framework-for-research-support-services.htm>

This webpage provides more detailed information about the Research Support Services Framework.

[6] National Institute for Health Research Clinical Research Network. 2016. Changes to arrangements for study set-up within the NHS in England. As of 9 May 2016: <https://www.crn.nihr.ac.uk/can-help/funders-academics/gaining-nhs-permissions/changes-to-arrangements-for-study-set-up-within-the-nhs-in-england/>

This webpage describes recent changes to the study set-up arrangements within the NHS in England.

[7] National Institute for Health Research. 2014; December. NIHR Christmas stats, Highlights: January 1<sup>st</sup> to December 1<sup>st</sup> 2014. As of 9 May 2016: <http://www.nihr.ac.uk/documents/about-NIHR/NIHR-Publications/NIHR%20Christmas%20xmas%20stats%202014.pdf>

This document provides an annual overview of the key statistics in relation to the objectives of the NIHR.

[8] National Institute for Health Research Clinical Research Network. 2016. Set-up service. As of 9 May 2016: <http://www.crn.nihr.ac.uk/can-help/life-sciences-industry/setup-service>

This webpage provides additional details on Model Clinical Agreements.

[9] Health Research Authority. n.d. Research Ethics Service (RES). As of 9 May 2016: <http://www.hra.nhs.uk/about-the-hra/our-committees/res>

This webpage contains full information on the Research Ethics Service.

#### 4.1.10. *Enabling research in care homes: the ENRICH programme*

##### Case study

The NIHR's Enabling Research in Care Homes (ENRICH) programme is the first national network to provide support for research engaging care homes and their residents, especially people with dementia.

In 2011, the NIHR Dementias and Neurodegeneration (DeNDRoN) Clinical Research Network established the ENRICH programme. This was followed at the beginning of 2012 by the launch of the ENRICH toolkit, a move publicly praised by industry [1]. Through the ENRICH toolkit, the programme has supported participating care homes to take part in a range of studies. As a result, there was a total NIHR investment in care home research of over £10 million in 2013, which was around 30 per cent of all dementia funding [1]. The toolkit is an electronic portal that provides advice and guidance for researchers, research staff and NIHR Local Clinical Research Networks on how to set up and conduct studies in a care home. It registered 500 hits in the first month of its existence [1].

The network of participating care homes has grown considerably. In 2012, BUPA care homes became the first corporate partner of ENRICH, adding 350 care homes to the network [1]. Today the network has more than 700 participating care homes in England and Scotland [2]. This offers a unique opportunity in dementia research, as it is estimated that 80 per cent of people living in care homes have a form of dementia or severe memory problems [3].

In late 2012, the ENRICH network was approached to support three studies funded as part of the NIHR's dementia themed call, with £3.5 million for care home research [1]. One of these studies is called the 'Enable Person-centred care for people with dementia and their carers: A cluster randomised controlled trial In Care homes (EPIC)', which is funded by the NIHR Health Technology Assessment programme. It aims to evaluate the clinical effectiveness and cost-effectiveness of Dementia Care Mapping™ (DCM™), a care home intervention used to support the implementation of person-centred care training for staff working with people with dementia living in care homes in England [4]. The EPIC study is being conducted in accordance with the principles of the ENRICH toolkit [4]. Professor Claire Surr, Chief Investigator, states that using existing networks and contacts has helped hasten the recruitment process, with 500 residents being recruited since June 2014 [5][6]. This exemplifies how the ENRICH programme is supporting research into dementia that will ultimately benefit the residents of the care homes.

An evaluation of the ENRICH programme was published in 2014. It looked at 33 recent studies and identified several ways in which ENRICH is beneficial. It was noted that membership of the network was perceived as a means of accessing research and networking with other care homes for mutual support, and that it had a positive impact on staff education and improved care. The evaluation also noted positive feedback from Care Quality Commission inspectors; increased volume of dementia research; and the chance for staff to express their opinions, concerns and ideas for improving residents' care [7].

Since its launch four years ago, the ENRICH toolkit has had more than 35,000 users. The tool has been updated since then, and the latest version contains revised guidance, a community blog, an online training tool and information on accessing funding opportunities [8].

The NIHR's ENRICH programme is bringing research on dementia closer to its beneficiaries; improving the participation of care home staff in bettering the residents' care; and facilitating uptake of research funding, which contributes to capacity building in dementia care.

## Evidence

[1] Department of Health. 2013. Delivering the Prime Minister's Challenge on Dementia: Delivering major improvements in dementia care and research by 2015: Annual report of progress. London: HM Government. As of 2 May 2016:

[https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/200030/9535-TSO-2900951-PM\\_Challenge\\_Dementia\\_ACCESSIBLE.PDF](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/200030/9535-TSO-2900951-PM_Challenge_Dementia_ACCESSIBLE.PDF)

Progress report on the Prime Minister's Challenge on Dementia

[2] Enabling Research in Care Homes. 2016. List of participants. As of 2 May 2016:

<http://enrich.nihr.ac.uk/participants>

List of participating care homes taking part in the Research Ready Care Home Network.

[3] Alzheimer's Society. 2014. Dementia 2014 report statistics. As of 2 May 2016:

<https://www.alzheimers.org.uk/statistics>

Alzheimer's Society statistics.

[4] Dementia Care Mapping EPIC trial. 2014. Evaluating the effectiveness and cost effectiveness of Dementia Care Mapping™ (DCM™) to enable person-centred care for people with dementia and their carers: A cluster randomised controlled trial in care homes study protocol. As of 2 May 2016:

[http://www.brad.ac.uk/health/media/healthmedia/DCM\\_EPIC\\_Protocol\\_v5.0\\_19-Dec-2014.pdf](http://www.brad.ac.uk/health/media/healthmedia/DCM_EPIC_Protocol_v5.0_19-Dec-2014.pdf)

Evaluation of the effectiveness and cost effectiveness of Dementias Care Mapping.

[5] Enabling Research in Care Homes. 2015. Overcoming the challenges of recruiting care homes to research. London: NIHR. As of 2 May 2016: [http://www.enrich.nihr.ac.uk/files/Case%20Studies/cs-10-Overcoming\\_the\\_challenges\\_recruiting%20\(new\).pdf](http://www.enrich.nihr.ac.uk/files/Case%20Studies/cs-10-Overcoming_the_challenges_recruiting%20(new).pdf)

Document outlining recruitment in the EPIC trial.

[6] EPIC trial. 2016. EPIC recruitment update. As of 2 May 2016:

<http://www.bradford.ac.uk/health/dementia/research/epic/epic-recruitment-update/>

Webpage updating on EPIC trial recruitment.

[7] Davies SL, Goodman C, Manthorpe J, Smith A, Carrick N, Iliffe S. 2014. Enabling research in care homes: An evaluation of a national network of research ready care homes. *BMC Medical Research Methodology* 14: 47. doi: 10.1186/1471-2288-14-47

The evaluation used a two-phase, mixed-methods approach. Phase 1 established a baseline of current and recent studies, including the National Institute for Health Research portfolio. Interviews were conducted with researchers working for the Dementias and Neurodegenerative Diseases Research Network (DeNDRoN) and care home managers. In phase 2, four DeNDRoN area offices recruited care homes to a care home network for their region. The phase 1 review revealed a small but increasing number of studies

involving care homes. Phase 2 proved the feasibility of care home research networks and their potential to increase recruitment to research and develop partnerships between health services and care homes.

[8] Enabling Research in Care Homes. 2015. New support for care home research – Meeting prime ministers Dementia 2020 vision. As of 2 May 2016: <http://enrich.nihr.ac.uk/newsitem/further-support-for-care-home-research-prime-ministers-dementia>

ENRICH webpage on meeting the Prime Minister's vision for Dementia in 2020.

## 5. Working with charities and the third sector on common agendas

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### 5.1. Summary

**Inclusive. Collaborative. Engaged.**

*NIHR works with charities and the third sector on common agendas to maximise the health gains from research investment and to reach patient groups at risk of being marginalised.*

NIHR's research infrastructure in the NHS helps to enable charities and the third sector to undertake high-quality, cost-effective research. Charities invested over £1.7 billion into studies enabled by and using NIHR infrastructure over the period 2009/10 to 2014/15, including £436 million in 2014/15 alone.

Partnering with charities enhances NIHR's ability to reach out to specific patient groups and to support major national campaigns. Equally, it allows charities to access the entirety of NIHR's infrastructure to realise patient benefits. For example:

- NIHR's network of Experimental Cancer Medicine Centres is jointly funded with Cancer Research UK and is increasing the number of patients taking part in trials of innovative new cancer treatments, such as those for refractory myeloma. More than 2,500 patient participants were recruited to 389 trials in 2015.
- England's largest programme to tackle stigma and discrimination against people with mental health, Time to Change, bases its interventions around principles of social contact validated as part of an NIHR research programme. The research team worked closely with the charities Mind and Rethink Mental Illness, who lead the programme.

Charities provide over a third of all public funding for medical research in the UK, and many national charities partner with NIHR. One example is Arthritis Research UK. This charity is working across the breadth of the health research innovation pathway and NIHR infrastructure, including with the University College London Hospitals Biomedical Research Centre, to establish the world's first centre for adolescent rheumatology; with NIHR's Translational Research Partnership, to begin the first translational research programme in Lupus; and with NIHR's Collaboration for Leadership in Applied Health Research and Care Greater Manchester, to promote self-management of their disease for patients with rheumatoid arthritis.

NIHR, in collaboration with the Association of Medical Research Charities – the UK's membership body representing 133 charitable research funding organisations – and other stakeholders, including the Health



Research Authority and the Medical Research Council, is implementing guidelines which will help reduce the burden of research funding on charities. The guidelines will provide a mechanism through which the NHS will pay for additional costs that could otherwise make the price of research prohibitively high.

NIHR works with charities to tackle urgent health issues where there are unmet research needs. Pooling resources with charities significantly speeds up the process of bringing new technologies into clinical practice. Examples of these partnerships include the following:

- The British Tinnitus Association is working as part of an NIHR-supported Priority Setting Partnership (via the James Lind Alliance) to inform research results into the first ever evidence-based clinical practice guidelines for tinnitus, which stand to benefit the 5 million people living with this condition in the UK.
- Globally more than 10,000 patients with a rare genetic form of diabetes have benefitted from a personalised medicine approach that allows them to control their blood sugar without the need for insulin injections. The screening method used to identify these patients arose from research funded via a strategic partnership with the Wellcome Trust, as well UK diabetes charities.
- Stroke survivors with cognitive impairment receive a diagnosis earlier and more efficiently as a result of NIHR's championing of a screening tool originally developed with funding from the Stroke Association.
- Researchers working in partnership with the charity Sue Ryder are improving practices on how to better communicate with patients and their families about end-of-life plans.

Networks of volunteers support research within their community. NIHR sponsors research to assess the impact and cost-effectiveness of these local, often experimental, initiatives. Below are two examples of NIHR randomised controlled trials which helped demonstrate significant benefits:

- One volunteer group now operates as its own charity, Speak with IT, to deliver enhanced, computer-based rehabilitative therapies for stroke victims with aphasia (a speech and language disorder) in the north-east of England. This follows results from NIHR's pilot trial indicating that this therapy improved patients' language abilities, and was more cost-effective, when compared to standard speech and language therapy and linked support groups.
- The charity Sing for Your Life reaches more than 1,000 elderly people in community and care settings each month. An NIHR-funded trial demonstrated that the singing programme the charity delivers significantly improves participants' quality of life and well-being.

Charity and third sector partnerships also provide a platform from which NIHR can undertake research into topics viewed as sensitive or challenging:

- The Equality Trust is an educational and campaigning organisation set up to share findings of an NIHR research programme examining the social and health-related determinants of inequality. The findings have been cited in World Health Organization policy documents and by senior policymakers from the United Nations and the International Monetary Fund.

### *5.1.1. Stratifying treatments for patients with maturity onset diabetes of the young*

#### Case study

Acting to speed up the processes through which new technologies can make a difference to patients' lives, the NIHR has facilitated a strategic partnership with the Wellcome Trust to support projects that target unmet, or poorly met, healthcare needs. Via a dedicated Health Innovation Challenge Fund (HICF), this initiative encourages companies, academia and clinicians to work together to translate research from the 'proof-of-principle' stage to improvements in patient care [1]. Using the NIHR's clinical research infrastructure at the NIHR Exeter Clinical Research Facility, Professors Andrew Hattersley and Sian Ellard at the University of Exeter Medical School have conducted research to help patients with rare genetic forms of diabetes. This research provides an example of what a joined-up, partnership approach to clinical research has achieved.

Diabetes caused by mutations in a single gene ('monogenic' diabetes) is rare and is often misdiagnosed as type 1 or type 2 diabetes. Estimates are that fewer than 5 per cent of people with monogenic diabetes are correctly diagnosed, with the result that up to 20,000 patients may be receiving inappropriate treatment [2]. Early work by the Exeter research team had developed genetic tests for several of these forms of diabetes. These are collectively termed maturity onset diabetes of the young, or MODY, given people affected usually show symptoms before the age of 25 [3].

Because genetic testing of all patients suspected of having MODY would prove prohibitively expensive, the team went on to develop a method of screening patients, by testing for by-products of insulin production that circulate in the bloodstream. With support from the HICF, as well as Diabetes UK, the Diabetes Foundation, and the European Union, the team was able to trial this approach, recruiting patients via the NIHR's Exeter Clinical Research Facility. The team showed that in certain cases, patients' blood glucose could be controlled using tablets rather than insulin injections, while in others, treatment could be stopped altogether [3].

The research has had significant impacts on practice and patient care. Through Professor Hattersley's membership on expert committees (including the International Society for Paediatric and Adolescent Diabetes and the World Health Organization), treatment guidelines for MODY now reflect the team's successes in applying a personalised medicine approach. More than 10,000 patients worldwide have had their treatment modified to remove the need for insulin injections, with improvements in their quality of life as a result of reduced discomfort and inconvenience [3].

As part of efforts to improve the availability and quality of information to guide healthcare practitioners and patients, the team also developed an online 'MODY calculator'. This resource allows clinicians to predict an individual's risk of MODY, by inputting information about their family history, clinical characteristics and test results. By providing a systematic approach to selecting patients who would benefit from further genetic testing, the MODY calculator helps to prevent unnecessary tests, and it has been used by more than 6,000 clinicians, scientists and patients [3].

The work demonstrates the value of the NIHR's bridging role between not-for-profit and other public and special interest groups, as well as providing infrastructure to support research that can transform the

lives of patients whose disease may otherwise be overlooked by common diagnostic and treatment pathways.

## Evidence

[1] National Institute for Health Research. n.d. Research Design Service: Health Innovation Challenge Fund. As of 2 May 2016: <http://www.rds.nihr.ac.uk/funding/funding-opportunities/hic/>

Information on the NIHR website detailing aims and objectives of the HICF.

[2] National Institute for Health Research. 2014. Using Pharmacogenetics to Improve Treatment in Early-onset Diabetes (UNITED). As of 2 May 2016: <https://clinicaltrials.gov/ct2/show/NCT01238380>

Clinicaltrials.gov listing of the UNITED trial, with information on monogenic diabetes and aims and objectives of the NIHR trial.

[3] Research Excellence Framework. 2014. Personalised medicine in patients with maturity onset diabetes of the young. [Case study 35590.] As of 2 May 2016:

<http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=35590>

REF case study outlining the contribution of NIHR-funded research to improved practices in diagnosing and treating MODY, and the support of a number of charitable partners.

### *5.1.2. Rehabilitating patients with speech and language difficulties following a stroke*

#### Case study

Aphasia is a problem affecting patients' ability to speak, to understand speech, and to read and write. It results from damage to the language region of the brain, often following a stroke, and is relatively common, affecting up to a third of stroke victims, or more than 50,000 people each year [1]. Speech and language therapy can help patients to recover their ability to communicate, however such treatment is rarely offered beyond three months post-stroke. In partnership with a number of stroke charities, the NIHR has enabled patients to receive further speech and language support, through piloting the use of a computer programme, called Step-by-Step, that helps to rehabilitate patients and restore their confidence in finding the right words [2].

Drawing on the support of the NIHR's Collaboration for Leadership in Applied Health Research and Care (CLAHRC) South Yorkshire, whose remit is to build research capacity – a team at the University of Sheffield developed an initiative to tackle some of the issues that people with aphasia face. These can include depression, family breakdown, unemployment, and social isolation [3].

The Sheffield team designed a pilot randomised controlled trial (RCT) to test the feasibility of using the Step-by-Step programme as an adjunct to standard speech and language therapy. The trial involved participants working through a library of more than 13,000 language exercises, for at least 20 minutes a day, 3 days a week, for 5 months [4]. To support participants in using Step-by-Step, the team recruited a network of volunteers from communication and stroke charities, including Speakability (now part of the Stroke Association) [5].

The trial recruited more than its original target of 30 participants. Results indicate a significant improvement in the number of words that participants receiving the Step-by-Step intervention could correctly identify, 5 months into their therapy. Working with the volunteer network meant that a speech and language therapist only needed to provide light-touch supervision, at the early stages of setting up the programme. Thus, in spite of the intervention's slightly higher lifetime costs compared with standard language therapy and linked support groups (£19,124 and £18,687 respectively), the team estimated that it would be cost effective (an incremental cost-effectiveness ratio of £3,058), given the improvement the team observed in patients' language abilities [4].

The patients and carers who took part in the pilot trial were so positive about their experiences in participating that in 2012 they launched their own charity, Speak with IT, to offer the Step-by-Step programme to other patients with aphasia in the north east of England [3]. Made up entirely of volunteers, the charity has trained 30 people to help more than 200 patients with aphasia, and is an active voice in the local community to raise awareness of the disease. Its CEO, Carl Palay, explained the value:

'The fact that Research at the University of Sheffield has shown using computer technology to treat the issues found with processing speech and language after a stroke is more effective than the usual stimulation offered in such cases, drives and inspires me to work towards making our support services available to as wide an audience as possible. For example, people using the computer software independently at home made significantly more improvement in finding the words they wanted than those who did not use computer treatment and our charity facilitates and supports this approach helping directly improve the quality of life of stroke survivors' [6].

With further funding from the NIHR's Health Technology Assessment programme, the Sheffield team are now leading a RCT of the computer therapy in twenty aphasia departments across the UK. In facilitating collaboration among patients, carers, volunteer groups and charities and through this research the NIHR is informing decisions around the use of this new model of treatment for patients with persistent aphasia.

## Evidence

[1] National Health Services. n.d. Aphasia. As of 2 May 2016:

<http://www.nhs.uk/Conditions/Aphasia/Pages/Introduction.aspx>

Information on aphasia, outlining causes and types of and treatments for the disease.

[2] National Institute for Health Research. 2009-2012. Evaluating cost effectiveness of computer therapy compared with usual stimulation for people with long standing aphasia: a pilot study

As of 2 May 2016: <http://www.nihr.ac.uk/funding/funded-research/funded-research.htm?postid=1981>

Details of the NIHR-funded Research for Patient Benefit pilot RCT of a computer-assisted course of speech and language therapy for patients with aphasia.

[3] National Institute for Health Research. 2012. NIHR Clinical Research Infrastructure Collaborations. Engaging with Medical Research Charities London: NIHR. As of 2 May 2016: <http://www.nihr.ac.uk/documents/industry/Brochures/Engaging-with-medical-research-charities.pdf>

Brochure providing case studies of the NIHR's engagement with the third sector and a number of impacts of this work.

[4] Palmer R, Enderby P, Cooper C, Latimer N, Julious S, Paterson G, Dimairo M, Dixon S, Mortley J, Hilton R, Delaney A, Hughes H. 2012. Computer Therapy Compared With Usual Care for People With Long-Standing Aphasia Poststroke. A Pilot Randomized Controlled Trial. *Stroke* 43: 1904-1911. doi: 10.1161/STROKEAHA.112.650671

Results of the Sheffield team's pilot RCT of a computer-assisted course of speech and language therapy for patients with aphasia, including sample size calculation for a full RCT and estimated cost-effectiveness of the pilot intervention.

[5] Collaboration for Leadership in Applied Health Research and Care. 2012. CLAHRCBITE Brokering Innovation Through Evidence: A bite-sized summary of a project within CLAHRC for South Yorkshire. As of 2 May 2016: <https://drive.google.com/file/d/0B1On41OBiiu3eW1id2VrOTVYNIU/view>

Summary project findings on cost effectiveness of computer aphasia treatment versus usual stimulation.

[6] SpeakwithIT. N.d. Latest News. As of 2 May 2016: <http://www.speakwithit.org/latest-news/>

Recent public-facing communications from the charity set up to promote further aphasia patient engagement with the Step-by-Step intervention, as trialled in the NIHR-funded study.

[7] National Institute for Health Research. n.d. HTA - 12/21/01: Clinical and cost effectiveness of aphasia computer therapy compared with usual stimulation or attention control long term post stroke (CACTUS). As of 2 May 2016: <http://www.nets.nihr.ac.uk/projects/hta/122101>

Details of the NIHR Health Technology Assessment programme-funded full RCT to evaluate the use of computer therapies for aphasia and inform care decisions by NHS commissioners, patients and relatives.

### *5.1.3. Developing a common research agenda for charity and patient groups involved in tinnitus research*

#### **Case study**

The NIHR Biomedical Research Unit (BRU) in hearing in Nottingham was established in 2008 and is the only such unit funded to undertake early translational research in deafness and hearing problems. Funded with an initial NIHR award of £3.75 million for four years, and awarded a further £6.25 million in 2012 [1], the Nottingham BRU is a partnership between the University of Nottingham and Nottingham University Hospitals NHS Trust, and works closely with the Medical Research Council Institute of Hearing Research. Drawing on close links with national charities, the Nottingham BRU is working with people who suffer from hearing-related problems and tinnitus.

Tinnitus is the perception of hearing a noise in the absence of any external source of sound. In the UK, there are more than 5 million people with tinnitus [2], costing the NHS £27million a year in hearing aids and/or counselling costs [3]. This condition affects primarily the elderly with 14 per cent of people aged over 50 suffering from tinnitus [2]. This makes it a burden on the healthcare system, especially considering the increasing aging population.

The BRU benefits from physical infrastructure comprising sound-insulated booths, and quiet testing rooms, including a child-friendly room, as well as equipment that allows for clinical and experimental assessments of hearing and researchers who offer expertise [1]. Leveraging existing capacity and capabilities, the BRU engaged with charities and industry in a partnership for a James Lind Alliance tinnitus priority-setting partnership (PSP). On this project, the BRU worked with the British Tinnitus Association (BTA) and the Judi Meadows Memorial Fund to identify the top 10 important questions for tinnitus research [4]. The programme ran from 2011 to 2012 and obtained the views of a wide range of stakeholders such as professional organisations, charities and patient support groups. The BRU offered expertise on how to conduct this process. Starting with 2,500 questions, the project involved several steps of refinement leading to a long list of 393 questions and, ultimately, 170 questions that were proposed to the tinnitus community for selection [4]. The 10 identified research uncertainties are meant to focus the research agenda by capturing important questions for both clinicians and patients. As recognised by the BTA Chief Executive, this project ‘gave a unique opportunity for a patient-led organisation to work with the BRU to deliver a project that was important to the whole of the tinnitus community – patients, clinicians and researchers’ [5].

The unique partnership among the NIHR, tinnitus charities and patient groups has identified important research questions. For example, the partnership led to exploring the potential of cognitive behavioural therapy (CBT) through a £259,000 grant awarded by the NIHR Research for Patient Benefit programme [5].

Another way in which the BRU is working with the BTA is through the creation of a BTA Head of Research position in 2015 [6]. The researcher is based at the BRU and works to facilitate tinnitus management within the NHS. An initial research study is investigating whether use of hearing aids and combination hearing aids improves tinnitus management [6].

By engaging in collaborations such as the one between the BRU in hearing in Nottingham and the BTA and by advancing common research agendas, the NIHR helps to achieve patient benefits. This research agenda is important in both national and international contexts because the BRU’s work is already achieving international impact. BRU research contributed to evidence-based clinical practice in tinnitus, with BRU work being featured in the clinical practice guidelines for tinnitus published by the American Academy of Otolaryngology on the assessment and management of bothersome and persistent tinnitus [7].

## Evidence

[1] Nottingham Hearing Biomedical Research Unit. 2016. About us. As of 2 May 2016: <http://www.hearing.nihr.ac.uk/about-us>

Webpage giving information about the Nottingham Hearing Biomedical Research Unit.

[2] Nottingham Hearing Biomedical Research Unit. 2016. Tinnitus etiology (causes) and management (treatment). As of 2 May 2016: <http://www.hearing.nihr.ac.uk/research/tinnitus-etiology-and-management>

Webpage providing information on the causes and treatment of Tinnitus, aimed at general readership.

[3] Nottingham University Hospitals. 2015. Do you suffer with tinnitus? As of 2 May 2016: <http://www.nuh.nhs.uk/communications-and-media/news/2015/july/do-you-suffer-with-tinnitus/>

Nottingham University Hospitals webpage providing information about the QUIET-1 trial, and inviting volunteers.

[4] British Tinnitus Association. 2013. The James Lind Alliance Tinnitus Priority Setting Partnership. As of 2 May 2016: <http://www.tinnitus.org.uk/the-james-lind-alliance-tinnitus-priority-setting-partnership>

Information about the James Lind Alliance Tinnitus Priority Setting Partnership.

[5] Nottingham Hearing Biomedical Research Unit. 2016. In research. The James Lind Alliance (JLA) Tinnitus Priority Setting Partnership top 10 uncertainties influence research and funding. As of 2 May 2016: <http://www.hearing.nihr.ac.uk/about-us/in-research>

Information about the Tinnitus Priority Setting Partnership

[6] Nottingham Hearing Biomedical Research Unit. 2015. British Tinnitus Association appoints head of research in innovative partnership. As of 2 May 2016:

<http://www.hearing.nihr.ac.uk/http://www.hearing.nihr.ac.uk/news/press-releases/article/british-tinnitus-association-appoints-head-of-research-in-innovative-partne>

Press release from Nottingham Hearing Biomedical Research Unit announcing the appointment of Dr Magdalena Sereda as their first Head of Research at the British Tinnitus Association.

[7] Nottingham Hearing Biomedical Research Unit. 2016. About us: Our successes. As of 2 May 2016: <http://www.hearing.nihr.ac.uk/about-us/successes>

Webpage providing information about the successes of the Nottingham Hearing Biomedical Research Unit.

#### *5.1.4. Allocating clinical research costs fairly*

##### *Case study*

Charities provide over a third of all public funding for medical research in the UK, consistently funding over £1 billion of research each year since 2008 [1]. The NIHR maximises the value of this funding through its support of infrastructure, such as facilities, centres and units dedicated to clinical research, and the UK-wide clinical research network [2]. The NIHR's partnership with the third sector has led to an array of achievements, with a number of these detailed in this chapter. It also prompted a review in how the NHS apportion research costs, to ensure that charity funding is directed towards the areas where it is likely to have the greatest impact.

In 2012, the Department of Health in England released updated guidance on attributing the costs of carrying out clinical research (known as AcoRD) to ensure that funders meet these costs fairly and transparently. It defined the types of cost that apply to clinical research, from those of the research study itself (research costs) to the costs of treating patients involved in the research (NHS treatment costs, and NHS support costs). It identified the costs that fall into each category and who should meet them. For the first time, the guidance also specifically set out the costs that charities should not be expected to pay,

including the local costs of managing trials, collecting research data and complying with regulatory requirements [3].

The AcoRD guidelines, subsequently adopted UK-wide, have acted to reduce the burden of research funding on charities, by providing a mechanism through which the NHS will pay for additional costs that could otherwise make the price of research prohibitively high [4].

To help implement the guidelines, the NIHR is working in collaboration with the Association of Medical Research Charities (AMRC) – the UK’s membership body representing 133 charitable research funding organisations – and other stakeholders, including the Health Research Authority and the Medical Research Council. Together, they have developed tools to help researchers to correctly apportion costs when applying for research funding from charities and other research funders. To ensure that only high-quality research would be eligible for the support, and in line with AMRC best practice, charities must offer their funding in open competition [4]

The importance of a fair and transparent process to encourage charities to fund research that maximises the NIHR’s support of clinical research is clear when one looks at the scale of this funding. Since 2009, charities have provided almost £1.7 billion of research funding to studies making use of the NIHR’s infrastructure. In 2014-15, charity funding accounted for over a quarter of all such external funding [2].

Other case studies present tangible examples of how the NIHR is collaborating with charities to advance the nation’s health and wealth: from Experimental Cancer Medicine Centres to trial new therapies for cancer, through to screening tools that prevent unnecessary insulin injections in patients with rare forms of diabetes.

## Evidence

[1] Association of Medical Research Charities. 2014. Charities spend £1.3bn on research in the UK. As of 2 May 2016: <http://www.amrc.org.uk/blog/charities-spend-13bn-on-research-in-the-uk>

Article from the UK representative body for medical research charities, detailing historical research spend.

[2] National Institute for Health Research. n.d. NIHR Leveraging investment. London: NIHR. As of 2 May 2016: <http://www.nihr.ac.uk/documents/about-NIHR/NIHR%20at%2010/Leveraging%20investment.pdf>

Summary document detailing the amounts and sources of funding of NIHR infrastructure.

[3] Department of Health. 2012. Attributing the costs of health and social care research. As of 2 May 2016: <https://www.gov.uk/government/publications/guidance-on-attributing-the-costs-of-health-and-social-care-research>

Guidance to provide a framework for the NHS and its partners to identify, attribute and recover costs associated with research in the NHS.

[4] Association of Medical Research Charities. 2014. AcoRD – costing research in the NHS. As of 2 May 2016: <http://www.amrc.org.uk/our-work/funding-clinical-studies/acord-costing-research-in-the-nhs>

AMRC guidance on the AcoRD guidance and its implications for charity research funding organisations.



### *5.1.5. Collaborating to improve studies of supportive, palliative and end-of-life care*

#### Case study

An increase in the number of people living with long-term and chronic illness means that the need to provide high-quality, supportive palliative and end-of-life care is more pressing than ever before. Advance care planning (ACP) enables patients to consider, discuss and, if they wish, document their wishes and preferences for future care, including decisions to refuse treatment in the event that they lose capacity to make decisions for themselves [1]. With support from the NIHR, researchers working in partnership with the charity Sue Ryder at the University of Nottingham's Sue Ryder Care Centre for the Study of Supportive, Palliative and End of Life Care have enabled improvements in practice on how to communicate better with patients and their families about end of life plans and have developed recommendations for health policy to improve the experience of death and dying for patients and their families. The centre's collaborative relationship with the charity Sue Ryder improves the uptake of its research into the provision of palliative and neurological care.

An NIHR-supported study into communication and decisionmaking in rehabilitation [1], undertaken by Dr Ruth Patty and colleagues, examined how practitioners raise sensitive issues and encourage involvement in decisionmaking. This research has informed professional practice and policy, as the findings have since been used by health and care professionals to improve how they communicate with patients about advance end-of-life care plans. Aside from the NIHR support, the Centre also benefitted from research grants from Burdett Trust for Nursing, Trent Cancer Network, and others [2].

This research informed the legislative and policy changes introduced in the Department of Health's End of Life Care Strategy and the 2007 Mental Capacity Act, which gave legal status to advance decisions to refuse treatment and nominations of lasting powers of attorney [3]. The Head of Programmes for Long-Term Conditions and End of Life Care at NHS Improving Quality described this research as 'influential' and said '[it] provided a foundation upon which further work and research has been based' [4]. In 2011, the Centre's analysis of staff's educational needs was also used to revise guidance for health and social care staff in the National End of Life Care Programme [3]. The research also informed professional practice at a high level when its research was cited in the Royal College of Physicians' evidence-based guidelines for ACP published in 2009 [5][6].

The research team actively engaged with the third sector in improving the understanding, implementation and uptake of ACP. The researchers worked actively with Dying Matters, a national coalition established by the National Council for Palliative Care to raise public awareness of and debate about ACP [8]. Since 2009, the coalition has gained 20,000 members from across the NHS, the voluntary and independent health and social care sectors, community organisations and academia [3]. The centre, jointly with the Dying Matters coalition and the National End of Life Care Programme, also co-developed an educational guide about ACP aimed at healthcare professionals. The guide is now available in seven languages.

The research has attracted considerable international attention. Its findings were presented at numerous international conferences, such as the inaugural International Advance Care Planning and End of Life Care conference [3]. It was also cited in the World Health Organisation's guidance for palliative care and

older people [7]. The centre's research also informed a European Council Symposium on the end of life decision-making process, when the Steering Committee on Bioethics agreed to develop European guidelines as part of its work programme [8].

The influence this research has had on policy and professional practice has been acknowledged, and the NIHR continues to support other research streams at the University of Nottingham's Sue Ryder Care Centre for the Study of Supportive, Palliative and End of Life Care. Similarly, the NIHR Programme Grant for Applied Research supported a new six-year research project titled Promoting Activity, Independence and Stability in Early Dementia (PrAISED) into maintaining independence, well-being and quality of life for people with early dementia by promoting activity and reducing falls and their adverse consequences [9].

## Evidence

[1] Pollock K, Wilson E. 2015; July. Care and communication between health professionals and patients affected by severe or chronic illness in community care settings: A qualitative study of care at the end of life. Southampton (UK): NIHR Journals Library: Health Services and Delivery Research 3.31. doi: 10.3310/hsdr03310

NIHR Final report detailing findings of study examining communication between health professionals at the end of life.

[2] Parry R. 2009. Practitioners' accounts for treatment actions and recommendations in physiotherapy: When do they occur, how are they structured, what do they do? *Sociology of Health & Illness* 31 (6): 835-53. doi: 10.1111/j.1467-9566.2009.01187.x

Peer-reviewed journal article with findings from a qualitative study about treatment actions and recommendations in physiotherapy.

[3] Research Excellence Framework. 2014. Improving understanding, implementation and uptake of advance care planning for end of life care. [Case study 27118.] As of 9 May 2016: <http://impact.ref.ac.uk/casestudies2/refservice.svc/GetCaseStudyPDF/27118>

This is the REF case study describing the impact of research into advance care planning undertaken by the University of Nottingham's Sue Ryder Care Centre for the Study of Supportive, Palliative and End of Life Care.

[4] Department of Health. 2012; October. End of Life Strategy: Fourth annual report. [pp. 8; 13.] London: Department of Health. As of 9 May 2016:

[https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/136486/End-of-Life-Care-Strategy-Fourth-Annual-report-web-version-v2.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/136486/End-of-Life-Care-Strategy-Fourth-Annual-report-web-version-v2.pdf)

Department of Health Strategy report for End of Life Care in NHS England.

[5] National End of Life Care Programme. 2011. Capacity, care planning and advance care planning in life limiting illness: A Guide for Health and Social Care Staff. As of 9 May 2016: [http://www.ncpc.org.uk/sites/default/files/ACP\\_Booklet\\_June\\_2011.pdf](http://www.ncpc.org.uk/sites/default/files/ACP_Booklet_June_2011.pdf)

Report by the National End of Life Care Programme, containing guidance for health and social care staff for advance care planning in cases of life limiting illness.

[6] Royal College of Physicians. 2009; February. Advance care planning: National guidelines. [Concise Guidance to Good Practice 12.] As of 9 May 2016:

<https://www.rcplondon.ac.uk/guidelines-policy/advance-care-planning>

[7] Seymour, JE, French, J, Richardson, E. 2010. Dying matters: Let's talk about it. *British Medical Journal* 341: c4860. doi: 10.1136/bmj.c4860.

Peer reviewed 'spotlight' article describing the changes in modern society and health care advances, their impact on how we deal with death and the best approach to managing dying in the future.

[8] World Health Organization Regional Office for Europe. 2011. Palliative care for older people: Better practices. Copenhagen: WHO Regional Office for Europe. As of 9 May 2016:

<http://www.eapcnet.eu/LinkClick.aspx?fileticket=UsdZAJEA5FI%3D&tabid=289>

World Health Organisation report for providing palliative care to older people.

[9] Sue Ryder Care Centre for the Study of Supportive, Palliative and End of Life Care. 2016. PrAISED: Promoting Activity, Independence and Stability in Early Dementia. As of 9 May 2016:

<https://nottingham.ac.uk/research/groups/srcc/projects/praised-dementia.aspx>

Study page with summary and contact details for the PrAISED study.

### *5.1.6. Screening to detect cognitive impairment and target rehabilitation in stroke survivors*

#### Case study

There are approximately 152,000 incidents of stroke a year in the UK [1]. The clinical response to stroke has commonly focused on physical disabilities rather than cognitive problems, although over 90 per cent of stroke survivors experience cognitive impairments that can be undetected by medical professionals [1]. Supported by an NIHR Programme Development Grant, the NIHR Clinical Research Network (CRN) and other funding sources, including the Stroke Association and Birmingham Guangzhou Brain and Cognition Centre, researchers from the University of Birmingham continue to advance a comprehensive stroke-specific screening tool, called the Birmingham Cognitive Screen (BCoS). This tool enables early and efficient detection of cognitive impairment after a stroke for a wider range of patients than is currently possible with existing methods [2]. This research has been influential in informing professional practice and its potential has been maximised through the formation of a social enterprise, Cognition Matters, which offers training for healthcare professionals and development of rehabilitation programmes. Developed by the researchers at the University of Birmingham and initially funded by the Stroke Association, the BCoS tool enables early and efficient detection of cognitive impairment after a stroke. The tool is more comprehensive in its range of assessment than those used in current clinical practice. It is able to assess a wider range of patients who would otherwise be untestable because of their difficulties with language and attention, and it does not require a specialised neuropsychologist for its administration [4].

The evaluation of the tool from 2012 concludes that ‘as a model based assessment, BCoS offers a quick and valid way to detect apraxia and predict functional recovery’ [2]. This conclusion was reiterated by another assessment from 2013, concluding that ‘[BCoS] can identify differential cognitive profiles across patient groups [and] help predict outcomes and inform rehabilitation’ [3].

The NIHR has supported further development of this screening tool and its associated training programme, in order to further advance the ways in which stroke survivors are assessed in the UK and internationally, as well as progressing professional practices in other areas, such as traumatic brain injury. This includes the BCoS Lite, funded by the NIHR, a current trial developing and validating a shorter version of the BCoS for more acute patients within six weeks of assessment [4]. This project also involves trialling of an associated rehabilitation intervention to improve cognitive and everyday functioning as indicated by the BCoS assessment.

The research has attracted widespread interest from the clinical and research communities in the UK and internationally. Since the launch of the BCoS tool in 2011, the research team has demonstrated the tool to over 120 health professionals and academics, which included clinical specialist psychologists and occupational therapists from the UK and abroad [4][5]. The research team continues their efforts to recruit further hospitals and associated services in the UK. The feedback from both clinicians and patients has been positive. As described by one of the clinicians,

‘The true strength of this assessment is that staff can see that the investment of the time to carry it out allows for clearer communication with the patient and the team and improves treatment planning. Using the same assessment tool across our pathway means that staff has improved communication about patients and saves time when moving patients across transition points in the pathway’ [4].

The widespread interest has led to development of this tool and its adaptation for assessment of patients with traumatic brain injury [4].

To maximise the potential of the BCoS tool and recover its costs from sales and training, this research led to a formation of a new social enterprise, Cognition Matters [6]. Since its establishment, this social enterprise has won a number of enterprise and social enterprise awards in recognition of the importance and potential impact of the project, including winning a Big Idea competition at the University of Birmingham in 2009, a Social Enterprise Catalyst Award from the Higher Education Funding Council for England and UnLtd in 2010, and the Enterprising Birmingham Business Plan competition in 2011 [7]. The innovativeness and effectiveness of this tool has also attracted international attention. The team received an investment from China [8], which led to the translation of the tool into three Chinese languages (Taiwanese Mandarin, Mainland Putonghua, and Cantonese version). The evaluation of the Cantonese version of the BCoS suggested that the tool was effective and claimed that it offers a ‘very promising tool for the detection of cognitive problems in Cantonese speakers’ [9]. The international uptake of the tool continues to expand, and the research team also received requests to translate the tool into additional languages, such as into Hindi Urdu, Spanish, Greek, French and Korean.

## Evidence

[1] Stroke Association. 2012; December. Saving lives: 20 years of investing in vital stroke research. Northampton: Stroke Association. As of 9 May 2016:

[http://www.thepossibilities.co.uk/assets/downloads/ResearchReport\\_Web\\_June2013](http://www.thepossibilities.co.uk/assets/downloads/ResearchReport_Web_June2013)

This report by the Stroke Association provides a summary and basic statistics on stroke and stroke research in the UK.

[2] Bickerton WL, Riddoch MJ, Samson D, Balani AB, Mistry B, Humphreys GW. 2012. Systematic assessment of apraxia and functional predictions from the Birmingham Cognitive Screen. *Journal of Neurology, Neurosurgery & Psychiatry* 83 (5): 513-21. doi: 10.1136/jnnp-2011-300968

This paper evaluates the validity and functional predictive values of the apraxia tests in the BCoS, using observational studies from a university neuropsychological assessment centre and acute and rehabilitation stroke care hospitals across England.

[3] Bickerton WL, Demeyere N, Francis D, Kumar V, Remoundou M, Balani A, Harris L, Williamson J, Lau JK, Samson D, Riddoch MJ, Humphreys GW. 2015. The BCoS cognitive profile screen: Utility and predictive value for stroke. *Neuropsychology* 29 (4): 638-48. doi: 10.1037/neu0000160

This study examined the utility of the Birmingham Cognitive Screen in discriminating cognitive profiles and recovery of function across stroke survivors, using a cross-section observational study which analysed cognitive profiles of 657 sub-acute stroke patients, 331 of whom were reassessed at 9 months.

[4] Research Excellence Framework. 2014. University of Birmingham Cognitive Screen for early identification of cognitive care pathways following stroke and other brain Injuries. [Case study 38806.] As of 9 May 2016: <http://impact.ref.ac.uk/casestudies2/refservice.svc/GetCaseStudyPDF/38806>

This REF impact case study on the BCoS outlines the details about the tools, provides its summarised research and clinical impact, and references the additional evidence.

[5] Humphreys GW, Bickerton W-L, Samson D, Riddoch MJ. 2012. BCoS cognitive screen. Psychology Press: London.

The manual is part of the test pack and provides details about the BCoS.

[6] Cognition Matters (homepage). 2016. As of 9 May 2016:

<http://www.cognitionmatters.org.uk/index.php>

This website provides details on the Cognition Matters social enterprise.

[7] Cognition Matters. 2016. Cognition Matters founders. As of 9 May 2016:

[http://www.bcos.bham.ac.uk/about\\_us.html](http://www.bcos.bham.ac.uk/about_us.html)

This webpage provides details of the Cognition founders and lists their awards in relation to the BCoS.

[8] University of Birmingham. 2015. Four University of Birmingham projects to receive funding from Guangzhou municipal government. As of 9 May 2016:

<http://www.birmingham.ac.uk/news/latest/2015/11/UoB-GMG-funding-181115.aspx>

This article provides details about international expansion of the BCoS and investment from China.

[9] Pan X, Chen H, Bickerton WL, Lau JKL, Kong APH, Rotshtein P, Guo A, Hu J, Humphreys GW. 2015. Preliminary findings on the reliability and validity of the Cantonese Birmingham Cognitive Screen in patients with acute ischemic stroke. *Neuropsychiatric Disease and Treatment* 11: 2377-2390. doi: 10.2147/NDT.S85698

This article provides the results of a study which uses the Cantonese version of the BCoS with a total of 98 patients with acute ischemic stroke and an additional 133 healthy individuals recruited as controls.

### *5.1.7. Basing interventions to reduce discrimination and stigma associated with mental health disorders around a principle of social contact*

#### Case study

Nine out of ten people with mental health problems report a negative impact of stigma and discrimination on their lives in the UK [1]. Stigma and discrimination limit recovery from illness, reduce social inclusion, have negative impacts on physical health, and stop people getting into employment [1]. To reduce stigma-related attitudes and behaviour and increase knowledge about mental illness, the NIHR has funded, through its Programme Grants for Applied Research scheme, a five-year research programme on mental health-related stigma and discrimination, SAPPHIRE, undertaken by researchers at the Institute of Psychiatry Psychology and Neuroscience at King's College London between 2007 and 2012 [2]. The research developed and tested original interventions based on the principle of 'social contact' between people with and without experience of mental health problems as the most important active ingredient in anti-stigma interventions [3].

The research resulted in the development and piloting of interventions suitable for the general population, and played a major role in the formation and evaluation of the Time to Change (TTC) campaign, the largest-ever mental health charity campaign in England [4]. Working closely with two leading mental health charities, Mind and Rethink Mental Illness, the research team made an important contribution to the development of the TTC social marketing campaign and locally based initiatives aiming to bring together people with and without experience of mental illness to reduce stigma [5]. Furthermore, the researchers led the evaluation of Phase 1 of TTC between 2008 and 2011. Together with Rethink Mental Illness, the researchers carried out a series of national phone surveys with 3,579 mental health service users using one of the tools developed as part of this project, the Discrimination and Stigma Scale (DISC). The evaluation concluded that experiences of discrimination reduced over the first four years of the TTC programme, from 91% in 2008 to 88% in 2011 [6]. Based on the results of this evaluation, the Department of Health announced £16 million in funding for TTC phase 2 [7]. The researchers continue to be an evaluation partner of TTC, collaborating with Mind and Rethink Mental Illness to track the progress and impact of the campaign and enabling the charities to improve the effectiveness of their interventions.

The research has also been influential in informing policy on mental health. In 2011, the UK government committed to 'supporting and working actively with Time to Change and other partners on reducing stigma for people of all ages and backgrounds' in the national mental health strategy 'No Health without Mental Health' [8]. In the subsequent Implementation Framework for this strategy, the three main

components of the evaluation of TTC phase 2 are listed as the methods for assessing progress towards the objective of ensuring that ‘fewer people will experience stigma and discrimination’ [9].

The research has also led to the development of a comprehensive set of measures and tools to assess stigma and discrimination in anti-stigma campaigns. It includes the Mental Health Knowledge Schedule (MAKS), consisting of stigma-related mental health knowledge domains and items about knowledge of mental illnesses, which was found to be a brief and feasible measure [10]. The Reported and Intended Behaviour Scale (RIBS) assesses reported past, current and intended behavioural discrimination. Rated by users and experts in stigma research, the scale has high internal consistency, test-retest reliability and consensus validity [11]. DISC is a psychometrically validated measure to assess experienced discrimination [12]. These measures are now used to evaluate anti-stigma campaigns in the UK, as well as internationally, including New Zealand where the DISC tool was featured in the government’s ‘*Like Minds Like Mine*’ national anti-stigma campaign [13]. Other tools, including MAKS, RIBS and DISC, have also been used by the Swedish government to evaluate Sweden’s anti-stigma campaign [14].

## Evidence

[1] Time to Change. 2008. Stigma shout: Service user and carer experiences of stigma and discrimination. London: Time to Change. As of 9 May 2016: <http://www.time-to-change.org.uk/sites/default/files/Stigma%20Shout.pdf>

This survey carried out at the beginning of Time to Change shows stigma and discrimination in mental health in the UK.

[2] King’s College London. 2016. SAPPHIRE research programme. As of 9 May 2016: <http://www.kcl.ac.uk/ioppn/depts/hspr/research/ciemh/cmh/research-projects/sapphire/index.aspx>

This webpage provides details of the NIHR-funded research programme SAPPHIRE, which underpinned the Time to Change campaign.

[3] Research Excellence Framework. 2014. Reducing mental health stigma across England. [Case study 41181.] As of 9 May 2016: <http://impact.ref.ac.uk/casestudies2/refservice.svc/GetCaseStudyPDF/41181>

The REF case impact case study provides a summary and details of the impact of the research supported by the NIHR and other funders.

[4] Time to Change. 2016. Evaluation reports. As of 9 May 2016: <http://www.time-to-change.org.uk/research-reports-publications/campaign>

This webpage includes the research papers essential to the formation of the Time to Change campaign.

[5] Time to Change. 2012. Background and achievements. London: Time to Change. As of 9 May 2016: <http://www.time-to-change.org.uk/sites/default/files/Background%20and%20achievements.pdf>

This webpage provides background information on the Time to Change campaign and explains the role of underpinning research from King’s College London in the formation of the campaign.

[6] Henderson C, Thornicroft G. 2013. Evaluation of the Time to Change programme in England 2008–2011. *British Journal of Psychiatry* 202 (s55): s45-48. doi: 10.1192/bjp.bp.112.112896

This peer-reviewed editorial piece describes the findings of an evaluation of TTC phase 1.

[7] HM Government. 2011. Press release: £20 million to knock down mental health stigma. As of 9 May 2016: <https://www.gov.uk/government/news/20-million-to-knock-down-mental-health-stigma>

This article describes how TTC phase 1 (2008–11) was evaluated and describes its results.

[8] Department of Health, HM Government. 2011. No Health without Mental Health: A cross-government mental health outcomes strategy for people of all ages. London: HM Government. As of 9 May 2016:

[https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/213761/dh\\_124058.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/213761/dh_124058.pdf)

This policy document outlines a cross-government mental health outcomes strategy and describes the role of TTC in this strategy.

[9] Centre for Mental Health, Department of Health, Mind, NHS Confederation Mental Health Network, Rethink Mental Illness, Turning Point. 2012. No Health without Mental Health: Implementation framework. London: HM Government. As of 9 May 2016: [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/216870/No-Health-Without-Mental-Health-Implementation-Framework-Report-accessible-version.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/216870/No-Health-Without-Mental-Health-Implementation-Framework-Report-accessible-version.pdf)

This best practice guidance by the Department of Health provides an implementation framework for the government's mental health strategy.

[10] Evans-Lacko S, Little K, Meltzer H, Rose D, Rhydderch D, Henderson C, Thornicroft G. 2010. Development and psychometric properties of the mental health knowledge schedule. *Canadian Journal of Psychiatry* 55 (7): 440-8. N/A

This peer-reviewed article provides further details on the MAKES tool.

[11] Evans-Lacko S, Rose D, Little K, Flach C, Rhydderch D, Henderson C, Thornicroft G. 2011. Development and psychometric properties of the reported and intended behaviour scale (RIBS): A stigma-related behaviour measure. *Epidemiology and Psychiatric Sciences* 2 (3): 263-71. doi:10.1017/S2045796011000308

This peer-reviewed article provides further details on the RIBS tool.

[12] Thornicroft G, Rose D, Kassam A, Sartorius N. 2007. Stigma: Ignorance, prejudice or discrimination? *British Journal of Psychiatry* 190 (3): 192-3. doi: 10.1192/bjp.bp.106.025791

This peer-reviewed article provides further details on the DISC tool.

[13] Wylie A, Brown R. 2011. Discrimination reported by users of mental health services: 2010 survey: Research report for Ministry of Health. Auckland: Mental Health Foundation of New Zealand. As of 9 May 2016: <https://www.mentalhealth.org.nz/assets/ResourceFinder/Discrimination-reported-by-users.pdf>

This report cites use of the tools developed by the NIHR-funded research described above.

[14] Hansson L, Stjernswärd S, Svensson B. 2014. Perceived and anticipated discrimination in people with mental illness – An interview study. *Nordic Journal of Psychiatry* 68 (2): 100-6. doi: 10.3109/08039488.2013.775339

This article cites use of the tools developed by this research.



### *5.1.8. Mapping inequality as a predictor of poor health and social care status*

#### Case study

Understanding the sources of income inequality has become a pressing issue around the world. Supported by funding from the NIHR, the research of Professor Kate Pickett and Professor Richard G. Wilkinson from the University of York helped establish the link between income inequality and social and health status, informing policy debates and Professors Pickett and Wilkinson are working with the third sector to improve public understanding of those issues.

Undertaken between 2007 and 2012, the studies examined social and health-related determinants of inequality, using ecological and multilevel cross-national comparisons and found that societies with lower levels of income inequality perform consistently better [1][2][3]. Their extensive international evidence links inequality to a wide range of social issues, including mental and physical health, drug use, obesity, educational performance, teenage births, violence, and social mobility. To improve the quality of life and well-being, their research recommended that more attention be paid to the social environment and the quality of social relations and that reducing material inequality improves the psychosocial well-being and social functioning of whole societies [4].

The research findings have been presented in 16 widely cited peer-reviewed journal articles and in a monograph *The Spirit Level: Why More Equal Societies Almost Always Do Better*, published by Penguin in 2009 [4]. *The Spirit Level* has sold more than 150,000 copies in its English edition and is published in 23 foreign editions [4]. The research and its implications have been influential in informing policy and public debates on inequality, and in 2009 led Pickett and Wilkinson to establish a not-for-profit educational and campaigning organisation, The Equality Trust. The organisation aims to improve the public understanding of social issues related to inequality and to inform political debate. It has widely engaged with the public, policymakers, and employers in the UK and internationally [5]. Among its many activities, The Equality Trust led an influential campaign, titled One Society, which aimed to ‘promote policies to take us towards a more equal society, and respond to political developments relating to top pay and income inequality’ [5].

The research, its implications and the resulting third sector work have had a considerable influence on informing public and policy debates on the determinants of inequality in society in the UK. The research findings and associated recommendations have been widely discussed by policy-makers nationally and internationally. The findings influenced the formation of local Fairness Commissions in the UK [6], which investigate and implement ways of reducing inequality in local areas such as recommending and campaigning for the payments of a living wage, prior to the introduction of the national living wage by the UK government in April 2016. The research has also fed in to numerous policy commissions, including the independent Living Wage Commission [7], the High Pay Commission [8] and the UK Drug Policy Commission [9]. It has also influenced the introduction of the Equality Act of 2010, which now includes a duty for local and national public bodies to ‘have regard to the desirability of reducing socio-economic inequalities’ in their decisionmaking [10].

Internationally, the research findings have been cited in numerous policy documents by international organisations and foreign governments. This includes the World Health Organisation’s Regional Office

for Europe in its policy document on addressing the social determinants of health [11], as well as the Canadian National Council of Welfare which cited the research in relation to strategies for reducing poverty and improving societal well-being [12]. The research conclusions and recommendations have also featured in the speeches of numerous prominent policymakers from international governmental organisations, including the United Nations, which commented on the impact of the research on the policy debates [13].

## Evidence

[1] Wilkinson RG, Pickett KE. 2006. Income inequality and population health: A review and explanation of the evidence. *Social Science & Medicine* 62 (7): 1768-84. As of 9 May 2016: <https://www.equalitytrust.org.uk/sites/all/themes/equalitytrust/images/inequality-and-health.pdf>

This peer-reviewed article provides the findings of the research underpinning this case study.

[2] Wilkinson RG, Pickett KE. 2007. The problems of relative deprivation: Why some societies do better than others. *Social Science & Medicine* 65 (9): 1965-78.

This peer-reviewed article provides the findings of the research underpinning this case study.

[3] Wilkinson R, Pickett K. 2010. *The spirit level: Why Greater Equality Makes Societies Stronger*. New York: Bloomsbury Press.

This monograph, written for a general readership, summarises the findings of the research and its implications.

[4] Research Excellence Framework. 2014. The impact of social inequality: Changing the public and policy debate. [Case study 43415.] As of 9 May 2016: <http://impact.ref.ac.uk/casestudies2/refservice.svc/GetCaseStudyPDF/43415>

This REF impact case describes the impact of this research.

[5] The Equality Trust. 2015. History. As of 9 May 2016: <https://www.equalitytrust.org.uk/history>

This webpage describes the history of The Equality Trust and how the research underpinned its formation.

[6] Sillett J, O'Donnell C. 2013; 13 August. Briefing: Fairness Commissions. [Policy Briefing.] London: Local Government Information Unit. As of 9 May 2016: <http://www.lgiu.org.uk/briefing/fairness-commissions/>

This policy brief provides details on the Fairness Commissions in the UK.

[7] Living Wage Commission. 2014; June. *Work that pays: The final report of the Living Wage Commission*. London: Living Wage Commission. As of 9 May 2016: [http://www.archbishopofyork.org/york//data/files/resources/3109/Work-that-pays\\_The-Final-Report-of-The-Living-Wage-Commission\\_w-3.pdf](http://www.archbishopofyork.org/york//data/files/resources/3109/Work-that-pays_The-Final-Report-of-The-Living-Wage-Commission_w-3.pdf)

This report describes the Living Wage Commission in the UK. Professor Pickett was one of the commissioners of this report.

[8] High Pay Commission. 2011. Cheques with balances: Why tackling high pay is in the national interest. [Final report of the High Pay Commission, UK.] : High Pay Commission. As of 9 May 2016: [http://highpaycentre.org/files/Cheques\\_with\\_Balances.pdf](http://highpaycentre.org/files/Cheques_with_Balances.pdf)

This report on tackling high pay cites the research in order to illustrate the link between social mobility and income inequality and strengthen the case for tackling high pay in the UK.

[9] UK Drug Policy Commission. 2012; October. A fresh approach to drugs: The final report of the UK Drug Policy Commission. London: UKDPC. As of 9 May 2016: <http://www.ukdpc.org.uk/wp-content/uploads/a-fresh-approach-to-drugs-the-final-report-of-the-uk-drug-policy-commission.pdf>

This report describes the link between international levels of drug use and income inequality based on the data provided by The Equality Trust.

[10] HM Government. 2010. Equality Act 2010 (c. 15). The National Archives. As of 9 May 2016: <http://www.legislation.gov.uk/ukpga/2010/15/introduction>

This webpage provides further information on the Equality Act 2010.

[11] World Health Organization Regional Office for Europe. 2012. Addressing the social determinants of health: The urban dimension and the role of local government. Copenhagen: WHO Regional Office for Europe. As of 9 May 2016:

[http://www.euro.who.int/\\_\\_data/assets/pdf\\_file/0005/166136/UrbanDimensions.pdf](http://www.euro.who.int/__data/assets/pdf_file/0005/166136/UrbanDimensions.pdf)

This WHO report cites the evidence from *The Spirit Level* to illustrate the importance of understanding and monitoring the link between social determinants of health and income inequality.

[12] Canadian National Council of Welfare. 2011. The dollars and sense of solving poverty. [National Council of Welfare Reports 130.] Ottawa: National Council of Welfare. As of 9 May 2016: [http://publications.gc.ca/collections/collection\\_2011/cnb-ncw/HS54-2-2011-eng.pdf](http://publications.gc.ca/collections/collection_2011/cnb-ncw/HS54-2-2011-eng.pdf)

This policy report describes the case for tackling poverty in Canada and cites *The Spirit Level* in its evidence.

[13] Moon B-K. 2013. Remarks at informal General Assembly thematic debate on inequality. As of 9 May 2016:

[http://www.un.org/apps/news/infocus/speeches/statments\\_full.asp?statID=1918#.UfDb943E](http://www.un.org/apps/news/infocus/speeches/statments_full.asp?statID=1918#.UfDb943E)

This webpage provides a copy of the full speech on inequality by United Nations Secretary-General Ban Ki-moon.

### *5.1.9. Partnering with charities to advance experimental medicine in cancer research*

#### Case study

In partnership with Cancer Research UK the NIHR and the health departments of the devolved administrations together established Experimental Cancer Medicine Centres (ECMC) to enable researchers and clinicians to work together towards developing new treatments for cancer [1][2]. Despite the historically long development cycle of oncology medicines (approximately 10 years), ECMCs are

already showing signs of impact in enhancing research capacities and focusing resources from public bodies, charities and industry into early phase clinical trials of cancer medicines.

The ECMC network was launched in 2007. To date there has been a joint investment by all the partners of £70 million. ECMC funding is competitive, encouraging bids from centres with a demonstrated track record of achievement in conducting research into experimental cancer medicines. Similar to that of the NIHR Biomedical Research Centres, ECMC funding is an infrastructure award, covering the costs of dedicated research nurses, laboratory technicians, administrators or pharmacists.

Bringing together public and charitable funding, ECMCs offer a high degree of flexibility and freedom in pursuing a broad area of research within experimental cancer medicine: centres are free to use the award in accordance with their local needs. There are currently 18 ECMCs and 9 paediatric centres across the UK [3]. In England, the NIHR provides support for the clinical infrastructure costs of research, while Cancer Research UK (CRUK) provides funding to meet the academic partner's infrastructure costs.

An impact of the ECMCs has been to increase the number of early trials of innovative new medicines. In 2014/15, more than 2,500 patients were recruited to 389 trials [3]. The success of ECMC supported research is evident by the progression of studies through different phases of development, that is, from pre-clinical to phase 2/3 trials. Examples of such studies are those on novel compounds for the treatment of melanoma, breast and ovarian cancer, non-small-cell lung cancer or chronic myelomonocytic leukaemia among others [3].

An example of a promising collaboration is that in myeloma research. The Myeloma UK Early Phase Clinical Trial Network, which was developed by the charity Myeloma UK, worked with the ECMCs to conduct the study 'Myeloma UK One', investigating the best combination of treatments for patients that relapsed or that have refractory myeloma. The study was set up in record time, with recruitment starting within 12 months from protocol design, compared with the usual two-year time-frame. This is an important achievement, one which supports the aim of bringing new medicines to patients in need more quickly [4].

A major ongoing ECMC-supported research study to advance stratified medicine is the 'Matrix trial'. Leveraging the ECMC network, the study aims to provide the right treatment to the right patient, building on knowledge of what makes the cancer cells grow and survive in that particular patient [5]. The study is being conducted in collaboration with the third sector represented by important industry players (AstraZeneca and Pfizer), and represents about £25 million worth of research [5]. The participating hospitals are coordinated by the respective ECMC in their region, with approximately 50 NHS trusts being involved in the programme [3].

The ECMCs have built research capacity, leveraging additional funding from universities, NHS Trusts and the private sector of £73.5 million (from a total of 48 companies or organisations). Commercial partnerships are encouraged in the ECMCs, with the private sector being a partner in 77 per cent of studies in the adult network and 60 per cent of those in the paediatric ones [3].

Other ways in which the ECMC network has developed research capacity include: supporting workshops (e.g. a 2014 Research Nurse workshop); developing knowledge hubs (e.g. the UK Therapeutic Cancer Prevention Network Group); and offering support in radiopharmacy trial set up through the CRUK,

ECMC and UK Radiopharmacy Group Taskforce [3]. In line with the NIHR's commitment to involving patients in research, the ECMCs have also engaged both patients and the public. This has involved gaining their insights into study development, study implementation and dissemination of results. The ECMC secretariat has set-up an ECMC Patient and Public Involvement (PPI) Group comprising representatives from the adult ECMCs (nominated by the ECMC leads), staff and PPI representatives. Patient representatives can also be found on ECMC steering committees/boards, as well as on a number of trial-specific steering groups [3].

The ECMCs are illustrative of how the NIHR, in partnership with CRUK, has managed to set up a clinical research network that draws on existing capacities and is attracting consistent further funding from industry to advance oncological research for patient benefit.

## Evidence

[1] Experimental Cancer Medicine Centre Network (homepage). 2016. As of 2 May 2016: <http://www.ecmcnetwork.org.uk/ecmc-network-18-centres-uk-wide>

Webpage with further details on the Experimental Cancer Medicine Centre Network.

[2] Experimental Cancer Medicine Centre. n.d. Paediatric Network. As of 2 May 2016: <http://www.ecmcnetwork.org.uk/ecmc-paediatric-network>

Webpage with further details on the Experimental Cancer Medicine Centre Paediatric Network,

[3] Experimental Cancer Medicine Centre Network. n.d. Annual Report 2014–15. London: EMC. As of 2 May 2016:

[http://www.ecmcnetwork.org.uk/sites/default/files/ECMC%20Annual%20Report%202014-15%20for%20web\\_1.pdf](http://www.ecmcnetwork.org.uk/sites/default/files/ECMC%20Annual%20Report%202014-15%20for%20web_1.pdf)

This is the ECMC annual report for 2014–15, highlighting the achievements of the network in the areas of collaboration within the network and with industry and discussing the supporting role of the ECMC secretariat.

[4] National Institute for Health Research. 2012. NIHR Clinical Research Infrastructure Collaborations engaging with medical research charities. London: NIHR. As of 2 May 2016: <http://www.nihr.ac.uk/documents/industry/Brochures/Engaging-with-medical-research-charities.pdf>

Guidance published by the National Institute for Health Research describing how to engage with medical research charities.

[5] Cancer Research UK. 2014. Revolutionary clinical trial aims to advance lung cancer treatment thanks to a Cancer Research UK and pharma partnership. London: Cancer Research UK. As of 2 May 2016: <http://www.cancerresearchuk.org/about-us/cancer-news/press-release/2014-04-17-revolutionary-clinical-trial-aims-to-advance-lung-cancer-treatment-thanks-to-cancer-research-uk-and>

Press release from Cancer Research UK announcing a new clinical trial aiming to advance lung cancer treatment through a partnership between pharma and Cancer Research UK.

### 5.1.10. *Exploring the benefits of community singing groups to improve health outcomes in elderly people*

#### Case study

Combining the arts and the sciences, and working alongside charities, researchers at the Sidney De Haan Research Centre for Arts and Health at Canterbury Christ Church University have deployed creative approaches to tackling health issues alongside a programme of research, and have delivered interventions to improve the lives of elderly people with a range of conditions [1].

The Canterbury team's work focussed on the well-being and health benefits of singing groups. The team had established an independent charity, Sing for Your Life, whose Silver Song Groups afforded opportunities for older people to take part in community singing [1].

With the NIHR's support, the team set out to conduct a randomised controlled trial to evaluate the effectiveness of these groups as a health promotion initiative [3]. The trial showed significant improvements in participants' reported quality of life measures of mental well-being, at the end of the 12-week intervention and 3 months after follow-up [1].

Linked work investigated the experiences of patients with respiratory disorders, specifically chronic obstructive pulmonary disease (COPD), engaged in a 36-week singing programme. In this case, the team found that participants perceived singing as both acceptable and beneficial for both their breathing, and their overall physical, psychological and social wellbeing [4].

The team has been able to transfer the findings of their research via the Sing for Your Life charity, which now reaches more than 1,000 older people in community and care settings per month. With engagement from local Parkinson's Society support groups, the team have established Skylarks, a network of singing for patients with Parkinson's. Testimonials capture the impacts of these groups on patients' wellbeing:

'My Mum was diagnosed with Parkinson's eight years ago and suffers from acute anxiety, especially in public situations. To say the singing group was a triumph would be an ENORMOUS understatement. It was the first time she has felt comfortable enough to stay for an entire group event in a very long time' [5].

Further charitable support from the Dunhill Medical Trust has enabled the team to establish an East Kent Singing and COPD network, with similarly positive patient testimonials:

'I go to the group with a tight chest, and leave feeling I can breathe again' [5].

The Royal Society for Public Health incorporated the research team's findings into national practitioner training in the arts, health and well-being. The team has also undertaken a number of local and international training events. Though perhaps unorthodox in its approach, these efforts to bring arts-based group therapy closer to evidence-based medical care, and involve the third sector, are paving the way for elderly people to enjoy a better quality of life that may also in time prove beneficial to their health.

## Evidence

[1] Research Excellence Framework. 2014. Arts, health and wellbeing research. [Case study 40585.] As of 2 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=40585>

REF case study describing the reach and significance of impacts derived from singing as a health and wellbeing intervention for adults within clinical and non-clinical populations.

[2] Clift S, Skingley A, Coulton S, Rodriguez J. 2012. A controlled evaluation of the health benefits of a participative community singing programme for older people (Silver Song Clubs). Folkestone: Sidney De Haan Research Centre for Arts and Health. As of 2 May 2016: [http://www.ahsw.org.uk/userfiles/Other\\_Resources/SSCRCTsummaryreportOct12.pdf](http://www.ahsw.org.uk/userfiles/Other_Resources/SSCRCTsummaryreportOct12.pdf)

Summary of the Canterbury research group's findings of a randomised controlled trial of singing groups as a health intervention.

[3] Skingley A, Clift S, Coulton S, Rodriguez J. 2011. The effectiveness and cost-effectiveness of a participative community singing programme as a health promotion initiative for older people: Protocol for a randomised controlled trial. *BMC Public Health* 11: 142. doi:10.1186/1471-2458-11-142

Protocol for a pragmatic randomised controlled trial of singing groups as a health intervention.

[4] Skingley A, Page S, Clift S, Morrison I, Coulton S, Treadwell P, Vella-Burrows T, Salisbury I, Shipton M. 2014. Singing for Breathing: Participants' perceptions of a group singing programme for people with COPD. *Arts and Health* 6 (1): 59-74. doi:10.1080/17533015.2013.840853

Results of a pre-test, post-feasibility and nested qualitative study of respiratory function and self-reported quality of life of patients with chronic obstructive pulmonary disease engaged in a 36-week singing programme.

[5] Research Excellence Framework. 2014. Singing, health and wellbeing. [Case study 40398.] As of 2 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=40398>

Further descriptions of the impacts on practice and outreach from singing as a health and wellbeing intervention, with details of specific efforts to reach elderly people with mental health disorders and chronic obstructive pulmonary disease.

## 6. Supporting Public Health Delivery

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### 6.1. Summary

#### **Healthy. Informed. Resilient.**

*NIHR's public health research promotes healthy behaviours and population-level interventions that lead to healthier lives and tackle health inequalities across the general population.*

NIHR's investment in public health research strengthens the country's resilience to disease. It helps to prevent disease through improved screening and diagnostics, increases emergency preparedness and promotes health in both medical and non-healthcare settings.

NIHR supports research into novel methods to screen for and prevent non-communicable diseases, which saves money and enables healthier lives. NIHR research into broader prevention initiatives also helps to reduce the impact of chronic conditions on the health system. Examples of NIHR-funded research in this area include the following:

- New interventions to reduce alcohol-related harm save primary care trusts an estimated £650,000 annually.
- Research into the use of pulse oximetry – a cost-effective method to detect critical congenital heart defects in newborns – means 92 per cent of babies with such defects are now diagnosed before leaving hospital.
- Studies of low-hazard nicotine products reduce the harm from smoking by providing the evidence to underpin smoking prevention strategies.
- Research investigating the potential of stratified care for nonspecific low back pain – where treatment is matched to patients' risk of a poor prognosis – is estimated to lead to more than £700 million in overall savings.
- Research into the clinical effectiveness and cost-effectiveness of screening for human papillomavirus is contributing to the evidence base for effective cervical cancer screening methods, both in England and internationally.

NIHR's support of vaccination research is an important component in preventing the spread of potentially life-threatening communicable diseases. NIHR research contributes to public preparedness for outbreaks and epidemics, enabling a rapid response in times of crisis. Examples of NIHR initiatives include:



- NIHR-supported research into meningococcal meningitis has led to policy changes on childhood immunisation and national vaccine coverage, which has contributed to better protection of the population against this dangerous condition.
- As part of the response to the H1N1 epidemic, NIHR put in place a rapid commissioning mechanism to fund a range of research initiatives to combat the epidemic. This contributed to increased vaccination coverage, with more than 500,000 children receiving an H1N1 vaccination within a few months of the epidemic beginning, and with a doubling in the number of pregnant women immunised against influenza in England between 2008 and 2015.

NIHR funds health promotion–related research that is designed to safeguard the public from health risk factors. It also provides evidence to inform national and international policy changes. Some examples of NIHR policy impact include:

- Banning the use of bisphenol A in baby bottles was a policy decision influenced by NIHR-funded research investigating the effects of human exposure to this chemical.
- Violence is being prevented through interventions that make innovative use of data shared from hospital accident and emergency departments.
- Understanding public attitudes to presumed consent for organ donation – which was facilitated by NIHR’s funding of studies of different national approaches – helped to prevent a costly change in policy and informed recommendations which contributed to a 50 per cent increase in registering of organ donors in the UK.

#### *6.1.1. Fostering the use of low hazard nicotine products amongst policies to prevent smoking*

##### Case study

Despite the progress in curbing smoking uptake, data show that smoking-related deaths and prevalence of tobacco-related illnesses remain of great concern in the UK. About 10 million adults still smoke in Great Britain, with the highest number of smokers aged 25–34 years old [1]. These numbers also translate into high costs: estimates place yearly NHS spending on smoking-related diseases at £2.7 billion, while the wider UK economy loses £2.5 billion as a result of sick leave and lost productivity [2].

NIHR-funded research has helped to extend the evidence base for interventions to reduce smoking uptake. Research undertaken at the University of Nottingham is credited with advancing knowledge on how to prevent people from taking up smoking and on smoking cessation, in particular in less studied groups, such as pregnant women and children. NIHR-funded research performed by this team of researchers has investigated the efficacy and safety of nicotine patches during pregnancy [3] and the role of hospital-based cessation practitioners to identify and treat smokers in secondary care [4]. These research areas were instrumental in fostering the use of low-hazard nicotine products as a harm reduction strategy, as well as contributing to the design and delivery of interventions which help to discourage people from taking up smoking.

This research has had further impacts through its adoption into policy. The Nottingham group’s findings informed several policy documents on smoking cessation and prevention, including: National Institute for

Health and Care Excellence (NICE) guidance on smoking cessation in community settings in 2008; NICE guidance on smoking cessation in pregnancy and after childbirth [5]; NICE guidance on smoking cessation in all NHS acute, maternity and mental health secondary care settings [6]; and the NICE update on evidence on school-based interventions to prevent the uptake of smoking among children and young people [7]. The Nottingham team has also informed policies on prohibiting point-of-sale tobacco displays in England, on plain tobacco packaging and on harm reduction [8].

While it is not possible to quantify the particular impact of only the NIHR-funded studies, this body of research should be considered in connection with the achievements of smoking cessation activities in the UK. One such success is the steady year-on-year decline (0.4%) of women known to be smokers at the time of delivery of a baby. Moreover, between the last quarter of 2015 and the first quarter of 2016, the proportion of pregnant women known to be smokers at the time of delivery had fallen below the national goal of 11 per cent for the first time [9]. In addition to reducing the suffering of smokers and their families and dependents, this type of work also contributes to wider economic savings to both individuals, their families, employers and the NHS.

## Evidence

[1] Action on Smoking. 2015. Fact sheet. As of 13 May 2016: <http://ash.org.uk/information/facts-and-stats/fact-sheets>

Figures on the amount of smoking in the UK.

[2] British Medical Association. 2016. Smoking statistics. As of 13 May 2016: <http://www.bma.org.uk/working-for-change/improving-and-protecting-health/tobacco/smoking-statistics>

Figures from the British Medical Association on smoking in 2016.

[3] Coleman T, Cooper S, Thornton JG, Grainge MJ, Watts K, Britton J, Lewis SA. 2012. A randomized trial of nicotine replacement therapy patches in pregnancy. *The New England Journal of Medicine* 366: 808-18. doi:10.1056/NEJMoa1109582

The research investigated the efficacy and safety of nicotine patches during pregnancy by recruiting participants who received behavioural cessation support and treatment with active nicotine patches (15 mg per 16 hours) or matched placebo patches. The findings of the study were that there was no significant difference in the rate of abstinence from the quit date until delivery between the nicotine replacement and placebo groups. Therefore, it was concluded that employing nicotine patches to behavioural cessation support for women who smoked during pregnancy did not significantly increase the rate of abstinence from smoking until delivery.

[4] Murray RL, Leonardi-Bee J, Marsh J, Jayes L, Li J, Parrott S, Britton J. 2013. Systematic identification and treatment of smokers by hospital based cessation practitioners in a secondary care setting: Cluster randomised controlled trial. *British Medical Journal* 347: f4004. doi:10.1136/bmj.f4004

The study investigated the effectiveness of the systematic default provision of smoking cessation support to all adult smokers admitted to hospital, relative to usual care. The intervention involved behavioural support and cessation pharmacotherapy for the duration of the hospital stay. According to the study's findings, this led to substantial improvements in smoking cessation among smokers admitted to hospital.

[5] National Institute for Health and Care Excellence. 2010. Guidance on smoking cessation in pregnancy and after childbirth. [NICE guidelines PH26.] As of 2 May 2016: <http://guidance.nice.org.uk/PH26>

The NICE guideline recommends that all pregnant women who smoke – and all those who are planning a pregnancy or who have an infant aged under 12 months – should be referred for help to quit smoking. It also mentions when and how nicotine replacement therapy and other pharmacological support should be offered.

[6] National Institute for Health and Care Excellence. 2013. Guidance on smoking cessation in all NHS acute, maternity and mental health secondary care settings. [NICE guidelines PH48.] As of 2 May 2016: <https://www.nice.org.uk/guidance/ph48>

This guidance aims to support smoking cessation, temporary abstinence from smoking and smoke-free policies in all secondary care settings. It recommends: strong leadership and management to ensure premises remain smoke free; all hospitals have an on-site stop smoking service; identifying people who smoke; offering advice and support to stop; providing intensive behavioural support and pharmacotherapy as an integral component of secondary care; integrating stop smoking support in secondary care with support provided by community-based services; ensuring staff are trained to support people to stop smoking while using secondary care services; supporting staff to stop smoking or to abstain while at work; and ensuring there are no designated smoking areas or staff-facilitated smoking breaks for anyone using secondary care services.

[7] National Institute for Health and Care Excellence. 2013. Evidence update on school-based interventions to prevent the uptake of smoking among children and young people. [NICE guidelines PH23.] As of 2 May 2016: <http://guidance.nice.org.uk/PH23>

The guidance aims to prevent the uptake of smoking by children and young people aged under 19. Among the recommendations, it mentions that information on smoking should be integrated into the curriculum and that anti-smoking activities should aim to develop decision-making skills and include strategies for enhancing self-esteem.

[8] Research Excellence Framework. 2014. Development and implementation of UK tobacco control policy. [Case study 27327.] As of 2 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=27327>

The case study highlights the achievements of the research conducted at the University of Nottingham aimed at preventing the harm to health caused by smoking. The contributions of the research are in the following areas: 1) smoke-free policy and passive smoking – the report the team produced on passive smoking and children received high media coverage and calls by NGOs for greater restrictions on smoking in the presence of children, particularly in cars; 2) point-of-sale legislation informing the 2010 Health Act – point-of-sale legislation in the 2011 coalition government's Tobacco Control Plan for England; 3) plain packaging – the systematic evidence review on plain tobacco packaging contributed to the Tobacco Control Plan; 4) smoking cessation and prevention – as shown by research in hospital patients, adolescents, pregnant women and people with mental disorders; and 5) harm reduction – the team produced a harm reduction report for the Royal College of Physicians that contributed to the

inclusion of harm reduction strategies in numerous policies, including a change in Medicines and Healthcare Products Regulatory Agency approach to licensing policy on nicotine products and informing the 2013 EU Tobacco Products Directive for the Environment, Public Health and Food Safety (ENVI) committee, to support permissive regulation of nicotine-containing products at the EU level.

[9] Health and Social Care Information Centre. 2016. Statistics on Women's Smoking at Time of Delivery: England Quarter 3, October 2015 to December 2015 Key Facts As on 13 May 2016: [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/508497/Statistics\\_on\\_Women\\_s\\_Smoking\\_Status\\_at\\_Time\\_of\\_Delivery\\_\\_England\\_-\\_Quarter\\_3\\_\\_2015-16\\_Report.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/508497/Statistics_on_Women_s_Smoking_Status_at_Time_of_Delivery__England_-_Quarter_3__2015-16_Report.pdf)  
Figures from the Health and Social Care Information Centre on prevalence of smoking among pregnant women at the time of delivery.

### *6.1.2. Sharing hospital A&E assault data as a model to prevent violence*

#### Case study

Violence contributes to lifelong ill health and early death. The WHO (World Health Organisation) highlights that many causes of death, such as heart disease, stroke, cancer and HIV/AIDS are the result of victims of violence engaging in such behaviours as smoking, alcohol and drug misuse, and unsafe sex in an attempt to cope with the psychological consequences of violence[1]. Therefore, violence prevention has important public health implications. At an individual level, violence prevention avoids physical and mental suffering. At a system level, it reduces the utilisation of several health services, including emergency department services. NIHR-funded research has contributed to the advancement of knowledge in the field of violence prevention. Building on work started in the mid-1990s, a team at Cardiff University has refined the Cardiff Model for Violence Prevention, a widely recognised best practice model on data sharing.

Created in 1996 by the Cardiff Violence Prevention Group, the model represents a multi-agency data-sharing approach using emergency unit data. It includes a monthly compiling of electronic data from patients attending emergency units as a result of violent acts, followed by the anonymisation of this data in view of sharing it through the local authority's Community Safety Partnership. These data, combined with others gathered through different police channels, inform violence prevention interventions put in place by different agencies, such as education authorities or transport authorities, that could supplement transport in dangerous areas [2][3].

The effectiveness of the Cardiff Model has been demonstrated over many years. It was found that this approach has led to a 4 per cent annual decrease in emergency unit use in Cardiff, despite a 1 per cent annual population increase in this city [3]. An evaluation also found a consistent decrease in violence inside high-risk premises where alcohol was sold and consumed [4]. The effectiveness of the Cardiff Model has also been demonstrated when compared with the other 14 most similar cities across the UK, where the method was not applied. The research was controlled for variables that are known to impact incidence and recording of violence, such as strength of the police force and city unemployment. The evaluation found that there was a 42 per cent decrease in violent crimes in Cardiff compared with the other cities, which was attributed to the Cardiff Model. The Cardiff Model has also been evaluated to assess economic benefits. It was found that in Cardiff, the model saved the city approximately £5 million

per annum from 2003 to 2006 and £6.9 million in 2007 [5]. The research has received wide recognition and adoption, being implemented in the UK as well as in other countries, such as the Netherlands [2].

NIHR funding has allowed the development of the Cardiff Model for Violence Prevention. While further refinement of the model is possible [6], this way of data sharing has resulted in positive public health outcomes and reduced costs and has led to safer societies.

## Evidence

[1] World Health Organization. 2014. Global status report on violence prevention 2014. [Joint report from WHO, the United Nations Development Programme and the United Nations Office on Drugs and Crime.] As of 2 May 2016:

[http://www.who.int/violence\\_injury\\_prevention/violence/status\\_report/2014/en/](http://www.who.int/violence_injury_prevention/violence/status_report/2014/en/)

The report gathers data from 133 countries and focuses mainly on national efforts addressing interpersonal violence, namely child maltreatment, youth violence, intimate partner and sexual violence, and elder abuse. The report, which was jointly published by the WHO, the United Nations Development Programme and the United Nations Office on Drugs and Crime, and calls for a scaling up of violence prevention programmes, stronger legislation and enforcement of existing regulations for violence prevention, as well as the provision of services for victims of violence.

[2] Research Excellence Framework. 2014. Shaping government policy in violence prevention. [Case study 3669.] As of 2 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=3669>

The case study offers a comprehensive overview on the development of the Cardiff Model for Violence Prevention, as well as on the policy impact it has had.

[3] Warburton AL, Shepherd JP. 2004. Development, utilisation, and importance of accident and emergency department derived assault data in violence management. *Emergency Medicine Journal* 21: 473-7. As of 2 May 2016: <http://emj.bmj.com/content/21/4/473.full>

The article represents an evaluation over a four-year period of the Cardiff model implementation. The main finding of the evaluation was that this model of data sharing was a powerful and effective means of targeting police and other local resources to bring about violence reduction. Such interventions were: the mounting of overt and covert police interventions targeted at violence hotspot licensed premises; the introduction of new half-hourly night time city centre bus services by transport authorities; and an assault awareness campaign in schools and public libraries.

[4] Warburton AL, Shepherd JP. 2006. Tackling alcohol related violence in city centres: Effect of emergency medicine and police intervention. *Emergency Medicine Journal* 23: 12-17. doi:10.1136/emj.2004.023028

The article present the results of a three-year study that investigated the correlation of alcohol-related assault injury in the city centre of Cardiff, with particular reference to 1) emergency department and police interventions; and 2) number and capacity of licensed premises. The study found that city centre assault injury prevention can be achieved through police/emergency department interventions.

[5] Florence C, Shepherd JP, Brennan I, Simon T. 2013. An economic evaluation of anonymised information sharing in a partnership between health services, police and local government for preventing violence-related injury. *Injury Prevention* 20: 108-114. doi:10.1136/injuryprev-2012-040622

The study assessed the costs and benefits of the Cardiff Model and found that this scheme led to substantial cost savings for the health service and the criminal justice system. These findings emerged from a comparison with 14 other cities in England and Wales designated as similar by the UK government, where the Cardiff Model was not implemented.

[6] Giacomantonio C, Sutherland A, Boyle A, Shepherd J, Kruithof K, Davies M. 2014. *Injury surveillance: Using A&E data for crime reduction guidance for police analysts and practitioners*. Coventry: College of Policing. As of 2 May 2016: [http://www.college.police.uk/About/What-do-we-offer/Documents/RR-851-CoP\\_AE\\_Guidance\\_report\\_final.pdf](http://www.college.police.uk/About/What-do-we-offer/Documents/RR-851-CoP_AE_Guidance_report_final.pdf)

The report offers guidance for organisations interested in violence reduction and who do not currently use A&E data. It draws on the knowledge of practitioners who work with the Cardiff Model and identifies a number of possible uses of A&E data, as well as common issues associated with the sharing and use of this information.

### *6.1.3. Commissioning research to reduce alcohol-related harm*

#### **Case study**

There are about 10.8 million adults in the UK who drink alcohol at levels that pose a risk to their health [1]. Frequent alcohol intake increases the risks of serious health afflictions, such as heart disease, stroke, liver disease, several types of cancer and pancreatitis. In addition, alcoholism can lead to several social challenges, such as homelessness, violence and family problems. All this adds up to high societal costs; the UK economy is losing £25.1 billion annually, while the health service is spending £2.7 billion annually on alcohol-linked conditions [2]. Therefore, research on how to reduce alcohol-related risks is very important to inform policies that will bring both health and economic benefits.

The NIHR is addressing these concerns by commissioning research on alcohol interventions. Examples of such research are the studies conducted at Newcastle University. Evidence gathered through a Cochrane Collaboration [3], which produced a systematic review of the wider evidence on screening and brief intervention effectiveness in primary care settings, was cited in policy documents [4]. This was credited with informing the public health community on how to act to prevent alcohol-related risk and harm across the population [2].

Researchers from Newcastle and Northumbria universities have also developed and promoted a method of screening and brief intervention for use by GPs and nurses in primary care. The screening helps to identify persons who would be at risk of alcohol-related harms (drinking above guideline levels), followed by an intervention consisting of advice or counselling to change drinking behaviour. The intervention includes a pack, entitled ‘How Much Is Too Much?’ that is aimed at patients who are able to control their drinking. The screening method has received wide recognition [4][5], and its impact can be traced on several levels. ‘How Much Is Too Much’ was included in six annual Directed Enhanced Service documents that were commissioned by the Department of Health and disseminated via Primary Care

Trusts [2], thereby reaching a wide population in England. This screening tool has also had policy impact, having been recommended in the National Institute for Health and Care Excellence (NICE) guideline on alcohol-use disorders [6]. This NICE guideline in turn informed the government's 2012 Alcohol Strategy, recommending routine alcohol screening to be carried out by NHS health professionals [5].

The positive impacts of the 'screening alcohol' intervention further translate into healthcare savings. The Department of Health estimated that the screening and brief advice could save a Primary Care Trust on average £650,000 annually, which in 2009 amounted to overall healthcare savings of around £100 million [7].

## Evidence

[1] Action on Smoking and Health. 2015. ASH facts at a glance – Smoking statistics. [November 2015.] As of 2 May 2016: [http://www.ash.org.uk/files/documents/ASH\\_93.pdf](http://www.ash.org.uk/files/documents/ASH_93.pdf)

Figures on smoking in the UK in 2015.

[2] Research Excellence Framework. 2014. Screening and brief interventions reduce alcohol consumption in England. [Case study 21743.] As of 2 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=21743>

The case study describes the research conducted by the team at Newcastle University, offering an overview of the evidence and impact from 1995 to 2013.

[3] Kaner EFS, Dickinson HO, Beyer FR, Pienaar EDED, Campbell F, Schlesinger C, Heather N, Saunders JB, Burnand B. 2007. Effectiveness of brief alcohol interventions in primary care populations. *Cochrane Database of Systematic Reviews* 2007 2:CD004148. doi:10.1002/14651858.CD004148.pub3

This research is a systematic review on assessing the effectiveness of brief intervention, delivered in general practice or based in primary care, to reduce alcohol consumption. It concludes that brief interventions consistently produced reductions in alcohol consumption. Longer duration of counselling was found to probably have little additional effect.

[4] National Audit Office. 2008. Reducing alcohol harm: Health services in England. London: National Audit Office. As of 2 May 2016: <https://www.nao.org.uk/wp-content/uploads/2008/10/07081049.pdf>

The report addresses alcohol misuse by investigating the role that NHS and its partners played in delivering on the hospital admissions indicator in England, as specified in the Public Service Agreement. It also mentions the Newcastle and Northumbria universities' brief intervention pack ('How Much Is Too Much?') when explaining brief advice (or brief interventions).

[5] UK Home Office. 2012. The government's Alcohol Strategy. London: HM Government. As of 2 May 2016: [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/224075/alcohol-strategy.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/224075/alcohol-strategy.pdf)

The strategy sets out proposals to reduce 'binge drinking', alcohol-fuelled violence and the number of people drinking to damaging levels and cites the NICE 2010 guidelines on alcohol-use disorders.

[6] National Institute for Health and Care Excellence. 2010. Alcohol-use disorders: Prevention. [NICE Guideline PH24.] As of 2 May 2016: <https://www.nice.org.uk/guidance/PH24>

On page 34 of this guideline, both ‘How Much Is Too Much?’ and the ‘Drink-Less’ pack are mentioned as ‘coordinated collections of evidence-based materials for use when screening and carrying out a brief intervention’.

[7] NHS. 2009. NHS 2010–2015: From good to great: Preventative, people-centred, productive. London: The Stationery Office. As of 3 May 2016: <http://www.official-documents.gov.uk/document/cm77/7775/7775.pdf>

The document highlights the NHS five-year plan that is meant to give involved actors a sense of direction on priorities in the NHS. It also offers financial considerations on savings resulting from proposed interventions.

#### *6.1.4. Immunising against meningococcal meningitis*

##### Case study

Based at the Oxford University Hospitals NHS Trust, in partnership with University of Oxford, the NIHR Biomedical Research Centre, Oxford (OxBRc) has been conducting translational research – translating basic/discovery science into clinical research – with the purpose of benefitting patients and the health system and achieving broader economic gains. Research on vaccines is one of 14 themes of research at OxBRc [1], supporting the work of the Oxford Vaccine Group. This group is part of the university’s Department of Paediatrics, which has made a contribution to public and global health solutions through advances in the areas of meningitis, influenza, pneumonia, tuberculosis, malaria, hepatitis and HIV/AIDS. In particular, the research on meningococcal meningitis led to UK and international childhood immunisation, increasing the protection against this disease.

Meningococcal disease is an infection that can often lead to death. Depending on the bacterial type, those who survive can experience disabilities, such as amputation, brain damage and epilepsy. The disease can be caused by five main groups of meningococcal bacteria – A, B, C, W and Y. There are two vaccines against most the common strains of meningococcal disease for babies. These are the Men ACWY vaccine (meningococcal groups A, C, W and Y) and the Men C vaccine (meningococcal group C) [2].

The team at the University of Oxford has been heavily involved in the evaluation of new meningitis vaccines for infants and young children [3]. They performed the first global clinical trials in infants for the Men ACYW vaccine [4], for a vaccine against a combination of two infections: Haemophilus influenza type b and serogroup C meningococcal infections [5] – meaning a combination vaccine for a type of flu and Men C. They also performed the first trials of the Men B candidate vaccine [6].

The Men B vaccine was the leading serogroup B meningococcal vaccine candidate and was subsequently marketed under the name Bexsero by Novartis vaccines (the license is now owned by GlaxoSmithKline). The team at Oxford led the first phase 3 infant study in Europe [7], which resulted in obtaining Bexsero’s authorisation by the European Medicines Agency in early 2013 [3]. As of 1 September 2015, the Bexsero vaccine has been added to the NHS childhood immunisation programme, making England the first country in the world to introduce a Men B vaccination programme that is publicly funded and that has



national coverage [8]. The reach of this immunisation programme is wide, considering that the group B meningococcal infection accounts for about 90 per cent of meningococcal infections in the UK, the equivalent of about 500–1,700 people every year having suffered from Men B disease in the past 20 years [2]. At the end of January 2016, the preliminary vaccine coverage estimates for the first routine cohort eligible for infant meningococcal B immunisation was 94 per cent for one dose and 84.8 per cent for two doses by six months of age [9].

The work on the MenB vaccine has also informed public debate, as the research received wide positive media coverage through newspapers, radio and online outlets [3].

The trials on the combination *Haemophilus influenzae* type b-serogroup C meningococcal meningitis vaccine led to the vaccine being used in the UK and other countries, including the USA and Australia. In the five years since the introduction of the vaccine there has been a 97 per cent decrease (from 78 deaths to 2) in meningitis C deaths for people under 20 years old in the UK [3].

The research on meningitis C vaccine conducted by this group also led to policy change on childhood immunisation. As a result of phase 4 studies, the team showed evidence that children vaccinated with serogroup C meningococcal vaccine in early childhood can lose immunity, which led to the recommendation of adolescent booster doses in the UK [10], as well as in other countries, such as Canada [11] and the USA [12].

These far-reaching impacts show that NIHR support of research conducted in a BRC on vaccines has contributed to better protection for the population in the face of a life-threatening condition.

## Evidence

[1] Oxford Biomedical Research Centre (homepage). 2016. As of 2 May 2016:  
<http://oxfordbrc.nihr.ac.uk/>

Webpage describing the organisation and role of the Oxford Biomedical Research Centre.

[2] Oxford Vaccine Group Vaccine Knowledge Project. 2016. Meningococcal disease. As of 2 May 2016:  
<http://www.ovg.ox.ac.uk/meningococcal-disease>

Webpage detailing the signs and symptoms of Meningococcal disease.

[3] Research Excellence Framework. 2014. Effective design development and evaluation of meningitis vaccines. [Case study 15529.] As of 2 May 2016:  
<http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=15529>

The case study offers an overview of the research performed by the University of Oxford, highlighting the impact and contributions of the study team.

[4] Snape MD, Perrett KP, Ford KJ, John TM, Pace D, Yu L, Langley JM, McNeil S, Dull PM, Ceddia F, Anemona A, Halperin SA, Dobson S, Pollard AJ. 2008. Immunogenicity of a tetravalent meningococcal glycoconjugate vaccine in infants: A randomized controlled trial. *The Journal of the American Medical Association* 299 (2): 173-84. doi:10.1001/jama.2007.29-c

The study presents the results from a randomized, open-label, controlled study of 225 UK and 196 Canadian 2-month-olds from August 2004 to September 2006. The study concluded that MenACWY was well tolerated and immunogenic in infancy.

[5] Pace D, Snape M, Westcar S, Oluwalana C, Yu LM, Begg N, Wysocki J, Czajka H, Maechler G, Boutriau D, Pollard AJ. 2008. A novel combined Hib-MenC-TT glycoconjugate vaccine as a booster dose for toddlers: A phase 3 open randomised controlled trial. *Archives of Disease in Childhood* 93 (11): 963-70. doi:10.1136/adc.2007.136036

To study presented in the article was aimed at investigating the immunogenicity and reactogenicity of a combined Haemophilus influenzae type b and Neisseria meningitidis serogroup C tetanus toxoid conjugate vaccine (Hib-MenC-TT) when administered as a booster dose in combination with a measles, mumps and rubella vaccine (MMR). The results supported the introduction of Hib-MenC-TT vaccine in the UK immunisation schedule to sustain protection of children against Hib and Men C disease.

[6] Findlow J, Borrow R, Snape MD, Dawson T, Holland A, John TM, Evans A, Telford KL, Ypma E, Toneatto D, Oster P, Miller E, Pollard AJ. 2010. Multicenter, open-label, randomized phase II controlled trial of an investigational recombinant meningococcal serogroup B vaccine with and without outer membrane vesicles, administered in infancy. *Clinical Infectious Diseases: an official publication of the Infectious Diseases Society of America* 51 (10): 1127-37. doi:10.1086/656741

The article presents the results from the first in infants of the leading serogroup B meningococcal vaccines. The study included a total of 147 infants from the United Kingdom. These were enrolled and randomly assigned to receive rMenB or rMenB+OMV at 2, 4, 6 and 12 months of age or a single dose at 12 months of age. The study concluded that the rMenB+OMV vaccine had the potential to protect infants from MenB disease.

[7] Gossger N, Snape MD, Yu LM, Finn A, Bona G, Esposito S, Principi N, Diez-Domingo J, Sokal E, Becker B, Kieninger D, Prymula R, Dull P, Ypma E, Toneatto D, Kimura A, Pollard AJ. 2012. European MenB Vaccine Study Group: Immunogenicity and tolerability of recombinant serogroup B meningococcal vaccine administered with or without routine infant vaccinations according to different immunization schedules: A randomized controlled trial. *The Journal of the American Medical Association* 307 (6): 573-82. doi: 10.1001/jama.2012.85.

The study aimed to determine the immunogenicity and reactogenicity of a multicomponent MenB vaccine (4CMenB) and routine infant vaccines when given either concomitantly or separately and found that a 4CMenB vaccine is immunogenic against reference strains when administered with routine vaccines at 2, 4, and 6 or at 2, 3 and 4 months of age.

[8] Meningitis Now. 2016. GAQs on the Men B vaccine (Bexsero). As of 2 May 2016: <https://www.meningitisnow.org/how-we-help/campaigns/beat-it-now/faqs-on-meningitis-b-vaccine/>

[9] Public Health England. 2016. Provisional vaccine coverage estimates for the new meningococcal B (MenB) immunisation programme for England, January 2016. [Infection report Volume 10 Number 8.] London: Public Health England. As of 2 May 2016: [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/503440/hpr0816\\_menb-vc.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/503440/hpr0816_menb-vc.pdf)

Infection report from Public Health England detailing the estimated coverage of the new meningococcal B immunisation programme in England.

[10] UK Joint Committee on Vaccines and Immunisation, Meningococcal Sub-Committee, Minutes of the meeting held on 18 February 2011.

This document represents the minutes of the meeting held on 18 February 2011 and cites articles representing the work on serogroup C meningococcal vaccines in Oxford.

[11] Centers for Disease Control and Prevention. 2011. Updated recommendations for use of meningococcal conjugate vaccines — Advisory Committee on Immunization Practices (ACIP), 2010. Morbidity and Mortality Weekly Report 60 (3): 72-6. As of 2 May 2016: <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6003a3.htm>

The US report summarizes two new recommendations: 1) routine vaccination of adolescents, preferably at age 11 or 12 years, with a booster dose at age 16 years; and 2) a 2-dose primary series administered 2 months apart for persons aged 2 through 54 years with persistent complement component deficiency (e.g. C5–C9, properidin, factor H or factor D) and functional or anatomic asplenia, and for adolescents with human immunodeficiency virus (HIV) infection. The CDC guidance cites the work of Oxford investigators on serogroup C meningococcal vaccines.

### *6.1.5. Appraising the environmental risks of bisphenol A (BPA) exposure in humans*

#### Case study

Bisphenol A (BPA) is used to produce polycarbonate plastics that are employed in the manufacturing of food and drink containers and other products. It is also used in the epoxy resins that line metal food cans and in dental sealants. BPA is absorbed by humans, and BPA metabolites are excreted in urine. The chemical is detectable in the majority of the human population (for example studies show it is in approximately 95 per cent of US population [1]). The NIHR supported research through the NIHR Collaborations for Leadership in Applied Health Research and Care (CLAHRC), conducted by a team at Peninsula College of Medicine and Dentistry, Exeter (known as PenCLAHRC), has demonstrated that the presence of BPA in the body is associated with hormonal imbalance and coronary heart disease [2]. This epidemiological research has informed a public health debate both in the UK and abroad, and a number of regulatory authorities worldwide are now tackling the need to reduce BPA residues in food and drink.

Research from PenCLAHRC represented the first cross-sectional epidemiological study investigating the effects of BPA on adult populations [3]. The study found that higher BPA exposure (judged by higher urinary concentrations of BPA) was associated with cardiovascular diagnoses. As this was a cross-sectional study, offering only a ‘snapshot’ of a situation in time, it was determined that a longitudinal study, following adults for a longer period of their life, was needed to provide further evidence. Subsequently, the team undertook the first forward-looking longitudinal study, which found that higher urinary BPA concentrations predict onset of coronary heart diseases [4]. Specifically, this evidence shows that BPA, alongside other known risk factors, such as smoking and obesity, could be an additional factor

contributing to the risk of developing heart disease. The PenCLAHRC article is cited in more than 180 scientific papers and in policy documents in Europe and the USA that have informed debate on the acceptable limit of BPA exposure.

Research undertaken at PenCLAHRC also showed a link between BPA and hormone imbalance. That is, men with higher concentrations of BPA also have higher concentrations of testosterone [5]. BPA may activate the oestrogen receptor ESRRA, which is involved in controlling the energy metabolism [6]. These findings are important because they show that BPA could have potential public health implications for the general population, and that BPA exposure should be further investigated in connection with other risk factors, which, combined, could lead to undesired health outcomes.

The research conducted by Professors Melzer and Galloway's team has stimulated international policy debate, having received wide media coverage in the academic literature, in international media (German television, the BBC) and in newspapers (*The Independent*, *The Times*, *Daily Mail*, *The New York Times*) [2].

The findings from the studies have been taken into consideration by many international bodies, such as the US Food and Drug Administration (FDA) [7], the European Food Standards Agency [8], the Advisory Board of the German Society of Toxicology [2] and Health Canada [2]. Specifically, in 2010, the FDA [2][9] stated having 'some concern' about BPA's safety, particularly for infants and young children, citing the research from PenCLARHC. The team's research contributed to the international body of evidence on BPA. Currently there is not a common view on the acceptable levels of BPA exposure in adults. However, there is more consensus when it comes to BPA exposure in babies. A ban on using BPA for baby bottles has come into effect in Canada (2008); Denmark and France (2010); several US jurisdictions (13 states, the District of Columbia and a few local jurisdictions [10]) (2011); and the European Union as a whole (2011) [2].

Internationally, policymakers are grappling with how to reduce the presence of BPA in food and drink to limit its prevalence in the human body. NIHR-supported research has contributed to a better understanding of exposure to BPA in humans.

## Evidence

[1] Calafat AM, Ye X, Wong LY, Reidy JA, Needham LL. 2008. Exposure of the U.S. population to bisphenol A and 4-tertiary-octylphenol: 2003–2004. *Environmental Health Perspectives* 116 (1): 39-44. doi:10.1289/ehp.10753

Evidence that BPA is detectable in 95% of the US population.

[2] Research Excellence Framework. 2014. The plastics chemical bisphenol A and its potential human health effects. [Case study 35614.] As of 2 May 2016:

<http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=35614>

The case study offers an overview of the BPA-centred research performed by professors Melzer and Galloway's team, highlighting the findings from the conducted research and the impact on policy.

[3] Lang IA, Galloway TS, Scarlett A, Henley WE, Depledge M, Wallace RB, Melzer D. 2008. Association of urinary bisphenol A concentration with medical disorders and laboratory abnormalities in

adults. *The Journal of the American Medical Association* 300 (11): 1303-10. doi:10.1001/jama.300.11.1303

The research was a cross-sectional study of BPA concentrations and health status in the general adult population of the United States. The analysis used data from the National Health and Nutrition Examination Survey 2003–2004. The study considered 1455 adults aged 18 through 74 years with measured urinary BPA and urine creatinine concentrations. The study concluded that higher urinary BPA concentrations were associated with cardiovascular diagnoses.

[4] Melzer D, Osborne NJ, Henley WE, Cipelli R, Young A, Money C, McCormack P, Luben R, Khaw K-T, Wareham NJ, Galloway TS. 2012. Urinary bisphenol A concentration and risk of future coronary artery disease in apparently healthy men and women. *Circulation* 125: 1482-90. doi:10.1161/CIRCULATIONAHA.111.069153

The study presents findings from a nested case-control analysis, measuring urinary (u) BPA in stored samples from a baseline clinical examination. The study compared uBPA concentrations in a case group who later developed coronary artery disease with those in a control group who remained free of coronary artery disease during follow-up. The participants were selected from the European Prospective Investigation Into Cancer and Nutrition (EPIC) Norfolk cohort, which is a prospective population study of 25,663 men and women aged 45 to 79 years, resident in Norfolk, United Kingdom, who completed a baseline questionnaire and attended a clinical examination. The research found that higher uBPA concentrations were associated with heart disease.

[5] Galloway T, Cipelli R, Guralnik J, Ferrucci L, Bandinelli S, Corsi AM, Money C, McCormack P, Melzer D. 2010. Daily bisphenol A excretion and associations with sex hormone concentrations: Results from the InCHIANTI adult population study. *Environmental Health Perspectives* 118 (11): 1603-1608. doi: 10.1289/ehp.1002367.

The study is a cross-sectional study using data from the InCHIANTI study, a prospective population-based study of Italian adults. The study included 715 adults between 20 and 74 years old. BPA concentrations were measured by liquid chromatography–mass spectrometry in 24 hour urine samples. The study found an association between higher daily excretion of BPA and total testosterone concentrations among men.

[6] Melzer D, Harries L, Cipelli R, Henley W, Money C, McCormack P, Young A, Guralnik J, Ferrucci L, Bandinelli S, Corsi AM, Galloway T. 2011. Bisphenol A exposure is associated with in-vivo estrogenic gene expression in adults. *Environ Health Perspect.* 119 (12): 1788-93.

The study looked at data from 96 adult men from the InCHIANTI population study. The study analysed in vivo expression of six estrogen receptor, estrogen-related receptor and androgen receptor genes in peripheral blood leukocytes. The study found a positive association between higher BPA concentrations and higher estrogen levels, concluding that higher levels of BPA are likely to function as a xenoestrogen.

[7] FDA Congressional Review of the Safety of BPA, Washington DC (September 2008)

United States Food and Drug Administration review for Congress on the safety of Bisphenol- A (BPA).

[8] European Food Safety Authority, 2010. Scientific opinion on bisphenol A: Evaluation of a study investigating its neurodevelopmental toxicity, review of recent scientific literature on its toxicity and

advice on the Danish risk assessment of bisphenol A. EFSA Journal 8 (9): 1829. As of 2 May 2016: [http://www.efsa.europa.eu/sites/default/files/scientific\\_output/files/main\\_documents/1829.pdf](http://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/1829.pdf)

Statement of the European Food Safety Authority on a study associating bisphenol A with medical disorders.

[9] Rodriguez JC. 2012. FDA advances petition to ban BPA in formula packaging. Law 360. As of 2 May 2016: <http://www.law360.com/articles/349745/fda-advances-petition-to-ban-bpa-in-formula-packaging>

Link to a press release announcing the plans by the US Food and Drugs Agency to push for a ban on using BPA in infant formula containers.

[10] Environmental Working Group. 2015. BPA in canned food: Regulation of BPA. As of 2 May 2016: <http://www.ewg.org/research/bpa-canned-food/regulation-bpa>

This is a link to an online article describing the recent ban by the US Food and Drugs Agency on use of BPA in infant formula containers yet use in canned food packaging is not regulated.

### *6.1.6. Diagnosing critical congenital heart defects in new-borns through advanced screening methods*

#### Case study

Congenital heart diseases (CHDs) are responsible for a large number of infant deaths. A systematic review found that CHDs accounts for 3 per cent of infant deaths [1], and the NHS highlights CHDs as one of the most frequent types of birth defects, found in up to 9 in every 1,000 babies born in the UK [2]. Depending on the seriousness of the heart defect, the child may require immediate life-saving surgery and life-long monitoring accompanied by medication to relieve symptoms or stabilise the condition. Therefore it is important to have an early diagnosis of CHDs. In the UK, within 24 hours after birth, a routine neonatal examination is performed on all newborns. Despite this, it is estimated that over 50 per cent of newborns with CHDs are incorrectly diagnosed [3]. NIHR-funded research has provided a cost-effective diagnosis for CHDs using pulse oximetry in neonatal screening. This research, described by *The Lancet* as ‘a new milestone in the history of congenital heart disease’ [4], not only is benefiting the UK population, but also has worldwide impact.

In 2005, a Health Technology Assessment programme–commissioned systematic review investigated the cost-effectiveness of newborn screening for CHDs to provide evidence for policy decisions on newborn CHD screening strategies and to identify future priorities for research [1][5]. This research identified two alternative newborn screening methods, pulse oximetry and echocardiography, to accompany the clinical examination and established that adding pulse oximetry in clinical examination is likely to be cost effective. Pulse oximetry is a test that uses a sensor to measure the oxygen level (oxygen saturation) of the blood. This level is important because low blood oxygen levels are often observed in CHDs. As a result of these findings, the Health Technology Assessment (HTA) programme commissioned research that led to a better understanding of the use of pulse oximetry as a population screening strategy [5]. The PulseOx trial, led by Andrew Ewer at University of Birmingham, is the largest UK study in this research area, having obtained data from 20,055 newborns and confirmed that pulse oximetry is a cost-effective way of

screening for CHDs. It is also a rapid, safe, non-invasive and painless method [6] that, when added to the regular clinical neonatal evaluation, led to a 92 per cent detection rate of CHDs of babies prior to discharge [7]. This means that it detects almost 30 additional cases of CHDs per 100,000 live births compared with clinical examination alone [6].

The PulseOx trial has had an impact at both the national and international levels. In the UK, the National Screening Committee has undertaken a pilot project, the Newborn Pulse Oximetry Screening pilot, which could lead to a national roll-out of pulse oximetry screening for CHDs [5]. The pilot has been rolled out in 15 NHS trusts across England. By the end of 2015, the pilot anticipated that pulse oximetry screening would be offered to approximately 38,000 newborn babies and was likely to result in the identification of around 300 babies with CHDs [8]. The HTA research has also impacted on clinical training in the UK, as clinicians have become more aware of pulse oximetry [5]. In 2010, a survey reported that only 7 per cent of UK neonatal units were routinely screening, while a follow-up survey in 2012 revealed that the pulse oximetry was routine practice in 36 (18%) of 204 units contacted. The 2012 survey results also found that of those not screening, 8 were in the process of introducing this practice and 111 were considering it but foresaw some obstacles [9]. The survey also revealed that there had been a positive change in opinion among UK neonatologists about pulse oximetry screening.

In addition to being cited in the international academic literature on pulse oximetry and informing public debate through wide media coverage in important newspapers, on radio and online [10], the PulseOx trial's international impact has included the adoption of pulse oximetry screening in different countries. In 2011, the US Secretary for Health and Human Services recommended the addition of pulse oximetry screening in the USA, directly referencing the work done in the UK [10][11][12]. In 2015, 43 (out of 50) US states had taken action towards newborn screening for CHD through legislation, regulations or hospital guidelines [13]. In a recent evaluation conducted by RAND Europe, an interviewee noted that the HTA research on CHDs informed a European initiative aimed at introducing pulse oximetry screening in such countries as France, Germany, Spain and Italy. The interviewee also mentioned that in July 2015 the Sri Lankan government introduced the use of pulse oximetry for newborn screening for CHDs [5][14].

NIHR-funded research has directly supported the introduction, nationally and internationally, of an effective and cost-effective additional screening method to detect CHDs. Screening is a public health primary prevention method, and the timely identification of CHDs will translate into better health outcomes for the affected population.

## Evidence

[1] Knowles R, Griebisch I, Dezateux C, Brown J, Bull C, Wren C. 2005. Newborn screening for congenital heart defects: A systematic review and cost-effectiveness analysis. *Health Technology Assessment* 9 (44). doi:10.3310/hta9440

The HTA-commissioned research provides evidence to inform policy decisions about the most appropriate newborn screening strategy for congenital heart defects and to identify priorities for future research that might reduce important uncertainties around such decisions. The study concluded that pulse oximetry is a promising alternative newborn screening strategy and recommends further evaluation to

establish better estimates of test performance, optimal timing, and diagnostic and management strategies. The alternative screening addition, echocardiography, was found to be associated with the highest detection rate, but it is a more costly strategy and has a 5 per cent false-positive rate.

[2] NHS Choices. 2015. Congenital heart disease. As of 2 May 2016: <http://www.nhs.uk/Conditions/Congenital-heart-disease/Pages/Introduction.aspx>

This is a link to a webpage on NHS Choices, aimed at patients and general readership, describing congenital heart disease, diagnosis and treatment.

[3] University of Birmingham. 2016. Pulse oximetry as a screening test for congenital heart disease in newborn babies (PulseOx). As of 2 May 2016:

<http://www.birmingham.ac.uk/research/activity/mds/trials/bctu/completed-trial-research/womens/pulseox/index.aspx>

This is a weblink to a brief report on the University of Birmingham website, describing the findings and implications of the completed PulseOx study in which pulse oximetry was used as a screening test for congenital heart disease in new born babies.

[4] A new milestone in the history of congenital heart disease. 2012. [Editorial.] *Lancet* 379 (9835): 2401. doi:10.1016/S0140-6736(12)61045-9

This *Lancet* editorial discussed the work done by Andrew Ewer at University of Birmingham and finds the screening method to be ‘a cheap and readily available – at least in developed countries – screening tool with good specificity, very high sensitivity, and a low false-positive rate, especially when used 24 h after birth.’

[5] Guthrie S, Bienkowska-Gibbs T, Manville C, Pollitt A, Kirtley A, Wooding S. 2015. The impact of the National Institute for Health Research Health Technology Assessment programme, 2003–13: A multimethod evaluation. *Health Technology Assessment* 19 (67): 1-291. doi: 10.3310/hta19670.

The research examines the impact of the NIHR HTA programme between 2003 and 2013. This case study examines the impact of the Newborn Screening for Congenital Heart Defects study, including the PulseOx trial. Using a payback methodology, the CHD research was found to have led to knowledge production, research targeting and capacity building, thereby informing policy and benefiting health and the health sector as well as contributing to broader social and economic benefits.

[6] Ewer A, Furnston A, Middleton L, Deeks JJ, Daniels JP, Pattison HM, Powell R, Roberts TE, Barton P, Auguste P, Bhojar A, Thangaratinam S, Tonks AM, Satodia P, Deshpande S, Kumararatne B, Sivakumar S, Mupanemunda R, Khan KS. 2012. Pulse oximetry as a screening test for congenital heart defects in newborn infants: A test accuracy study with evaluation of acceptability and cost-effectiveness. *Health Technology Assessment* 16 (2): v-xiii, 1-184. doi:10.3310/hta16020

This NIHR-commissioned research presents the findings from the pulse oximetry study. The research was undertaken to determine the accuracy of pulse oximetry. Acceptability of testing to parents was evaluated through a questionnaire; acceptability to staff was evaluated through focus groups. A decision-analytic model was constructed to assess cost-effectiveness. Among other things, the study found that pulse oximetry is a simple, safe, feasible test that is acceptable to parents and staff and that adds value to existing screening.



[7] Research Excellence Framework. 2014. Pulse oximetry screening to detect heart disease in newborn babies. [Case study 38778.] As of 2 May 2016:

<http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=38778>

These case studies offer an overview of the development of the HTA research as well as the impact of the studies, highlighting the achievements of the research team.

[8] Public Health England. 2015. Newborn pulse oximetry screening pilot under way. As of 2 May 2016: <https://phscreening.blog.gov.uk/2015/07/30/newborn-pulse-oximetry-screening-pilot-under-way/>

Press release from Public Health England announcing the start of the PulseOx screening trial for congenital heart disease in new born infants.

[9] Singh A, Ewer AK. 2012. Pulse oximetry screening for critical congenital heart defects: A UK national survey. *Lancet* 381 (9866): 535. doi:10.1016/S0140-6736(13)60278-0

The research presents the results from a survey taken between May and October 2012. The results show that pulse oximetry was routine practice in 36 (18%) of 204 units. The commonest concerns that were mentioned in relation to considering introduction into routine practice were resource issues, such as cost (63%), staff time (28%), availability of echocardiography (25%) and staff training (24%), as well as absence of local and national guidelines (36%). Less frequent concerns included excess false positives (10%), discharge delay (5%) and cross-infection (3%). In the 49 units not considering screening, the main reasons were staffing (57%), false positives (55%), availability of echocardiography (33%) and cost (31%).

[10] Research Excellence Framework. 2014. PulseOx: Detecting heart disease in newborn babies through pulse oximetry screening. [Case study 38797.] As of 2 May 2016:

<http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=38797>

These case studies offer an overview of the development of the HTA research as well as the impact of the studies, highlighting the achievements of the research team.

[11] Masimo Corporation. 2011. U.S. Health & Human Services makes critical congenital heart defect screening using motion-tolerant pulse oximetry a nationwide newborn screening standard. PR Newswire, 23 September. As of 5 May 2016: <http://www.prnewswire.com/news-releases/us-health--human-services-makes-critical-congenital-heart-defect-screening-using-motion-tolerant-pulse-oximetry-a-nationwide-newborn-screening-standard-130473518.html>

[12] Kemper AR, Mahle WT, Martin GR, Cooley WC, Kumar P, Morrow WR, Kelm K, Pearson GD, Glidewell J, Grosse SD, Howell RR. 2011. Strategies for implementing screening for critical congenital heart disease. *Pediatrics* 128 (5): e1259-67. As of 5 May 2016:

<http://pediatrics.aappublications.org/content/128/5/e1259.full>

Webpage with abstract for the paper, Strategies for implementing screening for critical congenital heart disease

[13] Centers for Disease Control and Prevention. 2015. State legislation, regulations, and hospital guidelines for newborn screening for critical congenital heart defects – United States, 2011–2014. As of 2 May 2016: <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6423a1.htm>

This document details US published legislation for the screening of critical congenital heart defects in newborns.

[14] Nationwide newborn screening for critical congenital heart disease (CCHD). 2015. The Island Newspaper [Sri Lanka], July 14. As of 2 May 2016: [http://www.island.lk/index.php?page\\_cat=article-details&page=article-details&code\\_title=128262](http://www.island.lk/index.php?page_cat=article-details&page=article-details&code_title=128262)

News report from Sri Lanka announcing the new screening initiative for newborns for critical congenital heart disease using pulse oximetry,

### *6.1.7. Examining public attitudes to presumed consent for organ donations*

#### Case study

In 2008, Spain had the highest rates of organ donation rate in Europe, with 35 donors per million of population, while the rate in UK was one of the lowest, at 13 per million of population [1]. At this time, the UK transplant waiting list consisted of about 7,000 people, with an approximately 8 per cent rise each year. In 2006–07 approximately 3,000 patients in the UK received an organ transplant, while approximately 1,000 patients died as of result of unavailability of organs or deterioration of health that made them no longer suitable to receive an organ [2]. To increase the number of available organs, a legislative change was proposed, to a default position that organs would be donated upon death unless individuals specifically opted out.

Against this data, and the availability of an ‘opt-out’ policy in such countries as Spain and Sweden, NIHR-funded research (through the Health Technology Assessment [HTA] programme) reviewed the impact of this type of legislation in other countries and analysed data on attitudes to presumed consent among the public, professionals and other stakeholders [3]. The research found that there was variation in the rates of organ donations among the different countries that had this opt-out regulation. While there was an increase in donation rates after the introduction of presumed consent in selected countries, the research found that presumed consent alone could not have triggered this change. The researchers concluded that a combination of legislation, availability of donors, transplantation system organisation and available infrastructure, available health system resources, as well as public attitudes and awareness of organ donations and transplantations contributed to the donor rates in those countries [3].

In response to these findings and arguments from other health professionals, in November 2008 the Organ Donation Taskforce advised the prime minister against introducing the opt-out legislation in the UK [2][4]. Chapters 11 (‘Impact of the introduction of an opt-out system on the number of organ donors’) and 12 (‘Attitudes of the public of an opt-out system’) were informed by the NIHR-funded research [4]. The taskforce argued that this type of change at that moment in time would be costly and challenging because it would erode public trust in the NHS. The government was advised to adopt non-legislative policy options and reassess the decision in five years’ time [4].

In 2013, it was reported that the number of people donating organs after death had risen 50 per cent since 2008 [5]. This translated to a 30 per cent increase in actual transplants, as some donors were unsuitable due to such factors as age. The highest increases in deceased donors were registered in Scotland and Northern Ireland – 74 per cent and 82 per cent, respectively [5].

All these increases in transplants translate not only into lives saved, but also into savings for the health system. The January 2008 Organ Donation Taskforce report [1] noted that the most significant economic benefits are found in the case of renal replacement therapy, that is, kidney transplantation instead of dialysis. While the average continuing annual cost for dialysis is £23,177, the cost of a transplant is £42,025 initially, followed by annual maintenance costs of £6,500. This makes it more cost effective to have a kidney transplant.

NIHR-supported research has provided evidence that informed policy in line with the capabilities and social realities of the NHS at the time. This prevented a costly change in policy that was anticipated to lead to a potential loss of public trust in the NHS and government [2]. It informed recommendations that led to 50 per cent increase in registering of organ donors. While shortages of organs are still a reality, the systematic review undertaken by the University of York with funding from the HTA programme is a valuable source of evidence that could help inform future policy changes. At the end of 2015, Wales became the first nation in the UK to introduce an opt-out system for organ donation [6].

## Evidence

[1] Department of Health. 2008. *Organs for transplants: A report from the Organ Donation Taskforce*. [285565.] London: Department of Health. As of 2 May 2016: [http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod\\_consum\\_dh/groups/dh\\_digitalassets/@dh/@en/documents/digitalasset/dh\\_082120.pdf](http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_082120.pdf)

This January 2008 report provides 14 recommendations that, taken together, are aimed to create a structured and systematic approach to organ donation in the UK. The report estimates that a 50 per cent increase in donation would result in an additional 1,200 transplants a year. Of these, more than 700 would be kidney transplants, which would translate in significant cost savings when compared with the costs of dialysis. The recommendations cover five broad aspects of donation, based on one overriding principle, namely, that there should be a UK-wide organ donation organisation. The five aspects are: 1) legal and ethical issues; 2) the role of the NHS; 3) organisational aspects of coordination and retrieval; 4) training; 5) public recognition of donors and their families and public promotion of donation.

[2] Research Excellence Framework. 2014. *Organ donation and presumed consent legislation*. [Case study 43462.] As of 2 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=43462>

The case study offers an overview of the research performed at the University of York, highlighting the findings from the conducted research and the impact on policy.

[3] Rithalia A, McDaid C, Suekarran S, Norman G, Myers L, Sowden A. 2009. A systematic review of presumed consent systems for deceased organ donation. *Health Technology Assessment* 13 (26): iii, ix-xi, 1-95. doi:10.3310/hta13260

The report presents the findings from the systematic review undertaken at the University of York. The research was aimed at examining the impact of a system of presumed consent for organ donation on donation rates and to review data on attitudes towards presumed consent. The following were included in the systematic review: five studies comparing donation rates before and after the introduction of legislation for presumed consent (before and after studies); eight studies comparing donation rates in countries with and without presumed consent systems (between-country comparisons); and 13 surveys of public and professional attitudes to presumed consent. Eight surveys of attitudes to presumed consent were from the UK public, with the most recent survey, undertaken in 2007, reporting that 64 per cent of respondents supported a change to presumed consent. The research concluded that presumed consent alone is unlikely to explain the variation in organ donation rates among countries.

[4] Department of Health. 2008. The potential impact of an opt out system for organ donation in the UK: An independent report from the Organ Donation Taskforce. [291525.] As of 2 May 2016: [http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod\\_consum\\_dh/groups/dh\\_digitalassets/@dh/@en/documents/digitalasset/dh\\_090303.pdf](http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_090303.pdf)

The report summarises the evidence that formed the basis of the taskforce's recommendation. The report cites the systematic review, acknowledging there was an apparent correlation between high donation rates and opt-out systems in countries around the world and that the presumed consent alone does not explain the variation in organ donation rates among the different countries. It also presents the arguments from health professionals about the potentially negative implications for clinical practice, such as the erosion of trust between clinicians and the patients and their families. Considering all the evidence, the report advises on a review in five years' time of opt-out systems, considering the results that would emerge from the implementation of the 14 recommendations of the taskforce in its report *Organs for Transplants* from January 2008.

[5] Lever A-M. 2013. Organ donation soars over past five years, says NHS Blood and Transplant. BBC, April 11. As of 2 May 2016: <http://www.bbc.com/news/health-22086086>

BBC News (England) release announcing the increase of organ donation over the past five years.

[6] Organ donation law 'revolution' starts in Wales. 2015. BBC, December 1. As of 2 May 2016: <http://www.bbc.com/news/uk-wales-34964382>

This is a link to a BBC News article reporting that Wales is the first nation in the UK to roll out an 'opt-out' system to organ donation.

### *6.1.8. Cracking the societal cost of back pain*

#### Case study

Each year approximately 3.5 million people in the UK experience back pain [1] and as a result, 6–9 per cent of adults visit their general practitioner (GP) each year [2]. This amounts to 14 per cent of consultations [3]. The total cost for direct healthcare resources is £1.6 billion [1]. In addition, there is a wider societal cost as a result of work absence due to back pain. These costs combined lead to an estimated equivalent of 1–2 per cent of lost gross national product [4]. NIHR-funded research has

investigated the potential of stratified care for nonspecific low back pain within physical therapy services in primary care and has demonstrated the clinical effectiveness and cost-effectiveness of this approach.

The STarT Back One model developed at Keele University represents a stratification of the management of back pain according to the patient's prognosis (low, medium, or high risk). It consists of a nine-item questionnaire administered to patients during their GP consultation. Patients are then allocated to different treatments according to their score on the questionnaire. Those in the 'low-risk' group are given advice about how to manage their back pain using self-care methods, whereas patients in the medium- and high-risk groups are referred to a physiotherapist [5]. A 2011 study funded by Arthritis Research UK [6] compared the clinical effectiveness and cost-effectiveness of stratified primary care (intervention) with non-stratified current best practice (control) and found that the stratified management approach resulted in improved primary care efficiency, with better health outcomes for patients with back pain compared with the non-stratified comparison group.

Based on these results, the NIHR supported the Implementation to improve Patient Care through Targeted treatment Back study (IMPACT Back) through the involvement of the Primary Care Research Network–North West. This study investigated the effects of implementing risk-stratified care for low back pain in family physician practice [7], in particular the impact on the physician's clinical behaviour, patient outcomes and costs to the system. The research involved 64 family physicians and 922 patients with low back pain. With a stratified approach to care, it was found that: 1) there were significantly more risk-appropriate referrals to physical therapy for medium- and high-risk patients; 2) there was a 30 per cent reduction in sickness certifications; and 3) there was a decrease in use of non-opioids – painkillers usually available without a prescription – and an increase in use of mild opioids, which is in line with back pain guidelines. The patient clinical outcomes were also better for the group that received stratified care, and there was a 50 per cent reduction in time off work for this group. This translates into a £400 saving per employed patient over 6 months. The calculated overall UK savings are than £700 million per annum [7].

To sum up, the IMPACT Back study shows that stratified care, in which prognostic screening is combined with matched treatment, is effective in primary care settings. These findings have important public health and economic implications, because they could result in changes in family physician practice. The National Institute for Health and Care Excellence (NICE) is currently undertaking a review of the guideline *Low Back Pain in Adults: Early Management* [8]. While a list of papers that will inform the guidelines is not available, one of the research questions the update will answer is 'What is the clinical and cost effectiveness of stratifying management of nonspecific low back pain or sciatica according to outcome of a risk assessment tool/questionnaire?' As IMPACT Back is the first study to investigate the implementation of stratified care for low back pain within primary care physician settings, the study results are likely to inform this NICE guidelines update. The STarTBack tool has been translated into 12 languages and implemented in several states in the USA (Utah, Idaho, Minnesota) [5].

## Evidence

[1] Maniadakis N, Gray A. 2000. The economic burden of back pain in the UK. *Pain* 84: 95-103. As of 2 May 2016: [http://intlifepain.org/BACKUP%20OF%20OLD%20SITE/Maniadakis\\_paper.pdf](http://intlifepain.org/BACKUP%20OF%20OLD%20SITE/Maniadakis_paper.pdf)

This paper reports the results of a 'cost-of-illness' study of the socio-economic costs of back pain in the UK.

[2] Dunn KM, Croft PR. 2005. Classification of low back pain in primary care: Using 'bothersomeness' to identify the most severe cases. *Spine* 30 (16): 1887-92. As of 2 May 2016: <http://www.ncbi.nlm.nih.gov/pubmed/16103861>

Study reporting on the use of a single question about 'bothersomeness' in primary care to classify the severity of lower back pain.

[3] Jordan KP, Kadam UT, Hayward R, Porcheret M, Young C, Croft P. 2010. Annual consultation prevalence of regional musculoskeletal problems in primary care: An observational study. *BMC Musculoskeletal Disorders* 11: 144. doi: 10.1186/1471-2474-11-144.

Journal article reporting the prevalence of musculoskeletal problems in primary care by region, based on observational data.

[4] Hestbaek L, Leboeuf YC, Manniche C. 2003. Low back pain: What is the long-term course? A review of studies of general patient populations. *European Spine Journal* 12 (2): 149-165.

Systematic and critical literature review of studies looking at low back pain in the general patient population.

[5] STarT Back (homepage). 2016. As of 2 May 2016: <http://www.keele.ac.uk/sbst/>  
Homepage for the STarT Back study at Keel University.

[6] Hill JC, Whitehurst DG, Lewis M, Bryan S, Dunn KM, Foster NE, Konstantinou K, Main CJ, Mason E, Somerville S, Sowden G, Vohora K, Hay EM. 2011. Comparison of Stratified Primary Care Management for Low Back Pain with current best practice (STarT Back): A randomised controlled trial. *Lancet* 378 (9802): 1560-71. doi: 10.1016/S0140-6736(11)60937-9

Results from the STarT Back randomised controlled trial comparing Stratified Primary Care Management for lower back pain with current best practice.

[7] Foster NE, Mullis R, Hill JC, Lewis M, Whitehurst DG, Doyle C, Konstantinou K, Main C, Somerville S, Sowden G, Wathall S, Young J, Hay EM. 2014. Effect of stratified care for low back pain in family practice (IMPACT Back): A prospective population-based sequential comparison. *Annals of Family Medicine* 12 (2): 102-11 doi:10.1370/afm.1625

Peer-reviewed article reporting results from a study aiming to determine the effects of implementing risk-stratified care for low back pain in family practice on physician's clinical behaviour, patient outcomes, and costs.

[8] National Institute for Health and Care Excellence. 2016. NICE guidelines on low back pain and sciatica in adults. [GID-CGWAVE0681] Expected publication date: September. As of 2 May 2016: <https://www.nice.org.uk/guidance/indevelopment/gid-cgwave0681>

National Institute for Health and Care Excellence (NICE) guidelines for the management of lower back pain in adults (in development.)

### *6.1.9. Preparing for flu pandemics through vaccine trials for children and pregnant women*

#### Case study

The H1N1 influenza, or ‘swine flu’, which first emerged in April 2009, was declared a pandemic by the World Health Organisation (WHO) in June 2009. This declaration meant that an exceptionally high proportion of the population was considered to be at risk of contracting it [1]. In response to this declaration, the NIHR established a coordinated, system-wide response to the flu pandemic that rapidly commissioned and published research looking into the treatment and management of H1N1 influenza [2][3]. The NIHR used both rapid investigator-led and commissioned routes to fund research through an open call with a one-week deadline, in addition to identifying key experts and working with them to develop research studies [3]. In the case of flu, children and pregnant women are often identified as high-risk groups, and therefore research investigating the safety of vaccines and antiviral treatment in these populations was particularly important. The NIHR has funded research on these groups, which informed a fast public health response, leading to the vaccination of children and early initiation of antiviral treatment for pregnant women. These efforts also informed policy at the national and international levels and offered an example of an efficient research response for future outbreaks.

Following the declaration of the swine flu as a pandemic, in preparations for the winter flu season in the autumn of 2009, the UK acquired two new influenza A H1N1 vaccines: Pandemrix and Celvapan [1]. Due to the urgent need to provide effective vaccines in a short amount of time, both vaccines had been licensed for use without having undergone testing on children. Therefore it was considered a national priority by the UK Scientific Advisory Group for Emergencies (UK-SAGE) to conduct research that would provide paediatric data on these vaccines. The University of Oxford’s Oxford Vaccine Group, which is linked to the NIHR Biomedical Research Centre in Oxford, was appointed to conduct this research with fast-tracked ethical and regulatory approvals, due to the time critical nature of the research [4]. After being awarded the research grant on 1 September 2009, the research team was able to redeploy resources [4] – including the hiring of 80 staff [5] using NIHR infrastructure. NHS permission was granted after 19 days [4] and the Research Ethics Committee’s favourable opinion was also granted rapidly.

Combined, these rapid actions allowed the first vaccine administrations to take place within a month of commencing the study. In total, the study recruited 943 children across five sites [1] and gathered rapid data received from parents monitoring adverse effects in their children. The team reported an interim analysis of the data by mid-November, informing the Joint Committee for Immunisation and Vaccination and the Department of Health that both vaccines were well tolerated by participating children [1]. As recognised in an open letter by the research team from the Oxford Vaccine Group published in *BMJ*, ‘The capacity of trials staff funded by NIHR proved essential, supporting the need for NIHR to invest in the clinical trials infrastructure’ [4].

The interim analysis offered a preliminary indication on immunogenicity superiority of the one vaccine [6]. The following year, the NIHR funded a subsequent study showing that 98 per cent of the children receiving the immunogenic superior vaccine maintained influenza A H1N1 antibodies above the

threshold of protection for one year following first administration, in comparison with only 51 per cent of the children receiving the other vaccine [7].

The immunisation policy for the 2009–10 influenza A H1N1 pandemic was informed by the work done at the Oxford Vaccine Group, and the research contributed to offering influenza vaccines to all children less than five years of age. More than 500,000 children in the UK had received an influenza A H1N1 vaccine by February 2010 [1]. This research was also used to inform the World Health Organization's global policy in this H1N1 outbreak [1].

Another at-risk group in the H1N1 influenza pandemic was pregnant women. Recognising this, the NIHR funded research on influenza A/H1N1 in pregnancy in a similar manner as the research for vaccines in children, through the Health Technology Assessment (HTA) funding programme. Making use of the UK Obstetric Surveillance System (UKOSS), which is a national NIHR-funded system to study rare disorders of pregnancy, researchers at the National Perinatal Epidemiology Unit at the University of Oxford received NIHR funding for a study of pregnant women hospitalised across the UK with 2009/H1N1 infection. They found that initiation of early antiviral treatment for pregnant women contributed to a 90 per cent reduction in the odds of admission for critical care [10][11]. As a result of using UKOSS, monthly analysis of data was possible, which enabled the Department of Health to undertake evidence-informed ongoing policy and guidance updates. The Department of Health changed the clinical algorithms – the sequence of clinical decisions in use to facilitate the fast availability of antivirals – specifically for pregnant women through the National Pandemic Flu Service [10]. Clinical guidelines were also updated in light of these findings [10][12].

The policy recommendation to offer pregnant women immunisation has been adopted subsequently in England as an ongoing recommendation that all pregnant women should be immunised against seasonal influenza [4][5]. As a result, the number of pregnant women immunised against influenza in England more than doubled between 2009 and 2015, to more than 280,000 [10][13][14]. At an international level, the UKOSS data informed recommendations issued by the European Centre for Disease Control and Prevention that indicate that universal influenza immunisation for pregnant women should be offered in Europe [10][15].

NIHR support yields lessons for a national public health response to pandemics, offering examples of how the UK system can deliver solutions in the face of such threats. As Professor Tom Walley (Director of NIHR Evaluations, Trials and Studies Coordinating Centre) said in his 2010 commentary for *The Lancet*: 'The success of NIHR in this particular case shows how it has transformed clinical research in the NHS'. The research on getting paediatric data on vaccines exemplifies how NIHR support allowed for a reduction in timelines related to setting up a clinical trial, while the research on pregnant women shows how real-time updates to clinical practice were possible as a result of research using existing system data collection methods.

## Evidence

[1] Research Excellence Framework. 2014. Preventing the spread of H1N1: Immunisation trials in UK children. [Case study 4868.] As of 2 May 2016:  
<http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=4868>



The case study presents the underpinning research and impact of the clinical trials undertaken by the Oxford Vaccine Group. It provides information on the results of the effects of the Pandemrix and Celvapan vaccines in children, supported by relevant publications.

[2] National Institute for Health Research Journals Library. 2016. H1N1 pandemic flu research. As of 2 May 2016: <http://www.journalslibrary.nihr.ac.uk/collections/h1n1-pandemic-flu-research>

The webpage offers a collection of research undertaken to support the Department of Health's response to the H1N1 'swine flu' pandemic. A total of 14 projects were funded, and they published their results in three themed issues of the journal *Health Technology Assessment*.

[3] Walley T, Davidson P. 2010. Research funding in a pandemic. *Lancet* 375 (9720): 1063-5. doi:10.1016/S0140-6736(10)60068-2

The article describes the NIHR response to the H1N1 epidemic.

[4] Pollard AJ, Reiner A, Tessa J, Sheasby E, Snape M, Faust S, Collinson A, Finn A, Heath PT, Miller E. 2009. Expediting clinical trials in a pandemic. *British Medical Journal* 339: b4652. doi:10.1136/bmj.b4652

This piece is a letter highlighting the progress on the setting up of the children's H1N1 vaccine trial, highlighting the success of the expedited approval process.

[5] The Oxford Vaccine Group newsletter. 2011. As of 2 May 2016: <http://www.ovg.ox.ac.uk/sites/default/files/Newsletter2011.pdf>

[6] Waddington C, Andrews N, Hoschler K, Walker W, Oeser C, Reiner A, John T, Wilkins S, Casey M, Eccleston P, Allen R, Okike I, Ladhani S, Sheasby E, Waight P, Collinson A, Heath P, Finn A, Faust S, Snape M, Miller E, Pollard A. 2010. Open-label, randomised, parallel-group, multicentre study to evaluate the safety, tolerability and immunogenicity of an AS03(B)/oil-in-water emulsion-adjuvanted (AS03(B)) split-virion versus non-adjuvanted whole-virion H1N1 influenza vaccine in UK children 6 months to 12 years of age. *Health Technology Assessment* 14 (46): 1-130. doi: 10.3310/hta14460-01.

This piece presents the results of the first study comparing the two vaccines performed by the Oxford team. The aim was to evaluate the safety, tolerability and immunogenicity of an AS03(B)/oil-in-water emulsion-adjuvanted (AS03(B)) split-virion vs non-adjuvanted whole-virion H1N1 influenza vaccine in UK children aged 6 months to 12 years. The results indicated that the adjuvanted vaccine, although reactogenic (producing common adverse reactions), was more immunogenic (inducing an immune response aimed at protecting the organism), especially in younger children, indicating the potential for improved immunogenicity of influenza vaccines in this age group.

[7] de Whalley P, Walker W, Snape MD, Oeser C, Casey M, Mouldale P, Harrill C, Andrews N, Hoschler K, Thompson B, Jones C, Chalk J, Kerridge S, Tomlinson R, Heath PT, Finn A, Faust S, Miller E, Pollard AJ. 2011. A 1-year follow-on study from a randomized, head-to-head, multicenter, open-label study of two pandemic influenza vaccines in children. *Health Technology Assessment* 15 (45): v-vi, xi-xiii, 1-128. doi:10.3310/hta15450

This piece presents the results from the one-year follow-on study. It aimed to assess the persistence of antibodies to H1N1 influenza one year after children aged 6 months to 12 years had been immunised

with two doses of either a non-adjuvanted whole-virion H1N1 influenza vaccine or an AS03B-adjuvanted split-virion H1N1 influenza vaccine. It also aimed also to assess the immunogenicity and reactogenicity in this population of a single dose of 2010–11 trivalent seasonal influenza vaccine. The research found that one year later, nearly all children who received two doses of the AS03B-adjuvanted split-virion pandemic H1N1 influenza vaccine had levels of antibodies deemed protective, while children who received two doses of whole-virion vaccine had lower levels.

[8] Vogel G. 2015. Why a pandemic flu shot caused narcolepsy. *Science*. doi:10.1126/science.aac8792

This article summarises the views that the Pandemrix vaccine is linked to the emergence of narcolepsy and discusses evidence that the nucleoprotein might be an important player in this link.

[9] Miller E, Andrews N, Stellitano L, Stowe J, Winstone AM, Shneerson J, Verity C. 2013. Risk of narcolepsy in children receiving an AS03 adjuvanted AH1N1 (2009) influenza vaccine in England. *British Medical Journal* 346: f794. doi: 10.1136/bmj.f794.

The objective of this research was to evaluate the risk of narcolepsy in children and adolescents in England targeted for vaccination with AS03 adjuvanted pandemic A/H1N1 2009 vaccine (Pandemrix) from October 2009. The authors' findings, which are consistent with those of a previous study conducted in Finland, found that the increased risk of narcolepsy after vaccination with AS03 adjuvanted pandemic A/H1N1 2009 vaccine indicates a causal association.

[10] Research Excellence Framework. 2014. Underpinning evidence-based policy for management of influenza in pregnant women. [Case study 9538.] As of 2 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=9538>

The case study presents the underpinning research and impact of the rapid study of pregnant women hospitalised across the UK with 2009/H1N1 infection using UKOSS. It also offers an overview of relevant publications.

[11] Yates L, Pierce M, Stephens S, Mill AC, Spark P, Kurinczuk JJ, Valappil M, Brocklehurst P, Thomas SH, Knight M. 2010. Influenza A/H1N1v in pregnancy: An investigation of the characteristics and management of affected women and the relationship to pregnancy outcome for mother and infant. *Health Technology Assessment* 14: 109-82.

The research was undertaken to assess rates of and risk factors for adverse outcomes following AH1N1v infection in pregnancy and to assess the adverse effects of the antiviral drugs and vaccines used in prevention and management. The study concluded that earlier treatment with antiviral agents is associated with improved outcomes for pregnant women and recommended that antiviral agents and vaccines should be provided promptly to pregnant women, particularly in the primary care setting.

[12] Department of Health. 2011. H1N1 2009: Winter flu: Updated guidance for providers of maternity services. London: Department of Health.

Department of Health guidance.

[13] Public Health England. 2013. Influenza. [Department of Health guidance on immunisation for influenza in pregnancy, updated for 2012–13 winter influenza season.] London: Department of Health. Green Book Chapter 19, volume 4-71.

Department of Health guidance on immunisation against influenza in pregnancy.

[14] Public Health England. 2015. Influenza immunisation programme for England GP patient groups: Data collection survey Season 2014 to 2015. London: Public Health England. As of 2 May 2016: [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/429612/Seasonal\\_Flu\\_GP\\_Patient\\_Groups\\_Annual\\_Report\\_2014\\_15.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/429612/Seasonal_Flu_GP_Patient_Groups_Annual_Report_2014_15.pdf)

[15] European Centre for Disease Prevention and Control. 2012. ECDC scientific advice on seasonal influenza vaccination of children and pregnant women. Stockholm: ECDC. As of 5 May 2016: <http://ecdc.europa.eu/en/publications/Publications/Seasonal%20influenza%20vaccination%20of%20children%20and%20pregnant%20women.pdf>

The document provides EU/EEA member states and EU bodies with relevant information to make an informed decision on routine vaccination of healthy children and pregnant women with seasonal influenza vaccine. The document is based on a systematic review of the literature, which encloses a UK study that used UKOSS data and the opinions of a group of independent experts.

#### *6.1.10. Piloting human papillomavirus testing as a cost-effective method for cervical cancer screening*

##### Case study

In the UK, there were 3,207 new cases of cervical cancer diagnosed in 2013 and 919 deaths in 2012 [1]. A 2014 report found that the annual costs of treating cervical cancer in England are over £44 million, borne by the NHS, the state and patients [2]. The high numbers of cervical cancer cases, combined with a high cost of treatment, signal the importance of having cost-effective screening methods to diagnose and identify cases in a fast and timely manner. NIHR-funded research found human papillomavirus (HPV) screening to be a cost-effective method of primary screening for cervical cancer [3].

HPV is considered to be the primary cause of cervical cancer and over three quarters of sexually active women get this virus at some point in their lives [4]. Approximately 70% of cervical cancers and precancerous cervical lesions are caused by two HPV types (16 and 18) cause [4]. The main method of testing for cervical cancer is cytology, which consists of taking a smear test of cervical cells and investigating the presence of lesions that could signal pre-cancerous or cancerous cells. Screening is a way of preventing cervical cancer. Finding out early about cellular changes in the cervix and treating these changes could improve the chances for women to stay healthy. This is important as untreated changes in the cervix could lead to cancer. Through the Health Technology Assessment (HTA) programme, the NIHR has funded research into the clinical effectiveness and cost-effectiveness of primary HPV screening in England [3][5].

Liquid-based cytology (LBC) is a method of preparing cervical samples for cytological examination. A randomised trial of human papillomavirus (HPV) testing in primary cervical screening (ARTISTIC) study, demonstrated that LBC and HPV testing combined was not superior to LBC alone. So combining the currently used method of screening with HPV testing did not give better results. However, the research did find evidence that HPV testing either as a triage or as an initial test triaged by cytology would be cheaper than the current way of cytology testing without HPV screening [5]. This suggests that using

HPV as a primary screening method to decide who should be offered cytological screening would be both clinically effective and cost effective.

Furthermore, provided the tests are carried out properly, the HPV testing gives either a positive or negative result; it is therefore more objective than examination of cytology for abnormalities because cytology screening is more dependent on the laboratory analyst [6]. Another finding of ARTISTIC was that the screening threshold for HPV recommended by the original manufacturer of the HPV test was leading to many false positives [5][6]. Based on this, the study has had an impact on industry, by establishing a threshold that resulted in fewer false positives and was still sensitive enough to ensure effective screening [5][6][8].

Subsequent NIHR-funded research, based on the results of the study, found that a HPV initial screen was more protective over a six- year period compared with current practice. This was based on the findings that for women that were HPV negative at baseline, the protection against lesions that could signal pre-cancerous or cancerous cells over 3 screening rounds and 6 years follow up was similar when compared to women with negative baseline cytology (current method of screening) after 2 screening rounds and 3 years. This finding showed an extended period of protection by a negative HPV result when compared with the cytology one and allows a safe lengthening of the screening interval [3][6]. The explanation for the longer duration of protection is that HPV signifies not only a risk of underlying disease but also a risk of developing a lesion. A HPV-negative outcome means a very low risk of having an underlying lesion and also a reduced risk of developing one over the next 6 years [3]. An independent assessment by RAND Europe found that this change would have a net benefit of nearly £3 million to the NHS, based on screening over 200,000 individuals per year [6].

The ARTISTIC trial triggered a national pilot of HPV primary screening [7][8] that began in 2013 and is being run at six sites across England. A 2015 evaluation of the ongoing pilot programme found that HPV primary testing achieves a higher detection rate of abnormal growth on the surface of the cervix, with a small increase also in the number of referrals to colposcopy, following positive screening results [9][10].

The UK National Screening Committee, which is responsible for the UK National Screening Programme in England, acknowledged the findings from the pilot trials together with other international evidence, and recommended that the cervical cancer screening programme should adopt HPV screening as the primary screening test for cervical cancer.

In sum, NIHR-funded research has contributed to the evidence base for effective cervical cancer screening methods, both in England and internationally [8]. The implications of this body of research are felt both in the quality of the screening method, which now is more exact and allows a longer timespan between screening times, and in the healthcare system costs.

## Evidence

[1] Cancer Research UK. n.d. Cervical cancer statistics. As of 9 May 2016:

<http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/cervical-cancer>

Statistics from Cancer Research UK on Cervical Cancer.

[2] Salter J. 2014. Revealing the true cost of cervical cancer...: Behind the screen. London: Demos. As of 9 May 2016: [http://www.demos.co.uk/files/Behind\\_the\\_screen\\_-\\_web.pdf?1402772155](http://www.demos.co.uk/files/Behind_the_screen_-_web.pdf?1402772155)

The report presents in detail the financial implications of cervical cancer, looking at its impact not just on individuals but also on the NHS and state more widely.

[3] Kitchener HC, Canfell K, Gilham C, Sargent A, Roberts C, Desai M, Peto J. 2014. The clinical effectiveness and cost-effectiveness of primary human papillomavirus cervical screening in England: Extended follow-up of the ARTISTIC randomised trial cohort through three screening rounds. *Health Technology Assessment* 18 (23): 1-196 doi:10.3310/hta18230

This is the NIHR HTA report of the research that describes the second study on the clinical effectiveness and cost-effectiveness of HPV as a primary screening method.

[4] World Health Organization Regional Office for Europe. 2016. Cervical cancer. As of 9 May 2016: <http://www.euro.who.int/en/health-topics/Life-stages/sexual-and-reproductive-health/activities/cervical-cancer>

The report provides an economic analysis of the impact of the HTA programme. One case in the report is the potential economic benefits of the recommendations from the ARTISTIC study.

[5] Kitchener HC, Almonte M, Gilham C, Dowie R, Stoykova B, Sargent A, Roberts C, Desai M, Peto J, ARTISTIC Trial Study Group. 2009. ARTISTIC: A randomised trial of human papillomavirus (HPV) testing in primary cervical screening. *Health Technology Assessment* 13 (51): 1-150. doi: 10.3310/hta13510

This is the NIHR HTA report of the research that describes the ARTISTIC trial.

[6] Kitchener HC. 2015. Report to the National Screening Committee June 2015. As of 9 May 2016: [http://legacy.screening.nhs.uk/policydb\\_download.php?doc=555](http://legacy.screening.nhs.uk/policydb_download.php?doc=555)

The report finds that there is grade A evidence to support a switch from primary cytology to primary HPV testing in cervical screening.

[7] Guthrie S, Bienkowska-Gibbs T, Manville C, Pollitt A, Kirtley A, Wooding S. 2015. The impact of the National Institute for Health Research Health Technology Assessment programme, 2003–13: A multimethod evaluation. *Health Technology Assessment* 19 (67): 1-291. doi: 10.3310/hta19670.

The study reviewed the impact of the programme, from 2003 to 2013, on health, clinical practice, health policy, the economy and academia. The ARTISTIC study is also discussed in the report.

[8] Moss S, Gibney A. 2015. HPV primary screening pilots: Evaluation report of the National Screening Committee. As of 9 May 2016: [http://legacy.screening.nhs.uk/policydb\\_download.php?doc=560](http://legacy.screening.nhs.uk/policydb_download.php?doc=560)

The paper reports on the results of baseline testing in the first 18 months of the pilots.

[9] Stubbs R. 2016; 13 April. HPV primary screening in the cervical screening programme. As of 9 May 2016: <https://phescreening.blog.gov.uk/2016/04/13/hpv-primary-screening-in-the-cervical-screening-programme/>

This blog post from 13 April 2016 mentions that, based on the review of the results from the English HPV primary screening pilot sites and international evidence, the UK National Screening Committee

recommended at its January meeting that HPV primary screening should be adopted by the screening programme.

[10] Kitchener 2015. Report to the National Screening Committee. As of 13 May 2016: [http://webcache.googleusercontent.com/search?q=cache:uLep9GZKk60J:legacy.screening.nhs.uk/policydb\\_download.php%3Fdoc%3D555+%&cd=2&hl=en&ct=clnk&gl=us](http://webcache.googleusercontent.com/search?q=cache:uLep9GZKk60J:legacy.screening.nhs.uk/policydb_download.php%3Fdoc%3D555+%&cd=2&hl=en&ct=clnk&gl=us)

Report to the UK National Screening Committee by the Chair of the Advisory Committee for Cervical Screening

## 7. Putting patients and the public at the heart of all stages of research

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### 7.1. Summary

#### **Engaged. Prioritised. Involved.**

*NIHR is making health research more relevant to patients and to the public it benefits by involving members of the public at all stages of research, from setting priorities to communicating and implementing study findings, as well as improving public awareness of research and actively improving public participation in research studies.*

One of the main aims of patient and public involvement (PPI) is to further improve the quality of research by including patient's perspectives on how and why the research is being conducted. The hope is that, by involving patients who will be directly involved in, and benefit from, the outputs of the research, patient-centred research will be more targeted and relevant and have an impact on the provision of services and care.

INVOLVE is an NIHR-funded national public involvement centre and advisory group that seeks to ensure that patients and the public are effectively involved in all stages of research. As acknowledged in the international evidence gathering for the *Going the Extra Mile* report,<sup>6</sup> INVOLVE has been a world leader in raising the awareness, importance and quality of public involvement over the past 20 years. It is one of the few (and longest-running) programmes of its kind in the world. Thus, through its promotion of PPI in research, NIHR is changing research culture and acting as a beacon of PPI best practice.

Examples of PPI supported by NIHR are numerous and cover the entire research process, from setting priorities for what kind of research is undertaken and how, to defining research outcomes and disseminating findings:

- Since 2008, the NIHR-funded Devices for Dignity (D4D) initiative has provided a platform for patients and the public to submit their ideas and become part of the healthcare innovation process. D4D focuses primarily on renal technologies, assistive and rehabilitative technologies, urinary continence management and paediatric technologies. D4D gives patients and the public an opportunity to underline which outcomes matter when thinking about the development of interventions and devices.

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<sup>6</sup> National Institute for Health Research. 2015. *Going the extra mile: Improving the nation's health and wellbeing through public involvement in research*. London: NIHR. As of 9 May 2016: <http://www.nihr.ac.uk/documents/about-NIHR/NIHR-Publications/Extra%20Mile2.pdf>

- A study of people at risk of cardiovascular disease who also have a severe mental illness received an award from the Mental Health Research Network for outstanding service user involvement. Patient engagement helped to make the intervention more acceptable and meaningful for research users and helped to shape future research.
- The Non-Executive Children’s Board at the NIHR/Wellcome Trust Cambridge Clinical Research Facility for Experimental Medicine has enabled children to have a voice in the service development of the facility and has led to changes in service re-design – for example, making the Clinical Research Facility more child friendly and helping inform the design of study-specific patient information.
- Funded by NIHR’s School for Primary Care Research, research to develop a smartphone app called the PainRecorder involved patients with musculoskeletal conditions in the actual design and functionality of the app, as well as in what kinds of data would be useful to collect. Their involvement resulted in changes to the app which better reflected the user experience.
- The James Lind Alliance seeks to involve the public in setting priorities for research. Funded by charities and supported by NIHR, it was established to give patients an equal voice with carers and clinicians through Priority Setting Partnerships. These identify and prioritise the Top 10 ‘unanswered questions’ concerning the effects of treatments on which they would like research to focus. Since 2007, approximately 50 partnerships have been convened, enabling more patients, carers and clinicians to get involved in the decisionmaking process, and informing future research funding.

In addition to helping research to be patient-led and patient-centred, the following efforts have resulted in more people participating in all stages of research:

- The Join Dementia Research initiative is a national online service that makes it easier for people with dementia, their carers and members of the public to register their interest in taking part in dementia research. The service then matches people to suitable studies. By expanding the pool of interested research participants, it aims to improve the speed of study delivery and, ultimately, to support advances in treatment.
- A study on testing and treatment for prostate cancer involved patients and the public to inform the phrasing of participant information, leading to high levels of participation in the study.
- At the regional level, NIHR’s Clinical Research Network is helping to match patients to relevant clinical trials and accelerating the pace of research. Over the past five years, more than 3 million individuals have participated in clinical research studies supported by the Clinical Research Network.

Finally, efforts supported by NIHR are raising awareness among the public and within the scientific community about the importance of PPI and the ways in which people can become involved. One of the central aims of these efforts is to be inclusive and to reach those groups which are usually not involved in research, as shown by the following example:

- The Generation R initiative provides a platform for children to engage with and learn about research both nationally and internationally. Generation R is giving children and young people a



role in informing research, from funding applications through to the design and validation of materials used as part of clinical trials.

### *7.1.1. Conducting research for the people, with the people: INVOLVE*

#### Case study

Established in 1996, INVOLVE is now funded by, and an integral part of, the NIHR, with the aim to support active public involvement in NHS, public health and social care research [1]. As such, INVOLVE is the only government-funded national advisory group seeking to ensure that patients and the public are involved in research, working from within the healthcare system itself. INVOLVE aims to embed patient and public involvement (PPI) throughout the research process, from identifying, prioritising and commissioning topics that form the focus of research studies, through to the design, conduct and communication of research studies and their findings.

The premise of PPI is that research should be conducted ‘with’ or ‘by’ the public or service users through their active involvement in research organisations or projects, rather than merely with their participation [2]. In practice this means that INVOLVE works to ensure that researchers, research commissioners, research funders and the public have access to the support and guidance that they need [1]. This includes significant online resources, including guidance, briefing documents and a PPI evidence library that anyone can add to [3]. INVOLVE also matches members of the public who want to participate in research with those carrying out research, through linking to the NIHR-hosted website People in Research [4].

Through its role, INVOLVE has raised awareness of the importance of PPI and improved the quality of research and different pathways to achieving patient benefits in these areas. A recent review by the NIHR concluded that the existence of INVOLVE has been crucial to the development of public involvement in NIHR, in the UK and internationally [5]. Stakeholders also felt that INVOLVE was instrumental in encouraging PPI across the research sector in the past 10 years [5]. This is also reflected in the research literature, where INVOLVE is often flagged as an example from which other countries and sectors can learn [6]. The examples below illustrate the different ways in which INVOLVE has achieved this.

Demonstrating the wide reach of INVOLVE, the INVOLVE website attracted 1.2 million visitors in 2014-15, with 54,600 people accessing briefing notes and 33,600 people visiting the PPI evidence library [7]. Alongside this reach is a wide network one can access through invoDIRECT, an online, searchable, directory of more than 100 networks, groups and organisations that support active public involvement in the NHS, public health and social care research [7].

INVOLVE also facilitates invoNET, a network of different members, working to build evidence, knowledge and learning about public involvement in NHS, public health and social care research. Membership covers a range of stakeholder groups including researchers, research funders and health and social care practitioners [8]. The purpose of the network is share, strengthen and disseminate the knowledge base of public involvement in research [9]. invoNET activities include round table events, most recently around the evidence base for impact of public involvement in research [10]. An example of the growing evidence base feeding in to these resources is a recent survey by the NIHR Clinical Research

Network indicating that 80 per cent of studies with PPI achieved their patient recruitment on time and on target [11].

Finally, INVOLVE supports specific programmes to raise awareness of research amongst particular groups of the public and patients. INVOLVE has a strong commitment to ensuring equality and diversity, guided by the principles of the Equality Act 2010 [12]. Recently significant focus has been raising awareness and developing the knowledge base around involvement of children and young people in research [12]. This includes ‘This Is My Story’: an animation of a young man who, initially new to research, becomes meaningfully involved [13].

Through its unique set-up and collaborative nature, INVOLVE will continue to have an important ongoing role in contributing to the nation’s research agenda, and supporting improvements in how patients and the public are involved at all stages in its formation and delivery [5].

## Evidence

[1] INVOLVE. 2015. INVOLVE Strategy 2012–15. As of 2 May 2016:

<http://www.invo.org.uk/posttypeorgpub/involve-strategy-2012-2015/>

Presents INVOLVE strategy for 2012–15.

[2] INVOLVE. 2015. What is public involvement in research? As of 2 May 2016:

<http://www.invo.org.uk/find-out-more/what-is-public-involvement-in-research-2/>

An explanation of what public involvement means and definitions of related terms.

[3] INVOLVE. 2015. Evidence library. As of 2 May 2016: <http://www.invo.org.uk/resource-centre/libraries/evidence-library/>

Introduction to the evidence library on the INVOLVE website.

[4] People in Research (homepage). 2016. As of 2 May 2016: <http://www.peopleinresearch.org/>

Homepage for People in Research, an initiative matching members of the public with researchers.

[5] National Institute for Health Research. 2015. Going the extra mile: Improving the nation’s health and wellbeing through public involvement in research. London: NIHR. As of 2 May 2016: <http://www.nihr.ac.uk/documents/about-NIHR/NIHR-Publications/Extra%20Mile2.pdf>

*Going the Extra Mile* is a report outlining the NIHR’s vision for PPI, the current status of PPI and recommendations for action based on the Breaking Boundaries strategic review.

[6] Parsons S, Starling B, Mullan-Jensen C, Tham S, Warner K, Wever K. 2016. What do pharmaceutical industry professionals in Europe believe about involving patients and the public in research and development of medicines? A qualitative interview study. *BMJ Open* 6: e008928. doi:10.1136/bmjopen-2015-008928

A paper reporting on a qualitative study exploring European-based pharmaceutical industry professionals’ beliefs about PPI.

[7] National Institute for Health Research. 2015. Taking stock: INVOLVE Coordinating Centre March 2015. London: NIHR. As of 2 May 2016: <http://www.invo.org.uk/wp-content/uploads/2015/04/INVOLVETakingStock2015.pdf>

A report by the INVOLVE Coordinating Centre outlining recent activities and achievements.

[8] INVOLVE. 2015. Current members. As of 2 May 2016:

<http://www.invo.org.uk/communities/invonet/current-members/>

List of invoNET members.

[9] INVOLVE. 2015. invoNET. As of 2 May 2016: <http://www.invo.org.uk/communities/invonet/>

Overview of invoNET, a network to build evidence and learning about public involvement in research.

[10] INVOLVE. 2015. News and events. As of 2 May 2016:

<http://www.invo.org.uk/communities/invonet/news-and-events/>

Information on news and events related to invoNET.

[11] Johns T, Crossfield S, Whibley C. 2015. Closed study evaluation: Measuring impacts of patient and public involvement and research quality and performance. London: NIHR CRN.

Survey collating information from 281 studies on the NIHR Clinical Research Network.

[12] INVOLVE. 2015. How we work with others. As of 2 May 2016: <http://www.invo.org.uk/about-involve/how-we-work-with-others/>

Overview of how INVOLVE addresses equality and diversity in working with others.

[13] INVOLVE. 2015. Involving children and young people. As of 2 May 2016:

<http://www.invo.org.uk/find-out-more/how-to-involve-people/involving-children-and-young-people/>

Information on how involving children and young people can help research.

### *7.1.2. Shaping health services to improve patients' physical and mental health*

#### Case study

Severe mental illnesses (SMI), such as schizophrenia and bipolar disorder, affect 0.5 to 1 per cent of the UK population [1][2]. The cost of schizophrenia for society amounts to £11.8 billion per year, of which £7.6 billion is spent in the public health sector [3, 4]. Previous research conducted at University College London found that people with schizophrenia are at greater risk of cardiovascular diseases (CVD) [5]. People with SMI use primary care and GP services more often than people without SMI [6], and this interaction could provide the opportunity for screening for CVD. Combining these two findings, NIHR funded a project called PRIMROSE (Prediction and management of cardiovascular risk for people with severe mental illnesses).

The PRIMROSE project is a five-year programme of research started in 2011 to improve the detection and management of CVD risk in people with SMI in primary care [7]. PRIMROSE has benefited extensively from the involvement of service users, which has had a major impact on the research project [8].

This involvement has been achieved through the help of Rethink, a charity for people with mental illnesses. Rethink facilitated the employment of a service user researcher on the research team, who acted as a gatekeeper and ensured high-quality involvement of a broad range of service users and carers, which in turn significantly influenced the elaboration of the new intervention. The service users came together

through two groups: 1) the Lived Experience Advisory Panel, a panel of service users and carers that meets once a year and that contributes to steer the project; and 2) the Intervention Development Group, which has two or three meetings per year and provides input during all stages, from grant application through to development [8]. These groups also helped identify barriers to the implementation of the intervention and ways to overcome them, making the intervention more acceptable and meaningful for service users [8].

An example of the Intervention Development Group's contribution has been the shaping of the nurses' training programme. The group suggested that stigma should be included in the curricula and that there should be considerations for ensuring that nurses are at ease working with people with SMI. A person with SMI involved in the project stated: '[Being involved in the study is] something that I feel really matters – the shocking statistic of people with severe mental illness like myself – the fact that our life expectancy is so dramatically reduced. It feels really important in that way for all service users. It also matters to me personally because I'm trying to reduce my own risk factors for cardiovascular disease' [8].

The design of the intervention also involved a series of focus groups with health professionals, service users and carers. The service users' focus groups were coordinated and facilitated by the Rethink researcher. In total, the focus group research involved 75 people: GPs, nurses, service users, community mental health staff and carers providing detail about the existing procedures and the perceived barriers and facilitators to delivering interventions for lowering CVD risk for people with SMI in primary care [9].

These findings informed the next step of the research programme, namely, a study to compare the effectiveness of the designed behavioural intervention to lower CVD risk which is delivered by a practice nurse or healthcare assistant, within standard care offered in general practice [9]. The study recruited 69 GP practices and 174 patients between January 2014 and the middle of 2015 [10].

While the full results from the PRIMROSE project are not yet available, this work has already shown the positive impact on the involved practice nurses and service users, in line with the NIHR's commitment to involve the public and the patients in research that concerns them. Overall, through the design and implementation of this new intervention, the programme aims to inform how to best shape GP services, therefore optimising the health care system and translating the results into better services for people with SMI.

## Evidence

[1] National Audit Office. 2007. Helping people through mental health crisis: The role of crisis resolution and home treatment services. London: HMSO. As of 2 May 2016:

<https://www.nao.org.uk/report/helping-people-through-mental-health-crisis-the-role-of-crisis-resolution-and-home-treatment-services/>

The National Audit Office webpage on health and social care describes the role of the Crisis Resolution and Home Treatment services

[2] Goldner EM, Hsu L, Waraich P, Somers JM. 2002. Prevalence and incidence studies of schizophrenic disorders: A systematic review of the literature. *The Canadian Journal of Psychiatry* 47: 833-43. As of 2 May 2016: <https://ww1.cpa-apc.org/Publications/Archives/CJP/2002/November/goldner.pdf>

This journal article is a systematic review of prevalence and incidence studies of schizophrenic disorders

[3] Andrew A, Knapp M, McCrone P, Parsonage M, Trachtenberg M. 2012. Effective interventions in schizophrenia: The economic case. [A report prepared for the Schizophrenia Commission.] London: Personal Social Services Research Unit. As of 2 May 2016: [http://eprints.lse.ac.uk/47406/7/\\_libfile\\_repository\\_Content\\_Knapp,%20M\\_Effective%20Interventions%20in%20schizophrenia%20the%20economic%20case\\_Effective%20Interventions%20in%20schizophrenia%20\(LSERO\).pdf](http://eprints.lse.ac.uk/47406/7/_libfile_repository_Content_Knapp,%20M_Effective%20Interventions%20in%20schizophrenia%20the%20economic%20case_Effective%20Interventions%20in%20schizophrenia%20(LSERO).pdf)

This is a discussion paper from the LSE on effective interventions in schizophrenia.

[4] Nuffield Trust. 2014. NHS spending on the top three disease categories in England. London: Nuffield Trust. As of 2 May 2016: <http://www.nuffieldtrust.org.uk/node/2530>

This Nuffield Trust webpage provides a chart on the top three categories of NHS spending in England

[5] Research Excellence Framework. 2014. Improving management of schizophrenia and severe mental illnesses in general practice. [Case study 22421.] As of 2 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=22421>

The case study offers mainly an overview of the MRC-funded research to identify and reduce cardiovascular disease in NHS patients with severe mental disorders undertaken by the team at University College London. Most of the research had been done before the Primrose programme.

[6] Osborn D, Levy G, Nazareth I, King M. 2008. Suicide and severe mental illnesses: Cohort study within the UK general practice research database. *Schizophrenia Research* 99 (1-3): 134-8. As of 2 May 2016: <http://www.ncbi.nlm.nih.gov/pubmed/18155881>

This webpage provides an abstract of the Schizophrenia Research journal article, *Suicide and severe mental illnesses: Cohort study within the UK general practice research database*.

[7] PRIMROSE (homepage). 2016. As of 2 May 2016: <http://www.ucl.ac.uk/primrose>

The webpage of the PRIMROSE programme offers an overview of the programme, the latest publications and two newsletters that inform on the progress of the programme.

[8] Staley K. 2013. The PRIMROSE programme – A case study illustrating the impact of service user and carer involvement. London: NIHR. As of 2 May 2016: <http://www.nihr.ac.uk/CCF/PGfAR/CCF-PGfAR-PPICaseStudyPRIMROSE.pdf>

This case study describes the impact of service user and carer involvement on the PRIMROSE programme, offering testimonials by different persons involved in the research.

[9] Burton A, Osborn D, Atkins L, Michie S, Gray B, Stevenson F, Gilbert H, Walters K. 2015. Lowering cardiovascular disease risk for people with severe mental illnesses in primary care: A focus group study. *PLoS ONE* 10 (8): e0136603. doi:10.1371/journal.pone.0136603

Original research article from the follow on study.

[10] Clinical Research Network. 2015. News Flash (May). As of 2 May 2016: [https://www.ucl.ac.uk/primrose/CRN\\_May\\_Newsletter2015](https://www.ucl.ac.uk/primrose/CRN_May_Newsletter2015)

This is a link to the PRIMROSE study newsletter.

### 7.1.3. *Inviting patients and the public to take part in research: OK to ask and Join Dementia Research*

#### Case study

People participate in research studies for a variety of reasons. Sometimes they hope to benefit personally, and in other instances they want to help others [1]. According to the NIHR Clinical Research Network, 95 per cent of the population stated they valued participation in research; however only 21 per cent stated they would be comfortable broaching the subject of their participation in research with a doctor [2]. To inform the public about the benefits of taking part in research and opportunities to do so, the NIHR has led a number of campaigns.

In 2013, the NIHR launched the OK to Ask campaign to coincide with International Clinical Trials Day (20<sup>th</sup> May), making the UK the only country in the world to run an awareness campaign to get people to take part in clinical research [3]. The campaign is now heading into its fourth year. OK to Ask encourages patients and their carers to ask NHS professionals about how they might take part in clinical research, as well as raising the profile of research participation. This reminds all healthcare professionals, whether research-active or not, to be research-aware [2].

As well as focusing on the 20<sup>th</sup> May, OK to Ask has active social media influence, such as Facebook and Twitter, where it uses the hashtag #NIHRoktoask. The OK to Ask campaign also draws support from charities, such as Sparks [4], MND [5] and the British Liver Trust [6], which highlight public participation in clinical research.

Each year, OK to Ask runs a survey to evaluate the impact of the campaign. In 2015, the survey was distributed to 15 Clinical Research Facilities. Although the survey cannot determine the number of people who have taken part in research as a result of campaigns, it showed that 97 per cent of respondents (n=825) would recommend research participation.

Looking more broadly, we see that in 2015, 618,453 patients and members of the public took part in 4,932 NIHR Clinical Research Network Portfolio studies. This means that over the past five years more than 3 million people have had the opportunity to participate in research supported by the NIHR Network [7].

While OK to Ask sought to raise awareness from all patients, some services were developed to be more topic focused than others, such as Join Dementia Research. In February 2015, the NIHR launched this national service, through an online and telephone service, in collaboration with the Alzheimer's Society, Alzheimer's Research UK and Alzheimer Scotland [8]. In the UK alone, 850,000 people live with dementia, a disease that requires a deeper understanding of its causes and possible treatments. Join Dementia Research encourages the public (both people with and people without dementia) to take part in research in a number of different areas, including, for example, cognitive tests, talking therapies, nutrition, drug trials, and genetics [9].

A benefit of *Join Dementia Research* is that it provides a pool of volunteers from which researchers can choose, the only requirement being that the studies have ethics approval [10]. This means that commercial as well as academic studies are eligible to use this resource, something particularly useful for

PhD candidates. The *Join Dementia Research* service has attracted 16,785 volunteers, 4,758 of whom have enrolled in 62 dementia studies across 115 NHS, University and commercial Research organisations [11]. A July 2015 survey of volunteers demonstrated that over 80 per cent of respondents had an increased awareness of dementia research taking place due to *Join Dementia Research* and two-thirds believe that the service has made it easier to get involved in dementia research [12]. The availability of volunteers to participate in studies has enabled studies to start in a timely manner without the historic issues with recruitment, and to have sufficient participants to make relevant findings at a population level. When asked about the value of taking part in research one couple said, 'It's for future generations and anything that we can do to help anybody with memory problems doesn't cost a thing, does it?' [13]

Recent figures show that 98 percent of NHS Trusts and 41 percent of general medical practices were actively engaged in clinical research. The NIHR has led campaigns and services, and encouraged thousands of patients and members of the public to engage directly with clinical research, demonstrating the value of taking part and increasing the number of individuals and institutions participating in research across the nation.

## Evidence

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*Join Dementia Research* information for researchers.

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Introduction to *Join Dementia Research*.

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Video presentation of the results of the 2015 *Join Dementia Research* survey.

[13] NIHR Join Dementia Research. n.d. Taking Part in the CATField Study: Video. As of 10 May 2016: <http://news.joindementiaresearch.nihr.ac.uk/taking-part-catfield-study-video/>

Volunteer testimony based on their participation in a dementia study through NIHR *Join Dementia Research*.

#### 7.1.4. Setting the research agenda through public, patient and clinician consultation

##### Case study

The James Lind Alliance (JLA), established in 2004, brings through patients, carers and clinicians together Priority Setting Partnerships (PSPs) in order to identify and prioritise the top 10 'unanswered questions' in different areas of health concerning the effects of treatments on which they would like research to focus [1]. A paper by Tallon et al. published in *The Lancet* in 2000, identified a research mismatch, meaning that research being conducted was not necessarily aligned with 'consumer'-identified needs [2]. To address this, the ultimate aim of the JLA is to ensure that funders are aware of patients' and clinicians' research priorities [3] and thus can advise on the best match. The NIHR funds the JLA to facilitate recruiting and training of JLA Advisers, coordinating PSPs, and looking after central JLA



communications. Usually each PSP is responsible for its own funding and organisation, which generally comes from one PSP-associated organisation or partners, or from a charity [4][5]. In 2015, a report on the Mesothelioma PSP was published, and a survey was launched for the Alcohol Related Liver Disease PSP, the first two examples of PSPs fully funded by the NIHR [6].

Since the first JLA PSP was conducted in 2007 on asthma, nearly 50 other PSPs have been conducted [7], translating into more than 70 articles and publications, as found on the JLA website [8]. PSPs focus on a range of health areas, including acne, hair loss, miscarriage and tinnitus. Between 2004 and 2015, 31 PSPs were completed and the work of PSPs attracted the participation of more than 26,000 individuals, enabling more patients, carers and clinicians to get involved in the decisionmaking process and thus informing future research funding [9]. For example, the Dementia PSP published a paper praising the involvement of patients and the public in the priority setting process claiming it ‘provided a broader perspective to the research agenda and in particular highlighted the need for research into care and organisation of care and delivery of people with dementia services’ [10].

The impact of the JLA PSPs and their potential for future impact has contributed towards addressing the ‘mismatch’ issue identified in 2000 by Tallon et al. and in a more recent research article by Crowe et al. in 2015 [2][11]. For example, not only do the JLA PSPs set priorities for research based on public, patient and clinician consultations, but this information is made public online.

One marker of the impact of PSPs can be found when selected research priorities are commissioned through the NIHR and other funders. The NIHR, in particular, uses some of the PSPs’ priorities to inform the research topics for commissioned calls. However, in some cases, funding for PSP priorities is difficult to track, especially if the funding comes externally to the NIHR, from a charity, for example. However, the JLA conducted a tracking exercise of NIHR funded priorities. Although not exhaustive, this exercise revealed that, as of February 2016, 26 identified priorities from 12 PSPs went to tender or were commissioned.

The funding outcomes of PSP identified priorities are not always systematically monitored; however, a selection of examples is presented in the next section. First, examples of the unanswered questions have been picked up in NIHR funded calls. For example, those from the Childhood Disability PSP were picked up by the NIHR’s Health Technology Assessment (HTA) and the Health Services and Delivery Research (HS&DR) programmes [12]. These programmes allocated funding to three of the ten issues identified as a result of the Childhood Disability PSP [12]. In 2013, the Dementia PSP released its priorities, 2 of which have been commissioned under the NIHR HS&DR funding programme [13][14]: one evaluating specialist nursing support for carers started in November 2015, and another, focusing on acute care for those with dementia, will start in July 2016 [13][14].

In response to the Sight Loss and Vision Partnership PSP a clinical trial was funded to understand ‘how outcomes from cataract surgery can be improved’. Following the Sight Loss and Vision Partnership PSP, the Efficacy and Mechanism Evaluation (EME) Programme has provided funding to test how keratoconus is treated in children and youths [15]. In 2016, the results of the Palliative and End of Care PSP led Marie Curie, a charitable organisation working with terminal illness, in association with the Motor Neuron Disease Association, to issue a call for research around the priorities identified in the PPI consultation [16]. Outside of the UK, this PeolcPSP inspired the All Ireland Institute of Hospice and

Palliative Care (AIIHPC) which used the PeolcPSP's top 28 unanswered questions to identify local priorities.

The PSPs, facilitated by the JLA, provide an opportunity for the public and patients to interact with clinicians and to contribute to the research agenda by identifying issues that are important to them and which will ultimately impact on their health, well-being and quality of life.

## Evidence

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Information from the JLA website

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This source explains the work of the James Lind Alliance, including figures for the number of PSPs completed and outlining some implications for the JLA

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[11] Crowe S. 2015. Symposium Report: Learning from JLA Evaluations - Shaping Future JLA Method, JLA Symposium 23 June 2015. As of 2 March 2016:

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This news item provides an update on the outcomes of the Childhood Disability PSP which have been explored by the British Academy of Childhood Disability Strategic Research Group and the NIHR.

[13] NIHR Evaluation, Trials and Studies. n.d. HS&DR - 14/154/07: Evaluation of specialist nursing support for carers of people with dementia. As of 27 April 2016:

<http://www.nets.nihr.ac.uk/projects/hsdr/1415407>

Information on a HS&DR funding call

[14] NIHR Evaluation, Trials and Studies. n.d. HS&DR - 14/154/09: Optimising acute care for people with dementia: a mixed-methods study. As of 27 April 2016:

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News item on the progress made by the PeolcPSP.

News item on the progress made by the PeolcPSP.

### 7.1.5. Putting patients at the heart of inventions to preserve dignity and independence

#### Case study

In 2008, the NIHR piloted two Healthcare Technology Cooperatives (HTCs), one of which was Devices for Dignity (D4D) [1] which sits in the Sheffield Teaching Hospitals NHS Foundation Trust [2]. In general, the HTCs are designed to work on issues of high relevance to patients and healthcare services and to create new medical devices, technologies and interventions [1]. Specifically, D4D works to deliver innovative technology solutions to support people with long-term conditions, preserving their dignity and independence. Following the pilot, in 2013, D4D became one of eight NIHR HTCs. It focuses on urinary continence management, renal technologies, assistive and rehabilitative technologies, and paediatric technologies [2].

All HTCs have a Patient and Public Involvement and Engagement plan, and they report on this on an annual basis. As just one example, D4D involves patients and the public at several levels, from inclusion of two PPI members on its steering committee, to having PPI representatives in each clinical area [1]. In addition, D4D's Renal Technologies theme includes a PPI lead/project manager who represents D4D as a co-applicant on research grants.

Thus, in more than 90 per cent of its projects, D4D engages with the public in a variety of ways, from conception to the iterative development of a product to optimise its utility and impact on patients [3]. For example, research users were involved in design workshops to rethink the neck collar for patients with motor neuron disease who have to wear a collar to support their neck [4].

When evaluating the experience of a subset of users involved in D4D research, it was found that all users (n=13) 'felt comfortable' and 'felt listened to' in participating in a project. Over half felt that they had 'had an impact on the project', and over 80 per cent stated that they were 'extremely likely' to want to get involved in further research in the future. As a result of feedback from this evaluation more information is being provided to users about subsequent stages of the research, so they can follow up on what they have contributed to [1].

To engage and involve patients and the public in its research programme, D4D ran a national *Independence and Dignity* survey [5] and hosted an event in June 2015 called *My Dignity Means: A Patient-led Event*, which was planned by a patient advisory group. The *My Dignity Means: A Patient-led Event* and preceding survey led the D4D team to identify issues, challenges and needs of individuals. Subsequently the team developed plans to mitigate some of the more prominent issues. For example, some patients alluded to the fact that they could not find satisfactory reviews of products or devices. As a result, D4D has begun collaborations with a number of its partners to launch a website where reviews of devices can be found [6]. The survey has also allowed the D4D team to assess patients' unmet needs, and inform the direction of further research. A secondary impact of the survey has led D4D to establish a partnership with Parkinson's UK on urinary continence management, although this is still under development [6].

In 2014, D4D also hosted a very successful 'hackathon' event in collaboration with Sheffield Hallam University and NIHR Collaboration for Leadership in Applied Health Research and Care (CLAHRC) for

Yorkshire and Humber, which focused on meeting unmet patient needs through improving the design of existing products, such as drinking devices, patient hoists and rollator, which are all currently under development [1].

The products and services that D4D develops in collaboration with patients and the public have also had an impact on health services delivery. An 'electronic bladder diary and clinical web portal' called ELAROS 24/7 was devised through a collaborative effort between Medipex and Innovations North, in collaboration with patients [7]. The purpose of this software is to help patients monitor and manage their symptoms, and to help assess and diagnose patients for lower urinary tract symptoms [7]. The impact of such an invention reduces patients' reliance on GP services or hospital referrals and helps patients to manage their condition. In 2013, ELAROS 24/7 was established as a company in its own right [7]. ELAROS 24/7 claims to have reduced referrals to secondary care by 30 per cent, appointment and diagnostics costs by 35 per cent, and the use of pharmacology by 10 per cent [8].

Funded by the NIHR, D4D has been able to identify issues relating to living with long-term conditions and has placed patients' needs at the core of its work, with the aim of improving patient well-being. As a consequence, D4D has had health services delivery and societal impacts through the results of its public-patient involvement and the development of patient-focused devices and technologies. Furthermore, D4D has created networks across the third sector and industry highlighting the HTC's commitment to taking a holistic approach to improving patients' lives.

## Evidence

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[5] Devices for Dignity Healthcare Technology Cooperative. n.d. Listening to you. As of 2 May 2016: <http://www.devicesfordignity.org.uk/ppc>

This webpage outlines the ways in which D4D interacts with patients and listens to their views.

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[8] ELAROS 24/7 (homepage). n.d. As of 2 May 2016: <http://www.elaros247.org.uk>

Website for ELAROS 24/7, which became a company in its own right with its product conceived under D4D.

### *7.1.6. Involving patients and the public in research through new methods and fora*

#### Case study

The NIHR School for Primary Care Research (SPCR) is a partnership among nine leading academic centres for primary care research in England. It was established to increase the evidence base for primary care practice. One of the departments is in Manchester, where the ‘Primary Care Research in Manchester Engagement Resource’ (PRIMER) group is located. This group of patients, carers and members of the public promotes the involvement of the public in shaping research and works with researchers at the University of Manchester and across the SPCR [1].

As an innovative approach to involving patients and the public in the research process, PRIMER have run ‘hack days’ in 2014 and 2015. These were co-designed with patients and the public, who facilitated some of the sessions at the event.

At the events, members of the public pitched their research ideas to each other and to researchers, and they then worked through how to develop the ideas using a research toolkit. Benefits included helping people to understand the process and challenges of competition and bidding through raising awareness of the steps and considerations that researchers need to think about in applying for funding. Another main benefit was that the interactive nature of the day broke down barriers between researchers and the public. Following the involvement, some individuals have teamed up with research teams: for example, one is sitting on a research advisory group and another individual now has an NIHR fellowship award to undertake a PhD [2].

PRIMER has also co-developed and co-delivered training with users, to provide input on how the public experience working with researchers, and to develop master classes on communications and how to set up and sustain public and patient involvement (PPI) groups [3].

One example of a patient inspired research project, where patients and the public have been central to the delivery of the research is ISIS (identifying, signposting and supporting carers) [4]. In this instance a member of the public, Mrs May Griffiths, who was part of the PRIMER team, identified an issue around ‘hidden carers’. These are individuals who support others with health problems but do not identify as a carer, and who are therefore less likely to access available support. As a ‘hidden carer’ for many years, Mrs

Griffiths recognised the issue. She collaborated with researchers in Manchester, and was named as a co-applicant on the application, which was funded by the NIHR Collaboration for Leadership in Applied Health Research and Care (CLARHC) Greater Manchester. Mrs Griffiths worked as a research team member and is an author of the publication describing the research findings [5]. In addition, the group used a steering group to act as ‘critical friends’, providing advice in advance of data collection on protocols and processes, during the study to reflect on progress and emerging findings, and afterward to validate the findings and make recommendations.

Another example of PPI in primary care research is the development of the PainRecorder, by a team of researchers in collaboration with patients and the public. When treating musculoskeletal conditions, such as arthritis it is important to understand the intensity of pain and its impact on quality of life over time to assess responses to treatment, and to ensure that correct medication and management is provided for the patient. Intermittent appointments with medical professionals are unlikely to identify these changes in a timely manner, unless accompanied by a diary to show regular monitoring by the patient. Paper diaries are often poorly completed and cumbersome, and information might be outdated by the time it reaches the practitioner. Research conducted at the University of Keele and funded by the NIHR SPCR, developed a smartphone application (called the PainRecorder) to digitally record information on pain and on the impact of pain on everyday life.

Patients and the public were heavily involved in the research through collaboration with the university’s research user group, who formed an advisory group. Members had a range of experience in using mobile technology. This was important, because the app had to be appropriate for use by a broad range of users. They provided input and advice on 1) the collection of data that was relevant to patients; 2) the appearance of the PainRecorder app itself; and 3) the functions and ease of use of the app [6].

Initially, the user group commented on specific aspects of the design, and ranked their importance for usability. The group made a number of suggestions around the data to be collected, as well as the presentation. For example, the user group felt that data should be entered at least twice a day, to reflect changes over time, including pain at night, and it highlighted the need to link pain to impact on activity. These features were incorporated into the design, and the group reconvened to test the device. In terms of usability, it was important for the user to be able to choose how to progress from one page to another, by clicking or sweeping to make it as user-friendly as possible, taking into account different levels of familiarity with digital technology [6].

The research group has now received follow-on funding from NIHR to conduct further testing on the validity of data collected and the methods for analysing and storing it, and on the clinical acceptability and utility of the app in informing patient treatment [7][8].

## Evidence

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Conference proceedings on an oral presentation of the study to date and next steps.

### *7.1.7. Engaging children and young people in research: Generation R*

#### Case study

Medicines can have different effects on children than on adults and young people, and the two groups also experience disease and services differently. In this context, Professor Dame Sally Davies, Chief Medical Officer, stressed that young people's involvement in healthcare research was 'not important but essential' [1]. She underlined the developmental and psychosocial impacts of treatments on children and the effects of offering a degree of autonomy to young people by inviting them to be part of the research



and decision-making process [1]. Involving children in the design and delivery of clinical research is important in two distinct ways. First, it empowers children to take part in research on health and healthcare matters that concern them. Second, it allows research to respond to children's concerns and ideas and to tailor solutions to their needs. GenerationR, a community for the involvement and participation of children in research, has provided a platform for children to engage with and learn about research both nationally and internationally. This has led to benefits with a global reach, including greater participation of young people's voices in research, through improvements to the way young people are engaged and involved in research.

GenerationR (R for research) was created in 2013 by five Young Persons Advisory Groups (YPAGs) based in Birmingham, Bristol, Liverpool, London and Nottingham [2] funded by NIHR [2]. These groups are made up of about 15 young people between the ages of 8 and 19. Some of the members have themselves been participants in clinical trials; others are simply interested in learning more about clinical research. They meet every six weeks so that their views, and those of their guardians/carers, can contribute to the design and delivery of clinical research [2][3]. In addition to these local meetings, the YPAGs have become involved in national and international collaborations that have led to the organisation of events.

In 2012, recognising the importance of coming together and sharing experience, the five YPAGs, with continued support from the NIHR, began to collectively organise and eventually formed a national YPAG: GenerationR [1]. GenerationR was launched at an event in September 2013 which engaged more than 160 stakeholders from charities, the research community, and industry. It was expected that this would help to demonstrate the value of patient and public interaction with researchers, improve research studies, and understand appropriate patient reported outcome measures [1]. The event was organised by representatives from each of the YPAGs and five parent representatives, as well as members of the Medicines for Children Research Network, a part of the NIHR Clinical Research Network (CRN) [1]. It was highly praised by international delegates, with one stating that this 'example of involvement in research of young people in the UK is really an inspiration for researchers in other countries' [4]. Eleven recommendations emerged from the event's round table discussions, centring on research ethics, dissemination of research results, and access to treatment, and considering the future of research and the next generation [1].

One of the recommendations from the GenerationR meeting was to find 'alternative and innovative ways of engaging with more young people and families building links with charitable organisations and parent/young people's groups'. This recommendation was acted upon in four ways. First, in January 2014, a Young People's Mental Health Advisory Group was established within GenerationR. This topic-specific group seeks to 'share good practice in service user and carer involvement,' and to promote research into mental health issues involving young people and highlighting their perspectives [5]. Second, GenerationR was further formalised in the creation of an interactive website, created in collaboration with the James Lind Initiative, with support from NIHR. The website was launched in May 2015, which awareness of young people's involvement in health research using blogs, games and quizzes [2].

Third, in October 2015, a follow-on event was convened involving 30 individuals (young people, the NIHR, the Nuffield Council on Bioethics, the JLA, the Royal College of Paediatrics and Child Health, the Health Research Authority, charities and industry) [6]. The GenerationR Alliance was initiated at the event, recognising the need to be aware of children and young people's (CYP) involvement in research, and to encourage interested parties to collaborate. Finally, GenerationR has also been involved in

international activities with other children's and young person's groups in the USA, Canada and Scotland, and through collaboration with the global pharmaceutical company, Pfizer. These efforts have led to the formation of the international Children's Advisory Network (iCAN) [7]. iCAN held its first summit in June 2015, and included two delegates from GenerationR [8]. There are plans for another summit in June/July 2016, which is predicted to attract 150 members of iCAN - young people, parents and advisors [9].

Another recommendation arising from the founding meeting of GenerationR in 2013 was to 'develop a systematic way to measure the impact of involvement activities' [8]. This was achieved through an evaluation of children's involvement in the Clinical Research Network, which gave as examples 10 cases where illustrating the involvement of children or young people in health research [10]. These case studies have shown how children and young people have informed research from funding applications through to the design and validation of materials. An example is the Supporting Parents with A Child with Arthritis (SPACe) study [10]. Researchers consulted a YPAG on the design of information leaflets for children and young people in advance of a randomised trial [10]. The YPAG was useful in suggesting a summary overview of the content at the start of each leaflet and in advising that an age bracket should not be a feature of the leaflets (validating the researchers' initial line of thinking) [10]. No further changes to the information leaflets were deemed necessary [10]. The research team believes that these leaflets were helpful in the subsequent successful recruitment to the study [10].

GenerationR is about empowering and stimulating children to get involved in research. The NIHR CRN has set up this initiative to involve future generations and to shed the stigma around involvement and participation in medical research. Overall, YPAGs and Generation R have provided young people with a platform to share their ideas with researchers and industry, and to be ambassadors for participation in research.

## Evidence

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Clinical Research Network webpage explaining the Young Person's Advisory Group.

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National Children's Bureau Evaluation of children's involvement in the NIHR Clinical Research Network.

### *7.1.8. Exemplifying public involvement as a means to improve the effectiveness and efficiency of research*

#### *Case study*

The NIHR Clinical Research Network (CRN) delivers clinical studies in the NHS. One element of this is to involve patients and the public to enhance participation, and ensure study design reflects public's priorities and needs. NIHR CRN can support researchers in a number of ways from training workshops to inform and advise patients and the public about ways in which they can be involved in research [1], to awareness campaigns, toolkits and guidance [2].

NIHR has played a leading role in establishing public involvement as good practice in clinical research. This is increasingly backed up by the evidence on how it can positively impact on research. For instance, an important thing to take into account is not holding study clinics too early in the day, so that elderly people using bus passes can attend. Practices like this support people to participate in research. To assess the benefits of patient involvement in recruitment to trials, the NIHR Mental Health Research Network (a topic-specific part of the CRN prior to the reorganisation in 2015) undertook a study to look at all 374 studies listed on the MHRN portfolio database between its inception and October 2011 [3].

The study found that patient and public involvement had increased over time, although in some areas of research it was limited. The study considered two different types of involvement – described as researcher-initiated collaboration versus consultation only. Studies funded by the NIHR were associated with a significantly higher level of collaboration, and had the smallest proportion of studies in the consultation-

only category. This suggests that the emphasis on patient involvement is more pervasive for the NIHR than for any other funder. Interestingly, studies that involved patients to a greater extent were more likely to have achieved recruitment targets, showing a benefit of involvement [3].

This work has been followed up across the entire NIHR CRN portfolio, by looking at the impact of PPI on research quality and performance, using closed studies supported by the CRN between 2012 and 2014 [4]. In a sample of 281 studies, 69 per cent of studies included patient and public involvement at some stage of their research. Patients and the public were most commonly involved in the development of the study protocol and identification of relevant ethical issues. When asked about the impact of PPI on research quality and performance, nearly 50 per cent of study teams highlighted the value of improving the information provided to patients, 38 per cent felt that PPI enhanced the credibility of the research team, and 30 per cent claimed the involvement reduced the burden for participants, by ensuring that the recruitment procedures to studies were sensitive to the needs of the patient [3]. In line with the findings from the MHRN study above, this research found that 80 per cent of studies with PPI recruited to time and target, as opposed to 69 per cent of studies that had no PPI element.

This research shows that public and patient involvement in research provides benefits to the quality of the research, and supports the recruitment of individuals through the NIHR CRN. Over the past ten 10 years, the NIHR has stressed the importance of PPI in the research it funds and supports, and there now seems to be growing evidence that this correlates with studies achieving performance targets, which seems to correlate with high levels of PPI and achieving clinical trial targets.

## Evidence

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Webpage on building research partnerships.

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### 7.1.9. Avoiding over-treatment in prostate cancer: The ProtecT trial

#### Case study

The NIHR has funded studies whose innovative methods of engaging patients in research have enabled groundbreaking findings and established new models for patient involvement in future research. The ProtecT trial of ‘active monitoring’ to avoid over-treatment in prostate cancer – a field in which recruitment has proven difficult – successfully increased participation rates by using embedded qualitative analysis of recruitment processes to produce patient-friendly study information.

More than 40,000 new cases of prostate cancer are diagnosed in the UK each year, making it the most common cancer in UK men [1]. This rate is expected to rise as the country’s population ages [2], leading to an increase over the 2012 death rate of 10,837 per year [3]. However, the value of screening for and early detection of prostate cancer is disputed due to the risk of over-diagnosis and over-treatment [4]. Radical treatments in men with localised, ‘low-risk’ prostate cancer can severely impact quality of life by affecting sexual, rectal and urinary function [5]. In response, NIHR-funded researchers have developed active monitoring as an alternative to radical treatments. Active monitoring aims to avoid over-treatment by continually reassessing patients with prostate cancer and only beginning radical treatment in those who show progression [6].

The ProtecT trial, funded through the NIHR’s Health Technology Assessment programme, compares active monitoring with surgery and radiotherapy in a randomised controlled trial. In order to be successful, the trial had to overcome the longstanding barrier of patients’ reluctance to participate in prostate cancer trials. Patients are less likely to participate in trials which assess differences in complications of treatment, but not differences in survival [7]. To address this challenge, the research team used qualitative research methods to examine the process through which patients diagnosed with prostate cancer were asked to participate in the study. Interviews with patients and analysis of recordings of recruitment appointments showed that the way in which the different treatments involved in the trial were presented had a significant impact on participation rates [7]. This resulted in a different approach to recruitment, in which recruiters avoided words which tended to be misinterpreted by patients. Researchers presented treatments as equal in keeping with the ‘uncertainty principle’, which holds that a study can only be considered an RCT if the patient does not know which of the trial arms will benefit them [8]. These changes led to an increase in the randomisation rate from 40 per cent to 70 per cent, with more patients finding all treatments involved in the trial acceptable [7].

Thanks to improved recruitment, the ProtecT study became the largest-ever randomised controlled trial in localised prostate cancer, with more than 1,500 patients with prostate cancer participating [9]. Although the results have yet to be published, emerging findings from the study have already had a major impact on policy and practice. ProtecT informed the 2010 decision not to introduce screening for prostate cancer in the UK – a high-profile decision on an extremely contentious issue – as evidenced by its citation in a Department of Health appraisal of options for screening [10]. In addition, conservative approaches, such as active monitoring, are central to NICE guidelines on diagnosis and treatment of prostate cancer [11], and evidence from ProtecT has been cited in Department of Health advice to GPs [12]. Finally, an independent review published in *The Lancet* states that ‘ProtecT has affected clinical

practice, even before announcement of its results, by allowing the UK to reaffirm its policy of no routine screening' [13].

In addition to enabling the development of an evidence base that has informed policy, the innovative use of qualitative methods to involve patients in research has had a broader impact on research practice. For example, a member of the research team, Professor David Neal, was appointed to a group established by the Department of Health to produce an 'informed decision making aid', which has since been adopted by the NHS [6]. Professor Neal also led the development for the Department of Health of a website for patients which explains conservative treatments of localised prostate cancer [6]. In this way, by funding the ProtecT trial, the NIHR has facilitated the development of patient-centred approaches to research that have the potential to improve recruitment for future trials, thus improving the quality of evidence produced.

## Evidence

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[12] Burford DC, Kirby M, Austoker J. 2010. Prostate cancer risk management programme information for primary care: PSA testing in asymptomatic men: Evidence document. London: NHS Cancer Screening Programmes. As of 9 May 2016:

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Journal article providing a review of the Health Technology Assessment in the UK

### *7.1.10. Embedding patient and public involvement through the infrastructure*

#### Case study

One of the recommendations that emerged from the strategic review of PPI in the NIHR was that ‘[a]ll NIHR...infrastructure organisations should have a strategy, framework or plan that covers the promotion and advancement of public involvement, participation and engagement in research’ [1]. Today, individual NIHR centres, units and facilities have patient and public involvement (PPI) and engagement strategies, which are often co-designed with members of the public [2][3][4]. This has led to concrete examples where PPI activities and other engagement and awareness-raising efforts have helped to improve the quality and relevance of research and raise awareness of research undertaken.

Across England, the NIHR’s Collaborations for Leadership in Applied Health Research and Care (CLAHRCs) conduct high-quality applied health research across the NHS to provide benefits to patient outcomes through bringing together local NHS providers and commissioners with academics and other relevant partners. Patients and the public often inform the research undertaken, improving its quality and

relevance. One example of this is the Transfer of Care at 17 project, from the East of England CLAHRC, which focused on mental health issues for young people in foster care [5]. The study found that foster carers needed additional training and access to psychological services to support young people in their care. As a result, the research team co-developed with young people a training course for foster carers and subsequently produced two videos to raise awareness about going into and leaving foster care. These videos have been viewed collectively more than 11,000 times on YouTube, and three young people involved in the project received a Cambridgeshire County Council Award for the best research/creative team [5]. The film has been integrated into a skills training for carers, social workers and other professionals delivered by The Fostering Network, a UK-based foster charity.

In 2013, the NIHR/Wellcome Trust Clinical Research Facility (CRF) in Cambridge established a Non-Executive Children's Board – which has grown in size and in 2015 was made up of 35 children aged 5–16 who have participated in studies on the CRF and those who have never participated in research, their parents and CRF staff members – to discuss views on how to improve services and make the CRF more attractive and engaging for children.

The ideas from the children have helped create brighter, more child-friendly rooms, including turning an office into a children's phlebotomy room and preparation of rooms to be age/gender appropriate. The children have also had a say in what toys, DVDs, games, books and even tablet computers are provided within the facility, along with a children's activity menu. The Children's Board also enables children's input into the design of patient information. Children's views on patient information sheets have informed the information provided to children prior to consenting to participating in research studies.

Through the Children's Board, the CRF has been able to develop its understanding of the patient experience. It shares research-related stories more widely with visitors, staff, patients and members of the public, using case studies. The Children's Board has also provided input into three Photo Story Books to explain participation in research [6][7]. These story books, which are targeted at three different age groups (under 6, 6–10 and 11 and over), help to provide information about what visiting the CRF and participating in research involves. Inspired by this, two NHS clinics for allergies and diabetes created story books, which were helpful in recruiting patients to studies [7].

The Children's Board is currently being evaluated through a small qualitative study called Children's Experience of Engaging in Research (CHEER). The aim of the evaluation is to gather views from children, their families and CRF staff on the Children's Board and to understand the benefits of engaging this group in the ongoing delivery of research by the CRF [8].

In addition to actively involving patients in different stages of research, many NIHR centres, units and facilities host engagement events which are designed to keep the public informed of research and opportunities to participate in research studies or become involved in research. For example, the NIHR Newcastle Biomedical Research Centre (BRC) on Ageing and Chronic Disease has a programme entitled Research and Innovation Matters [9]. This programme delivers more than 15 major public events each year with a focus on the themes of ageing and chronic disease. The events are usually aligned to national disease weeks or days to strengthen links to national and local patient groups. The centre also holds a series of debates to promote lively dialogue on key issues that arise, such as sharing patient data, ethics and governance for research, and patient involvement in early-phase research. The events are co-designed with



patients and members of the public to ensure that the content is relevant, appropriate and interesting. Across the programme, the BRC reaches thousands of interested individuals, and each event is filmed to ensure it can reach as wide and diverse an audience as possible.

Research occurring in NIHR-supported centres, units and facilities, such as BRCs, Biomedical Research Units, CLAHRCs and CRFs, have PPI strategies and activities to improve the quality and relevance of research and raise awareness of the research being undertaken.

## Evidence

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## 8. Creating opportunities for economic and social returns

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### 8.1. Summary

**Entrepreneurial. Affordable. Effective.**

*NIHR creates opportunities for economic as well as social returns on health research investment, including a more effective and affordable NHS.*

NIHR supports cooperative partnership models of working among companies, clinical academics and clinicians which improve patient health and benefit the economy. This is facilitated through NIHR's support of the research infrastructure in the NHS, which is made up of world-class research centres, units, facilities and NIHR's Clinical Research Network, which provides total coverage in England. This infrastructure plays an important role in supporting the wider health research system by supporting, enabling and delivering research through partner organisations. In 2014/15, NIHR provided £227.8 million of funding for the research infrastructure, which supported a further £130 million of research funding from industry, £436 million from charities and £354 million from research councils.

Commercial contract studies are an important part of this wider picture. In 2014/15, the Clinical Research Network supported the delivery of 4,932 open studies, 1,079 of which were from the life sciences industry. Commercial contract studies are also involving ever-greater patient numbers: 78 per cent of NHS Trusts recruited nearly 35,000 participants in 2014/15, making use of the nationwide NIHR Clinical Research Network, which acts as a unifying platform for delivery of research studies. The efforts of the Clinical Research Network are complemented by NIHR's Office for Clinical Research Infrastructure, which provides a dedicated conduit for global industry to connect with the other NIHR-funded research infrastructure of centres, units and facilities, integrated within the world's largest single-payer healthcare system.

NIHR's investment in research infrastructure also facilitates public-private partnership models that connect 'home-grown' NHS research expertise with high tech manufacturing facilities. The following are examples of commercial licences and companies that are in place as a result of NIHR-funded early research:

- Autolus is developing therapies that re-programme the body's own immune cells as a treatment for cancer. It has now raised £70 million of private capital through two rounds of funding.
- Synairgen has licenced experimental therapies to lessen the impact of viral infection in asthmatics, initially developed through proof-of-concept funding via NIHR's Southampton Respiratory Biomedical Research Unit.

In addition to research studies, NIHR invests in proof-of-concept trials that traditional investors might consider high risk, thus helping entrepreneurs bring advanced prototypes to market. The following are two successful examples:

- ‘Smart specs’ help the visually impaired by augmenting users’ vision. Funding from NIHR’s Invention for Innovation programme enabled researchers at the University of Oxford to produce an advanced prototype tailored to patients’ needs.
- ‘Bionic eye’ prostheses in patients are a global first at the NIHR/Wellcome Manchester Clinical Research Facility; they use a retinal implant to combine artificial and natural sight to combat a form of blindness that affects millions of people worldwide.

NIHR also seeks to quantify the economic impacts of new therapies based on evidence. This has always been done, but is especially important in today’s climate of low growth. For example:

- Aiming to maximise public health gains at a price affordable to the NHS as a whole, NIHR’s Health Technology Assessment (HTA) programme conducts pragmatic research to inform policy recommendations on new drugs, devices and diagnostics. One estimate places the net benefit of putting a sample of 10 HTA study findings into practice at £3 billion, by implementing interventions shown to be either cost effective or cost saving to the NHS.
- Targeting patients at the greatest risk of malnutrition – estimated at 30 per cent of hospital patients – using a simple screening tool developed at NIHR’s Southampton Biomedical Research Centre could save the NHS £200 million.
- Improving the evidence for deciding if and when to vaccinate over-65-year-olds against pneumonia, informed by research at the London School of Hygiene and Tropical Medicine’s Health Research Protection Unit, is ensuring that resources within the NHS are spent in a cost-effective manner.
- Supporting clinicians to develop new medical devices and involve the NHS more closely in innovation, a cooperative partnership between clinicians, academics and industry at Queen Mary University of London developed a surgical stapler to resect the bowel. This device is improving patients’ lives while saving £12,000 per patient per year in treatment costs.

NIHR also helps to drive different stages of the translational pathway. A nationwide platform of Clinical Research Facilities is attractive to foreign manufacturers looking to trial innovative drugs, devices and diagnostics. Equally, NIHR’s funding of research consortia around rare diseases generates uniquely detailed data within patient cohorts. For example:

- A consortium that supports 5,000 patients with a rare form of liver disease and which has developed strong ties among industry partners, local clinical trials infrastructure and NIHR’s Clinical Research Network is generating new avenues for research – prompting one US-based pharmaceutical company to move its entire manufacturing outfit to the north-east of England.

### *8.1.1. Holding patient-focused research to account: The value and impacts of the Health Technology Assessment (HTA) programme*

#### Case study

Basing medical treatments on evidence of what works, while supporting difficult decisions on what is affordable within a cost-constrained NHS, requires pragmatic and sometimes controversial research. The NIHR Health Technology Assessment (HTA) programme is the largest dedicated research programme within the NHS and a primary source of clinically relevant research directed at policymakers and medical practitioners. Predating the NIHR's establishment, since 1993 the HTA has funded more than 700 independent research studies to assess the effectiveness, costs and broader impacts of healthcare treatments – aiming to maximise health gains at a price affordable to the NHS as a whole.

The National Institute for Health and Care Excellence (NICE) is tasked with considering evidence of the cost-effectiveness of drugs, medical devices and diagnostics before formulating policy recommendations on which of them the NHS should incorporate into clinical practice. Feeding in to this process, the HTA acts as a trusted evidence provider – funding clinical trials and evidence syntheses that inform NICE clinical guidelines and expand the quality and range of treatments available to patients within the NHS [1].

Eleven case studies written up as part of this report – of which this case study forms a part – refer to HTA funding as contributing to the impacts they describe. Several of these case studies involve research undertaken with a commercial partner. These range from targeted and safer forms of radiotherapy for patients with breast cancer, to new continuous infusion pumps to mimic the body's own production of insulin for patients with diabetes.

HTA funding is also having macro-level effects by supporting research to improve the quality and cost-effectiveness of current medical practice. To work out the potential returns arising from the HTA's investments, an independent study by RAND Europe examined the benefits that would arise from adopting new medical interventions into the NHS. It took a small sample (10 of a total of 743) HTA-funded studies of interventions with high potential impact, shown either to be cost-effective, or cost saving, compared with standard NHS care. To work out a monetary value of these benefits over a single year, the analysis assumed that the NHS would fully implement the HTA study findings and that any impacts were solely due to these findings [2].

The study estimated a potential net benefit from the 10 studies in the sample of £3 billion, based on a value of £20,000 per quality-adjusted life year, or QALY. Thus, even if the NHS realised only 12 per cent of these studies' potential benefit, it would cover the entire cost of the HTA programme from 1993 to 2012 – approximately £367 million [2].

Underpinning the HTA's portfolio of work is an underlying principle that clinical research should not only use the most rigorous techniques, but also be needs-led, with a clear benefit to patients and practitioners. As a result, it has the freedom to fund research in areas where there is no direct commercial incentive. An example of the value of this work are the significant benefits – and resultant health cost savings – arising from the use of tranexamic acid as a life-saving treatment for patients at risk of bleeding

to death from traumatic injuries. This work is estimated to have the potential to save the equivalent of £26 billion and 100,000 lives a year across the globe.

The HTA programme provides a valuable justification for the NIHR's – and more broadly, the Department of Health's – use of resources on research.

## Evidence

[1] Guthrie S, Bienkowska-Gibbs T, Manville C, Pollitt A, Kirtley A, Wooding S. 2015. The impact of the National Institute for Health Research Health Technology Assessment programme, 2003–13: A multimethod evaluation. *Health Technology Assessment* 19(67): 1-291. doi:10.3310/hta19670

RAND Europe's independent evaluation of the impacts of the HTA programme.

[2] Guthrie S, Hafner M, Bienkowska-Gibbs T, Wooding S. 2015. Returns on research funded under the NIHR Health Technology Assessment (HTA) programme: Economic analysis and case studies. Santa Monica, California: RAND Corporation. As of 9 May 2016:

[http://www.rand.org/pubs/research\\_reports/RR666.html](http://www.rand.org/pubs/research_reports/RR666.html)

RAND Europe's independent evaluation of the economic returns from the HTA programme.

### *8.1.2. Stimulating medical innovation in hard-to-research areas, and developing new technologies to improve patients' quality of life*

#### Case study

The NIHR has brought industry and clinicians together to innovate in areas where conducting randomised controlled trials is difficult, such as surgery. In 2008, the NIHR designated two centres – one in London, and one in Sheffield – as pilot Healthcare Technology Cooperatives (HTCs) [1]. The initiative recognised two parallel needs: to support clinicians in developing new medical devices and to involve the NHS more closely in the process of innovation. Each centre acted as a hub where clinician-led collaborative teams, industry, academia, device users and patients could work together as a 'national resource', to benefit both health and wealth [2].

An example of the success of this cooperative model is the work of Professor Norman Williams and colleagues at Queen Mary University of London, and their efforts – via the Enteric Healthcare Technology Cooperative – to improve continence in patients who would otherwise require an ostomy (an operation to create an opening in the wall of the intestine).

The surgical team at Queen Mary developed a method of treating lower bowel cancer that made it possible to reconnect the bowel, so that a patient could evacuate naturally rather than having a stoma fitted. The method is known as the Anterior Perineal Plane for Ultra Low Anterior Resection or APPEAR procedure. Amongst other tools, this operation depended on the team developing a new surgical stapler and grasping device [2].

The NIHR's support, alongside funding from the Technology Strategy Board, the Engineering and Physical Sciences Research Council and the Medical Research Council [2], created an environment where Queen Mary consultants and an external healthcare company could work together as a mutual

partnership. It allowed them to build up entrepreneurial skills and capabilities while drawing on the detailed knowledge of nurses and other professionals who work with patients on a day-to-day basis [2].

The team successfully developed the innovative APPEAR approach, with multicentre trials indicating that it reduced the need for a stoma in two-thirds of patients, saving £12,000 per patient per annum in avoided stoma management costs. The innovative stapler and grasper designed for the APPEAR procedure was awarded the Worshipful Company of Cutlers' Surgical Prize 2011. Also Professor Williams and Queen Mary secured patents to enable international commercial exploitation [3], and they have leveraged over £6.6 million in public funding since 2012 [4].

Following an evaluation by RAND Europe, the Healthcare Technology Cooperative model was deemed a success, with both pilot centres receiving renewed funding. A crucial factor in the evaluation was to recognise that innovations (such as the APPEAR procedure) generate not only financial returns from industry (via direct commercialisation), but also wider benefits to the NHS and to patients, for which there is no direct commercial return [2].

Overall, the NIHR's support for Healthcare Technology Cooperatives demonstrated the value in industry involvement, by bringing people together who did not previously know or work with each other. By increasing the availability of partners from the outset of the project, it reduced pressure on clinicians – who are often the ones with primary ideas for innovation – as the sole node determining success or failure. In 2013, following an open funding competition, the NIHR provided funding for an additional six centres to be designated as Healthcare Technology Cooperatives: spanning trauma, wound management, cardiovascular disease, colorectal therapies, and mental health. Its investment of over £6 million is aimed at furthering the benefits of this programme to UK industry and translating them into improvements in health and quality of life of patients [1].

## Evidence

[1] National Institute for Health Research. 2015. Enteric Healthcare Technology Co-operative: Annual Review 2014–2015. London: NIHR. As of 2 May 2016:

<http://www.bowelfunctionhtc.org.uk/publications/annual-review?download=27:enteric-htc-annual-review-2014-2015>

Information on the Imperial HTC and recent achievements, as part of its annual report.

[2] Kryl D, Marjanovic S, Chonail SN, Ridsdale H, Yaqub O. 2011. Healthcare Technology Cooperatives: Filling a niche in the English R&D landscape. Santa Monica, Calif.: RAND Corporation.

As of 2 May 2016: [http://www.rand.org/pubs/technical\\_reports/TR932.html](http://www.rand.org/pubs/technical_reports/TR932.html)

RAND Europe's independent evaluation of the first round of the HTC programme, evaluating achievements and impacts of the two pilot HTCs, with detailed case studies.

[3] Research Excellence Framework. 2014. Development and validation of innovative colorectal surgery procedures. [Case study 18369.] As of 2 May 2016:

<http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=18369>

REF case study detailing work of the Imperial team and underpinning research into innovative surgical devices, including references to the NIHR's renewal of the HTC.

[4] National Institute for Health Research. 2015. Healthcare Technology Co-operatives (HTCs). As of 2 May 2016: <http://www.nihr.ac.uk/about/healthcare-technology-co-operatives.htm>

Information on the NIHR HTC programme, including a list of current HTCs and funding amounts.

### *8.1.3. Encouraging the life sciences industry to invest in UK health research*

#### Case study

As part of an annual investment of over half a billion pounds in health research infrastructure, the NIHR provides facilities, staff and support for first-class research that sustains collaborations with industry partners. The annual industry investment leveraged by the NIHR's infrastructure support has quadrupled, from £33 million in 2009/10 to £130 million in 2014/15, and there has been a five-fold increase in industry-backed studies, from 514 to 3,008 per year, over the same period. Overall, NIHR Biomedical Research Centres and Units have supported more than 4,000 collaborative and contract studies with industry since 2009-10 [1].

The NIHR Office for Clinical Research Infrastructure (NOCRI) acts as a conduit for global industry, research charities and other national and international government agencies to connect and partner with the NIHR. It provides a managed process for collaborative research – helping companies to understand the clinical potential of drugs, devices and diagnostics in development, and expediting their access to groups of patients among the 60 million people who use the NHS. It also acts as a signpost for the various routes via which industry might best make use of the expertise, facilities and services sustained by the NIHR's support [2].

NOCRI has helped to broker substantive partnerships with industry. One example is the announcement in 2014 of Teva Pharmaceutical Industries Ltd's intention to invest £12 million into UK clinical trials. As part of the deal, Teva would provide funding of up to £600,000 towards dementia research [3]. NOCRI's role in this instance was to facilitate and streamline Teva's access to specific avenues of NIHR support, such as the Dementia Translational Research Collaboration, an initiative that draws together a number of world-leading specialist clinical and academic partners in UK dementia research [4]. Teva's aim was specifically to focus on early-stage work, to understand drug targets, mechanisms and new approaches to treating dementia.

An example of a current project planned since Teva's announcement is the project at University College London Hospitals' Biomedical Research Centre, to study whether signs of inflammation in nerve cells in the brain can act as an early indicator of Alzheimer's disease. The study team hopes that this would provide information for trials of new therapies that target neuro-inflammation: 'a very exciting new direction', as noted by the UCL Dementia Research Centre's clinical trials lead [5].

By providing dedicated routes to partner and collaborate with global players in the life sciences industry, through such initiatives as NOCRI, NIHR is helping to bring direct investment into the UK economy. As part of a foreword to the UK government's Investing in UK Health and Life Sciences strategy, Prime Minister David Cameron said,



‘As a result of increasing R&D costs, the old “big pharma” model is becoming more difficult to maintain. In its place is a new focus on translational medicine – more early stage clinical trials with patients, more external innovation, more collaboration’.

This strategy highlighted NOCRI’s role as ‘a single point of entry’ for life science companies to engage with NIHR infrastructure, as part of an announcement of record levels of investment – £800 million over five years – into Biomedical Research Centres and Units [6]. By creating ‘unique research partnerships’, this initiative is establishing collaborations among academia, the NHS and industry with the potential to drive significant improvements to the health of the nation, as well as making a major contribution to growth [2].

## Evidence

[1] National Institute for Health Research. 2015. Growth through health research: The NIHR as an engine for growth. London: NIHR. As of 5 May 2016: <http://www.nihr.ac.uk/documents/about-NIHR/NIHR-Publications/NIHR%20Growth%20Through%20Health%20Research%20-%20Interactive%20Spreads%20March%202015.pdf>

This brochure outlines a number of the ways in which the NIHR’s provision of people, programmes, infrastructure and systems are contributing to UK growth. It contains a variety of statistics on the increasing amounts of industrial collaboration with the NIHR, narrative descriptions of routes through which the NIHR provides support, and case studies of particular initiatives involving industry.

[2] National Institute for Health Research. 2012. NIHR Office for Clinical Research Infrastructure (NOCRI): Connecting Excellence. London: NIHR. As of 5 May 2016: [http://www.nocri.nihr.ac.uk/media/10756/NOCRI%20Corporate%20Brochure\\_LR%20-%20FINAL%20REVISED%204%20Oct,%202012.pdf](http://www.nocri.nihr.ac.uk/media/10756/NOCRI%20Corporate%20Brochure_LR%20-%20FINAL%20REVISED%204%20Oct,%202012.pdf)

This brochure is aimed at corporate partners seeking to find out more information about NOCRI. It contains information on the UK’s presence as a global player in the life sciences industry and on the NIHR’s role in supporting a number of industry-focussed and collaborative initiatives, in particular translational research partnerships.

[3] National Institute for Health Research. 2014a. Global pharmaceutical company, Teva, announces health research collaboration with NIHR. As of 5 May 2016: <http://www.nocri.nihr.ac.uk/news-and-events/news/global-pharmaceutical-company,-teva,-announces-health-research-collaboration-with-nihr/>

NOCRI’s announcement of Teva’s intention to invest £12 million in UK clinical trials, including £600,000 in dementia research.

[4] National Institute for Health Research. 2014b. Dementia Translational Research Collaboration (TRC). As of 5 May 2016: <http://www.nihr.ac.uk/about/dementia-translational-research-collaboration.htm>

Information on the NIHR’s dementia-themed translational research collaboration, noting details of NOCRI’s role in bringing together different elements of NIHR-supported infrastructure.

[5] University College London Hospitals Biomedical Research Centre. 2015. UCL and Teva study to research role of inflammation in neurodegeneration. As of 5 May 2016:

<http://www.uclhospitals.brc.nihr.ac.uk/news/ucl-and-teva-study-research-role-inflammation-neurodegeneration>

Announcement from UCL Hospitals NIHR Biomedical Research Centre on Teva's funding of a two-year study to investigate inflammation in microglia cells as a predictor of disease in 20 patients with early-stage or mild Alzheimer's.

[6] HM Government. 2011. Investing in UK health and life sciences. London: HM Government. As of 5 May 2016: [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/32451/11-1428-investing-in-uk-health-and-life-sciences.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/32451/11-1428-investing-in-uk-health-and-life-sciences.pdf)

The UK government's 2011 strategy document for the UK life sciences sector, announcing planned investments in Biomedical Research Centres and Units, as one of a number of efforts to support translational research in the NIHR.

#### *8.1.4. Advancing revolutionary cancer treatments from concept through to venture capital*

##### Case study

The nature of the NIHR's support, underpinning research at all stages of the translational pathway – directly by funding people and projects, and by supporting research infrastructure and systems – acts to 'crowd in' other public and private funders [1]. The collaborative nature of this process is exemplified by the work led by Dr Martin Pule at the joint University College London (UCL)/UCL Hospitals (UCLH) NHS Foundation Trust Biomedical Research Centre (BRC), which seeks to advance the very latest genetic and immune-based technologies as a treatment for cancer.

The premise of this research – namely genetically re-engineering the body's own immune cells (T-cells) to attack cancer cells rather than viruses – is to develop an alternative to the often imprecise and toxic forms of chemo- and radiotherapy currently available for treating cancer. However, ensuring the safety and scalability of such ground-breaking therapeutics, based on manipulating living material rather than simple chemical or protein-based drugs, is a significant challenge [2].

As part of infrastructure funding totalling over £100 million directed towards the UCL/UCLH BRC, the NIHR has supported Dr Pule's pioneering work through the early proof-of-concept stages and then, via a therapeutic innovation bridging fund, towards its clinical application. By combining this 'home grown' scientific expertise with significant parallel investments in specialist production facilities, the UCL/UCLH BRC has developed a unique resource to manufacture clinical-grade gene and cell therapies [3].

In 2015, building on promising results from initial trials of T-cell therapy in patients with end-stage leukaemia in the United States [2], and capitalising on interest from pharmaceutical companies in this area [4], the UCL team announced its formation of a 'spin-out' company, Autolus [5]. The company launched following a £30 million investment by Syncona Partners LLP, itself a commercial subsidiary of the Wellcome Trust, whose profits are redirected back to support the Wellcome Trust's charitable mission [6].

The team must develop these advanced technologies further if they are to programme T-cells precisely enough to be used widely across the NHS [5]. Bringing these new therapies to trial will be a careful process involving small numbers of patients, thus requiring close integration with specialist referral clinics [5]. To achieve this, Autolus is embedded within the clinical trials infrastructure that NIHR provides, through its support of UCL/UCLH BRC [5].

Recent funding announcements suggest there could be further growth for Autolus. Later in 2015, as part of its Invention for Innovation programme, the NIHR committed over £3 million towards further research at UCL to deliver a safe, scalable and cost-effective version of the T-cell therapy [7]. In March 2016, Autolus announced a further £40 million of investment from two companies, Woodford Investment Management and Perceptive Bioscience, to help move its work into the clinic [8].

## Evidence

[1] National Institute for Health Research. 2015. Growth through health research: The NIHR as an engine for growth. London: NIHR. As of 2 May 2016: <http://www.nihr.ac.uk/documents/about-NIHR/NIHR-Publications/NIHR%20Growth%20Through%20Health%20Research%20-%20Interactive%20Spreads%20March%202015.pdf>

This brochure outlines a number of the ways in which the NIHR's provision of people, programmes, infrastructure and systems are contributing to UK growth. It contains a variety of statistics on the increasing amounts of industrial collaboration with the NIHR, narrative descriptions of routes through which the NIHR provides support, and case studies of particular initiatives involving industry.

[2] Turtle CJ, Sommermeyer D, Berger C, Hudecek M, Shank DM, Steevens NN, Budiarto TM, Karimi M, Chaney CN, DeVito AM, Heimfeld S, Jensen MC, Riddell SR, Maloney DG. 2014. Therapy of B cell malignancies with CD19-specific chimeric antigen receptor-modified T cells of defined subset composition. [Abstracts and Program of the 56th American Society of Hematology Annual Meeting and Exposition, San Francisco, CA.] As of 2 May 2016: <https://ash.confex.com/ash/2014/webprogram/Paper75620.html>

Announcement of the results of an early trial of CAR T-cell-based therapies in 27 adults with refractive acute lymphoblastic leukaemia, of whom 24 went into remission and 6 remained disease-free after a year.

[3] Dr Nick McNally, Director of Research Support, UCL/UCLH BRC. Pers. comm. 31 March 2015.

[4] Brower V. 2015. The CAR T-Cell Race. The Scientist. As of 2 May 2016: <http://www.the-scientist.com/?articles.view/articleNo/42462/title/The-CAR-T-Cell-Race/>

Commentary tracking recent advances in T-cell-based therapies, including industry investment and discussions of the safety challenges surrounding this 'living' anti-cancer technology.

[5] Autolus. 2015. Syncona LLP and UCL Business PLC announce the formation of Autolus Limited, a cancer immunotherapy company. As of 2 May 2016: <http://www.autolus.com/syncona-llp-and-ucl-business-plc-announce-the-formation-of-autolus-limited-a-cancer-immunotherapy-company/>

Press release detailing Syncona LLP's commitment of £30 million in Series A financing to develop and commercialise the work of Dr Martin Pule and colleagues in T-cell engineering.

[6] Syncona Partners LLP. 2016. About Syncona. As of 5 May 2016: <http://www.synconallp.com/about/>

Information on Syncona's remit and corporate set-up as a subsidiary of the Wellcome Trust.

[7] Europe PubMed Central. 2015. Next generation CAR19 studies. As of 2 May 2016: <https://europepmc.org/grantfinder/grantdetails?query=pi:%22Pule+M%22+gid:%22II-C3-0714-20005%22>

Information on Dr Martin Pule's Invention for Innovation (i4i) challenge funding to develop a timely and cost-effective strategy for delivering T-cell therapies on the NHS.

[8] University College London/University College London Hospitals Biomedical Research Centre. 2016. £40 million towards developing revolutionary T-cell cancer treatments. As of 2 May 2016: <http://www.uclhospitals.brc.nihr.ac.uk/news/%C2%A340-million-towards-developing-revolutionary-t-cell-cancer-treatments>

UCL/UCLH BRC's most recent announcement of a second round of funding for Autolus, totalling £40 million, from Woodford Investment Management LLP and Perceptive Bioscience Investments Ltd.

### *8.1.5. Generating the evidence to support difficult decisions around vaccination policy in a cost-constrained healthcare system*

#### Case study

The NIHR's remit to improve both the health and wealth of the nation places a duty of care on it to provide evidence to help prevent treatments being put into practice when doing so would place an unjustifiably high cost burden on the NHS as a whole. Deciding which treatments ought not to be deployed in a cost-constrained health system remains a complex task. Research at the NIHR-funded Health Protection Research Unit (HPRU) at the London School of Hygiene and Tropical Medicine (LSHTM) is helping to improve the evidence for making these difficult decisions, such as if and when to vaccinate elderly people against pneumonia, which in England and Wales hospitalises six to seven people over 65 years of age, every day.

The NIHR set up the HPRU programme as a series of partnerships between universities and Public Health England, a body formed in 2013 to protect the public from infection-borne and environmental hazards [1]. In 2014, LSHTM received more than £10 million over five years from the NIHR to establish three new HPRUs. The remit of one of these HPRUs – focussed on immunisation – is to conduct research to enhance the protective impact and safety of vaccinations, and ensure a more equal sharing of the benefits of vaccination across society [2].

In the case of pneumonia vaccination, a team at the London HPRU led by Dr Albert Van Hoek sought to establish whether healthy 65 year-olds would benefit from a vaccination – PCV-13 – against types of pneumonia responsible for up to a fifth of such infections in the elderly [3]. Previous clinical trials in the Netherlands had demonstrated PCV-13 to be effective in preventing 75 per cent of severe disease caused by the types of pneumococcal bacteria included in the vaccine [4]. However, in the UK, a fully immunised child already receives three doses of this vaccine before the age of four [3].

The research team took into account the current burden of disease among the elderly, as well as the indirect benefits of the childhood vaccination programme on future cases of the disease. The results

indicated that the future impact of the childhood vaccination programme would, as a result of improving 'herd immunity' amongst the general population, reduce the chances of these types of pneumonia affecting those over 65 years of age. The team concluded that even if the PCV-13 were free, as opposed to costing £50 per dose, any immunisation programme in the elderly would not be cost effective [5].

Based on this research, in November 2015 the body responsible for advising on UK vaccination policy – the Joint Committee on Vaccination and Immunisation – decided not to recommend introducing PCV-13 vaccination to those over 65 years of age [6]. The committee noted the importance of the HPRU's cost-effectiveness analysis in bringing the evidence on vaccination of the elderly up to date [7].

Although pneumonia remains a serious problem in the elderly, by establishing the low likelihood that a further PCV-13 vaccination programme would be a cost-effective way to tackle infections, NHS resources can be diverted to other routes to tackle this disease. Through its investment in HPRUs, such as that at the LSHTM, the NIHR has enabled the UK to implement policy in contrast to that of countries such as the United States – where the PCV-13 vaccine has been introduced – with estimated savings of up to £25 million per year to the UK taxpayer [3].

## Evidence

[1] National Institute for Health Research. 2015. Health Protection Research Units. As of 2 May 2016: <http://www.nihr.ac.uk/funding/health-protection-research-units.htm>

The NIHR's description of the remit of its HPRU programme, noting its establishment in 2013, principal (disease) topic areas, and initiatives funded since April 2014.

[2] The Chariot Views from the London School of Hygiene & Tropical Medicine. 2014. Over £10m in grants awarded for health protection research. As of 2 May 2016: <http://blogs.lshtm.ac.uk/news/2014/01/17/over-10m-in-grants-awarded-for-health-protection-research/>

The London School of Hygiene and Tropical Medicine's announcement of NIHR funding awards to establish three new HPRUs aimed at strengthening research across a range of public health priority areas.

[3] National Institute for Health Research Health Protection Research Unit in Immunisation. 2016. Giving 65 year olds PCV-13 pneumococcal vaccine not cost-effective. As of 2 May 2016: <http://immunisation.hpru.nihr.ac.uk/news/giving-65-year-olds-pcv-13-pneumococcal-vaccine-not-cost-effective>

Press release announcing results of the LSHTM study of PCV-13 cost-effectiveness in the elderly.

[4] Bonten M, Huijts S, Bolkenbaas M, Webber C, Patterson S, Gault S, Van Werkhoven CH, Van Deursen A, Sanders E, Verheij T, Patton M, McDonough A, Moradoghli-Haftvani A, Smith H, Melleliu T, Pride M, Crowther G, Schmoele-Thoma B, Scott D, Jansen K, Lobatto R, Oosterman B, Visser N, Caspers E, Smorenburg A, Emini E, Gruber W, Grobbee D. 2015. Polysaccharide Conjugate Vaccine against Pneumococcal Pneumonia in Adults. *The New England Journal of Medicine* 372: 1114-1125. doi:10.1056/NEJMoa1408544

Results of a trial in the Netherlands involving 84,496 adults 65 years of age or older immunised with PCV-13, indicating its effectiveness in preventing pneumococcal disease.

[5] Van Hoek AJ, Miller E. 2016. Cost-effectiveness of vaccinating immunocompetent  $\geq 65$  year olds with the 13-valent pneumococcal conjugate vaccine in England. Public Library of Science ONE 11 (2): e0149540. doi:10.1371/journal.pone.0149540

Results of a study examining the cost-effectiveness of introducing PCV-13 vaccination to adults aged 65 or over in the UK, in addition to existing child vaccination and vaccination of those over 65 years old in clinical risk groups.

[6] Joint Committee on Vaccination and Immunisation. 2015. Interim JCVI statement on adult pneumococcal vaccination in the UK. London: HM Government. As of 2 May 2016: [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/477966/JCVI\\_pnemococal.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/477966/JCVI_pnemococal.pdf)

November 2015 statement from the Joint Committee on Vaccination and Immunisation, the independent body that advises UK health departments on the provision of vaccination and immunisation services, noting the increasing likelihood that a programme of PCV-13 vaccination in the elderly would not be cost effective given the impact of childhood PCV-13 vaccination.

[7] Joint Committee on Vaccination and Immunisation. 2015. Minute of the meeting on 7 October 2015 [Draft.] London: JCVI. As of 2 May 2016: <https://app.box.com/s/iddfb4ppwkmjtusir2tc/1/2199012147/46319285265/1>

Minutes of the 7 October 2015 Joint Committee on Vaccination and Immunisation meeting considering evidence from the LSHTM HPRU research as part of its decision whether to immunise over-65-year-olds with the PCV-13 vaccine.

### *8.1.6. Preventing malnutrition in clinical settings via a user-friendly screening tool: The Malnutrition Universal Screening Tool (MUST)*

#### Case study

More than 3 million people in the UK – 1 in 20 adults – are malnourished or at risk of malnutrition. Disease-related malnutrition is estimated to cost the UK taxpayer in excess of £20 billion every year, or roughly 15 per cent of the total public expenditure on health and social care [1]. People in healthcare settings are at a particularly high risk of malnutrition – estimated at 30 per cent of hospital patients and 35 per cent of care home residents [1]. Establishing and addressing these risks has been a primary focus of research supported by the NIHR's Southampton Biomedical Research Centre (BRC) for Nutrition, Lifestyle and Healthy Ageing.

Led by Professor Marinos Elia, researchers at the University of Southampton's Institute of Human Nutrition created and validated the Malnutrition Universal Screening Tool (MUST) – a user-friendly and simple technique for identifying and managing patients at risk of malnutrition [2]. The research underpinning this tool identified a series of three simple risk indicators for malnutrition based on patients' past, present and future nutritional status, and combined these to create a score that healthcare practitioners can use as the basis of a care plan [2]. Crucially, the research also developed and tested a series of surrogate measures to allow practitioners to estimate patients' height and weight – and thus

enable them to still carry out the necessary calculations – when patients are bed-bound (for example in elderly, infirm or unconscious patients) [2].

The team began to roll out the MUST tool into clinical practice in the early 2000s, and it saw significant uptake following the NIHR's BRC award to Southampton in 2007 [2]. To raise public awareness of the tool, the research team undertook substantial advocacy efforts – via chairing a number of malnutrition-related associations – and sought to incorporate recommendations for its use into policy reports and national action plans [2]. The MUST tool also won the IT Innovation Award at the Health Business Awards 2008 [3].

In 2012, the National Institute for Health and Care Excellence (NICE) incorporated recommendations to use MUST as a screening tool for malnutrition into its Quality Standard on Nutrition Support in Adults [4]. At the time, only two other NICE guidelines had been estimated to provide greater cost savings to the NHS [1]. Current estimates suggest that by targeting the patients at greatest risk of malnutrition, these guidelines – if implemented widely – could save the NHS in England in the region of £200 million in a single year [1].

The Southampton team noted that significant further upfront investment is required if these cost savings are to be realised [5]. Nonetheless, by providing a supportive framework for the Southampton BRC team's continuing research efforts, the NIHR is enabling high quality studies that can inform further improvements in the quality and cost-effectiveness of care to reduce the burden of avoidable malnutrition on the nation's health and wealth.

## Evidence

[1] Elia, M. 2015. The cost of malnutrition in England and potential cost savings from nutritional interventions (full report on behalf of Malnutrition Action Group of BAPEN and the National Institute for Health Research Southampton Biomedical Research Centre). London: NIHR. As of 2 May 2016: <http://www.uhs.nhs.uk/Media/Southampton-Clinical-Research/BRCdownloads/ECONOM-REPORT-FULL-18.11.15.pdf>

Joint report detailing the costs of malnutrition and providing an impact analysis of implementing the NIHR Southampton BRC-supported NICE clinical guidelines/quality standard on nutritional support in adults.

[2] Research Excellence Framework. 2014. MUST: A new tool for combating malnutrition in the UK and Overseas. [Case study 44143.] As of 2 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=44143>

REF case study detailing the work of the Southampton team on developing, testing and implementing the MUST screening tool, providing evidence of its uptake into practice and the resulting health and wider socioeconomic impacts.

[3] BAPEN. 2008. BAPEN with Southampton University Hospitals Trust wins IT Innovation Award 2008 for 'MUST'. As of 2 May 2016: [http://www.bapen.org.uk/pdfs/press\\_releases/press\\_40.pdf](http://www.bapen.org.uk/pdfs/press_releases/press_40.pdf)

Press release announcing the Southampton team's prize at the 2008 Health Business Awards.

[4] National Institute for Health and Care Excellence. 2012. NICE quality standard [QS24]. As of 2 May 2016: <https://www.nice.org.uk/guidance/qs24>

NICE's quality standard to define clinical best practice to care for adults in the hospital or community who are either malnourished or at risk of malnutrition.

[5] University Hospital Southampton NHS Foundation Trust. 2013. The Cost of Malnutrition in the UK Economic Report. As of 2 May 2016: [http://www.uhs.nhs.uk/ClinicalResearchinSouthampton/Our-research/Nutrition-](http://www.uhs.nhs.uk/ClinicalResearchinSouthampton/Our-research/Nutrition-research/Ourresearchandimpacts/Impactcasestudies/ThecostofmalnutritionintheUKeconomicreport.aspx)

[research/Ourresearchandimpacts/Impactcasestudies/ThecostofmalnutritionintheUKeconomicreport.aspx](http://www.uhs.nhs.uk/ClinicalResearchinSouthampton/Our-research/Nutrition-research/Ourresearchandimpacts/Impactcasestudies/ThecostofmalnutritionintheUKeconomicreport.aspx)

Online summary of key findings from the joint NIHR-BAPEN report on malnutrition.

### *8.1.7. Attracting foreign companies to conduct world-first trials of retinal implants that combine artificial and natural sight*

#### Case study

By providing dedicated national clinical research infrastructure in the NHS, through its Biomedical Research Centres, Biomedical Research Units, and Clinical Research Facilities, the NIHR is enabling world-leading clinical trials to take place. A recent global first brought together public, charitable and industry support to trial an innovative device for restoring sight – the Argus II retinal implant system. Trials of this device, manufactured by US company Second Sight Medical Products Inc, are bringing foreign investment to the support of UK research, for a group of patients who may be the first of millions to benefit from such advances in medical technology [1].

Leading the research is a group at the Manchester Vision Regeneration Laboratory, part of the joint NIHR/Wellcome Trust Manchester Clinical Research Facility (MCRF). Their work sought to build on previously successful trials of the Argus II system, namely, an artificial implant, or 'bionic eye', which uses wireless signals from a camera worn by the user to stimulate an array of electrodes placed directly onto the surface of a patient's retina [2]. Argus II was the first device of its kind to be approved as a means to induce visual perception, and therefore restore a degree of sight, in patients with retinitis pigmentosa, a rare hereditary disease that causes progressive damage to the light-sensitive cells in the retina and, ultimately, complete blindness [3].

The Manchester team set out to expand use of the Argus II system by trialling its use in a more common form of retinal disease, namely, 'dry' age-related macular degeneration (AMD), which is the leading cause of blindness in the Western world. Patients with dry AMD progressively lose their central vision, while retaining peripheral vision [4].

In July 2015, 80-year-old Ray Flynn became the first participant in the Manchester research study to receive the Argus II implant, and thus the first patient with dry AMD to combine artificial and natural vision using a retinal prosthesis. Within a day of the surgery he was able to identify the orientation of patterns on a screen, not previously possible as a result of the loss of his central vision. Remarkably, he was able to sense the outline of people and objects with his eyes closed – demonstrating that the system was functioning in addition to his natural vision [5].



Having previously relied exclusively – and exhaustingly – on his peripheral vision, Ray was positive about the impact of the research and its potential to help other patients in the future [6]. Following his operation, he said:

Before when I was looking at a plant in the garden it was like a honeycomb in the centre of my eye. That has now disappeared. I can now walk round the garden and see things’ [6].

Trials of the implant at the NIHR/Wellcome Trust MCRF are ongoing in a number of other patients with dry AMD. The research team are hopeful that by working in partnership with the manufacturers of this advanced technology, their work will pave the way for the use of this technology in the 44,000 people in the UK, and more than 20 million worldwide, who are living with this debilitating condition.

## Evidence

[1] Central Manchester University Hospitals. 2015. Five blind patients with AMD will receive groundbreaking Argus II ‘bionic eye’ treatment at Manchester Royal Eye Hospital. As of 2 May 2016: <http://www.cmft.nhs.uk/media-centre/latest-news/five-blind-patients-with-amd-will-receive-groundbreaking-argus-ii-%E2%80%98bionic-eye%E2%80%99-treatment-at-manchester-royal-eye-hospital>

Announcement of the Manchester research team’s intention to begin trialling the Argus II system in patients other than those with retinitis pigmentosa, whom the system had originally been developed to treat.

[2] Second Sight. n.d. Argus® II Retinal Prosthesis System. As of 2 May 2016: <http://www.secondsight.com/g-the-argus-ii-prosthesis-system-pf-en.html>

Information on the Argus II retinal implant from its manufacturers.

[3] Chuang AT, Margo CE, Greenberg PB. 2014. Review. Retinal implants: a systematic review. *British Journal of Ophthalmology* 98: 852 As of 2 May 2016: <http://bjo.bmj.com/content/98/7/852.abstract>  
Systematic review and discussion of the body of research underpinning a range of retinal implant devices, including the Argus II ‘bionic eye’ system.

[4] Chopdar A, Chakravarthy U, Verma D. 2003. Age related macular degeneration. *British Medical Journal* 326 (7387): 485-488. As of 2 May 2016: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1125371/>

Review and discussion of AMD providing information about the disease and future impacts in the Western world, in the context of an ageing population.

[5] Central Manchester University Hospitals. 2015. Manchester Royal Eye Hospital and Second Sight announce global surgical first with Manchester patient. As of 2 May 2016: <http://www.cmft.nhs.uk/media-centre/latest-news/manchester-royal-eye-hospital-and-second-sight-announce-global-surgical-first-with-manchester-patient>

Announcement of initial trials of the Argus II system in the first patient with dry AMD to receive the implant, Ray Flynn.

[6] Khomami N and agencies. 2015. British pensioner first to have central vision restored through bionic eye. The Guardian. As of 2 May 2016: <http://www.theguardian.com/uk-news/2015/jul/21/bionic-eye-pensioner-manchester-vision-restored>

One of a number of news articles announcing the early success of Ray Flynn's surgery and its impact on his vision.

### *8.1.8. Forging clinical, academic and industrial partnerships for patients with a rare form of liver disease*

#### Case study

Primary biliary cholangitis (PBC) (formerly called primary biliary cirrhosis) is a long-term liver disease affecting a few thousand people in the UK. For reasons that remain poorly understood, PBC arises when the body's immune system attacks the bile ducts that transport bile from the liver, which can lead to liver damage and sometimes liver failure [1]. Professor David Jones, an NIHR Senior Investigator at Newcastle University, has built up a consortium to focus research efforts on this rare condition and has successfully engaged a number of industry partners [2]. Given that up to 40 per cent of patients with PBC do not respond to the only licensed treatment, ursodeoxycholic acid, research to improve treatment options for these patients is essential [3].

Underpinning the PBC consortium's success is the world's largest PBC research cohort – originally set up by Professor Jones in 2008 – which currently collects detailed information on the nature and progression of the disease from more than 5,000 patients [3]. In addition to funding from the Medical Research Council, the consortium draws on several branches of NIHR's support, from direct funding for Professor Jones as a member of the NIHR faculty, to infrastructure support (both via the NIHR Newcastle Biomedical Research Centre (BRC), and as one of a series of NIHR Rare Disease Translational Research Collaborations [4]), to programme funding for specific research studies, such as a current study investigating treatments for profound fatigue in patients with PBC [5].

The value of the UK PBC consortium is manifold. The research cohort has enabled clinicians to build up a uniquely detailed database of medical information, helping to identify cases of PBC and describe the varying clinical features of patients' disease. It has also acted as a springboard to develop clinical trials of new treatments, allowing researchers to group patients according to the specific genetic and biological characteristics of their illness. These features, together with the intellectual and infrastructural support provided by access to the NIHR Clinical Research Network, and a health system with a strong focus on health economics, combine to form an environment Professor Jones describes as being 'like catnip to industry' [6].

The UK PBC consortium has indeed benefitted from productive relationships with industry since its inception. One USA based pharmaceutical company that was an early consortium partner has since moved its entire manufacturing outfit to the north-east of England, as a result of the strong ties it has developed with clinical trials infrastructure. A further nine industry partners – ranging from small biotech start-ups to some of the world's largest pharmaceutical companies – are currently involved with the consortium [6].

By providing a platform where industry and academia can build on each other's strengths, the NIHR is helping to ensure that early-stage research efforts to find new treatments for rare diseases, such as PBC, stand the best chance of success as they progress through the clinical pathway. Through its cross-cutting support of such initiatives as the PBC consortium, these partnerships are working to bring improved treatments to the few, as well as the many.

## Evidence

[1] National Health Services. n.d. Primary biliary cirrhosis. As of 2 May 2016: <http://www.nhs.uk/conditions/Primary-biliary-cirrhosis/Pages/Introduction.aspx>

Information on PBC, including causes, treatments and prevalence.

[2] National Institute for Health Research. 2015. Growth through health research: The NIHR as an engine for growth. London: NIHR. As of 2 May 2016: <http://www.nihr.ac.uk/documents/about-NIHR/NIHR-Publications/NIHR%20Growth%20Through%20Health%20Research%20-%20Interactive%20Spreads%20March%202015.pdf>

This brochure outlines a number of the ways in which the NIHR's provision of people, programmes, infrastructure and systems are contributing to UK growth. It contains a variety of statistics on the increasing amounts of industrial collaboration with the NIHR, narrative descriptions of routes through which the NIHR provides support, and case studies of particular initiatives involving industry.

[3] UKPBC Winter Newsletter. 2015. As of 2 May 2016: <http://www.uk-pbc.com/newsevents/UK-PBC%20Winter%20Newsletter.pdf>

Update from the UK PBC research cohort, containing information on patient numbers in the cohort as of winter 2015, as well as ongoing research efforts.

[4] National Institute for Health Research Rare Diseases Translational Research Collaboration. n.d. Themes. As of 2 May 2016: <http://rd.trc.nihr.ac.uk/themes-2/>

Information on the NIHR's infrastructure funding to support research into rare diseases, including Professor Jones's work on gastrointestinal disorders, such as PBC.

[5] National Institute for Health Research. 2013. EME - 10/90/03: Rituximab for the Treatment of Fatigue in Primary Biliary Cirrhosis. As of 2 May 2016: <http://www.nets.nihr.ac.uk/projects/eme/109003>  
Listing of a current PBC study funded by the NIHR's Efficacy & Mechanism Evaluation programme.

[6] Medical Research Council. 2015. Industrial strength research. As of 2 May 2016: <http://www.mrc.ac.uk/news/browse/industrial-strength-research/>

News article describing the requirement for industry and academia to work together to improve health and wealth, using the UK PBC cohort as an example of success in this area.

### *8.1.9. Helping to drive innovation by investing in early-stage inventions*

#### Case study

Recognising the need for dedicated funding to help bring prototype innovations to market, the NIHR established the Invention for Innovation (i4i) programme, in order to advance new medical devices,

technologies or interventions into areas of clinical need. As well as supporting proof-of-concept and prototyping trials, traditionally seen as particularly high risk – and therefore less attractive to many investors – the programme supports researchers in commercialisation activities. These include securing intellectual property protection, developing business plans, and bringing venture funders into the picture [1]. It also enables researchers to consider and address the challenges of introducing innovative medical products into the practice within the NHS [2].

A recent evaluation of the i4i programme found that a majority of i4i-supported projects completed a prototype and began testing or began a pivotal clinical trial within the project's lifetime. The programme also led to six spin-out companies and a number of late-stage prototypes (i.e. that are nearly ready for market) [1].

An example of the impact of i4i is 'smart specs', a visual aid developed by a team led by Dr Stephen Hicks at the University of Oxford. With the support of £650,000 from i4i in 2011, the project aimed to help people with poor vision by enhancing the brightness of images according to their proximity [3]. A pilot feasibility study provided evidence that a wearable display helped users with very limited residual sight to avoid nearby objects [3]. Building on what the principle investigatory described as 'a clunky proof of principle', i4i's support enabled the team to develop a functional device that also engaged the user [1]. An ongoing collaboration with the Royal National Institute of Blind People provided the team with a valuable route to engage patients and to consider which types of visual impairment might benefit from a device to enhance wearers' perceptions of nearby objects.

By focusing on the needs of individuals with visual impairment, and building a device around these individuals' views of how it should feel and what would be useful, the team developed an advanced prototype designed to work for a number of different patients [1]. One participant in the early trials of the device remarked:

'What is great about these glasses is that you can see through them and make the most of the vision you've got. They add to what you see with extra information. It's like having a sixth sense, an extra superpower (though it's what most people do every day) – knowing where to look and pick out objects from what's around you. It's very exciting' [4].

The team went on to achieve considerable successes. Following from i4i's support, the team won the Royal Society Brian Mercer Award for Innovation, as well as industry funding via a Google Impact Challenge award of £500,000, to help gather health economic data required to build a business case before commercialisation [1].

The team are now conducting further trials in patients, as they develop a commercial product that they intend to retail for less than £300. Their work, and i4i's support, demonstrates the value of investment at an early stage in the development of medical devices, and provides the starting point for future public private partnerships in an area that few conventional research funding streams would ordinarily invest in [1].

## Evidence

[1] Marjanovic S, Krapels J, Sousa S, Castle-Clarke S, Horvath V, Chataway J. 2015. The NIHR Invention for Innovation (i4i) programme: A review of progress and contributions to innovation in

healthcare technologies. Santa Monica, Calif.: RAND Corporation. As of 2 May 2016: As of 5 May 2016:

[http://www.rand.org/content/dam/rand/pubs/research\\_reports/RR1100/RR1101/RAND\\_RR1101.pdf](http://www.rand.org/content/dam/rand/pubs/research_reports/RR1100/RR1101/RAND_RR1101.pdf)

RAND Europe's evaluation of the i4i programme, which consisted of surveys of i4i-funded principal investigators and key informant interviews from a sample of 170 projects.

[2] National Institute for Health Research. n.d. Invention for Innovation. As of 5 May 2016: <http://www.nihr.ac.uk/funding/invention-for-innovation.htm>

The NIHR's landing page for the Invention for Innovation (i4i) programme, with details of its remit and how to apply for funds.

[3] Hicks SL, Wilson I, Muhammed L, Worsfold J, Downes SM, Kennard C. 2013. A depth-based head-mounted visual display to aid navigation in partially sighted individuals. PLOS ONE. doi:10.1371/journal.pone.0067695

Results of the Oxford team's pilot of a low-resolution visual aid – 'smart specs' – on small initial cohorts of healthy and severely visually impaired individuals, to determine feasibility of their use to navigate a short obstacle course.

[4] University of Oxford. 2014. Smart glasses for people with poor vision being tested in Oxford. As of 5 May 2016: <http://www.ox.ac.uk/news/2014-06-17-smart-glasses-people-poor-vision-being-tested-oxford-1>

Press release noting positive results of the early i4i-supported trials of the smart glasses, with testimonials from the principal investigator and patients who took part.

### *8.1.10. Trialling therapies to lessen the impact of viral infection in people with asthma*

#### Case study

By supporting the development of innovative treatments that address gaps in therapeutic options, NIHR Biomedical Research Centres (BRCs) and Biomedical Research Units (BRUs) help to create commercial potential while improving patient outcomes and saving the NHS money. This is illustrated by the Southampton Respiratory BRU's involvement in work towards a new treatment designed to reduce exacerbations of respiratory illness, whose potential impact has attracted major investment from the pharmaceutical industry.

In 2006, the British Thoracic Society reported that respiratory diseases cause the deaths of 1 in 5 people in the UK [1]. However, the effectiveness of existing treatments in managing these extremely prevalent conditions has been limited. A person in the UK has a potentially life-threatening asthma attack every ten seconds [2], while exacerbations of chronic obstructive pulmonary disease (COPD) are the second most common cause of emergency admission to UK hospitals [3]. As a result, respiratory diseases cost the NHS £3 billion per year and cause the loss of nearly 25 million work days annually in the UK [1].

Researchers at the University of Southampton, led by Professor Stephen Holgate, have been working for more than 20 years to understand the underlying mechanisms of respiratory diseases. Building on the

finding that asthma attacks are caused by viral infections [4], the team has sought to develop novel therapeutics to prevent or reduce the severity of attacks. This led to the discovery of a new drug, interferon beta (IFN $\beta$ ), which has been developed by Synairgen, a spin-out company founded in 2003 by Professor Holgate and colleagues. Clinical trials of the drug were conducted through the NIHR Southampton Respiratory BRU and the NIHR Wellcome Trust Clinical Research Facility (WTCRF). Synairgen CEO Richard Marsden describes the BRU and the NIHR WTCRF as ‘invaluable’ to the project, stating that ‘This specialist respiratory research capability, integrated with both the regional asthma service and the NIHR WTCRF means that high quality and challenging clinical trials can be completed in a timely manner’ [5].

The results from phase 1 trials enabled Synairgen to raise £6 million in 2009 and £2.5 million in 2011 to drive the completion of phase 2 [6]. These trials demonstrated the safety and efficacy of IFN $\beta$  in preventing attacks in moderate-severe asthma [6]. The findings of this research have had substantial commercial impact and have the potential to save the NHS money while improving patient outcomes. Synairgen has patented the use of inhaled IFN $\beta$  as a treatment for asthma and COPD exacerbations in Europe, the United States and Japan. It will be developed in partnership with AstraZeneca as part of a licensing agreement worth \$232 million [5]. Synairgen now employs around 25 people [6].

In addition, the NIHR, through the Southampton Respiratory BRU, has awarded the University of Southampton £7.3 million in follow-on funding for further work on innovative treatments for respiratory illnesses [6]. This research, also funded by the Medical Research Council, has produced proof of concept for disease mechanistic networks in asthma sufferers – a development with potentially major implications for novel therapies [7].

Regarding potential impact for patients, trials have shown that IFN $\beta$  is effective against the majority of exacerbations in moderate-severe asthma, which affects around 10 per cent of all asthma sufferers in the UK [1]. Such exacerbations account for around half of the total healthcare cost of asthma, meaning that the NHS stands to realise major cost savings [8]. Moreover, a reduction in the number of work days lost in the UK due to COPD, as well as improving quality of life, would benefit the country’s economy by reducing the annual loss of productivity and income tax [9].

## Evidence

[1] British Thoracic Society. 2006. The burden of lung disease: 2<sup>nd</sup> edition. London: The British Thoracic Society. As of 9 May 2016:

<https://www.brit-thoracic.org.uk/document-library/delivery-of-respiratory-care/burden-of-lung-disease/burden-of-lung-disease-2006/>

[2] Asthma UK. 2014. Asthma UK Strategy 2014–2017: Reduce risk of asthma attacks. London: Asthma UK. As of 9 May 2016:

<https://www.asthma.org.uk/globalassets/about/asthma-uk-strategy-2014-17.pdf>

[3] National Health Service Medical Directorate. 2012. COPD Commissioning Toolkit: A resource for commissioners. London: NHS. As of 9 May 2016:

[https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/212876/chronic-obstructive-pulmonary-disease-COPD-commissioning-toolkit.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/212876/chronic-obstructive-pulmonary-disease-COPD-commissioning-toolkit.pdf)

[4] Papadopoulos NG, Bates PJ, Bardin PG, Papi A, Leir SH, Fraenkel DJ, Meyer J, Lackie PM, Sanderson G, Holgate ST and Johnston SL. 2000. Rhinoviruses infect the lower airways. *Journal of Infectious Diseases* 181 (6): 1875-84. As of 9 May 2016: <http://jid.oxfordjournals.org/content/181/6/1875.full.pdf>

[5] National Institute for Health Research Southampton Respiratory Biomedical Research Unit. 2016. Lynchpin in \$220M fight against breathlessness. As of 9 May 2016:

[http://www.uhs.nhs.uk/ClinicalResearchinSouthampton/Our-research/Respiratory-research/Ourresearchandimpacts/Impactcasesstudies/Lynchpinin\\$220Mfightagainstbreathlessness.aspx](http://www.uhs.nhs.uk/ClinicalResearchinSouthampton/Our-research/Respiratory-research/Ourresearchandimpacts/Impactcasesstudies/Lynchpinin$220Mfightagainstbreathlessness.aspx)

[6] Research Excellence Framework. 2014. Breathing new life into the treatment of respiratory illnesses. [Case study 44146.] As of 9 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=44146>

[7] Hinks TS, Zhou X, Staples KJ, Dimitrov BD, Manta A, Petrossian T, Lum PY, Smith CG, Ward JA, Howarth PH, Walls AF, Gadola SD, Djukanovic R. 2015. Innate and adaptive T cells in asthmatic patients: Relationship to severity and disease mechanisms. *Journal of Allergy and Clinical Immunology* 136 (2): 323-33. doi: 10.1016/j.jaci.2015.01.014

[8] National Asthma Education and Prevention Program. 2002. National Asthma Education and Prevention Program: Expert panel report: Guidelines for the diagnosis and management of asthma update on selected topics: 2002. *Journal of Allergy and Clinical Immunology* 110 (5): s141-219.

[9] Fletcher M, van der Molen T, Barnes N, Walsh J. 2011. COPD: The new workplace epidemic. Washington: COPD Foundation. As of 9 May 2016: <http://www.copdfoundation.org/pdfs/copd-uncovered-report-2011.pdf>

## 9. Enabling clinical research excellence

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### 9.1. Summary

**Informed. Clinical. Excellent.**

*NIHR connects academia, the NHS and other parts of the healthcare system. This enables NIHR to fund world-class early translational research and provide a rapid response to research priorities.*

NIHR funding and support increases the national research infrastructure in the NHS and resources available to researchers and clinicians. It provides the facilities and environment for academic and NHS researchers to leverage further funding from other partners, such as charities and industry. Examples of NIHR impact through collaborative structures include:

- Biomedical Research Centres and Biomedical Research Units increase research capacity and capabilities by providing research infrastructure in the NHS and opportunities for research and clinical personnel to develop multidisciplinary skills, with over £918 million in research funding leveraged in 2014/15 from NIHR's charity, industry and public research funding partners.
- Clinical Research Facilities are providing a purpose-built environment equipped with the latest technology to conduct cutting edge experimental medicine research, leading to promising innovative treatments, devices and diagnostics, such as a new ultrasound technique for treating bone cancer, which alleviates pain almost immediately.
- NIHR's BioResource provides a database of public and patient volunteers willing to participate in research trials and studies with a view to having an impact on health and healthcare. To date, 75,000 individuals have signed up to BioResource and are available to participate in studies.
- Collaborations for Leadership in Applied Health Research and Care (CLAHRCs) are partnerships bringing together local providers of NHS services and NHS commissioners, universities, other relevant local organisations and the relevant Academic Health Science Network that conduct applied health research and implement evidence-based solutions to improve health. An example is the My Medication Passport – a booklet and app that holds a register of an individual's medication and other details – which empowers patients and helps them to inform medical professionals about their own medical history.

NIHR also provides funding for rare diseases and niche areas. Collaborations targeting early translational (that is, experimental medicine) research on specific diseases include the following:

- NIHR's Translational Research Partnerships create frameworks for national coordination to meet therapeutic needs in special areas, including a collaboration with Novartis that could lead



to a new treatment for Sjogren's syndrome, an autoimmune disease that affects the glands that produce tears and saliva.

- The Rare Diseases Translational Research Collaboration successfully supports 56 projects in the field of rare diseases, including 9 jointly funded with industry. This research benefits the 7 per cent of the UK population who suffer from rare diseases and enhances knowledge of disease mechanisms that are applicable to more common diseases.

Experienced, well-trained research staff are the foundation of robust research. NIHR funds three national schools that bring together leading academic centres in England and contribute to the professional training of researchers. The research outputs from the schools have informed national and international policy on a range of subjects:

- At the School for Primary Care Research, studies are contributing to policy change, including research which found that a mobile device that measured patients' blood pressure while they were ambulatory was more accurate and cost effective than either clinical or home monitoring. The National Institute for Health and Care Excellence (NICE) has since updated its hypertension guidelines to recommend ambulatory monitoring, and the research is also cited in South African guidelines for hypertension.
- Studies at the School for Public Health Research aim to improve the evidence base for applied public health practice, such as investigating whether the availability of cheap beers and ciders encourages people to cut down on drinking or whether bringing welfare advice on such problems as debt and benefits together with delivery of medical care would reduce costly demands for health services.
- The School for Social Care Research is engaging research fellows, contributing to researchers' professional development, and supporting studies that are benefiting the social care system. A study looking at the barriers faced by unpaid carers led to changes in guidance documents issued by several national charities and was cited during readings of the Health and Social Care Act 2012 in the House of Commons.

NIHR also provides resources to help advance knowledge and facilitate future research. It makes the findings of research freely and transparently available and provides resources to facilitate access to research resources, including public and patient volunteers, in the following ways:

- NIHR promotes the dissemination of research findings by requiring all NIHR-funded study outputs to include a short 'plain English' summary that can be easily understood by the general public.
- It also makes resources freely accessible online, including infographics, annual reports, booklets and research reports. NIHR's Journals Library, the first of its kind to be established by a health research funder, comprises 165 published issues of five open access, permanently available peer-reviewed journals. It recorded 260,000 website visits in 2015.
- NIHR's Research Design Service provides valuable advice on research design and methodological considerations and helps researchers improve the patient and public involvement component of their research. The service worked with more than 2,800 research teams in 2014/15 and helps lead to more successful and impactful research, as observed by researchers and funders alike.

### *9.1.1. Driving impacts across the UK higher educational sector through research*

#### Case study

In 2014, UK universities higher education institutions (HEIs) underwent the Research Excellence Framework (REF), the largest and most comprehensive peer-reviewed exercise in research impact assessment of its kind in the world. For the first time, this exercise required institutions to submit evidence-informed narrative statements – ‘impact case studies’ – to demonstrate the non-academic impacts of that research, conducted at their institution had had between 2008 and 2013.

The REF impact case studies provide a rich source of narrative material with which to explore the mechanisms by which research is benefiting society [1]. As part of its remit to deliver research-based evidence to the NIHR, the Policy Research in Science and Medicine (PRiSM) unit, a joint venture between RAND Europe and The Policy Institute at King’s College London, conducted an analysis of these impact case studies to understand how NIHR funding and support was delivering impacts via UK HEI [2].

The study found that nearly 16 per cent of the total number of life science themed impact case studies submitted to the REF referenced the NIHR’s support, spanning REF submissions from HEIs across the country. These case studies described nearly 250 instances of the NIHR’s support noted within universities’ descriptions of how their research was improving society [2].

Notable amongst the case studies was a high degree of cooperative funding between different public and charitable research funding agencies. Almost half of those that referenced the NIHR support noted charity funding, and over a third noted support from one or more of the UK Research Councils [2].

The vast majority (more than 90 per cent) of NIHR-supported case studies described and provided evidence for research contributing to regional or national impacts (e.g. local or UK-wide implementation of health practices based on research findings). These ranged from improvements to school dental screening practices, to better ways of ensuring minority groups have access to stroke care, to gender-sensitised weight loss programmes [2]. These case studies have formed the basis for a number of the narratives detailed further within this report.

The study also found that NIHR-supported research at UK HEIs had impacts outside of the UK . It transpired that a little under half (45 per cent) of the case studies provided evidence of research contributing to changes in international practice. This included widespread changes in healthcare procedures, service delivery or training. Some examples are the use of NIHR’s Collaborations for Leadership in Applied Health Research and Care supported tranexamic acid to prevent bleeding in trauma patients and NIHR Patient Safety Translational Research Centre supported surgeons’ deployment of a safety checklist, used by more than 1,800 healthcare organisations worldwide [2].

Similarly high proportions of case studies (over 40 per cent) noted contributions to direct impacts on patients. A majority substantiated these claims by providing evidenced figures on the scale of public benefits, for instance changes in patient outcomes observed as part of published research findings. Although it is difficult to quantify absolute numbers of patients benefitting from the support referred to

in the case studies, over a quarter provided evidence of the research impacting the lives of more than a thousand people; among those, a handful of studies impacted more than a million people.

The evidence shows that NIHR investment in research carried out in UK HEIs sustains a swathe of health, social and economic impacts. Given the generic health relevance of much of the research noted as receiving NIHR support, it also provides reassurance that the NIHR is acting in line with its broad mandate, to support ‘the health and wealth of the nation’.

## Evidence

[1] King’s College London and Digital Science. 2015. The nature, scale and beneficiaries of research impact: An initial analysis of Research Excellence Framework (REF) 2014 impact case studies. London: King’s College London. As of 29 April 2016: <http://www.kcl.ac.uk/sspp/policy-institute/publications/Analysis-of-REF-impact.pdf>

This high-level analysis examined the full corpus of 6,679 non-redacted case studies submitted to the 2014 REF exercise, of which the above NIHR sub-analysis formed a cohort.

[2] Kamenetzky A, Hinrichs-Krapels S, Wooding S, Grant J. 2016. An analysis of the impact of research supported by the National Institute of Health Research. Policy Research in Science and Medicine (PRiSM) Unit. RAND Europe and King’s College London. As of 29 April 2016: <http://www.kcl.ac.uk/sspp/policy-institute/publications/Impact-of-NIHR-research.pdf>

A retrospective analysis of instances of NIHR support referenced within impact case studies submitted by UK higher educational institutions, as part of the 2014 Research Excellence Framework UK-wide research assessment exercise.

### *9.1.2. Underpinning stronger partnerships through translational research infrastructure*

#### Case study

Launched in 2011, the NIHR Translational Research Partnerships (TRPs) and Translational Research Collaborations (TRCs) were developed to bring together the UK’s leading academic and NHS organisations with the life sciences industry and drive the translation of fundamental biomedical research into clinical settings. Creating translational research infrastructure through TRPs and TRCs had originally been envisioned in the UK’s government plan to establish the UK Life Sciences Super Cluster in 2009 [1]. Following the therapeutic capability clusters (TCC) pilot initiative in 2010-11, the NIHR became responsible for transforming this initiative into a long-term programme [2]. There are currently two TRPs, namely, Inflammatory Respiratory Disease and Joint and Related Inflammatory Disease, which allow the NHS, clinical academic researchers and life science companies to work together to focus on inflammatory respiratory diseases such as asthma, and joint-related inflammatory diseases, such as arthritis.

Four objectives are at the centre of the formation of TRPs: 1) deliver world-class translational research, which will result in optimal routes for clinical development and ultimately new treatments for patients; 2) encourage genuine collaboration between the UK’s leading universities, NHS organisations and life

science companies; 3) facilitate rapid and efficient interactions between life science companies and investigators who are participating in the TRPs; and, 4) promote and enhance the UK's reputation as a world-class centre for translational research [3].

In practice, the partnerships established a consortium of centres of excellence formed by a university and NHS organisations, and represented by a Clinical Academic Lead, and these were selected by an international review panel based on their expertise and capabilities in the designated field. The TRPs thus provided a single point of access for life sciences companies, from first contact and entry into the centres of excellence through to the completion of a study. The benefits to commercial partners can be seen in better access to recognised experience in current exploratory development protocols; experience in pathophysiology and disease mechanisms; and expertise in modelling, enabling technologies and infrastructure, including imaging, biobanks, accredited laboratory facilities [3].

The collaborative opportunities created by the TRPs are expected to speed up the advancement of new therapies into treatments for major health conditions. As the partnerships were only established in the last five years, there is a lack of robust evidence of their expected impacts. However, there are early examples of the TRPs helping clinical academia and other partners, including industry and charities, work more collaboratively. The collaboration between Novartis and the NIHR TRP to start the first commercial trial of a new treatment for Sjogren's syndrome [4] is one example. Sjogren's syndrome is the second most common autoimmune condition after rheumatoid arthritis. This represents an example of how the TRP can aid in the development of a new treatment in areas of unmet need. Another example is the TRP in Joint and Related Inflammatory Diseases, which collaborated with Arthritis Research UK and its Experimental Arthritis Treatment Centres in a joint call for industry-collaborative clinical studies. This joint call will leverage an additional £1 million in research charity funding and will fund three studies, including the first Translational Research Partnership research programme in Lupus [5].

In addition, the NIHR supported the formation of two TRCs. The TRCs bring together groupings of expertise from across different parts of the NIHR infrastructure to enhance the translation into patient benefit and collaboration in specific therapeutic areas. Currently, there is a TRC in Rare Diseases and a TRC in Dementia. These collaborations brought together NIHR Biomedical Research Centres and Units with relevant research themes to collaborate in translating discoveries from basic scientific research in rare diseases and dementia into benefits for patients. In other words, they created instruments of national coordination to increase research collaboration and speed up translation in the areas of high unmet therapeutic need. The TRC in Rare Diseases has a focus on 'deep phenotyping' patients with rare diseases, and it works closely with the other NIHR research infrastructure for rare diseases research .

While the evidence of impact of the TRCs is yet to emerge due to their relatively recent formation, recent examples illustrate some results of efficient collaboration enabled by the TRCs [5]. For example, the TRC in Dementia recently received funding from Parkinson's UK to search for Parkinson's biomarkers in blood and cerebrospinal fluid using proteomics. This research has the potential to be advantageous as blood is easily accessible and a blood test can be repeated to obtain measures of change. The Tracing Parkinson's study is also funded by Parkinson's UK and is the largest in-depth study of people with Parkinson's, recruiting more than 2,000 people across 70 UK study centres [6]. The NIHR Dementia TRC is also part of the UK Dementia Research Platform, a platform which aims to create the world's

largest population study for use in dementias research, with 2 million participants aged 50 and over. The NIHR TRC supports the efforts of the UK Dementia Research Platform by providing experimental medicine infrastructure and capabilities.

## Evidence

[1] HM Government Office for Life Sciences. 2009. Life Sciences Blueprint. London: Department for Business, Innovation and Skills. As of 9 May 2016: <https://www.biocity.co.uk/file-manager/Group/reports2009/2009-07-ols-life-science-blueprint.pdf>

This policy document provides a background to and rationale for the formation of the therapeutic capability clusters, the predecessors of the TRPs.

[2] HM Government. 2011. New research partnerships set to boost patient treatments and economic growth. As of 9 May 2016: <https://www.gov.uk/government/news/new-research-partnerships-set-to-boost-patient-treatments-and-economic-growth>

This webpage provides a press release with an announcement of the formation of the NIHR TRPs.

[3] National Institute for Health Research. 2011. Translation Research Partnerships. London: NIHR. As of 9 May 2016: <http://www.nihr.ac.uk/documents/about-NIHR/Briefing-Documents/4.10-Translational-Research-Partnerships.pdf>

This NIHR brochure sets out the background, vision and objectives for the TRPs and provides an overview of centres currently participating in the two NIHR TRPs.

[4] BusinessWire. 2015. NIHR announces pioneering study to test new treatment for Sjogren's syndrome. As of 9 May 2016: <http://www.businesswire.com/news/home/20141209005436/en/NIHR-Announces-Pioneering-Study-Test-Treatment-Sjogren%E2%80%99s>

This webpage provides an announcement of the start of a 'pioneering study' to test a new treatment for Sjogren's syndrome.

[5] Internal document from the Department of Health.

[6] National Institute for Health Research Office for Clinical Research Infrastructure. 2015. NIHR Dementia Translational Research Collaboration: Engaging with NHS and industry to advance dementia research. London: NIHR. As of 9 May 2016: <http://www.nihr.ac.uk/industry/NIHR%20Dementia%20Translational%20Research%20Collaboration%20Booklet.pdf>

This document provides an overview of the objectives and activities of the two TRCs.

### *9.1.3. Supporting UK leadership in rare diseases research*

#### Case study

Rare diseases are defined as those found in less than 0.5 per cent of the population [1]. There are more than 5,000 rare diseases and collectively these affect 7 per cent of the UK population [2]. Research into this field is important not only for bettering the lives of these patients, but also for advancing research into understanding disease mechanisms that are applicable to more common diseases. The NIHR's Rare

Diseases Translational Research Collaboration (RD-TRC) is providing the infrastructure to facilitate research with the potential to bring about novel treatments that will improve lives and reduce costs [1].

The RD-TRC includes NIHR Biomedical Research Centres, Biomedical Research Units and Clinical Research Facilities, thereby drawing on multiple areas of the NIHR research infrastructure [1]. Beginning in 2013, the NIHR has made an initial four year investment of £5 million per annum in the RD-TRC, with the intention to improve the research infrastructure and support costs for 'deep phenotyping' training and capacity development for translational research into rare diseases.

The RD-TRC is already having an impact on the research landscape in rare diseases. This is shown by increased participation in their funding calls, new partnerships with industry, uptake of their Fellowship Scheme, and increased involvement of patients and their carers.

At the end of 2015, the RD-TRC was supporting 56 research projects including 9 jointly funded with industry. There has been an increase in interest and applications in these schemes over time [2]. The projects have increased the knowledge base in the case of several rare diseases such as: Osteogenesis Imperfecta, Duchenne muscular dystrophy and Alpha-1- antitrypsin deficiency, among others [2]. The RD-TRC advances research through the gathering of 'deep phenotyping' data on patients living with rare diseases [2]. These data are available to NIHR-funded and other researchers for the purposes of research into new diagnostics and treatments, including through combining with genomic data. Furthermore, results from RD-TRC-supported studies have been disseminated within the clinical and scientific communities at international meetings and in peer-reviewed publications [2]. This increases the possibility of formulating new research questions based on RD-TRC findings.

The RD-TRC has also managed to foster partnerships with industry, both multinational pharmaceutical companies and small start-ups [2]. As the RD-TRC can only fund the phenotyping aspects of studies, the industry partner that is invited to collaborate is responsible for meeting other financial costs that arise in this complex area of research. The latest joint funding call with the NIHR Office for Clinical Research Infrastructure has resulted in nine studies with industry, two of which are phase 2 trials. This leveraging expands the potential impact that the RD-TRC can have in translating research into practice. For example, research into the phenotyping of IgA Nephropathy (N) has already led to the team having talks with pharmaceutical companies to continue the funding which will enable further phenotyping and establish a new cohort of 3,000 IgAN patients from across the UK. Researchers leading another study into congenital hyperinsulinism in infants received £2.3 million in funding from Innovate UK for a partnership with the biotechnology firm Heptares Therapeutics to develop novel treatment approaches [2].

In terms of capacity building, researchers involved with the RD-TRC benefit from special training that further advances research capacities. This includes training in research methodology and governance particular to rare disease research, as well as guidance on how to involve patients and the public in research. Since the launch of RD-TRC, there have been two rounds of fellowship calls, which provide funding for seven PhD and five post-doctoral qualifications [2].

The involvement of patient groups has contributed to an upward trend in patient recruitment and participation, with more than 9,500 patients recruited by the end of the RD-TRC's second year (well over

300% of the target it had set itself). The RD-TRC has a Patient Advisory Group, which held its first meeting in November 2015. This group connects patients and researchers using social media tools. Consideration of the public and patients is further supported by producing ‘plain English’ study summaries and disseminating research findings via the RD-TRC website and twitter account [2].

Overall the RD-TRC exemplifies the way in which the NIHR’s research infrastructure is contributing to a greater early translational and clinical research capability in this field and keeping the UK at the cutting edge of international research in this field [1]. In the words of a patient beneficiary, it has filled an important gap in the advancement of research: ‘...that’s the gap that RD-TRC has filled very effectively and has allowed us to move from meeting one patient and identifying a rare defect, to coordinating a population of several hundred patients in the UK and making a strong case to the Department of Health for specialised service commissioning and for clinical trials, which we believe have an excellent hope of addressing some components of the conditions we are dealing with’ [3].

### Evidence

[1] National Institute for Health Research. 2016. Rare Diseases Translational Research Collaboration (TRC). As of 9 May 2016: <http://www.nihr.ac.uk/about/rare-diseases-translational-research-collaboration.htm>

This webpage describes the Rare Diseases Translational Research Collaboration.

[2] National Institute for Health Research. 2016. Rare Diseases Translational Research Collaboration: Review 2013–2015: February 2016. London: NIHR. As of 9 May 2016: <http://rd.trc.nihr.ac.uk/wp-content/uploads/2016/03/2013-15-Review-web-version-spreads-small.pdf>

The report presents an overview of research activities conducted by the NIHR Rare Diseases Translational Research Collaboration in the three years of its existence.

[3] National Institute for Health Research. 2015. Rare Diseases Translational Research Collaboration Newsletter 10. As of 9 May 2016: <http://rd.trc.nihr.ac.uk/wp-content/uploads/2015/12/RD-TRC-Newsletter-10.1.compressed.pdf>

The newsletter contains accounts from patients from the TRC Research Symposium – Turning Lives Around – Segmental Overgrowth Study.

#### *9.1.4. Opening up access to ‘big data’ with tools to support life sciences research*

The NIHR has put in place a range of initiatives and resources that enable easier access to research data and tools to support excellence in academic research. These include both the NIHR ‘big data’ initiatives, as well as the NIHR policies on open access. The NIHR is committed to improving access to data as this will help ‘the nation stay at the forefront of pioneering health research and a favoured location for life sciences industry studies’ [1]. With this objective, the NIHR has established or joint-funded several initiatives and sources, including the Clinical Practice Research Datalink (CPRD), the Clinical Record Interactive Search, the NIHR Health Informatics Collaborative, the MRC-NIHR phenome centres, the

NIHR BioResource with the MRC, the NIHR National Biosample Centre, and the Farr Institute of Health Informatics Research.

The Clinical Practice Research Datalink, created by the NIHR in partnership with the Medicines and Healthcare products Regulatory Agency, as a new, enhanced service that constituted a £60 million investment over 10 years. The CPRD provides a secure service which enables researchers to obtain high-quality, anonymised data for different types of health research [2]. It provides one of the largest databases of longitudinal medical records from primary care in the world, currently representing more than 11.3 million patients from 674 practices in the UK. This includes 4.4 million active patients (6.9% of the UK population) meeting quality criteria who are broadly representative of the UK general population in terms of age, sex and ethnicity [3]. To date, the CPRD data have been extensively used for observational research in over 1,000 published peer-reviewed journal articles [4]. As illustrated in the literature, many peer-reviewed publications using the CPRD data have had a direct impact on public health in all major therapeutic areas, including cardiovascular disease, cancer, and digestive diseases [5]. The impact of the CPRD data can also be seen in clinical guidelines, and guidance documents including technical guidance which often inform decisionmaking in healthcare. According to a recent systematic review of CPRD studies in English guidance and guidelines since 2000 [6], 23 clinical guidelines or studies have referenced studies using data from the CPRD.

The impact of the NIHR-provided support can also be illustrated by the MRC-NIHR National Phenome Centre in London and the regional centre in Birmingham. Established in conjunction with the MRC, the phenome centres offer access of the UK research community to a world-class capability in metabolic phenotyping. The centres helps researchers to better detect the onset of several diseases and develop more effective treatments. The phenome centres represent an important step towards harnessing the full promise of precision medicine [7]. Early detection and tailoring of treatment are anticipated to contribute not only to significant improvements in patient health but also to cost savings to the NHS. Evidence of the potential impact of the centres is emerging through developments such as the intelligent knife (iKnife), a device that can provide near-real-time information on the biological makeup of tissue by analysis of the aerosol released during electrosurgical dissection [8]. Another example of the emerging impact of the phenome centres is a recent study which used an exploratory metabolic phenotyping approach identified that a specific pattern of metabolites detectable in urine samples is associated with increased BMI [9].

## Evidence

[1] National Institute for Health Research. 2016. NIHR 'big data'. As of 29 April 2016: <http://www.nihr.ac.uk/policy-and-standards/nihr-big-data.htm>

This website provides an overview of the NIHR 'big data' initiatives.

[2] Department of Health. 2011. The Government plan for a secure data service: Strengthening the international competitiveness of UK life sciences research. London: Department of Health. As of 29 April 2016:

[https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/215337/dh\\_131242.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/215337/dh_131242.pdf)



The document provides an overview of this new service, and explains the delivery and refinement of this service and the products it offers.

[3] Herrett E, Gallagher AM, Bhaskaran K, Forbes H, Mathur R, van Staa T, Smeeth L. 2015. Data resource profile: Clinical Practice Research Datalink (CPRD). *International Journal of Epidemiology* 44 (3): 827-36. doi: 10.1093/ije/dyv098

This article reviews the Clinical Practice Research Datalink (CPRD) and its contribution to health research.

[4] Clinical Practice Research Datalink. 2016. Bibliography. As of 29 April 2016: <https://www.cprd.com/bibliography/>

This website provides the bibliographic details on the studies using the CPRD.

[5] Kousoulis AA, Rafi I, de Lusignan S. 2015. The CPRD and the RCGP: Building on research success by enhancing benefits for patients and practices. *British Journal of General Practice* 65 (631): 54-5. doi: 10.3399/bjgp15X683353

This editorial provides examples of and references to different therapeutic areas where the CPRD data showed a direct impact on public health.

[6] Oyinlola JO, Campbell J, Kousoulis AA. 2015. The use of real world evidence to influence practice: A systematic review of CPRD studies in English guidances and guidelines. *Value in Health* 18 (7): A565. doi: <http://dx.doi.org/10.1016/j.jval.2015.09.1852>

This journal article provides evidence of the use of CPRD studies in clinical guidances and guidelines.

[7] Dzau VJ, Ginsburg GS, Van Nuys K, Agus D, Goldman D. 2015. Aligning incentives to fulfil the promise of personalised medicine. *Lancet* 385 (9982): 2118-9. doi: [http://dx.doi.org/10.1016/S0140-6736\(15\)60722-X](http://dx.doi.org/10.1016/S0140-6736(15)60722-X)

This article uses an example of the National Phenome Centre to illustrate the potential of personalised medicine.

[8] Balog J, Sasi-Szabó L, Kinross J, Lewis MR, Muirhead LJ, Veselkov K, Mirnezami R, Dezső B, Damjanovich L, Darzi A, Nicholson JK. 2013. Intraoperative tissue identification using rapid evaporative ionization mass spectrometry. *Science Translational Medicine* 5 (194): ra93. doi: 10.1126/scitranslmed.3005623.

This article provides further details on the iKnife and summarises the initial results of the use of the iKnife as a means to differentiate between cancerous and non-cancerous tissue when compared with histological analysis of samples from 81 patients undergoing surgery for tumour resection.

[9] Elliot P, Poma JM, Chan Q, Garcia-Perez I, Wijeyesekera A, Bictash M, Ebbels TM, Ueshima H, Zhao L, van Horn L, Daviglius M. 2015. Urinary metabolic signatures of human adiposity. *Science Translational Medicine* 7 (285): 285ra62. doi: 10.1126/scitranslmed.aaa5680

This journal article provides the findings of a study enabled by the National Phenome Centre.

### *9.1.5. Creating impact with collaborative approaches to research through infrastructure merging academia and practice*

#### Case study

Since 2008, the NIHR has made a major investment in partnerships between higher education institutions and local health services called Collaborations for Leadership in Applied Health Research and Care (CLAHRCs). In October 2008, the NIHR funded nine CLAHRCs for a five year period. In the next round, 13 sites were funded for five years starting from 2014. The NIHR has invested up to £114 million in these collaborations over the 10 year period. The aim is to increase capacity and capability to produce and implement research evidence through sustained interactions between academics and services which will, in turn, improve patient outcomes. CLAHRCs bring together the local providers of NHS services and NHS commissioners, who host the collaboration, working with universities, other relevant local organisations and the relevant Academic Health Science Network. The sites primarily focus on research targeted at chronic disease and public health interventions [1].

Since 2008, the CLAHRCs have demonstrated a substantial portfolio of world-class applied health research and significant track records in translating research findings into improved outcomes for patients. A number of evaluations have been conducted to understand the benefits of this model to funding.

Soper et al. found that CLAHRCs infrastructure and ways of working have strengthened local networks and relationships; built capacity in their local academic and NHS communities to undertake and use research that meets the needs of the service; developed research and implementation methodologies; and added to understanding of the complex relation between research and implementation [2]. This is in line with the findings of Rycroft-Malone et al., that showed that the 'mechanisms of collaborative action, relationship building, engagement, motivation, knowledge exchange and learning are important to the processes and outcomes of CLAHRCs' activity, including their capacity for implementation' [3]. Rycroft-Malone et al. noted that impacts were affected by the CLAHRCs' approach to implementation, quality of collaboration, commitment and ownership, and degree of sharing and managing knowledge [4].

By acting to bring together the perspectives of academics and clinical practitioners, CLAHRCs provide an infrastructure where researchers and NHS communities can work together to solve health issues. This way of working has strengthened local networks and relationships [1]. For example, CLAHRC East of England assessed screening measures for children for autism spectrum conditions, and produced a shortlist of tests which could be used by frontline clinicians. This has led to children with these conditions being diagnosed faster, and has improved their access to receiving the support they require [5].

Another issue, identified in Cambridgeshire as important in the local community was moving young people from care to independent living. The CLAHRC worked with the local councils and NHS Foundation Trust to understand factors that influence the transition and the quality of support they receive. The research found that poor mental health impacted on the transition, and that young people needed greater support in identifying these issues and receiving treatment. As a result, three films have been made which are used UK-wide in the training of prospective carers [5].

Another example is the development of My Medication Passport by CLAHRC Northwest London. The concept for this came from a public focus group and CLAHRC researchers worked with patients and

clinicians to develop a booklet and app to hold a register of an individual's medication and other details to empower patients and enable them to inform healthcare professionals about their medication and healthcare needs. The passport is felt to be of particular value to vulnerable patient groups and those using a wide range of health and social care services. The passport was launched in 2013, and a recent report of the impact of the CLAHRCs states that 100,000 booklets had been ordered and nearly 10,000 apps have been downloaded across 37 countries [5].

Overall, the NIHR has put in place the infrastructure to enable collaboration between academics and clinical practitioners. These ways of working have strengthened local networks and relationships; built capacity in their local academic and NHS communities to undertake and use research that meets the needs of the service; developed research and implementation methodologies; and added to understanding of the complex relation between research and implementation.

## Evidence

[1] National Institute for Health Research. 2015. Collaborations for Leadership in Applied Health Research and Care (CLAHRCs). [Briefing paper 4.05 CLAHRCs Version 9 (January 2015)]. London: NIHR. As of 9 May 2016: <http://www.nihr.ac.uk/documents/about-NIHR/Briefing-Documents/2016/4.05-Collaborations-for-Leadership-in-Appiled-Health-Research-and-Care.pdf>

NIHR briefing paper describing the set-up and structure of the CLAHRCs as funded by the NIHR.

[2] Soper B, Yaqub O, Hinrichs S, Marjanovich S, Drabble S, Hanney S, Nolte E. 2013. CLAHRCs in practice: Combined knowledge transfer and exchange strategies, cultural change, and experimentation. *Journal of Health Services Research & Policy* 18 (3): s53-64. doi: 10.1177/1355819613499903

[3] Rycroft-Malone J, Wilkinson J, Burton CR, Harvey G, McCormack B, Graham I, Staniszewska S. 2013. Collaborative action around implementation in Collaborations for Leadership in Applied Health Research and Care: Towards a programme theory. *Journal of Health Services Research & Policy* 18 (3): s13-26. doi: 10.1177/1355819613498859.

Independent evaluations of CLAHRCs, reviewing their mechanism of collaboration to conduct results and produce impact.

[4] Rycroft-Malone J, Wilkinson J, Burton C, Andrews G, Ariss S, Baker R, Dopson S, Graham I, Harvey G, Martin G, McCormack B, Staniszewska S, Thompson C. 2011. Implementing health research through academic and clinical partnerships: A realistic evaluation of the Collaborations for Leadership in Applied Health Research and Care (CLAHRC). *Implementation Science*. 19 (6): 74. doi: 10.1186/1748-5908-6-74

[5] National Institute for Health Research. n.d. World class research making a difference: Collaborations for Leadership in Applied Health Research and Care. London: NIHR. As of 9 May 2016: <http://www.clahrc-em.nihr.ac.uk/clahrc-em-nihr/documents/nihr-clahrc-world-class-research-making-a-difference.pdf>

Impact brochure published on behalf of the NIHR by the NIHR CLAHRC East Midlands describing the success of the CLAHRCs since their piloting in 2008.

### *9.1.6. Constructing the facilities to conduct high quality patient-focussed research*

#### Case study

Clinical Research Facilities (CRF) are dedicated, purpose-built facilities with specialist clinical research and support staff from universities and NHS Trusts working together on patient-oriented commercial and non-commercial early translational (experimental medicine) research [1]. The CRF Network enables researchers to collaborate, which, in turn, helps to ensure there is a diffusion of knowledge which can advance the field.

The decision to invest in the CRFs was taken as a result of the success of the five Wellcome Trust Clinical Research Facilities that were set up in 1997 [2]. These indicated that the new environments, which fostered collaborations between basic and clinically trained researchers, led to improvements in healthcare. In 2006, the NIHR, in partnership with other funders in the UK Clinical Research Collaboration, offered a £84 million investment to set up the CRFs [2]. This capital funding was dedicated to building facilities and acquiring necessary equipment. The NIHR also funded NHS infrastructure costs for the CRFs, such as clinical research nurses, technicians, and facility maintenance costs.

Currently NIHR supports 19 CRFs impacting a large number of patients. The facilities allow for the conduct of both commercial and non-commercial experimental medicine studies, as private companies can also access the facilities for their research studies, with appropriate cost recovery by the NHS. From 1 September 2012 to 31 March 2017, the CRFs will receive £102 million of funding from NIHR [1][2]. CRFs around the country are realising research milestones and achieving benefits for patients. The NIHR Alder Hey Clinical Research Facility in Liverpool specialises in experimental medicine and early-phase trials for children and babies, including the first ever administration of new therapeutic agents in children and babies [3]. In 2013, just one year after opening, it provided patients with access to research studies from 18 different commercial partners, including one 'global first' in which a patient in Liverpool was the first in the world to be enrolled in a research study [4]. At the NIHR/Wellcome University College London Hospitals CRF, they began the first-in-man trial of a new treatment for hepatocellular cancer, the second most common cause of cancer death worldwide, but for which there is only one drug currently available for treatment of the advanced stage of the disease [4].

Though experimental medicine is, by definition, early phase, research at the CRFs is already providing benefits to patients. The NIHR Imaging CRF supports more than 100 research studies where imaging is used to monitor the responses of patients to novel treatments and therapies [5]. For example, a new Magnetic Resonance-guided High Intensity Focussed Ultrasound technique is being developed as a way of treating cancers. In particular where cancers have spread to the bone, this technique has shown promise in nine clinical trial participants, helping to significantly reduce the patients' pain almost immediately. In November 2015, the results of this clinical trial using this technique received attention in the national media for its potential and for its promise to not only alleviate pain, but also help treat tumours without recourse to surgery [6]. At the NIHR/Wellcome Trust Birmingham Clinical Research Facility, two studies being carried out into new therapies for hepatitis C are having success. In one trial 11 patients were randomised and cured of the disease, while another trial cured 6 patients. Though these are small, early

successes, they show the promise of CRFs to help early translational medicine translate into patient benefits [7].

The CRFs can also help to support the research process, making research more efficient across the system. To cite but one example, the Exeter NIHR Clinical Research Facility has established a ‘biobank’ – a large collection of data and tissue samples which can be used for research purposes – and has recruited 8,000 volunteers into the Exeter 10,000 biobank and research register. There have been several benefits to research efforts realised already from this biobank, including: benefits to 90 different projects which were able to access a pre-screened database of research volunteers and achieve a 50 per cent response rate to studies; providing more than 20,000 samples for biomarker analysis; multiple publications in academic journals; and the generation of more than £10 million in external funding which utilises the data from this project [8].

Translating experimental research into concrete health outcomes is a lengthy process. However having a dedicated and purpose-built environment, equipped with the latest technology, enables researchers to conduct cutting edge research that will translate into benefits for the patients. In addition NIHR funding for CRFs is essential for fostering NHS collaboration with industry in experimental medicine [1], an area that historically can be less attractive for industry due to the associated costs, lengthy research and development cycle and high rates of failure.

## Evidence

[1] National Institute for Health Research. 2016. Clinical Research Facilities (CRFs) for Experimental Medicine. As of 9 May 2016: <http://www.nihr.ac.uk/about/clinical-research-facilities-for-experimental-medicine.htm>

This webpage provides information on Clinical Research Facilities for Experimental Medicine

[2] National Institute for Health Research. 2015. Clinical Research Facilities for Experimental Medicine. [4.4 Clinical Research Facilities for Experimental Medicine Version 8 (July 2015).] London: NIHR. As of 9 May 2016: <http://www.nihr.ac.uk/documents/about-NIHR/Briefing-Documents/4.4-Clinical-Research-Facilities-for-Experimental-Medicine.pdf>

The document is a brief summarising how NIHR Clinical Research Facilities for Experimental Medicine are contributing to NIHR’s vision.

[3] Alder Hey Children’s Charity (homepage). As of 9 May 2016: <http://www.alderhey.nhs.uk/research/nihr-alder-hey-clinical-research-facility/>

[4] University College London Hospitals National Institute for Health Research Foundation Trust. 2015. NIHR/Wellcome UCLH Clinical Research Facility: Cancer trials portfolio. London: University College London Hospitals NHS Foundation Trust. As of 9 May 2016: <http://www.uclhospitals.brc.nihr.ac.uk/sites/default/files/CRF%20Cancer%20Newsletter%20-%20Sept%202015.pdf>

[5] The Royal Marsden. n.d. Imaging CRF Research Highlights. As of 9 May 2016: <https://www.royalmarsden.nhs.uk/our-research/our-research-facilities/nihr-imaging-clinical-research-facility/research-highlights>

[6] McKie R. 2015. High-power sound waves used to blast cancer cells. The Guardian, October 31. As of 9 May 2016: <https://www.theguardian.com/science/2015/oct/31/ultrasound-cancer-research-hifu-bone-trial>

[7] National Institute for Health Research. 2014. NIHR/Wellcome Trust Birmingham Clinical Research Facility activities and highlights, 2014. London: NIHR. As of 9 May 2016: <http://www.research.uhb.nhs.uk/wp-content/uploads/2014/08/Annual-Report-NIHR.pdf>

[8] National Institute for Health Research. 2015. NIHR 2014 annual report. London: NIHR.

### *9.1.7. Strengthening capacity to apply academic excellence in healthcare through NIHR schools*

#### Case study

Improving the health and wealth of the nation through research relies on strong research capabilities and trained researchers. To create an environment that fosters research excellence in specific fields, the NIHR has funded three national schools: the School for Primary Care Research, the School for Public Health Research and the School for Social Care Research [1]. These schools represent collaborations between academic centres that allows for: research synergies leading to robust and high-quality evidence that informs policy in healthcare; capacity building in each area; and improvements in research awareness in the schools' respective fields [1]. Examples of benefits and selected impacts from each of the schools are discussed briefly below.

The School for Primary Care Research (SPCR), established in 2006, has funded 326 studies (2016 data) [2], with a focus on epidemiology, diagnosis, treatment, management and prognosis of illnesses in primary care; service delivery of primary care; and methodological developments to address primary care research questions. SPCR has undertaken projects in a number of themes, including a stream of work on hypertension. In this field, projects include a number of patient self-monitoring and self-management trials, a systematic review of individual patient data meta-analysis of self-monitoring of blood pressure, and a prospective register of trials for ongoing meta-analyses. Research from the SPCR found that ambulatory monitoring of blood pressure is more accurate than both clinic and home monitoring in diagnosing hypertension. The research also showed the cost-effectiveness of ambulatory monitoring of blood pressure. Taking into account the improvements in accuracy, a NICE Guideline Development Group recommended that ambulatory blood pressure measurement should be implemented for the routine diagnosis of hypertension in primary care, and this is reflected in the 2011 NICE Hypertension Guideline [3][4][5]. The research also informed the South African Hypertension guideline of 2011 [5]. The findings of the research were also reported widely in the media, including by the BBC [4].

SPCR work has also been impacting on patient-centred care and the management of long-term conditions. The school's research on the effectiveness of self-care strategies in non-communicable diseases was considered by the World Health Organization (WHO) guideline development group, which is currently using the findings in formulating WHO guidelines [6][7].

The School for Social Care Research (SSCR), established in May 2009, has commissioned more than 60 research studies [8] spanning a range of subjects in the area of social care, from preventing and reducing

the need for social care and support, to promoting choice and independence, balancing care and work, developing solutions to changing needs, and providing evidence to help deliver integrated services [9]. The research has been widely disseminated in 59 articles and journal papers, 18 methods reviews and 11 scoping reviews [10]. One example of SSCR research that has had a wider benefit is a study on overcoming the barriers faced by unpaid carers to remaining in employment. The project, undertaken in 2011, found that there were approximately 315,000 unpaid carers aged 16–64 in England. These were predominately women who had left full-time or part-time employment to provide care, a cost which amounted to £1.3 billion a year in public expenditure. The research also found little evidence that councils systematically provide services to support carers who are at risk of leaving their employment [11]. The study's findings were cited in more than 20 media outlets, including *BBC News*, *The Guardian* and *Community Care*. The research has informed policy around unpaid care and employment, such as policy and practice documents by the Government and Employers for Carers (2013), the Alzheimer's Society (2013), the King's Fund (2013), the West Sussex Public Health Research Unit (2013) and Carers UK (2012), and it was cited in the House of Commons during the second reading of the 'Care Bill'. Carers UK used the work to show the costs of caring to the government, and it is cited in several of their reports [11]. The scoping study is being followed by a further SSCR study to continue enlarging the evidence base to inform 'replacement care' for working carers in England [11].

Another example of impact which resulted from a research partly funded in the later stages by the SSCR is the impact on improving policy and practice to support mental health [12]. A wide body of research led from within the Personal Social Services Research Unit in the LSE (London School of Economics and Political Science) Health and Social Care group over the past two decades has sought to establish an economic case for interventions to prevent mental illness, to develop solutions to address mental health needs and to actively promote mental health well-being. In particular, work funded by the school on community capacity building to promote mental health and prevent mental health disorders provided an input to the government's Mental Health Strategy for England (2011) and the Mental Health Strategy for Scotland 2012–2015 [12].

The SPHR established in 2012 has supported more than 38 projects (2014 data) [13]. The SPHR is a relatively new endeavour and it is not yet possible to see the full impact of its research. This school targets three main public health challenges, namely, alcohol, ageing well and health inequalities, and it has already produced evidence on a number of possible public health interventions. For example, there is ongoing research to understand whether giving residents control over decisions about their neighbourhoods improves health and well-being outcomes. This research is acknowledged by NICE for its potential to contribute to future guidelines developments [14]. Another study is investigating the impact of the availability of cheap beers and ciders on drinking habits, while other research is looking at whether bringing welfare advice on such problems as debt and benefits together with delivery of medical care would reduce costly demands for health services [15].

All three of the schools represent collaborations among leading academic centres in England and contribute to capacity building and development of research networks where fellows are able to disseminate their research and build partnerships [1]. For example, the SSCR has engaged more than 192 Fellows (2012 data) from London School of Economics and Political Science and the universities of

Bristol, Kent, Manchester and York [7]. More than 90 trainees have received awards through the SPCR that furthered their research careers [6], while the SPHR funded 140 researchers during its first year [16]. The three schools demonstrate how the NIHR has pooled together capacities and talent from some of the best academic centres in the country and has enabled them, through funding, to conduct high-quality and timely research.

## Evidence

[1] National Institute for Health Research. 2015. Schools for Primary Care, Social Care and Public Health Research. [Version 10 (July 2015).] London: NIHR. As of 9 May 2016: <http://www.nihr.ac.uk/documents/about-NIHR/Briefing-Documents/3.3-Research-Schools.pdf>

This document provides an overview of the three schools.

[2] School for Primary Care Research (homepage). 2016. As of 9 May 2016: <http://www.spcr.nihr.ac.uk/>

This is the homepage for the School for Primary Care Research.

[3] National Institute for Health and Care Excellence. 2011. Hypertension in adults: Diagnosis and management NICE guidelines. [CG127.] As of 9 May 2016:

<https://www.nice.org.uk/guidance/cg127/evidence>

This webpage outlines evidence for the Hypertension in Adults: diagnosis and management NICE Guidelines.

[4] National Institute for Health Research School of Primary Care Research. n.d. Annual report for the 2011–12 financial year. London: NIHR. As of 9 May 2016: <http://www.spcr.nihr.ac.uk/research-old/nihr-spcr-annual-report-2011-12-w.pdf>

NIHR School of Primary Care Research Annual Report for the 2011 – 2012 financial year.

[5] Research Excellence Framework. 2014. Hypertension: Improving routine diagnosis of hypertension in primary care. [Case study 38796.]

Research Excellence Framework case study on hypertension from the University of Birmingham

[6] National Institute for Health Research School of Primary Care Research. n.d. Annual report for the 2012–13 financial year. As of 9 May 2016: [http://www.spcr.nihr.ac.uk/projects/spcr\\_annual-report2012-13.pdf](http://www.spcr.nihr.ac.uk/projects/spcr_annual-report2012-13.pdf)

NIHR School of Primary Care Research Annual Report for the 2012 – 2013 financial year.

[7] School for Primary Care Research. 2015. Top 10 achievements in 10 years. News 2015 (6): 2. As of 9 May 2016: [https://gallery.mailchimp.com/c031c9cc29b4b899935088b4a/files/Winter\\_05.pdf](https://gallery.mailchimp.com/c031c9cc29b4b899935088b4a/files/Winter_05.pdf)

Newsletter for the School for Primary Care Research.

[8] National Institute for Health Research School for Social Care Research. Projects. As of 9 May 2016: <http://www.sscr.nihr.ac.uk/projects.php>

List of current projects on the School for Social Care Research website.



[9] National Institute for Health Research School for Social Care Research. n.d. School for Social Care Research: Annual report 2009–2010. As of 9 May 2016:

[http://www.sscr.nihr.ac.uk/PDF/SSCR\\_annual\\_report\\_2009-2010.pdf](http://www.sscr.nihr.ac.uk/PDF/SSCR_annual_report_2009-2010.pdf)

NIHR School for Social Care Research annual report for 2009 – 2010

[10] National Institute for Health Research School for Social Care Research. 2016. Publications. As of 9 May 2016: <http://www.sscr.nihr.ac.uk/publications.php>

List of project outlines for the School for Social Care Research.

[11] National Institute for Health Research Journals Library. 2012. Overcoming barriers: Unpaid care and employment in England. As of 9 May 2016: <http://www.journalslibrary.nihr.ac.uk/nihr-research/school-for-social-care-research/unpaid-care-and-employment>

NIHR Journals Library webpage on the project, Overcoming barriers: Unpaid care and employment in England

[12] Research Excellence Framework. 2014. Improving policy and practice to promote better mental health. [Case study 40639.] As of 9 May 2016:

<http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=40639>

Research Excellence Framework on Improving policy and practice to promote better mental health from the London School of Economics & Political Science.

[13] National Institute for Health Research School for Public Health Research. 2014. Advisory Board meeting notes, 23rd October 2014. As of 9 May 2016: <http://sphr.nihr.ac.uk/wp-content/uploads/2015/04/SPHR-23rd-Oct-2014-Adv-Board-Notes-web.pdf>

These are the minutes from the 2014 Advisory Board meeting, which highlight the developments of the school in the past year.

[14] National Institute for Health and Care Excellence. 2016. Public health guideline on community engagement (NG44): Relevant ongoing NIHR research: February 2016. As of 9 May 2016: <https://www.nice.org.uk/guidance/ng44/resources/nihr-research-2368402381>

The document mentions the *Communities in Control Study Phase 1 & 2: An Evaluation of a Natural Policy Experiment in Community Empowerment* among the literature that could inform future updates of the NICE guideline.

[15] National Institute for Health Research School for Public Health Research. 2016. Pioneering new approaches to public health research: Insights from the NIHR School for Public Health Research. As of 9 May 2016: [http://sphr.nihr.ac.uk/wp-content/uploads/2016/02/Pioneering-New-Approaches-SPHR-NIHR-A4-Web-download-vesion-r1\\_single-pages-2.pdf](http://sphr.nihr.ac.uk/wp-content/uploads/2016/02/Pioneering-New-Approaches-SPHR-NIHR-A4-Web-download-vesion-r1_single-pages-2.pdf)

[16] National Institute for Health Research School for Public Health Research. 2013. Advisory Board meeting notes, 14th June 2013. As of 9 May 2016: <http://sphr.nihr.ac.uk/wp-content/uploads/2013/11/Notes-Actions-SPHR-14-June-2013-Adv-Board-SPHRweb.pdf>

These are the meetings from the 2013 Advisory Board meeting, which highlight the developments of the school in the past year.

### *9.1.8. Raising the quality of funding proposals across the research sector*

#### Case study

The NIHR-funded Research Design Service (RDS) provides confidential and free-of-charge support to health and social care researchers across England on design and methodology when writing their grant applications to both the NIHR and other national funders of research that is peer-reviewed [1]. Researchers often need support in developing their ideas and working up study designs in order to increase the chance of success in obtaining funding and avoiding inefficiencies in both the application and research stages [2]. During 2014-15, 2,837 researcher teams benefited from RDS advice on the development of new projects. From the 1,582 funding applications supported by RDS, 375 full or one-stage applications were successfully funded and 208 outline applications were shortlisted [3]. This illustrates that RDS provides valuable research advice with relatively high success rates of projects securing funding.

The RDS advice is recognised by the applicants who positively rate its support. There are numerous examples from all regions in England highlighting the value of RDS support [4]. One such example is the Guildford Hypertension 2000 study, a randomised trial of exercise interventions to increase levels of physical and sporting activity. The researcher felt that the RDS played a key part in the development of the application, helped identify relevant people for conducting the study conduct such as GPs and case officers and offered advice on the design of the research [4].

The quality of RDS support is also recognised by funders. In the case of the Self-Management of Analgesia and Related Treatments at the End of life (SMARTe) project, whose application was supported by RDS, the NIHR Health Technology Assessment (HTA) review panel commented on the patient and public involvement (PPI) strategy that ‘This is the best inclusion of patients and public inclusion ... seen on any application’ [4].

The support that RDS provides in the area of PPI is manifold. A 2015 evaluation of 10 case studies from across 5 RDS regions showed that researchers were supported through such mechanisms as being put in touch with PPI groups and receiving advice on training, and on how to engage patient and the public throughout the research, and details on how to provide reimbursements for PPI representatives [5].

The RDS is an important enabler for relevant and impactful research. This can be seen in the project on improving management of Type 1 diabetes in the UK with the Dose Adjustment For Normal Eating (DAFNE) programme as a research test bed. This successful NIHR Programme Grant for Applied Research (PGfAR) work benefited from RDS Yorkshire’s advice. The resulting research contributed to a better understanding of why some patients benefit from training more than others and helped develop models to enhance the accessibility and effectiveness of this training. More than 20,000 people with Type 1 diabetes in the UK have been trained to use DAFNE, and the Department of Health now supports structured education for all individuals with diabetes [6]. The programme’s findings were disseminated in more than 20 publications. Subsequently the RDS Yorkshire supported the development of a follow-on research programme to secure a subsequent NIHR PGfAR award in 2015.

In addition to offering individual support to researchers, the RDS also organises workshops at the programme level. More than 180 people registered for a series of four events held for PGfAR and Programme Development Grants programmes [3].

The NIHR-funded RDS is enabling researchers to develop stronger applications that secure funding. This reduces the risk of waste in research and enables the conduct of high quality clinical research.

## Evidence

[1] Research Design Service (homepage). 2016. As of 29 April 2016: <http://www.rds.nihr.ac.uk/>

Homepage for the Research Design Service

[2] Ioannidis JPA, Greenland S, Hlatky MA, Khoury MJ, Macleod MR, Moher D, Schulz KF, Tibshirani R. 2014. Increasing value and reducing waste in research design, conduct, and analysis. *Lancet* 383: 166-75. doi: 10.1016/S0140-6736(13)62227-8

Journal article on increasing value and reducing waste in research design, conduct, and analysis.

[3] National Institute for Health Research Research Design Service. n.d. Information on the RDS submission from the reporting year 2014–15, provided by the Research Design Service.

Facts and figures on the support provided by the NIHR Research Design Service 2014 – 2015

[4] RDS Case Studies 2013–2014: Submitted to NIHR/DH April 2014. Information provided by the Research Design Service.

These are a range of case studies that present projects that received RDS support and the accounts of researchers that benefited from it.

[5] Green G and Eyles C. 2015. Review of case studies on RDS support for public involvement. Provided by the Research Design Service.

The review presents identified themes from the analysis of 10 cases, which present the range and breadth of RDS support for PPI and the impact that this had.

[6] Heller S, Lawton J, Amiel S, Cooke D, Mansell P, Brennan A, Elliott J, Boote J, Emery C, Baird W, Basarir H, Beveridge S, Bond R, Campbell M, Chater T, Choudhary P, Clark M, de Zoysa N, Dixon S, Gianfrancesco C, Hopkins D, Jacques R, Kruger J, Moore S, Oliver L, Peasgood T, Rankin D, Roberts S, Rogers H, Taylor C, Thokala P, Thompson G, Ward C. 2014. Improving management of type 1 diabetes in the UK: The Dose Adjustment For Normal Eating (DAFNE) programme as a research test-bed: A mixed-method analysis of the barriers to and facilitators of successful diabetes self-management, a health economic analysis, a cluster randomised controlled trial of different models of delivery of an educational intervention and the potential of insulin pumps and additional educator input to improve outcomes.

Programme Grants for Applied Research 2 (5). As of 29 April 2016:

[http://www.journalslibrary.nihr.ac.uk/\\_\\_data/assets/pdf\\_file/0017/131624/FullReport-pgfar02050.pdf](http://www.journalslibrary.nihr.ac.uk/__data/assets/pdf_file/0017/131624/FullReport-pgfar02050.pdf)

This is the full NIHR grant report for this programme.

### *9.1.9. Facilitating research through dedicated Biomedical Research Centres and Biomedical Research Units*

#### **Case study**

In April 2007, 12 NIHR Biomedical Research Centres (BRCs) were established across England through partnerships between leading NHS organisations and universities [1]. Following a second, new open competition in 2011, 11 NIHR Biomedical Research Centres were designed and funded. The centres conduct early translational research which aims to transform scientific breakthroughs into treatments for patients. The first round of BRCs was followed by the establishment in 2008 of the first round of 16 NIHR Biomedical Research Units (BRUs). In 2012, a second round of 20 BRUs was funded to conduct early translational research in areas of clinical need and high disease burden [2]. Compared with the BRCs, the BRUs are small in critical mass and specialised in a specific disease identified by the Department of Health. The BRU funding helps the NHS/University partnerships further their research capacity.

The BRCs and BRUs have advanced clinical excellence by creating research capacity in the NHS through the provision of physical infrastructure in order to conduct clinical research, acquire new research skills and capabilities, and establish new organisational structures, systems and functions [2][3]. Each of these areas is discussed below.

The capital funding provided by the Department of Health and the NIHR as part of the BRC and BRU awards (for example new physical infrastructure, such as translational research laboratories and clinical trial facilities) has been used in several cases to attract further funds from different actors. A 2013 evaluation found that BRCs are more successful in attracting additional funding than comparative international centres of excellence. It was calculated that for every £1 invested, the BRCs generate between £3.50 and £18 [4]. Year-on-year since 2009, there has been an increase in the funding leveraged across BRCs and BRUs, with figures for 2014-15 totalling in excess of £1 billion.

There is evidence to suggest that BRCs and BRUs have built and increased capabilities and capacity in health research. Funding has been used to open new positions and attract high-profile researchers from overseas and industry settings [3]. Professional training has also been supported through the scheme, often leading to the development of multidisciplinary skills for young researchers. Through the establishment of expert advisory boards and committees with international experts, BRCs have elevated the international competitiveness of the partnering institutions in translational research. Research forums, new research roles for clinical staff, and the introduction of ICT systems have resulted in changes in research management and governance [3].

As an organisational structure, the BRCs and BRUs are illustrative of how the NIHR is creating an environment conducive to achieving clinical research excellence by bringing together academia and the NHS. In particular, the contractual set-up of BRCs has transformed relationships between the NHS and academia by bringing them closer together to work on translational research [3]. With respect to BRUs, an evaluation concluded that NHS and academic partners are collaborating more closely than they were before the establishment of these structures. The evaluation documented changes in attitudes and mind-

sets of the involved parties towards mutual collaboration, with more interest in taking research forward jointly [2].

The BRCs are considered by international observers as examples of good practice in promoting translational research, with particular strengths in the institutional set-up that fosters integrated working, reduces fragmentation of actors and offers access to population-level data [4]. One element that is credited to this success is the feedback and accountability to the NIHR, as the funder [4]. The BRCs and BRUs also allow for links between industry and academia. At the Oxford BRC, developing vital sign data fusion technology for the emergency department and the cancer centre was possible in collaboration with private actors. This technology is valued by the clinical staff [4], as it allows for continual monitoring of patients' vital signs and alerts staff to the deterioration in patients' conditions.

Another way in which these structures have strengthened relationships is by raising awareness among clinicians and academics of the mutual reliance and interdependence of their activities that link quality of research and the quality of patient care [3]. This was done by attracting a larger number of both clinicians and academics into these collaborative and translational research organisations [3]. The BRCs also foster more transparent and effective research management and governance structures, as academics are more engaged in NHS trust boards and committees [3]. BRCs have contributed to raising public awareness about translational research among the general public and have achieved better patient involvement through the use of patient advisory boards, information leaflets and research aimed at capturing patients' opinions about research [3]. In parallel, greater public participation in clinical trials has happened by engaging with other parts of the NIHR; namely, the NIHR Clinical Research Network.

BRCs enhance the relevance of research for patients and the NHS. For example, the application process required academic and NHS partners to jointly review their research portfolios and set priority themes for research, placing patients' needs at the centre of the applications [3]. Research from the BRCs provides examples of positive impact on patient care, as patients have increased access to novel treatments and technologies that would otherwise become available to them only after a significant delay. Furthermore, by providing access to data from health services research, the BRCs help to improve patient care. For example, research on infection conducted at the Oxford BRC has allowed the combination of actors to bring together samples from the hospital, access to clinical databases and molecular sequencing technology [4]. This research informed actions to cut the transmission of infections at hospital level and is developing new techniques and applications with potential long term economic impact.

Finally, BRCs are also thought to have contributed to an increase in the status and importance of research in the NHS. This can be seen in the enhancement of interdisciplinary translational research through collaboration with university departments beyond medical schools. Moreover, the BRCs and BRUs contribute to overall academic productivity through their publication activity. Year on year, there has been an increase in the publications produced, with nearly 8,000 publications from BRCs and BRUs in 2014-15 demonstrating active dissemination of their research to the international community.

Overall, the NIHR BRCs and BRUs are engaging academia, clinicians and patients through translational research partnerships that help produce world-class outputs [1]. This scientific endeavour translates into benefits not only for patients but also in terms of economic engagements as a result of pairing academic talent with industry's scale-up and commercialisation capabilities.

## Evidence

[1] NIHR 2016. Biomedical Research Centres. As of 07 April 2016:

<http://www.nihr.ac.uk/about/biomedical-research-centres.htm>

Webpage describing Biomedical Research Centres.

[2] Marjanovic, S., Soper B, Ismail S., Reding A., Ling T.. Changing the translational research landscape: A review of the impacts of Biomedical Research Units in England. Santa Monica, CA: RAND Corporation, 2009. [http://www.rand.org/pubs/technical\\_reports/TR798.html](http://www.rand.org/pubs/technical_reports/TR798.html)

The report describes a review of the BRU scheme by conducting a perceptions audit of senior executives involved in the scheme. The review explored what impact these executives felt the scheme is having on the translational research landscape.

[3] Marjanovic, S, Soper B., Shehabi A., Claire C., Reding A. and Ling T. 2009. Changing the translational research landscape: A review of the impacts of Biomedical Research Centres in England. Santa Monica, CA: RAND Corporation. [http://www.rand.org/pubs/technical\\_reports/TR787.html](http://www.rand.org/pubs/technical_reports/TR787.html)

The report represents a review of the BRC scheme, undertaken by RAND Europe and commissioned by the DH 18 months after the BRCs were established. The review consists of a perceptions audit of senior executives involved in the scheme.

[4] Hinrichs S., Henham M-L., Jeffries R., Grisaffi T., Van Stolk C. 2013 Assessing the value of NIHR Biomedical Research Centres. RAND Europe. (Unpublished report).

The report investigates the returns and outputs that three BRCs have produced in order to assess the value of funding NIHR BRCs. The study had two approaches: (1) case studies of individual NIHR BRCs and (2) international benchmarking of NIHR BRCs against comparable international centres for translational research.

### 9.1.10. *Managing a shared knowledge resource: the case of the Journals Library and BioResource*

#### Case study

The NIHR's research systems and resources, and research infrastructure in the NHS helps to connect researchers with the world-class data or participants required to conduct groundbreaking research. As one component of this, the NIHR BioResource helps to match researchers to volunteers who meet the criteria for participation in their studies. Another resource is the NIHR Journals library which provides researchers throughout the global system, and also the public, to access the outputs of the NIHR-funded research.

A report prepared for the Minister for Universities and Science describes open access to journals as 'a public benefit which enhances transparency, scientific integrity and rigour, stimulates innovation, promotes public engagement, and improves efficiency in research' [1]. The work towards open access to NIHR research outputs began in 1997 with the first publication of the journal *Health Technology Assessment*, which constitutes a record of 98 per cent of research published under the Health Technology Assessment (HTA) programme [2]. Following the success of the HTA journal, the model has been

extended with research outputs from four more NIHR research programmes, the Efficacy and Mechanism Evaluation, Health Services and Delivery Research, Programme Grants for Applied Research and Public Health Research programmes now with journals of their own as part of the NIHR Journals Library.

The peer reviewed reports held in the Library, which is the first of its kind to be established by a health research funder, present detailed information on the research project, and are designed to complement articles in other peer-reviewed journals, which typically contain much less information. The rate of publication has continued to increase since the library's inception. In total 165 issues were published in 2015, including 97 issues in the *Health Technology Assessment* series alone. The Journals Library's value as a relevant and interactive database, and not simply a repository of past research, is illustrated by usage figures: in 2015, the website received 260,000 visits. The average number of citations per article published in *Health Technology Assessment* over a two-year period has also increased from 1,443 in 1999 to 4,106 in 2015 [3]. Though this citation count in itself is cannot be used as a formal metric of scientific impact, it does tell us that that the articles in the journal are being used and cited by other researchers in the field.

In addition to providing access to existing data, the NIHR's efforts help to drive the generation of new data where it is most needed. The NIHR BioResource aims to support recruitment for early translational research (experimental medicine) studies by creating a panel of volunteers who are willing to be recalled by genotype and phenotype. The initiative began with the Cambridge BioResource, which was established in 2006, and it has since been expanded to include a further seven centres throughout England, all based around existing NIHR Biomedical Research Centres (BRCs) and Biomedical Research Units (BRUs). Each BioResource has a different focus corresponding with the research at the corresponding BRC or BRU. For example, the South London and Maudsley (SLAM) BioResource for Mental Health has a focus on research into psychiatry and neurology. To date, 75,000 volunteers have signed up to the BioResource [4].

The BioResource has proved valuable a basis for studies that further scientific knowledge and advance translational research. For example, the HaemAtlas project used blood from donors recruited through the Cambridge BioResource to advance understanding of hematopoiesis, the process through which blood cellular components are formed [5]. The blood obtained from the BioResource participants has enabled the HaemAtlas team to perform 'the most comprehensive analysis of gene expression in hematopoietic cells to date' [5], which led to the identification of genes that help to determine lineage commitment and cell function. The HaemAtlas team has stated that the data produced by the study 'will be invaluable for future studies on hematopoiesis and the role of specific genes and will also aid the understanding of the recent genome-wide association studies' [5]. The BioResource has also been acknowledged for its contribution to studies published in high-impact journals including *Nature* and *Cell* [6][7].

By connecting researchers to the people who can provide samples for research studies, the NIHR's investment in providing an available resource to advance knowledge and research is helping to lay the foundations for future innovation and thus ensuring the UK's continued leadership in health research.

## Evidence

[1] Tickell A. 2016. Open access to research publications: Independent advice. [Advice to the Minister for Universities and Science.] As of 9 May 2016:

[https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/499455/ind-16-3-open-access-report.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/499455/ind-16-3-open-access-report.pdf)

Document on open access to research publications.

[2] National Institute for Health Research. n.d. About the NIHR Journals Library.

As of 9 May 2016: <http://www.journalslibrary.nihr.ac.uk/about>

Webpage describing the NIHR Journals Library

[3] SCImago Journal & Country Rank (homepage). n.d. As of 9 May 2016: <http://www.scimagojr.com/>  
Data from SCImago.

[4] National Institute for Health Research. 2015. The NIHR BioResource. As of 9 May 2016:  
<http://www.nihr.ac.uk/policy-and-standards/the-nihr-bioresource.htm>

This webpage describes the NIHR BioResource.

[5] Watkins N, Gusnanto A, De Bono B, De S, Miranda-Saavedra D, Hardie D, Angenent W, Attwood A, Ellis P, Erber W, Foad N, Garner S, Isacke C, Jolley J, Koch K, Macaulay I, Morley S, Rendon A, Rice K, Taylor N, Thijssen-Timmer D, Tijssen M, Van der Schoot CE, Wernisch L, Winzer T, Dudbridge F, Buckley CD, Langford C, Teichmann S, Göttgens B, Ouwehand W. 2009. A HaemAtlas: Characterizing gene expression in differentiated human blood cells. *Blood* 113 (9): e1-9. doi: 10.1182/blood-2008-06-162958

Journal article on HaemAtlas featuring in *Blood*.

[6] Hunt KA, Mistry V, Bockett NA, Ahmad T, Ban M, Barker JN, Barrett JC, Blackburn H, Brand O, Burren O, Capon F, Compston A, Gough SC, Jostins L, Kong Y, Lee JC, Lek M, MacArthur DG, Mansfield JC, Mathew CG, Mein CA, Mirza M, Nutland S, Onengut-Gumuscu S, Papouli E, Parkes M, Rich SS, Sawcer S, Satsangi J, Simmonds MJ, Trembath RC, Walker NM, Wozniak E, Todd JA, Simpson MA, Plagnol V, van Heel DA. 2013. Negligible impact of rare autoimmune-locus coding-region variants on missing heritability. *Nature* 498 (7453): 232-5. doi: 10.1038/nature12170

Journal article featuring the Cambridge BioResource in *Nature*.

[7] Lee JC, Espéli M, Anderson CA, Linterman MA, Pocock JM, Williams NJ, Roberts R, Viatte S, Fu B, Peshu N, Hien TT, Phu NH, Wesley E, Edwards C, Ahmad T, Mansfield JC, Geary R, Dunstan S, Williams TN, Barton A, Vinuesa CG; UK IBD Genetics Consortium, Parkes M, Lyons PA, Smith KG. 2013. Human SNP links differential outcomes in inflammatory and infectious disease to a FOXO3-regulated pathway. *Cell* 155 (1): 57-69. doi: 10.1016/j.cell.2013.08.034

Journal article featuring the Cambridge BioResource in *Cell*



## 10. Supporting, training and developing a diverse workforce in the NHS and academia

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### 10.1. Summary

**Skilled. Motivated. Diverse.**

*NIHR supports training and development opportunities to develop a diverse workforce and to embed the practice and mindset of clinical research throughout the NHS and academia.*

In order to achieve clinical research excellence, research teams must possess technical knowledge and be skilled in working together to overcome difficulties, spark new ideas and inspire other researchers. NIHR is training a highly skilled workforce and developing and retaining the best clinical, health service and public health research professionals. It is also enabling leading clinicians to embark on, and successfully develop, their academic careers while continuing their clinical training.

NIHR supports more than 5,000 trainees through a range of NIHR research funding or training awards. This comprehensive range of research training opportunities includes the prestigious Fellowship Programme and the academic career pathway for doctors and dentists. These and other NIHR training programmes support people at an individual level to realise their full personal skills and potential. By offering multiple fellowships and career development awards, NIHR creates follow-on funding opportunities that enable NIHR clinical researchers to follow a sustainable career path and build a research portfolio. This research is also likely to benefit the wider health and social care landscape, both nationally and internationally. For example:

- Between 2006 and March 2015, NIHR funded 165 Doctoral Research and Clinical Doctoral Research Fellows in England. These fellowships have had a demonstrable impact on individuals' careers and have created a skilled research and clinical academic workforce in both medical and non-medical professions.
- NIHR is giving 27 NIHR Research Professors the unique opportunity to conduct clinical research which can, and is, moving from 'bench to bedside' and from 'campus to clinic' by translating research into benefits for patients, healthcare and society.
- Through its Leadership Programme, NIHR is supporting researchers throughout NIHR to become efficient and effective managers and leaders, in order to help improve the way research is conducted within organisations and at the system level.

- NIHR has developed a massive open online course ('MOOC'), in partnership with the Digital Learning Team at the University of Leeds, which was taken by 8,845 people from more than 80 countries worldwide.

A well-trained research team is a foundation for delivering high-quality research outputs. NIHR offers health professionals support to develop research skills and gives them protected time to conduct research alongside their clinical duties. This provides more flexibility and choice for individuals to determine career pathways that span both clinical and research roles. The following efforts are helping to embed research and its findings into the health system:

NIHR's Mentorship for Health Research Scheme supports allied health professionals, healthcare scientists, nurses and midwives in their professional development, helping them to gain valuable skills in clinical research.

- Since 2006, the Integrated Academic Training (IAT) pathway has provided research training for more than 2,000 doctors and dentists. This spans the Academic Clinical Fellowships (early-career research during specialist training) to the intermediate NIHR Clinician Scientist awards. Many Clinician Scientists continue to progress on the clinical academic pathway; pursuing joint academic and research careers.
- NIHR is supporting a new training programme for carers of people suffering from anorexia nervosa, which has now been taken up by the two largest eating disorder charities in the UK. The programme is also recommended by the USA-based international charity FEAST and forms the basis of both NHS and international services, including those in the USA and Australia.

#### *10.1.1. Investing in research talent in the NIHR faculty: evidence from the NIHR leadership programme*

##### Case study

The NIHR's continuous commitment to foster high-quality research that would benefit the UK population relies on high-performing research teams. Well-functioning teams require good leadership. Academic and clinical leadership pose different challenges when compared with other private or public sector organisations, and therefore there is a need for programmes tailored specifically for research and healthcare settings.

To address this gap, the NIHR has developed and funded the NIHR Leadership Programme. Launched in 2009, the programme is a collaboration among the NIHR, the NHS and Ashridge Business School [1]. It is designed to benefit clinical research in NHS England and contribute towards to the nation's 'health and wealth' [1]. It aims to build leadership skills in the NIHR faculty at junior to senior levels [2]. The impacts of the programme span benefits to UK individual researchers and their teams, institutional benefits of improved leadership and systems benefits in strengthening relationships across the NIHR community.

The programme helps participants gain leadership skills that improve their work. A pair of independent evaluations by RAND Europe found that participants noticed an increase in confidence building and approaches to leadership, which also benefits their training and development. In terms of research

performance, senior leaders felt they had improved by being able to overcome challenges individually and as a team, and in approaching the role more creatively and innovatively [3]. Other groups reported similar results, attributing an ability to build self-confidence as a result of the leadership programme [3]. Some reported greater levels of productivity as a researcher, and trainees specifically developed skills in financial and physical resources management [4].

By developing skills which aided the participants' professional development and decision-making and the implementation of efficient processes within their work places [3] the programme has also benefited organisations as a whole [4]. Among other examples, participants in the programme have reported improvements in an ability to respond to structural change within organisations and translational research capacity strengthening within their networks.

The benefits of the NIHR Leadership Programme can be interpreted at a wider scale. Participants' ability to better express their team's objectives to wider and different audiences as well as the interaction with R&D Managers within NHS Trusts suggest a greater engagement between researchers at different levels and across disciplines [3]. Other benefits at a system level included strengthened relationships within the NIHR community as a whole, which could lead to a more sustainable NIHR. In particular, participants across the programme reported that the programme allowed them to strengthen pre-existing relationships or build new ones. Senior leaders in particular commented on the positive effect this had on pursuing more collaborative opportunities with all researchers in the system, even those who might be competitors on grant applications.

The NIHR leadership programme is also credited with having enabled participants to scope new or strategic research areas across the NIHR, such as those supported by the Strategic Collaborations Initiative. The Leadership Programme was seen as critical in providing the time and support for people to raise awareness of cross-cutting, strategic issues for the NIHR. In addition, many reported improved cooperation between the NIHR and NHS [4], one of the main objectives of introducing a component of the leadership programme which addressed NHS R&D managers.

On the whole, the NIHR Leadership Programme has enabled individuals to grow and develop as researchers. It has not only been positively evaluated, but it has also recognised internationally. In 2015, the programme was recognised by a European Foundation for Management Development Excellence in Practice Gold Award for 'Faster and Easier Clinical Research: Developing a Thriving National Community of NHS R&D Directors and Managers' under Organisational Development [5]. By understanding the wider impact and implications of their role in healthcare research, the participants will contribute to better research both within their organisations and across the NIHR community.

## Evidence

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Webpage explaining the NIHR Leadership Programme.

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List of winners of European Foundation for Management Development awards.

### 10.1.2. *Mentoring the next generation of health researchers*

#### Case study

Achieving academic excellence, demonstrated through research impacts that advance the health of the nation, is central to the NIHR's mission. To achieve this, it is essential to have well-trained research teams that not only possess technical knowledge, but also work together to overcome difficulties, spark new ideas and inspire other researchers. The NIHR has invested in developing such a workforce. One example is the NIHR Mentorship for Health Research scheme. Established in 2012, the scheme is designed to support and accompany allied health professionals and healthcare scientists, nurses, and midwives in their professional development [1], with the overall aim of supporting UK's 'next generation of clinical academic leaders' [2]. This programme's impact has been measured primarily at the individual level where it has proven beneficial. It is expected that, in time, these benefits will be seen at a sector level, as these researchers will benefit organisations and the entire research and health care system across the country.

The scheme consists of pairing Health Research Training Fellows with a relevant individual who is a recognised leader in a given field, and can act as a mentor. Once fellows and mentors have been matched, mentoring activities take place through face-to-face and/or online interaction [2]. The scheme therefore intends to act as a catalyst for establishing a community of mentorship practice in clinical academic careers.

In the long run, the mentorship programme aims to create a culture of sharing ideas and continuous learning that will advance knowledge. Given that the scheme is in its first few years, an assessment of the

wider organisational and system-level impacts is not yet available. However there is evidence that the scheme is beneficial at an individual level. An evaluation conducted by the University of Huddersfield, covering year 1 of the mentorship scheme found that participants both mentees and mentors looked favourably on the scheme and reported a range of benefits from taking part in it. The evaluators analysed applications to the scheme to understand applicants' expectations, and conducted an online survey and semi-structured interviews.

They found that mentorship scheme had an impact on individuals in their approach to work and their professional development. In particular, the mentees felt they have had developed a series of skills that would help them advance their professional career and help them deliver high quality research. By being able to talk about professional issues and their development with their mentor, as well as by improving their networking skills, many mentees stated that they were able to achieve their personal goals [3]. Furthermore, the scheme benefited the participants' approach to research by improving their learning capacities and their approach to understanding research purpose and related tasks, including the dissemination of findings. The scheme also helped bolster personal traits in mentees who felt they had grown more confident and resilient to the challenges that often come with research, for example winning research grants and getting published.

The scheme was also beneficial for the mentors who reported that they found value in being able to support their mentee and to watch their mentee's development. This evaluation finding highlights an important benefit of the scheme, which is that it brings value to both parties involved.

The evaluation of the mentorship scheme shows how NIHR funding is supporting the development of future clinical leaders who are expected to produce high-quality research. The scheme's demonstrated success at the individual level could also result in wider organisational and system benefits as these individuals become leaders in the system. Some mentees have expressed interest in becoming mentors, thereby [3] broadening the benefit they received to the clinical academic community. The changes observed in individuals show that the Mentorship scheme has had value in terms of training and teaching, and in terms of research through helping to forge future clinical academic leaders.

## Evidence

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### 10.1.3. *Forming a community of clinical research nurses*

#### Case study

Clinical research nurses are an integral part of the research team working on research studies, and engaging with patients, through recruitment, follow-up and collection of data. There are approximately 4,000 NIHR Clinical Research Nurses who assist in conducting valuable research [1]. In order to help build a coherent and valuable community of Clinical Research Nurses, the NIHR has outlined a Competency Framework for Clinical Research Nurses in 2011 [2], and provides training and development opportunities at the local level that better prepares these nurse to deliver high-quality patient care. A number of strategic priorities were also created which aim to help nurses to develop professionally, known as the 6Cs (communication, compassion, care, courage, competence and commitment). These efforts have led to the development of a range of skills for nurses which have better prepared them to deliver high quality patient care, as well as deliver improvements to policy and practice.

The NIHR's support has resulted in a policy change, as represented by the introduction of the Competency Framework for Clinical Research Nurses [2]. This framework facilitated the adoption of relevant competences for nurses which reflect the challenges and opportunities of clinical research in the UK and set out the ethical and legal requirements that accompany these activities in order to conduct studies that meet desired standards of quality and safety.

The development of the 6Cs nursing strategy has further contributed to shaping the role of a Clinical Research Nurse. These 6Cs are intrinsic to the work of a Clinical Research Nurse. They require that individuals be capable of challenging and highlighting wrongdoing and willing to incorporate the research results into their practice [3].

These policy instruments have shaped training that benefits Clinical Research Nurses, enabling them to deliver better health care. For example, the Norfolk and Suffolk Comprehensive Local Research Network commissioned an Advanced Research in Practice course which was tailored around the 2011 Research Nurse Competency Framework and followed a survey that identified few training and career development opportunities in the research practitioner workforce. The course, run in 2011 and 2013, provided opportunities for individuals to practice presentation skills and to become better informed on the conduct of clinical research [3].

The Cambridge NIHR/Wellcome Trust Clinical Research Facility also provides training for Clinical Research Nurses. Here clinical nurses at the site are required to do one day of Emergency Scenario Simulation Training per year and staff have reported increased confidence in their approach to emergency situations as a result [4].

Clinical Research Nurses' abilities have also been recognised by the patients, for example at the NIHR Southampton Biomedical Research Unit (now Centre) in Nutrition, Diet and Lifestyle. In a longitudinal study of children with Crohn's disease, conducted between December 2010 and April 2013, the nurses were recognised for their calmness, mutual respect, being approachable supportive knowledgeable listeners; and their ability to integrate research into clinical care [4].

The wide range of skills developed by the Clinical Research Nurses was captured in an NIHR publication highlighting a number of successful Clinical Research Nurses. The interviewees stated that, through their role, they were able to help build local research, change research cultures, further develop a specific set of skills that a research nurse needs, develop research management abilities, better foster patient and public involvement, inform the public and support primary care [4]. For example, one nurse moving from industry to the NIHR praised many aspects of the role, including working with patients, having autonomy, and having opportunities for career advancement. In addition, as a Cancer Research Network Good Clinical Practice facilitator she is part of a team that has trained 30,000 individuals across the Comprehensive Local Research Network, and she felt there had been a positive shift in the standing of research in her areas over time [5].

The NIHR commitment to support a community of Clinical Research Nurses can also be seen in efforts to encourage communication in the Clinical Research Nurses community. Examples include the use of social media (#CRNurses on Twitter), through a monthly newsletter, CONNECT; and 'Celebrating the Clinical Research Nurse' meetings [6].

## Evidence

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[3] National Institute for Health Research Clinical Research Network. n.d. 6Cs Live! London: NIHR. As of 2 May 2016: <http://www.nihr.ac.uk/documents/faculty/6Cs%20Flyer.pdf>

[4] National Institute for Health Research. n.d. Our work: Celebrating the Clinical Research Nurse 2014. London: NIHR. As of 2 May 2016: <https://www.crn.nihr.ac.uk/wp-content/uploads/Healthcare%20professionals/CCRN%202014%20Our%20Work%20Final.pdf>

[5] National Institute for Health Research. n.d. Our voices: Celebrating the Clinical Research Nurse. London: NIHR. As of 2 May 2016: <http://www.nihr.ac.uk/documents/faculty/Nurses%20Voices%202014%20V2.pdf>

[6] National Institute for Health Research. n.d. Clinical Research Nurses. As of 2 May 2016: <http://www.nihr.ac.uk/our-faculty/clinical-research-nurses.htm>

#### 10.1.4. *Cultivating tomorrow's health research capacity by funding doctoral research*

##### Case study

The NIHR provides PhD positions for promising medical and non-medical healthcare professionals through two award schemes: the Doctoral Research Fellowship (DRF) and the Clinical Doctoral Research Fellowship (CDRF). These fellowships have supported early-stage clinical researchers in entering into, and for the most part, remaining in combined academic and clinical settings, thereby contributing to a strengthened clinical research capability across the health service.

The DRF awards successful applicants with three years of funding (or four to five years if they pursue their PhD part-time). The CDRF is suitable for applicants who have at least one year's experience in clinical practice in a non-medical profession who are interested in pursuing research. Fellows are awarded with salary costs, in addition to their PhD tuition fees and their research project costs [1].

In 2015, the NIHR Trainees Coordinating Centre (TCC) invited 165 previous NIHR Doctoral Research Fellows and Clinical Doctoral Research Fellows who were awarded and completed their fellowship between 2006 and March 2015 to report on their career pathway since receiving the fellowship. Eighty individuals responded and the information gathered illustrates their career paths [2].

The NIHR TCC found that funded fellowships feed into the academic and healthcare landscape with the majority of respondents working in academia, and one quarter working in the health/healthcare sector. By far, the largest proportion of respondents work in an academic role as a (senior) research associate or as a (senior) lecturer [2]. Over half of the respondents direct or lead a research team, and over a third reported having supervised PhD candidates, suggesting that they are designing, directing and guiding research in their area of expertise [2]. Furthermore, since completing their PhD nearly half of those surveyed had been successful as the lead applicant on one or more competitive grants or awards [2]. The overwhelming majority of respondents remain working in England, showing that the NIHR has invested in researchers who are using their skills to further research and help train future healthcare workers in the nation [2].

In terms of individual-level impacts, almost all respondents stated that they use the knowledge and skills gained as a result of their NIHR DRF/CDRF in their current role. These findings show, at least in part, that the fellowships have contributed to building a cohort of skilled researchers feeding in to the healthcare research landscape and having some impact on treatment and patient care [2].

There is an expectation that the research undertaken by all funded fellowships has a benefit to patients and the broader public within five years of the end of award. The examples below are just two ways in which doctoral research fellows are meeting this expectation.

Dr Kyla Thomas is currently an NIHR Clinical Lecturer having completed her NIHR DRF in December 2013 [3]. Dr Thomas' work as a Doctoral Research Fellow focused on Varenicline, a smoking cessation medicine, and its neuropsychiatric side effects [3]. This work was undertaken using the NIHR funded Clinical Practice Research Datalink and a systematic review of randomised controlled trials in order to assess the risks and benefits of the drug [3]. The study found that the drug was not linked with an increased risk of death or serious neuropsychiatric illnesses such as depression, suicide attempt and



suicidal ideation. In fact, its benefits in reducing smoking had knock-on effects on users' levels of anxiety as they quit smoking [4]. Dr Thomas stated that the reduction in prescription of Varenicline on the basis of unproven neuropsychiatric effects is cause for concern and must be taken seriously by policymakers given the drug's success in enabling people to quit smoking [4]. The research was one of several studies considered by the Food and Drug Administration in the United States in its safety review of Varenicline in October 2014 which resulted in updates to Varenicline's label [5]. Pfizer, the manufacturer of Varenicline, has recently published results of a large RCT of 8,144 smokers in 16 countries. This study provides further evidence for the efficacy and safety of Varenicline compared with other smoking cessation drugs [6].

Dr Sonia Saxena is currently an NIHR Career Development Fellow, having previously completed an NIHR DRF and NIHR Postdoctoral Fellowship [3]. Dr Saxena is a GP who leads research in the Child Health Unit at Imperial College, London [3]. Her research showed children whose GPs are easy to access are less likely to visit A&E than those whose GPs are less able to provide appointments [7]. The study published in the journal *Pediatrics* suggested that modest changes in the provision of GP appointments – such as providing more after-school appointments between the times of 5-7pm – could prevent thousands of visits to emergency departments a year and was widely covered in news and social media [8][9]. The paper was cited in written evidence to the recent Health Select Committee's enquiry into proposed 7 day working reforms in primary care [10].

Over 300 NIHR funded Doctoral Research and Clinical Doctoral Research fellowships have been awarded since 2006. These fellowships have had a demonstrable impact on individuals' careers and provided the English academic and healthcare landscape with a skilled research and clinical academic workforce, in both medical and non-medical professions.

## Evidence

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Journal article on the neuropsychiatric safety of pharmaceutical products.

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[http://www.eurekalert.org/pub\\_releases/2016-01/icl-eat011916.php](http://www.eurekalert.org/pub_releases/2016-01/icl-eat011916.php)

News article on Dr. Sonia Saxena's work.

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News item on the release of the Health Select Committee report on Primary Care.

### *10.1.5. Building a research ready workforce: Good Clinical Practice training*

#### **Case study**

Good Clinical Practice (GCP) training is a requirement of the Research Governance Framework for Health and Social Care (2005) and regulations around the conduct of clinical trials for anyone seeking to conduct clinical research [1]. GCP is the 'international ethical, scientific and practical standard' [1] for clinical research. Training is delivered through the NIHR Clinical Research Network (CRN) [1], and a strong partnership with Medicines and Healthcare Products Regulatory Agency. The GCP has demonstrated its value at an individual level, in the workforce and abroad.

GCP training is provided either face-to-face or online for research in a variety of settings, including primary, secondary, and paediatric care. There is also GCP for the management of investigational

medicinal products and for Adults Lacking Capacity [2]. GCP is designed to help deliver robust research outcomes that ultimately impact on the patient, through ensuring that good data are collected and that people are recruited into studies.

Since 2009, more than 109,000 individuals have followed the GCP training. Owing to the increase in research activities which require GCP-trained staff, demand for GCP training has also increased in recent years. Between 2009 and 2013, approximately 30,000 individuals accessed the training [3]. However, in the 2015-16 financial year, approximately 24,917 individuals followed the e-learning version of the training [1]. This steady stream of individuals following GCP training ensures that there is an available workforce to undertake research. As a result, this centralised provision provides better value for public money, according to an interviewee from the CRN.

At an individual level, the GCP allows researchers to reflect on the clinical research process, understanding how and why data have been collected which is a key benefit to the individual. The GCP also harmonises the language used among clinical researchers enabling informed conversations about their approach and good practice towards research locally. In addition, the face-to-face training provides clinical researchers with an opportunity to network, something that is not always possible given the nature of their work. Individuals commented that the training was an 'extremely educative programme' bringing the user 'up-to-date with GCP' and that it was 'practical and thought provoking' [3].

The NIHR GCP training model has also been adopted abroad, and the CRN delivers it to the Peter MacCallum Cancer Centre (PMCC) in Australia. The PMCC was 'keen...to embed this programme within [its] research culture' and as of 2014, 10 per cent of the PMCC staff had received GCP training [3]. The former PMCC Head of the Clinical Trials Unit commented that '[s]taff who have had the training have an enhanced understanding of the central importance of GCP' and that the NIHR GCP training model has made a 'significant change' to the PMCC [4].

Without GCP training, clinical research would not be able to happen in the UK. However, aside from fulfilling a legal requirement, GCP training seems to offer some benefits to individuals and, as a model, has affected clinical research training abroad.

## Evidence

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[3] National Institute for Health Research Clinical Research Network. 2013. Good Clinical Practice. London: NIHR.

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[4] National Institute for Health Research. 2014. NIHR Clinical Research Network Good Clinical Practice model goes global. As of 12 May 2016: <https://www.crn.nihr.ac.uk/blog/news/nihr-clinical-research-network-good-clinical-practice-model-goes-global/>

### 10.1.6. *Honing the skills of non-professional carers of people with eating disorders*

#### Case study

It is estimated that 725,000 people in the United Kingdom are affected by an eating disorder [1]. Young people are most likely to be affected by anorexia nervosa which is most likely to start occurring in people at the age of 16 or 17 [1], and bulimia, which is more common, is likely to occur in late adolescence at 18 or 19 years of age [1]. Eating disorders negatively impact on those close to sufferers. In the case of adolescents with an eating disorder, more often than not they are cared for by their parents, almost all of whom would like more information on how to help their children [2]. It is estimated that up to 30 per cent of carers experience ‘clinical levels of depression and anxiety’ which can compound sufferers’ stress and their feelings about their illness [2]. Supported by the NIHR, researchers at King’s College, London (KCL) investigated interventions to alleviate the negative emotional impact of eating disorders on sufferers and their carers. Results from the study have shown that reduced emotional expression in carers is effective in alleviating pro-anorexic beliefs among sufferers and their tendency towards emotional avoidance [2]. This has led to the adoption of training methods both in the UK and abroad which have demonstrated capacity for a beneficial impact on patient outcomes.

The NIHR funded some of the research through a Programme Grant for Applied Research (2007-2014) and Research for Patient Benefit funding (2011-2014), which were complemented by money from South London and Maudsley (SLAM) NHS Foundation Trust which specialises in mental health services [2][3]. The researchers developed three different training interventions: ‘The New Maudsley Method’, ‘Collaborative Care Skills Training’, and ‘Expert Carers Helping Others’ (ECHO) [2]. Studies examining the effects of the Collaborative Care Skills Training workshops showed that they helped to decrease carer burden and provided ‘valuable skills’ to carers [4]. Originally, this training intervention was developed in a series of six two-hour workshops which saw a great reduction in the number of carers reporting high levels of stress [2]. Other results included improvements among adult anorexia in patients whose carers became involved in their treatment [2]. Subsequently, given that workshops were not accessible to all, a ‘self-help intervention’ called ECHO, in the form of DVDs and a book, was developed [2], as well as a clinical handbook [2].

A randomised controlled trial (RCT) of the ECHO intervention revealed some beneficial impacts on patients. Six months following the intervention, inpatients showed ‘a small but sustained improvement in [...] quality of life and clinical symptoms’, with fewer ‘in-patient bed days’ in the subsequent six months [5]

These training interventions have been nationally and internationally recognised. First, NHS England’s 2013 Standard Contract for Specialised Eating Disorders makes specific reference to the use of the New Maudsley Method in the treatment of people with eating disorders [2][6]. Secondly, the South London

and Maudsley NHS Foundation Trust incorporates the New Maudsley Method into its service [7] and trains approximately 80 carers annually [2]. Third, both Beat and Succeed, two leading UK charities specialising in eating disorders, have adopted interventions as a result of this study, as have charities and services in the USA and Australia [2][8][9][10]. Finally, the study produced a book for carers, *A Skills-based Learning for Caring for a Loved One with an Eating Disorder: The New Maudsley Method*, which had sold roughly 16,000 copies as of July 2013 [2][11]. Another book detailing the interventions and aimed at clinicians, has received recommendations from a number of NHS services in England (Cambridgeshire, Oxford, and South Yorkshire) and in New York and St. Louis in the USA [2].

NIHR funding has contributed to important work in the field of eating disorders. The work has been recognised and promoted internationally, supported by eating disorder charities. Carers, who often felt ill-equipped to manage their loved one's eating disorder, were provided with an opportunity to learn to manage their emotions, better deal with their loved one's eating disorder and, in some cases, train other carers. As a result, in the year following carers' training, practical improvements have been observed in patients, showing signs that the intervention is having a positive impact.

## Evidence

[1] NHS Choices. n.d. Eating disorders. As of 2 May 2016: <http://www.nhs.uk/Conditions/eating-disorders/Pages/Introduction.aspx>

Webpage detailing eating disorders and how they can be treated.

[2] Research Excellence Framework. 2014. An evidence based skills training intervention for carers of people with eating disorders improves care. [Case study 41188.] As of 2 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=41188>

Research Excellence Framework case study on training for carers of people with eating disorders.

[3] South London and Maudsley NHS Foundation Trust. n.d. About us. As of 2 May 2016: <http://www.slam.nhs.uk/about-us>

Webpage describing the South London and Maudsley NHS Foundation Trust.

[4] Pépin G, King R. 2013. Collaborative Care Skills Training workshops: Helping carers cope with eating disorders from the UK to Australia. *Social Psychiatry and Psychiatric Epidemiology* 48 (5): 805-812. doi: 10.1007/s00127-012-0578-6

Journal article testing the transferability of the Collaborative Care Skills Training workshops from the UK to Australia.

[5] Hibbs R, Magill N, Goddard E, Rhind C, Raenker S, Macdonald P, Todd G, Arcelus J, Morgan J, Beecham J, Schmidt U, Landau S, Treasure J. 2015. Clinical effectiveness of a skills training intervention for caregivers in improving patient and caregiver health following in-patient treatment for severe anorexia nervosa: Pragmatic randomised controlled trial. *British Journal of Psychiatry Open* 1 (1): 56-66. doi: 10.1192/bjpo.bp.115.000273

Journal article testing the effect of training for carers of people with anorexia nervosa on care.

[6] NHS Commissioning Board. 2013. NHS Standard Contract for Specialised Eating Disorders (Adults). [C01/S/a.] London: SLAM. As of 2 May 2016: <https://www.england.nhs.uk/wp-content/uploads/2013/06/c01-spec-eat-dis.pdf>

Service specifications: NHS Standard Contract for Specialised Eating Disorders (Adults).

[7] South London and Maudsley NHS Foundation Trust. 2013. Eating Disorders Service: Outpatient, day care, inpatient and step up. London: SLAM. As of 2 May 2016: [http://www.national.slam.nhs.uk/wp-content/uploads/2014/09/EDU-Service-booklet\\_FINAL.pdf](http://www.national.slam.nhs.uk/wp-content/uploads/2014/09/EDU-Service-booklet_FINAL.pdf)

[8] Beat. n.d. Self help. As of 2 May 2016: <https://www.b-eat.co.uk/about-eating-disorders/help-and-treatment/self-help>

Webpage outlining resources for coping with eating disorders.

[9] Succeed Foundation. n.d. Skills for Carers. As of 2 May 2016: <http://www.succeedfoundation.org/work/skillsforcarers>

Webpage describing the Skills for Carers project.

[10] New Maudsley Approach. n.d. Profiles. As of 2 May 2016: [http://www.thenewmaudsleyapproach.co.uk/About\\_Us.php](http://www.thenewmaudsleyapproach.co.uk/About_Us.php)

Webpage providing profiles of key people working with the New Maudsley Approach.

[11] New Maudsley Approach. n.d. Recommended reading. As of 2 May 2016: [http://www.thenewmaudsleyapproach.co.uk/Recommended\\_Reading.php](http://www.thenewmaudsleyapproach.co.uk/Recommended_Reading.php)

List of publications from researchers on the New Maudsley Approach.

### 10.1.7. *Expanding understanding of clinical research through a massive open online course (MOOC)*

#### Case study

Conducting people-based research means there is a dual engagement of professionals, current and future, and the public, who should both be involved in research. The success of this engagement relies on obtaining an understanding of what research entails within the UK healthcare system. The NIHR is achieving this educational endeavour through a variety of training including online courses. These types of courses are important because they are free and available to anyone. The online courses are managing to reach wider audiences than just those in the academic and clinical settings and are therefore contributing to dissemination of knowledge on clinical research.

In 2015, the NIHR Clinical Research Network (CRN) launched its first ‘massive open online course’ (MOOC) in partnership with the Digital Learning team at the University of Leeds. This free online course called ‘Improving Healthcare through Clinical Research’ was developed on the FutureLearn platform [1]. The course explained why and how the NIHR is conducting research and how the process of discovery is used to improve healthcare [2]. This MOOC’s ultimate objective is to achieve a better understanding of the challenges and benefits of conducting clinical research among a wide community of learners [3]. In order to reach a wider number of learners, it was designed at an introductory level [3]. The

course used case studies to cover various topics such as the way research can be used to find new solutions to treat and provide care for some of the major diseases including cancer and dementia; the impact of clinical research; and the ethical questions raised by clinical research [2].

While only one edition of the course has been run, there are indications of the impact this training has had, in terms of dissemination of information through high course completion rates and satisfaction with the course as expressed by the diverse range of participants.

On its opening day, 7,000 people had already registered for the MOOC [2]. This number rose to 8,845 people upon completion of the course with participants from more than 80 countries including patients, the public and healthcare professionals [3]. Though enrolment was lower than a typical MOOC, the diverse distribution of participants is illustrative of the wide audience the MOOC attracted. The majority of participants (48%) were already working in clinical research in healthcare while 24 per cent did not have any previous knowledge about clinical research [3].

An important indication of the quality of a MOOC is its completion rate. Often a high number of people sign up to such courses but do not follow through to the end. The average rate of completion for a MOOC is less than 7 per cent [4]. The NIHR course registered 14 per cent (1,223 persons) of the participants who followed the course until the end and nearly one quarter (2,004 persons) who returned to the course more than once. This success is also recognised by Fiona O'Neill (head of Workforce and Learning at the NIHR Clinical Research Network), who found this number to demonstrate a high level of engagement compared with the usual participation rate of a MOOC [3]. The high level of engagement was also seen in the number of questions and comments posted on the platform by the learners [3].

Another important indication of the quality of the MOOC is the participants' satisfaction. Overall, the majority of participants who completed the post course evaluation were extremely satisfied with the quality of the course, giving a high indication of the course effectiveness and quality. Over 90 per cent of participants rated the experience of attending the course as good or excellent, having met or exceeded their expectations and willing to recommend it to a friend [3]. Furthermore the participants expressed different ways in which the MOOC was valuable to them. One benefit the participants expressed was the flexibility that comes with attending the MOOC, as participants are able to log in at times convenient for them and to choose how intensively they want to get engage in the course [5]. Importantly, several participants mentioned that attending the course gave them confidence to take part in research [6]. The idea that 'people don't do research to you, they can't do research without you' [6] resonates with the NIHR's commitment to involve patients and the public in research.

The MOOC is a particular example of how NIHR has managed to use internet platforms to reach a wider audience among which young people that are contemplating a career in research, clinicians, or patients. The course is a promising tool to engage with a wider audience of learners, complementing the traditional outlets of knowledge dissemination such as scientific journals, conferences and workshops. The course will be run again with the aim of improving professional development among healthcare professionals and bringing awareness on research to wider audience of learners.

## Evidence

[1] Future Learn. n.d. Improving healthcare through Clinical Research. As of 5 May 2016: <https://www.futurelearn.com/courses/clinical-research>

This page is the MOOC registration page. It explains what the participant is expected to learn, directs readers to previous learners' highlights and explains the accreditation system.

[2] Clinical Research Network. 2015. Over 7,000 people sign up to 'Improving healthcare through clinical research' online course launched today. As of 3 May 2016: <https://www.crn.nihr.ac.uk/news/mooc-improving-healthcare-through-clinical-research-launches-today/?h=34>

This announcement from the Clinical Research Network, dated 2 November 2015, presents the MOOC the day it was launched.

[3] O'Neill F. Improving Healthcare through Clinical Research: Evaluation Report.

This document presents the course and its objectives, gives participant statistics and cites findings from the pre- and post-course evaluations.

[4] Parr C. 2013. MOOC completion rates 'below 7%': Open online courses' cohort much less massive at finish line. Times Higher Education. [9 May 2013.] As of 2 May 2016: <https://www.timeshighereducation.com/news/mooc-completion-rates-below-7/2003710.article>

[5] Clinical Research Network. 2016. Clinical research: MOOC will help you discover all you need to know. As of 3 May 2016: <https://www.crn.nihr.ac.uk/blog/news/clinical-research-mooc-will-help-you-discover-all-you-need-to-know/>

This page from the Clinical Research Network, dated 11 March 2016, presents the new version of the MOOC to be launched in June 2016 and the questions it aims to answer.

[6] National Institute for Health Research. 2016. Massive open online course (MOOC) highlights. As of 3 May 2016: <https://www.youtube.com/watch?v=N0fWv68k63g>

This 4:18 minute video presents the patients learning from the MOOC.

### 10.1.8. *Enhancing research leadership through NIHR professorships*

#### Case study

The NIHR Research Professorships are prestigious awards which give early-stage academic researchers the opportunity to enhance their research leadership and translation skills over a period of five years [1]. The NIHR is currently the only institute in England that funds research professorship awards of this kind. Between 2011 and 2015, 165 individuals were nominated by their higher education institution-NHS partnership, and 27 individuals were awarded an NIHR Professorship [2]. Selected individuals are chosen based on their potential to become research leaders and will gain access to the NIHR Leadership Programme [3]. Furthermore, NIHR professors, in collaboration with their nominating institution, create a personal leadership and development programme and some serve on other NIHR personal awards panels [2]. Professors are relieved of their local and regional administrative and managerial roles in order



to devote time to research. Given the programme's focus on the translation of research, NIHR professors are expected to maintain links with health services [1]. Healthcare professionals spend two sessions per week 'delivering service', and non-healthcare professionals, such as methodologists, must collaborate with clinical services [1][2]. Overall, NIHR professors must be able to demonstrate that their research can impact on healthcare from 'bench to bedside [1]' and from 'campus to clinic' [1].

Overall, the NIHR Professorship Award represents a two-pronged approach. At an individual level, the award cultivates promising research talent. At a macro-level, it is expected that the research conducted during the professorship will translate into practice with benefits for patients, healthcare and society. These awards are granted to individuals on course towards becoming professors, demonstrating the potential to become research leaders in their respective fields within a few years [1]. Although, the first cohort of NIHR Professorships have not yet completed their five years, the examples below highlight the story of two individual awardees and how they have benefited from becoming NIHR Professors and the wider impacts of their work.

Professor Waljit Dhillon at Imperial College London has been recognised with NIHR training awards such as the NIHR Clinician Scientist (2004), the NIHR Career Development Fellowship (2009) and the NIHR Research Professorship (2015) [4]. Professor Dhillon's work through the NIHR Research Professorship award concentrates on the use of hormones in reproductive health [5]. Professor Dhillon has shown the benefits of using the hormone kisspeptin in practice to help with IVF treatment in order to make it more safe, and effective [5]. Funded by the NIHR, the Medical Research Council and the Wellcome Trust, Professor Dhillon and his research team conducted a trial which tested kisspeptin in women with polycystic ovary syndrome [6]. The results revealed that kisspeptin resulted in more live births and was safer than hCG, the hormone traditionally used in IVF [6]. As of November 2015, 30 babies had been born to women who underwent this treatment, demonstrating how this research has been used in practice [6].

Another awardee who has had impact through her work is Professor Nadine Foster, a physiotherapist at the Arthritis Research UK Primary Care Centre at Keele University [5]. Professor Foster received the NIHR Professorship of Musculoskeletal Health in Primary Care in 2012 to lead research on treatments and outcomes for primary care patients with common musculoskeletal pain such as low back pain and knee pain [5][7]. One of her studies, IMPaCT Back, (Implementation to improve Patient Care through Targeted treatment) has highlighted the benefits of stratified care, in which patients' risk of persistent pain and disability is identified (low, medium and high risk) and then patients are matched with different treatments [8]. In comparison to usual primary care, stratified care led to less back pain related disability and fewer days lost from work, which has a financial impact. On average, cost-benefit analyses show that UK society would save £400 per employed person through this course of action and that the NHS would save £34 per patient using stratified care. Furthermore, the screening tool used to subgroup patients (the STarT Back tool) has been implemented across many NHS services, and Professor Foster's team estimate that £700 million could be saved if stratified care is implemented widely in general practice [8]. Her work on back pain has led to two large further research studies, a new five year programme funded through an NIHR Programme Grant for Applied Research, developing and testing stratified care for patients with

other musculoskeletal pain problems, and a new randomised trial, funded by the NIHR HTA programme, to test a new stratified care approach for patients with sciatica in primary care.

These are but two examples of how NIHR Professors have the opportunity to conduct research that can, and has been, translated into healthcare practice. This investment in individuals has the capacity to transform current practice and improve innovation in healthcare treatments.

## Evidence

[1] National Institute for Health Research. 2015. NIHR Research Professorships. As of 9 May 2016: <http://www.nihr.ac.uk/funding/research-professorships.htm>

Webpage describing the NIHR Research Professorship.

[2] Information communicated by the NIHR.

[3] National Institute for Health Research. 2014. NIHR Research Professorships: Guidance notes round 5. London: NIHR. As of 14 May: <http://www.nihr.ac.uk/documents/funding/Training-Programmes/TCC-RP-R5-2014-Guidance-Notes.pdf>

Guidance notes for NIHR Research Professorships.

[4] Imperial College London. n.d. Professor Waljit Dhillon. As of 9 May 2016: <http://www.imperial.ac.uk/people/w.dhillon>

Professor Dhillon's university webpage.

[5] NIHR Trainees Coordinating Centre. 2015. Case Study Compilation. Internal document. [Unpublished.]

NIHR case studies highlighting some accomplishments of its alumni.

[6] Sayers M, Myers M. 2015. New fertility treatment developed at Imperial could make IVF safer for mothers. As of 9 May:

[http://www3.imperial.ac.uk/newsandeventspggrp/imperialcollege/newssummary/news\\_4-11-2015-14-35-27](http://www3.imperial.ac.uk/newsandeventspggrp/imperialcollege/newssummary/news_4-11-2015-14-35-27)

News item covering some of Professor Waljit Dhillon's work.

[7] Keele University. n.d. Prof Nadine Foster. As of 9 May 2016:

<https://www.keele.ac.uk/pchs/staff/professors/nadinefoster/>

Prof. Foster's university webpage.

[8] National Institute for Health Research. 2015. Growth through health research: The NIHR as an engine for growth. London: NIHR. As of 5 May 2016: <http://www.nihr.ac.uk/documents/about-NIHR/NIHR-Publications/NIHR%20Growth%20Through%20Health%20Research%20-%20Interactive%20Spreads%20March%202015.pdf>

This brochure outlines a number of the ways in which the NIHR's provision of people, programmes, infrastructure and systems are contributing to UK growth. It contains a variety of statistics on the increasing amounts of industrial collaboration with the NIHR, narrative descriptions of routes through which the NIHR provides support, and case studies of particular initiatives involving industry.

### *10.1.9. Thriving as a clinical researcher: Individuals and impact from NIHR funding awards*

#### Case study

The NIHR faculty includes each person funded by the NIHR and engaged in activities across academia, the NHS and the third sector in England. The NIHR is committed to building a diverse research community whose work translates into quality care. The faculty's main goal is to build research capacity through attracting the best talent, facilitating research which is best for the public and patients, and supporting the training and academic needs of health and social care professionals [1]. NIHR training opportunities and funding awards are available to those who have an initial interest in research, have decided to pursue formal research qualifications, or have a research background. The benefits of such funding are two-pronged: first, individuals benefit from the awards they receive by progressing their research careers and building a research portfolio; second, this research has an impact on the wider health and social care landscape, both nationally and internationally.

The NIHR Trainees Coordinating Centre (TCC) manages a variety of funding awards to drive the development of skills and facilitate the research career pathway for methodologists, non-medical healthcare professionals, doctors and dentists. Among these awards are the Academic Clinical Fellowship, the In-Practice Fellowship, the Doctoral Research Fellowship, the Clinician Scientist Award, the Clinical Trials Fellowship, the Career Development Fellowship, and the Post-Doctoral Fellowship. Both the Academic Clinical Fellowship and the In-Practice Fellowship are pre-doctoral awards which provide medical professionals with the opportunity to improve their research skills through academic training or dedicated research time [2][3]. The Doctoral Research Fellowship provides funding for individuals to follow a 'customised research training programme' in their doctoral research, allowing them to develop their research skills [4]. Both the Post-Doctoral Fellowship and the Career Development Fellowship provide opportunities to early-stage or experienced post-doctoral researchers, respectively, as well as full time funding for up to three years [4]. Individuals can follow a training programme through the Clinical Trials Fellowships, exposing them to all aspects of clinical trials and building upon their interest and existing experience [5]. Clinician Scientist Awards are personal funding grants, designed to cover the salary costs of an individual and fund his or her research project or programme by way of enabling his or her development [6]. As might be expected, much of the impact of these fellowships has been seen at an individual level in terms of career progression within the health and social care research community; however, some of the research has influenced decisionmaking in policy and practice.

NIHR fellowships have an impact on individuals' research career trajectory, as evidenced by two Career Development Fellows. Awarded an NIHR Career Development Fellowship in 2014 (administered through the Institute of Neuroscience at Newcastle University), Dr Anna Basu is also an Honorary Consultant Paediatric Neurologist at the Great North Children's Hospital, Newcastle-upon-Tyne [7][8]. Having completed her PhD in 2007, Dr Basu was awarded a NIHR recognised, locally-funded Clinical Lectureship in 2010 before receiving an NIHR Clinical Trials Fellowship in 2013 [8]. During this time she led a trial comparing two forms of home-based parent-delivered therapy for children with unilateral cerebral palsy [9]. Dr Basu's research currently focuses on developing and piloting a parent-delivered early

therapy intervention for infants who have had a perinatal stroke. Dr Basu has also been supported as a co-investigator with NIHR Health Technology Assessment funding to assess the acceptability of a trial to understand the efficacy of standing frames for children's postural management [7]. Dr Carsten Flohr was the first dermatologist to hold an NIHR Clinician Scientist Award, followed by an NIHR Clinical Trials Fellowship and now an NIHR Career Development Award [10]. Dr Flohr participated in the NIHR Leadership Programme, has acted as a member of the Doctoral Research Fellowship Panel and is now on the Postdoctoral Fellowship Panel [7]. During his time as an NIHR Clinical Trials Fellow, he developed experience in trial design and the protocols for two multi-centre randomised controlled trials. Dr Flohr is now Head of the Unit for Population-Based Dermatology Research at St John's Institute of Dermatology, King's College London, where he leads a programme of research focused on childhood atopic eczema, including clinical trials. These studies are likely to have an impact on clinical practice both domestically and abroad [7].

Some healthcare professionals, such as Dr Jess Drinkwater, have received funding for initial research training, alongside clinical duties, that led to pursuing formal research qualifications. Since 2009, Dr Drinkwater has received three NIHR fellowships: an Academic Clinical Fellowship, an In-Practice Fellowship and a Doctoral Research Fellowship. Dr Drinkwater's research as an In-Practice Fellow investigated the role of patient and public involvement in service improvement in primary care [7]. After presenting her findings she was approached to work for her local Clinical Commissioning Group (CCG) to develop their engagement strategy. She co-wrote the engagement strategy (worth £200 000) and helped to deliver local training for patients and general practice staff on patient involvement. Both were directly influenced by the findings from her In-Practice Fellowship research. Dr Drinkwater and the CCG are now implementing the engagement strategy and hope it will lead to more patient-centred commissioning, ultimately resulting in improved patient experience across all health services for the people of Bradford. Dr Drinkwater's research as an In-Practice Fellow formed the foundations of her application for a Doctoral Research Fellowship. During this next fellowship she is working with multiple stakeholders to develop an intervention to strengthen the role of patient participation in service improvement in general practice [7]. Another researcher, Dr Hannah Christensen, a previous NIHR Post-Doctoral Fellow, completed her NIHR Research Development Award-funded PhD in 2007. As a post-doctorate researcher, Dr Christensen worked on an NIHR Programme Grant study called TARGET which investigated how to improve the quality of care given to children presenting to primary care with respiratory tract infections. Following this, Dr Christensen was awarded the NIHR post-doctoral research fellowship examining interventions for infectious disease control [7]. In parallel, Dr Christensen is a member of the NIHR Health Protection Research Unit [7]. In 2015, Dr Christensen's research findings in cost-effectiveness informed the Joint Committee on Vaccination and Immunisation's decision to roll out the Meningitis B vaccination in the childhood vaccination programme [7].

Other researchers have used NIHR funding to further an existing research career and have generated findings informing healthcare practice both nationally and internationally. Dr Morag Farquhar holds an NIHR Career Development Fellowship (CDF), and her work has helped to influence the development and evaluation of interventions across the Atlantic. Dr Farquhar's CDF, alongside funding from the charity Marie Curie, has afforded her the opportunity to lead the Living with Breathlessness study. The

purpose of this research is to improve care and support for both patients with advanced chronic obstructive pulmonary disease (COPD) and their carers. Alongside a Macmillan Post-Doctoral Research Fellowship, Dr Farquhar received an NIHR Research for Patient Benefit Award, to conduct research into breathlessness in advanced disease. Dr Farquhar's work in evaluating the Cambridge Breathlessness Intervention Service (BIS) has received national and international interest, from Australia and Canada in particular. In Canada, 'INSPIRED', an intervention for patients with advanced COPD, was modelled on the Breathlessness Intervention Service: 15 teams are rolling out INSPIRED pilots across the country, supported by the Canadian Foundation for Healthcare Improvement [7].

These are just a few examples of how the NIHR is funding individuals who are training for, conducting and evaluating ground-breaking and original research in their field. As a result, these individuals are translating their research findings to clinical practice or informing policy decisions both nationally and internationally.

## Evidence

[1] National Institute for Health Research. 2014. Our faculty. As of 9 May 2016: <http://www.nihr.ac.uk/our-faculty/>

Webpage introducing the NIHR faculty.

[2] National Institute for Health Research. 2016. NIHR In Practice Fellowships. As of 9 May 2016: <http://www.nihr.ac.uk/funding/in-practice-fellowships.htm>

[3] National Institute for Health Research. 2016. NIHR Academic Clinical Fellowships. As of 9 May 2016: <http://www.nihr.ac.uk/funding/academic-clinical-fellowships.htm>

Information on the Academic Clinical Fellowships.

[4] National Institute for Health Research. 2016. NIHR Fellowship programme. As of 9 May 2016: <http://www.nihr.ac.uk/funding/fellowship-programme.htm>

Information on the Fellowship programme.

[5] National Institute for Health Research. 2015. NIHR Clinical Trials Fellowships. As of 9 May 2016: <http://www.nihr.ac.uk/funding/clinical-trials-fellowships.htm>

Information on Clinical Trials Fellowships.

[6] National Institute for Health Research. 2016. NIHR Clinician Scientist Award. As of 9 May 2016: <http://www.nihr.ac.uk/funding/clinician-scientist-awards.htm>

Information on the Clinician Scientist Award.

[7] NIHR Trainees Coordinating Centre. 2015. Case Study Compilation. Internal document. [Unpublished.]

NIHR case studies highlighting some accomplishments of its alumni.

[8] Newcastle University Faculty of Medical Sciences. 2015. Dr Anna Basu. As of 9 May 2016: <http://www.ncl.ac.uk/medalsciences/research/groups/profile/anna.basu>

Dr Basu's academic webpage.

[9] Kirkpatrick E, Pearse J, James P, Basu A. 2016, Effect of parent-delivered action observation therapy on upper limb function in unilateral cerebral palsy: a randomized controlled trial. *Developmental Medicine & Child Neurology*. doi: 10.1111/dmcn.13109

Journal article from Dr Basu's research.

[10] King's College, London. n.d. Dr Carsten Flohr. As of 9 May 2016: <http://www.kcl.ac.uk/lsm/research/divisions/gmm/departments/dermatology/Groups/flohr/index.aspx>

Dr Flohr's academic webpage.

### 10.1.10. *Bridging academia and the clinic through training*

#### Case study

In improving the health and wealth of the nation, the NHS workforce needs individuals who bridge academic pursuits and clinical endeavours. The NIHR awards Academic Clinical Fellowships (ACFs), which give medical and dental professionals a chance to conduct research alongside their clinical duties, thereby creating highly trained research and clinical staff [1]. ACFs are one part of the Integrated Academic Training (IAT) Programme, which has been delivered by the NIHR since 2006. The IAT Programme follows from the recommendations of the Modernising Medical Careers and UK Clinical Research Collaboration's report of March 2005 [1].

Since this pre-doctoral fellowship programme began, the NIHR has funded 2,247 ACF posts, according to a communication with the TCC, with approximately 250 medical and dental trainees now starting the programme each year [2]. ACFs are designed to allow doctors and dentists to ring-fence 25 per cent of their time to engage in academic research or education research training, while simultaneously pursuing clinical training [1]. Awardees are eligible to use this protected academic or research time to apply for fellowships to support doctoral studies or to draft research proposals for future work [1]. This element demonstrates that the ACF is encouraging individuals to continue in research beyond the timescale of the fellowship.

In 2015, the NIHR TCC conducted an evaluation to determine the destination of ACFs who have completed the programme. Initial analysis of the findings shows individual-level impacts of the ACF, with the majority of individuals who participated in the programme reporting they went on to pursue joint academic and research careers. One previous award holder is Dr Damian Roland who started an ACF in 2009 and was subsequently awarded with an NIHR-funded Doctoral Research Fellowship [3]. In his PhD he examined and developed a new framework to evaluate medical education interventions. A Consultant and Honorary Lecturer in Paediatric Emergency Medicine, Dr Roland now works across Leicester Hospital and Leicester University [3]. Dr Roland's research centres on illness identification in children and young people, educational evaluation and using social media as a means of knowledge translation. He co-developed the Paediatric Observation Priority Score (POPS), which helps practitioners to confidently recognise when children are sick or when they are ready for safe discharge [3]. The success of POPS has meant it has been adopted in a number of hospital emergency departments in the UK [4]. Alongside the benefits to those who are awarded ACFs, there are several indications of benefits to the wider health research landscape.

In 2015, the Medical Research Council conducted a cross-funder review of early-career clinical academics, based on positions funded by the NIHR and five other research funders. Across all those surveyed who followed a research training fellowship (RTF) or a Clinician Scientist Fellowship since 2006, five per cent gained their first research experience through the NIHR ACF [5]. Furthermore, almost one in five individuals who followed a research training fellowship awarded by any of the six participating funders between 2012 and 2014 were influenced to get into research as a result of the NIHR ACF [5]. One in ten individuals stated that this was their main motivation to pursue research [5]. The report cites 'ACFs have become an important factor in piquing trainees' interest in research' [5]. In addition to this, Goldacre et al. (2011) surveyed ACFs appointed in 2008 and determined that ACFs had many reasons to pursue an academic career, including the 'challenge of research', having a 'varied and stimulating' career and being part of an 'intellectual environment' in an academic department [6]. The authors also found that 80 per cent of respondents had some intention to remain in the UK [6]. These findings suggest that the NIHR ACF programme is contributing towards creating clinical research capacity within the nation.

Overall, the ACFs allow the NIHR to develop its faculty at an early and key stage of individuals' careers. Supporting a protected environment, where trainees can develop both their clinical and research skills, grants individuals more choice in their career pathway.

## Evidence

[1] Academic Careers Sub-Committee of Modernising Medical Careers and the UK Clinical Research Collaboration. 2005. Medically- and dentally-qualified academic staff: Recommendations for training the researchers and educators of the future. London: Modernising Medical Careers and the UK Clinical Research Collaboration. As of 8 April 2016: [http://www.ukcrc.org/wp-content/uploads/2014/03/Medically\\_and\\_Dentally-qualified\\_Academic\\_Staff\\_Report.pdf](http://www.ukcrc.org/wp-content/uploads/2014/03/Medically_and_Dentally-qualified_Academic_Staff_Report.pdf)

2005 Recommendations for training researchers and educators.

[2] NIHR. 2015. NIHR Integrated Academic Training for doctors and dentists. As of 29 April 2016: <http://www.nihr.ac.uk/funding/integrated-academic-training.htm>

[3] NIHR Trainees Coordinating Centre. 2014. NIHR Case Study: Dr Damian Roland. Internal document. [Unpublished.]

NIHR case studies highlighting the work of Dr Damian Roland.

[4] University of Leicester. n.d. POPS -The Paediatric Observation Priority Score. As of 29 April 2016: <http://www2.le.ac.uk/departments/cardiovascular-sciences/research/cardiovascular-physiology-and-pathophysiology/emergency-medicine-group/research/pemla/pops/pops-front-sheet>

Information on the Paediatric Observation Priority Score

[5] Medical Research Council in collaboration with the Academy of Medical Sciences, British Heart Foundation, Cancer Research UK, National Institute for Health Research and Wellcome Trust. 2015. A Cross-Funder Review of Early-Career Clinical Academics: Enablers and Barriers to Progression. London: MRC. Prepared for IFF Research. As of 8 April 2016: <http://www.mrc.ac.uk/documents/pdf/review-of-early-career-clinical-academics/>

Research on the experiences of clinical academics early in their career.

[6] Goldacre MJ, Lambert TW, Goldacre R, Hoang UY. 2011. Career plans and views of trainees in the Academic Clinical Fellowship Programme in England. *Medical Teacher*. 33:11, e637-e643, DOI: 10.3109/0142159X.2011.610842

Research conducted to report on the basic demographic characteristics of trainees in 2008, their future career plans, and their views on incentives and disincentives in pursuing a clinical academic career.



## 11. Investing across the nation

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### 11.1. Summary

**Regional. Societal. Needs-based.**

*NIHR supports regionally driven research to address the distinct health priorities of different regional areas and to assist the national scale-up of local initiatives.*

NIHR recognises that the diversity of England's regions and their health profiles create unique challenges; therefore, it funds regionally focused studies that engage communities in research designed to meet their specific needs. NIHR also identifies innovations developed at the regional level which have the potential to be scaled up, and it funds research to build the evidence base for their wider implementation.

Where a region faces particularly high prevalence of a disease or difficulties in implementing effective treatment, NIHR supports research led from within the region and targeted at the affected population. The 13 NIHR Collaborations for Leadership in Applied Health Research and Care (CLAHRCs) play a valuable role in ensuring that research is sensitive to regional priorities and engages local populations. As a result, NIHR-funded projects have been able to produce targeted interventions that improve local patients' health. For example:

- The West Midlands CLAHRC supported the YouthSpace study to redesign mental health services for Birmingham's unusually large young adult population. The CLAHRC provided a platform for community engagement throughout the project, which found that the redesigned service could substantially reduce delays in treating young people for psychosis.
- A project involving the East Midlands CLAHRC led to the development of the Leicester Self-Assessment tool to aid early identification of diabetes risk in ethnic minority communities, who form a large proportion of the region's population and are among those most likely to suffer from diabetes.
- The CLAHRC South West Peninsula has supported work to implement redesigned pathways for stroke care, initially developed within the Royal Devon and Exeter NHS Foundation Trust, throughout the region. This builds on local operational research, which used computer modelling to identify ways to cut the time taken for a person who has suffered a stroke to receive vital clot-busting treatment, with waiting times cut by almost one half.

NIHR's community-based approach to generate reliable evidence for interventions, a number of those interventions have been adopted in other regions or at the national level. This has led to changes to policy and practice, which improve outcomes for more patients. Various projects illustrate this impact:

- A stroke registry designed for targeted use in London's ethnically diverse population was developed with NIHR support and has since been adopted by two-thirds of English hospitals. The registry gathers data which enables better prediction of stroke risk and long-term outcomes, which in turn facilitates evidence-based policy and practice in stroke services, as demonstrated by citation of the work in the National Stroke Strategy.
- A study on the energy efficiency of NHS buildings found that innovative ventilation of hospitals in the London Urban Heat Island could enhance patient safety by preventing overheating as far forward as 2080, even as climatic temperatures rise. The London findings on innovative ventilation have been identified by national-level NHS management as an influence on future policy; cited by the Department for Environment, Food & Rural Affairs (usually referred to as DEFRA) policy documents; and adopted internationally by private and public healthcare providers, including Skanska and the government of India.
- The Big Local study, supported by NIHR's School for Public Health, engages local residents in designing health promotion interventions in their local communities and is being monitored by NICE as a possible example of good practice for inclusion in its future Guidelines on Community Engagement.
- A multiregional study on care transitions engaged elderly people from each region, all of whom had recently experienced transitions, as members of the research team. The resultant patient-centred and locally focused findings have led to changes in policy in each of the study regions (Solihull, Leicester, Manchester and Gloucestershire).
- The Head Up project on combating neck weakness in motor neuron disease patients, conducted at Sheffield Hallam University, engaged a local patient group alongside a multidisciplinary team of experts, through NIHR's Devices for Dignity initiative. This active involvement of local stakeholders enabled the development of a neck support collar that responds to patients' needs by helping them to communicate and eat.

Where appropriate, NIHR itself seeks to drive scale-up of innovative regional interventions, by funding trials and adaptations which demonstrate their potential benefits for patients throughout the country. Examples include:

- The Football Fans in Training initiative, developed in Scotland, works through football clubs to provide a culturally sensitised weight loss programme for Scottish males. The evidence produced by an NIHR-funded evaluation – showing almost half of participants achieving a target weight loss likely to reduce obesity-related health risks – led to the roll-out of the initiative in sports clubs across England and Europe-wide.
- NIHR funded a trial to determine the potential benefits of wider uptake of the New Forest Parenting Programme, aimed at families of children with attention deficit hyperactivity disorder, which was originally developed and implemented in Southampton. NIHR support facilitated local clinical involvement in the study, the findings of which are expected to inform revised NICE guidelines.

NIHR's emphasis on regionally driven research ensures a flow of evidence-based health innovations that have the potential to improve lives on a national scale, aided by NIHR's willingness to support wider scale-up.

### *11.1.1. Retaining men's participation in weight loss programmes in Scottish football clubs*

#### Case study

In spite of obesity rates in UK males being some of the highest in Europe, fewer than a third of participants in weight management programmes are male [1]. The health effects associated with obesity – increased cases of diabetes, heart disease, stroke and cancer – are estimated to place a financial burden on the health system of £2 billion by 2030 [2]. Research into public health programmes to try to reverse the trend of rising obesity play an important part in the NIHR's portfolio. One such programme in Scotland targeted men in particular, to attract and retain their participation in a weight loss and healthy eating programme [2]. This programme was originally funded by the Scottish Premier League Trust (now the Scottish Professional Football League Trust) and the Chief Scientist Office of the Scottish government, with the evaluation funded through the NIHR.

The programme, titled Football Fans In Training (FFIT), was gender-sensitised and was designed to be delivered in Scottish Premier League football clubs by community coaches. It drew on prevailing conceptions of masculinity, such as men's feelings of connection and attachment to football clubs, camaraderie and team bonding, to help participants discuss sensitive subjects concerning their weight [1]. The programme consisted of both dietary components and physical activity tailored to individual fitness levels, such as an incremental walking programme and pitch-side training sessions in the football clubs' home grounds [1].

In 2011, the NIHR provided support for a team at the University of Glasgow to conduct a randomised controlled trial – the first of its kind – to evaluate the FFIT programme and determine how effective it was in helping participating men to lose weight [1]. The team engaged funders and participants at the early stages of designing the research protocol and during the pilot stages of the FFIT programme, in order to assess whether such interventions as the walking programme would motivate men sufficiently to re-engage with physical activity [1]. Throughout the programme they worked with football club coaches and undertook a number of public engagement activities – including a documentary later broadcast by the BBC following a number of the initial participants in the trial – to broaden the reach and accessibility of the research [1].

More than a thousand men registered their interest in the trial, with 747 going on to take part. Those receiving the FFIT intervention lost an average of 5 kg (approximately 5 per cent of their bodyweight) over the course of the programme, with almost half achieving a target weight loss likely to reduce obesity-related health risks [2]. Participants gave positive reports of their physical and mental well-being ... 'it's just quality time that I didn't have, because I didn't have a life...it's been life changing for me'. The team also found that the intervention, costing around £680 per participant, was also cost effective in terms of participants' health benefits estimated to accrue over the 12 months of the programme.

The Glasgow team's rigorous approach, afforded by the NIHR's support of a randomised controlled trial, delivered a robust evaluation of the FFIT programme's effects. This was noted by the Scottish government, which praised the success of the programme in attracting and engaging participants across income groups, in particular those at the lower end of the socioeconomic scale. The trial's results

informed further knowledge-exchange activities with NHS weight management services in the Lothian and Grampian regions, who in 2012 indicated their intention to extend the programme. Further programmes have since rolled out to tackle obesity among inmates in Perth prison and nationally and internationally among rugby clubs in England and New Zealand (RuFIT) [1]. In 2013, a major European-wide expansion of the programme received approximately €6 million in funding to roll out the intervention in 15 major football clubs across Europe (EuroFIT) [3].

## Evidence

[1] Wyke S, Hunt K, Gray C, Fenwick E, Bunn C, Donnan P, Rauchhaus P, Mutrie N, Anderson A, Boyer N, Brady A, Grieve E, White A, Ferrell C, Hindle E, Trew. 2015. Football Fans In Training (FFIT): A randomised controlled trial of a gender-sensitised weight loss and healthy living programme for men – end of study report. *Public Health Research* 3 (2). doi:10.3310/phr03020

Paper describing the randomised controlled trial on the weight loss and healthy living programme for men.

[2] Research Excellence Framework. 2014. Influencing policy, practice and services to improve obese men's health and well-being. [Case study 23615] As of 2 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=23615>

Research Excellence Framework case study on improving obese men's health.

[3] EuroFIT. n.d. Overview. As of 2 May 2016: <http://eurofitfp7.eu/impact>

Full write-up of the FFIT project, with information on background, methods, results and impacts.

### *11.1.2. Highlighting stroke risks in South London through a unique register to inform long-term care and policy*

#### Case study

Every year around 100,000 people in the UK have a stroke – making strokes the third largest cause of death after heart disease and cancer [1]. In order to understand how best to configure healthcare services to support the acute and long-term needs of stroke survivors, clinicians require a platform through which they can collect detailed information on stroke patients, their health outcomes, quality of life and quality of care. The longest-running of these platforms is the South London Stroke Register at King's College London [2].

By following stroke survivors for up to 10 years after the event, the registry data provide evidence on the long-term nature of the disease and on patients' ongoing (poor) outcomes [3]. In particular, it highlighted the persistently high nature of cognitive impairment in patients over time following their first stroke [4] and the prevalence of depression in over half of all stroke patients [5]. It also demonstrated the benefits of shortening patients' hospital stays, with appropriately supported rehabilitation in the community – a strategy found to be more cost effective in the long run than treating patients in general medical wards [6].

Building on this work, the NIHR invested over £1.3 million in research projects and programmes making use of the data held in the register [2]. The support has enabled the King's team to analyse information from more than 4,000 patients whose first stroke occurred between 1995 and 2012 [7].

As well as estimating the risks of stroke and the likelihood of it recurring, the team aimed to develop clinical tools to predict patients' long-term outcomes, such as problems with cognition, depression or anxiety. The NIHR's funding of a broad-reaching programme grant enabled the King's team to model the most effective methods of providing care and of understanding patients' needs, the better to provide services to meet those needs [7].

While overall the team found a declining incidence of stroke over the 15 years of data captured in the registry, the research highlighted significant disparities in stroke risk among patients in different ethnic groups, with black men at particularly high risk. The team highlighted a need for prevention strategies to address differences in risk among ethnic groups in culturally sensitive ways [7].

These and other detailed findings informed policy, including the National Stroke Strategy and a parliamentary Public Accounts Committee report on the need for a 'step change' in stroke care, in order to address patients' needs.

Data from the registry and this research also fed in to further studies examining the effects of reconfiguring stroke services to a series of eight 'hyper-acute' units in London. Providing continuous specialist care in these units within the first 72 hours of a stroke resulted in an estimated 12 per cent reduction in deaths at 90 days and cost savings of £5.2 million (£811 per patient) as a result of patients' reduced length of hospital stay [8].

With the NIHR's support, the King's team has been able to gather and analyse data as part of a unique resource to improve long-term stroke care. The team's findings around early supported discharge have informed national guidelines and have been implemented in 66 per cent of English hospitals – with clear indications that better organised and higher-quality care is leading to improved outcomes for patients [2].

## Evidence

[1] NHS Choices. 2014. Stroke. As of 2 May 2016:

<http://www.nhs.uk/conditions/Stroke/Pages/Introduction.aspx>

Information on stroke signs and symptoms, including information on the prevalence of stroke in the UK.

[2] Research Excellence Framework. 2014. South London Stroke Register: Informing innovation in stroke care. [Case study 41174.] As of 2 May 2016:

<http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=41174>

Research Excellence Framework case study detailing the NIHR's support of research making use of the South London Stroke Register, and the resulting impacts on patient care, practice and policy.

[3] Wolfe C, Crichton S, Heuschmann P, McKeivitt C, Toschke A, Grieve A, Rudd A. 2011. Estimates of outcomes up to ten years after stroke: Analysis from the prospective South London Stroke Register. *PLoS Medicine* 8 (5): e1001033. doi:10.1371/journal.pmed.1001033

Study highlighting long-term care needs of 3,375 stroke patients registered between 1995 and 2006

[4] Douri A, Rudd AG, Wolfe C. 2013. Prevalence of poststroke cognitive impairment. *Stroke* 44: 138-45. doi:10.1161/STROKEAHA.112.670844

Study highlighting levels of cognitive impairment in 4,212 patients registered between 1995 and 2010, and in particular the variation of patient outcomes by sociodemographic status.

[5] Ayerbe L, Ayis S, Rudd AG, Heuschmann PU, Wolfe CD. 2011. Natural history, predictors, and associations of depression 5 years after stroke. *Stroke* 42 (7): 1907-11.

doi:10.1161/STROKEAHA.110.605808

Study analysing data from 3,689 stroke patients registered between 1995 to 2006, to determine the longer-term natural history of depression.

[6] Saka O, Serra V, Samyshkin Y, McGuire A, Wolfe C. 2009. Cost-effectiveness of stroke unit care followed by early supported discharge. *Stroke* 40: 24-9. doi:10.1161/STROKEAHA.108.518043

Study using cost-effectiveness modelling to analyse the long-term (10 year) health service, societal and costs per quality-adjusted life year of different models of stroke care.

[7] Wolfe C, Rudd A, McKevitt C. 2014. Modelling, evaluating and implementing cost effective services to reduce the impact of stroke. *Programme Grants for Applied Research* 2 (2). doi:10.3310/pgfar02020

Write-up of the NIHR programme grant supporting population-based registry research using data from the South London Stroke Register. Details stroke incidence rates and trends, recurrence, survival, activities of daily living, anxiety, depression, quality of life, appropriateness and cost-effectiveness of care, and provides qualitative narratives of patients' perspectives.

[8] Hunter RM, Davie C, Rudd A, Thompson A, Walker H, Thomson N, Mountford J, Schwamm L, Deanfield J, Thompson K, Dewan B, Mistry M, Quoraishi S, Morris S. 2013. Impact on clinical and cost outcomes of a centralized approach to acute stroke care in London: A comparative effectiveness before and after model. *PLOS One* 8(8): e70420. doi:10.1371/journal.pone.0070420

Study pooling data from 307 'before' and 3,156 'after' patients either side of the introduction of a new hub-and-spoke model of hyper-acute stroke research centres and comparing patient outcomes with a previous model of 30 local hospitals receiving acute stroke patients.

### 11.1.3. *Scoring, detecting and mitigating the risk of diabetes*

#### Case study

NIHR funding has supported diabetes research that addresses regional needs but has the potential to be scaled up to the national level, resulting in improved health outcomes and cost savings for the NHS in patients with diabetes. The University of Leicester's Diabetes Research Centre (DRC) has links with both the NIHR Collaboration for Leadership in Applied Health Research and Care (CLAHRC) East Midlands and the NIHR's Leicester-Loughborough Diet, Lifestyle and Physical Activity Biomedical Research Unit (BRU). The DRC has developed and trialled risk assessment tools for the prevention of diabetes with support from the NIHR's Senior Investigator funding and Programme Grants for Applied Research (PGfAR) programmes. The tools were designed to meet the needs of the East Midlands, which has a high

concentration of ethnic minority groups among whom diabetes is particularly prevalent. The tools have the potential to drastically reduce NHS expenditure on diabetes.

The number of people in the UK with type 2 diabetes (T2DM) stands at around 2.5 million, and is increasing as the population ages and obesity rates rise [1]. A further 9.6 million people are at high risk of developing diabetes, mainly due to glucose disorders [2]. Despite T2DM being preventable, it is estimated that its treatment costs the NHS £8.8 billion per year [3]. However, prevention is made more challenging by the difficulty of detecting T2DM and glucose disorders [4], and there are barriers to uptake of screening in particular ethnic minority groups. These include time constraints and the inconvenience of visiting a GP practice [5].

To address this challenge, in 2008, the DRC conducted screening at 30 general practices in Leicestershire [6]. The data were used to develop two risk assessment tools for use in ethnically diverse populations: the Leicester Self-Assessment (LSA) tool (based on the patient's own knowledge) and the Leicester Practice Risk (LPR) tool (designed for risk assessment in general practice) [5][7]. LSA and LPR are the first risk assessment tools for T2DM to have been validated in a multi-ethnic UK population [8]. The PGfAR-funded study showed both these tools to be effective in detecting heightened risk of T2DM in general practice [8]. The early detection of T2DM risk and symptoms using such tools as LSA and LPR has been identified as a potential source of cost savings for the NHS. Research by the DRC has shown that the treatment cost per case of T2DM detected can be lowered by £100, to around £250, by using these risk assessment tools [9].

The development of LSA and LPR through regional-level trials has had national-level impacts on clinical practice, as well as policy, health and economic impacts. At the policy level, both tools have been included in National Institute for Health and Care Excellence (NICE) guidelines on the detection of T2DM risk [10][11]. This has been accompanied by the tools' uptake in clinical practice and various other settings, where programmes are overcoming the barriers to uptake of screening by targeting patients directly in locations other than GP practices and, in doing so, improving early detection and prevention of T2DM. NHS Clinical Commissioning Groups are using LSA at screening events nationwide, and it has been used in connection with the NHS Health Check programme, which aims to prevent heart disease, stroke, diabetes and kidney disease [4].

Early detection and prevention have also been promoted through the LSA tool's implementation in other settings, including faith centres (in Leicester) and pharmacies (nationally). In 2011, LSA was used in 700 pharmacies as part of a free health check initiative run by Diabetes UK and Community Pharmacy Wales, during which around 8 per cent of the 17,500 people who received the assessment were referred to their GP [4]. Tesco and Boots are also among a number of organisations, including the University of Leicester and the Royal College of General Practitioners, that have made LSA available on their websites; 260,000 people have completed a self-assessment through these websites [4].

Diabetes UK has been particularly active in promoting the use of LSA as a tool for early detection and prevention. The charity has been using the tool at road shows throughout the country since 2011, resulting in more than 20,000 risk assessments and more than 10,000 referrals in 2012 alone [4]. The positive impact of the use of LSA in this initiative has been highlighted by a Diabetes UK study, which

showed that of those assessed, 33 per cent subsequently increased their level of physical activity, 41 per cent started to eat more healthily, and 44 per cent visited their GP for screening [4].

## Evidence

[1] Diabetes UK. 2015. Major drive to prevent illness with launch of national type 2 prevention programme. As of 2 May 2016: [https://www.diabetes.org.uk/About\\_us/News/Major-drive-to-prevent-illness-with-launch-of-national-Type-2-prevention-drive/](https://www.diabetes.org.uk/About_us/News/Major-drive-to-prevent-illness-with-launch-of-national-Type-2-prevention-drive/)

News item on launch of national Type 2 Diabetes prevention programme

[2] Public Health England. 2015. National NHS diabetes initiative launched in major bid to prevent illness. As of 2 May 2016: <https://www.gov.uk/government/news/national-nhs-diabetes-initiative-launched-in-major-bid-to-prevent-illness>

Press release on NHS Diabetes prevention programme.

[3] Public Health England. 2014. Adult obesity and type 2 diabetes. As of 2 May 2016: [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/338934/Adult\\_obesity\\_and\\_type\\_2\\_diabetes\\_.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/338934/Adult_obesity_and_type_2_diabetes_.pdf)

Public Health England Paper describing the relationship between diabetes and obesity.

[4] Research Excellence Framework. 2014. Pre-diabetes and type 2 diabetes: Risk-assessment tools for early detection and prevention. [Case study 35209.] As of 2 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=35209>

Research Excellence Framework case study on pre-diabetes and Type 2 diabetes

[5] Gray LJ, Davies MJ, Hiles S, Taub N, Webb DR, Srinivasan BT, Khunti K. 2012. Detection of impaired glucose regulation and/or type 2 diabetes mellitus, using primary care electronic data, in a multi-ethnic UK community setting. *Diabetologia* 55 (4): 959-66. doi: 10.1007/s00125-011-2432-x

Journal article on a UK multi-ethnic community setting and detection of impaired glucose regulation and Type 2 diabetes.

[6] Webb DR, Gray LJ, Khunti K, Srinivasan B, Taub N, Campbell S, Barnett J, Farooqi A, Echouffo-Tcheugui JB, Griffin SJ, Wareham NJ, Davies MJ. 2011. Screening for diabetes using an oral glucose tolerance test within a Western multi-ethnic population identifies modifiable cardiovascular risk: The ADDITION-Leicester study. *Diabetologia* 54 (9): 2237-46. doi: 10.1007/s00125-011-2189-2

Journal article on screening for diabetes.

[7] Gray LJ, Taub NA, Khunti K, Gardiner E, Hiles S, Webb DR, Srinivasan BT, Davies MJ. 2010. The Leicester risk assessment score for detecting undiagnosed type 2 diabetes and impaired glucose regulation for use in a multi-ethnic UK setting. *Diabetic Medicine* 27 (8): 887-95. doi: 10.1111/j.1464-5491.2010.03037.x

Journal article on the Leicester risk-assessment score.

[8] Gray LJ, Khunti K, Edwardson C, Goldby S, Henson J, Morris DH, Sheppard D, Webb D, Williams S, Yates T, Davies MJ. 2012. Implementation of the automated Leicester Practice Risk Score in two



diabetes prevention trials provides a high yield of people with abnormal glucose tolerance. *Diabetologia* 55 (12): 3238-44. doi: 10.1007/s00125-012-2725-8

Journal article on the Leicester Practice Risk Score in two trials on the prevention of diabetes.

[9] Khunti K, Gillies CL, Taub NA, Mostafa SA, Hiles SL, Abrams KR, Davies MJ. 2012. A comparison of cost per case detected of screening strategies for type 2 diabetes and impaired glucose regulation: Modelling study. *Diabetes Research and Clinical Practice* 97 (3): 505-13. doi:10.1016/j.diabres.2012.03.009

Journal article comparing costs per detected Type 2 diabetes or impaired glucose regulation case through screening strategies.

[10] Chatterton H, Younger T, Fischer A, Khunti K, Programme Development Group. 2012. Risk identification and interventions to prevent type 2 diabetes in adults at high risk: Summary of NICE guidance. *BMJ* 345: e4624. doi:10.1136/bmj.e4624

Summary of NICE guidelines.

[11] National Institute for Health and Care Excellence. 2012. Preventing type 2 diabetes: Risk identification and interventions for individuals at high risk. [Public Health Guidance PH38.] As of 2 May 2016: <http://www.nice.org.uk/PH38>

NICE guidelines on the prevention of Type 2 diabetes in people at high risk.

#### *11.1.4. Using natural ventilation to cool hospital buildings and reduce energy consumption*

##### Case study

NIHR support for research on energy-efficient health buildings is an example of NIHR investment in research that meets local needs while achieving wider impact. NIHR-funded research on the use of natural ventilation and passive cooling in health buildings has addressed the need, particularly in London, for sustainable and cost-effective improvements to the energy efficiency of NHS building stock.

NHS buildings are major contributors to the UK's carbon emissions accounting for around 3 per cent of total carbon dioxide emissions and 30 per cent of public sector emissions, at an annual cost of over £400 million on heating and lighting [1][2]. Although the Department of Health (DH) has set targets for NHS organisations for the reduction of emissions, it was reported in 2008 that these would not be met if trends in emissions continued [3]. In addition to posing environmental risks, poor ventilation and cooling endanger patients. The DH has reported that 'During relatively mild heatwaves, excess death rates are significantly, but avoidably, higher in this country' [4]. Moreover, climate change and increasing use of electronic equipment in healthcare both exacerbate these issues [1], which are especially severe within the London Urban Heat Island (LUHI).

A team of researchers led by Professor Alan Short of the University of Cambridge has been studying low-energy ventilation and cooling of non-domestic buildings for more than 20 years. Their initial research led to the design of buildings ranging from educational facilities to a brewery, before the DH asked the research team to apply the principles of their work to health buildings. This was followed by NIHR-

funded research which modelled the future resilience of NHS building stock, including a hospital in the LUHI, based on projected temperature increases by 2030, 2050 and 2080. Having found that the majority of existing building stock was at risk of overheating by 2080, the research team determined that energy-saving cooling and ventilation solutions could prevent overheating for the period up to 2080 [5]. These findings led to the conclusion that improved cooling and reduced emissions could be achieved without the costly replacement of NHS building stock – including within the LUHI, where the risk of overheating is highest [1]. The research team also found that the same principles of passive cooling and natural ventilation could be applied to new build hospitals with equally positive results [6].

These groundbreaking findings have had a significant impact on policy, with the potential to result in environmental, health and economic impacts. The Acting Director of the Estates and Facilities Policy Division of the NHS stated that this research ‘demonstrated that the existing estate is capable of being sustainably improved to achieve levels of ventilation and cooling which will extend the estates’ functional suitability for the foreseeable future,’ and that ‘Cambridge University’s research [is] at the heart of government policy on making the country resilient to climate change.’ [7] In addition, the Department for Environment, Food and Rural Affairs (DEFRA) has cited the research in its National Adaptation Programme on responding to climate change [8]. Outside the UK, research by Short’s team has been used in the United States by healthcare consortium Kaiser Permanente as evidence for initial moves away from policies prohibiting natural ventilation in hospitals [9]. Changes to policy have been accompanied by changes in building design. Skanska, a multinational infrastructure development company, has incorporated findings by Short’s team into their approach to building hospitals in the UK and abroad [10], and Short is collaborating with the Indian government on a prototype hospital to be used in the design of more than 600 hospitals [1].

The ongoing impact of the research has major potential implications for the NHS’s approach to climate change and environmental sustainability. For example, members of the research team have an advisory role in the redevelopment of Watford General Hospital, which has been described as ‘the first NHS project to deliberately factor in climate change implications’ [11]. Moreover, improved resilience to rising temperatures has important implications for patient safety given the abovementioned health consequences of overheating [5]. Finally, by demonstrating the potential of existing NHS building stock to be made more energy efficient and less vulnerable to overheating, the research has saved the NHS money by helping to prevent unnecessary demolition and rebuilding [1].

## Evidence

[1] Research Excellence Framework. 2014. Low-energy design strategies for healthcare buildings in a changing climate. As of 3 May 2016: <http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=23400>

Research Excellence Framework case study on design for healthcare buildings.

[2] NHS Sustainability Development Unit. 2008. Saving carbon, improving health: A draft reduction strategy for the NHS in England – A consultation document.

This is a consultation document on a carbon reduction strategy for the NHS.

[3] Department of Health. 2008. Estate Returns Information Collection (ERIC). As of 2 May 2016: <https://data.gov.uk/dataset/eric-annual-returns>

This webpage provides data on Estate Returns Information Collection.

[4] Department of Health. 2008. Heatwave plan for England: Protecting health and reducing harm from extreme heat and heatwaves. As of 2 May 2016:

[https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/429384/Heatwave\\_Main\\_Plan\\_2015.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/429384/Heatwave_Main_Plan_2015.pdf)

This document outlines a heatwave plan for England.

[5] Short CA, Cook M, Cropper PC, Al-Maiyah S. 2010. Low-energy refurbishment strategies for health buildings. *Journal of Building Performance Simulation* 3 (3): 197-216.

doi:10.1080/19401490903318218

Journal article on energy saving strategies in the refurbishment of healthcare buildings.

[6] Short CA, Al-Maiyah S. 2009. Design strategy for low-energy ventilation and cooling of hospitals. *Building Research and Information* 37 (3): 1-29. doi:10.1080/09613210902885156

Document on a low-energy cooling and ventilation systems design strategy in hospitals

[7] Letter from Acting Director of the NHS Estates & Facilities Policy Division.

[8] Department for Environment, Food and Rural Affairs National Adaptation Programme. As of 15 May 2016: [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/209866/pb13942-nap-20130701.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/209866/pb13942-nap-20130701.pdf)

[9] Letter from Chief Design Engineer, Kaiser Permanente.

[10] Letter from Head of Sustainability, Skanska Infrastructure Development.

[11] Letter from Chief Executive, Great Ormond Street Hospital.

### *11.1.5. Redesigning local youth mental health services to provide care right through to young adulthood*

#### Case study

Evidence suggests that three-quarters of all psychiatric illness begins before the age of 25. NIHR-funded studies of care practice reveal that young people between 16 and 25 years old have the highest incidence of mental health illness of any age group but the worst access to mental healthcare services [1]. With this in mind, a team supported by the NIHR Collaboration for Leadership in Applied Health Research and Care (CLAHRC) West Midlands led a study examining how to radically redesign mental health services for young people in Birmingham [2].

Drawing on its connections among universities in Birmingham and a number of health and social care organisations, CLAHRC West Midlands funded the team to look in detail at the damaging impacts that can arise from bottlenecks in receiving treatment among young people with mental health illnesses. In particular, the team explored the vulnerabilities of 16- to 18-year-olds who either disengage, or become lost, as they transition to adult mental health services, in particular among black and other minority ethnic groups [2].

To address these issues, the team worked with local service users in Birmingham – often quoted as being ‘one of Europe’s youngest cities’ due to its high proportion of under-25-year-olds – to devise an

experimental youth pathway, Youthspace, in partnership with the Prince's Trust. Targeted at those between 14 and 25 years old, this low-stigma, youth-friendly intervention deployed youth teams and an interactive website to reach out to young people with mental health illnesses. The team also aimed to improve health-seeking behaviours, with a public health campaign targeting young people in the early stage of psychosis through bus and newspaper advertisements, as well as via the Youthspace website [2].

Early results of the impact of the Youthspace initiative showed its success in reducing the delays young people experienced in waiting for treatment for psychosis – from 285 to 104 days compared with those in a control arm [2]. Though only a proof-of-principle, the West Midlands team's results indicate that this new method of service delivery allowed carers to engage and assess young people without the need for interim contact by secondary mental health services [3].

Building on the Birmingham pilot, the team's model of a mental health service that responds to the needs of young people right through to the age of 25 has sparked local, national and international interest. Based on the West Midland team's research, Birmingham now offers a mental health service to children, young people and young adults right through to the age of 25. Responding to this, other local clinical commissioning groups are looking to adapt their services [2]. In addition to having impacts on practice, the work is influencing policy, with the Department of Health's *Future in Mind* proposal citing the Birmingham model and noting interest in its further deployment [4]. The work is also noted in an international review of youth mental health services 'for the 21st century' [5].

Most importantly, with the support of the NIHR's CLAHRC West Midlands, the Youthspace initiative is making a real difference to young people's lives. One teenager noted the impact of the support she received:

'Taking part in Youthspace has made me turn my anger into a positive to create change for other young people. Youthspace has given me the opportunity to develop my skills and grow as an individual. I have finally been able to use my skills and experiences to make that change. If it wasn't for the Prince's Trust and Youthspace giving me these opportunities I wouldn't be here today [6].'

## Evidence

[1] Singh SP, Paul M, Islam Z, Weaver T. 2010. Transition from CAMHS to Adult Mental Health Services (TRACK): A study of service organisation, policies, process and user and carer perspectives. London: Queen's Printer and Controller of HMSO. As of 3 May 2016: [http://www.nets.nihr.ac.uk/\\_\\_data/assets/pdf\\_file/0010/64288/FR-08-1613-117.pdf](http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0010/64288/FR-08-1613-117.pdf)

Results of an NIHR Service Delivery and Organisation-funded project to examine the transition of young people with mental health illness to adult mental health services.

[2] CLAHRC Super BITE. 2015. Brokering Innovation Through Evidence. As of 3 May 2016: [https://www2.warwick.ac.uk/fac/med/about/centres/clahrc/impact/bites/clahrc\\_wm\\_superbite\\_youthmhservices\\_june2015.pdf](https://www2.warwick.ac.uk/fac/med/about/centres/clahrc/impact/bites/clahrc_wm_superbite_youthmhservices_june2015.pdf)

A summary of research activity translating to impacts on health and social care services by the West Midlands CLAHRC.

[3] Connor C. 2015. Don't turn your back on the symptoms of psychosis: the results of a proof-of-principle, quasi-experimental intervention to reduce duration of untreated psychosis. Virtual Conference Library. As of 3 May 2016: <http://iaymh-vcl-2015.eppic.org.au/content/dont-turn-your-back-symptoms-psychosis-results-proof-principle-quasi-experimental>

Presentation of the results of the West Midlands CLAHRC's experimental youth pathway, YouthSpace.

[4] Department of Health, NHS England. 2015. Future in mind: Promoting, protecting and improving our children and young people's mental health and wellbeing. London: Department of Health. As of 3 May 2016:

[https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/414024/Childrens\\_Mental\\_Health.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/414024/Childrens_Mental_Health.pdf)

Recent proposal to promote, protect and improve children and young people's mental health and wellbeing.

[5] McGorry P, Bates T, Birchwood M. 2013. Designing youth mental health services for the 21<sup>st</sup> century: examples from Australia, Ireland and the UK. *The British Journal of Psychiatry* 202 (s54): s30-s35. As of 3 May 2016: <http://bjp.rcpsych.org/content/202/s54/s30>

Discussion of youth mental health services in three countries, highlighting examples of new care pathways and efforts to redesign services around patients' needs.

[6] National Institute for Health Research. n.d. World class research making a difference. London: NIHR. As of 2 May 2016: <http://www.clahrc-em.nihr.ac.uk/clahrc-em-nihr/documents/nihr-clahrc-world-class-research-making-a-difference.pdf>

Brochure outlining the impact of the NIHR's investment in CLAHRCs as a means to bring together NHS providers and commissioners with academics, local organisations, industry and health research infrastructure.

#### *11.1.6. Addressing the needs of local patients with motor neurone disease*

##### **Case study**

Motor neurone disease (MND) – a neurological condition that causes damage to the nerves that control the body's muscles – affects around 5,000 people in the UK. Neck weakness is one of a number of highly distressing and challenging symptoms that progressively impact on patients' independence. MND patients had reported that existing collars, designed principally to immobilise the neck following trauma or surgery, did not provide satisfactory support or allow for sufficient movement. Building on early infrastructure support from Devices for Dignity (D4D) and with funding from the NIHR's Invention for Innovation programme (i4i), a multidisciplinary team at the University of Sheffield and Sheffield Hallam University has come together to create a novel collar to help overcome neck weakness in patients with motor neurone disease (MND) [1].

Representatives from Dementias and Neurodegeneration (DeNDRoN) – a neurodegenerative disease and dementia-specific speciality group within the NIHR Clinical Research Network – initially took MND

patients' concerns on existing neck collars to D4D [2]. Responding to this, D4D brought together a team comprising a neurologist, a physiotherapist, an occupational therapist, a nurse and a team of designers, who engaged members of the local Sheffield MND Association to tackle the problem of how to engineer an improved neck support [1].

Actively listening to patients' needs and responding to their requests can be a powerful tool to empower them in managing their own care. The local MND Association patient group fed in to the early stages of the project, meeting regularly with the team to refine design concepts for a more user-friendly neck support, and to conduct early testing. Their input and involvement helped to secure funding from i4i to build a prototype, which was then trialled on volunteers as part of the Head-Up project [3].

By drawing on a diverse skill set from across Sheffield's healthcare and design experts and by working with patients to understand their needs, the team developed a collar that sat lower on the patient's neck and offered support along the contours of the neck muscles. The device enabled users to adjust the levels of support it provided by inserting a range of shapes. It was also designed with aesthetics in mind, so as to look more like an item of clothing than a medical device [1].

The team's initial tests showed that the device made it easier for the wearer to communicate, eat and maintain eye contact than did previous supports. It afforded users a greater range of movement and provided more support for its weight and size when compared with other supports [4]. The Sheffield team is now trialling the Head Up device on 20 patients with MND, with engagement from the local MND Association in helping to recruit patients to the study [5].

By responding to local patients' needs and providing the means to bring together experts from different areas to collaborate, the NIHR has helped the Sheffield team develop an innovative product with potential for improving the quality of life of thousands of individuals living with MND in the UK.

## Evidence

[1] McDermott C, Langley J, Stanton A, McCarthy A, Clarke Z, Baxter S, Shaw P, Heron N, Reed H, Quinn A, Judge S, Squire G, Wells O. n.d. Developing neck support technology. So David can raise his head with dignity. As of 3 May 2016: <https://www.shu.ac.uk/ad/changinglives/neck-brace>

Sheffield Hallam University's write-up of the Sheffield Support Snood project.

[2] Lab4Living. n.d. 'Head-Up' developing new neck supports. As of 3 May 2016: <http://research.shu.ac.uk/lab4living/head-up-developing-new-neck-supports>

Announcement from the design team Lab4Living of i4i funding, referencing DeNDRoN's role in initiating the idea for the project.

[3] Marjanovic S, Krapels J, Sousa S, Castle-Clarke S, Horvath V, Chataway J. 2015. The NIHR Invention for Innovation (i4i) programme: A review of progress and contributions to innovation in healthcare technologies. Santa Monica, Calif.: RAND Corporation. As of 3 May 2016: [http://www.rand.org/pubs/research\\_reports/RR1101.html](http://www.rand.org/pubs/research_reports/RR1101.html)

RAND Europe's evaluation of the NIHR's i4i programme, featuring the Head-Up project as one of a number of case studies.

[4] Pancani S, Rowson, J, Tindale W, Heron N, Langley J, McCarthy AD, Quinn A, Reed H, Stanton A, Shaw PJ, McDermott CJ, Mazza C. 2016. Assessment of the Sheffield Support Snood, an innovative cervical orthosis designed for people affected by neck muscle weakness. *Clinical Biomechanics* 32: 201-206. doi:10.1016/j.clinbiomech.2015.11.010

Write-up of phase 1 of the Head-Up project, testing the novel device against other neck supports on 12 healthy volunteers.

[5] Sheffield Institute for Translational Neuroscience. n.d. Head-up. As of 3 May 2016: <http://sitran.org/clinical-studies/headup/>

Current status of the Head-Up project as it tests the neck support device on 20 users with MND.

### *11.1.7. Empowering local communities to advance research and improve public health*

#### **Case study**

The NIHR School for Public Health Research (SPHR) is one of three NIHR-funded national schools. Established in 2012, the SPHR has supported more than 35 projects (2014 data) [1]. The school is promoting research into three main areas: alcohol, ageing well and health inequalities. Within the health inequalities theme, the school is preoccupied with investigating how health interventions could address or avoid perpetuating inequalities.

One of the cornerstones of health promotion interventions is community engagement, as recognised in the Ottawa Charter for Health Promotion [2]. The NIHR SPHR is undertaking a project evaluating the impact of community level control over action to improve the community's neighbourhood [3]. This evaluation project relies on input from the public at all stages of the research, from design to dissemination. Intermediate findings are providing community groups with data that enhance their learning, which is an important element considering that greater community control on decisionmaking should rely on objective information. The latest evidence suggests that collective control can make significant contributions to curbing health inequalities; therefore the evaluation also seeks to identify ways to support greater control by communities [3].

The evaluated initiative, Big Local, has received over £200 million from the Big Lottery Fund and will involve more than 150 communities across England over the next 15 years [4]. The main aim is to give residents living in disadvantaged places control over actions meant to improve their areas. Each community can receive at least £1 million, as well as other support, to design interventions to improve their neighbourhoods. The overall evaluation funded by the NIHR SPHR is being led by Liverpool and Lancaster Universities Collaboration for Public Health Research (LiLaC), one of the eight academic centres of public health excellence that form the SPHR. It also involves collaborations with other current SPHR member institutions [4]. The evaluation is paying great attention to public involvement, in line with the NIHR's expectation that patients and the public are actively involved in the research NIHR funds. A Resident Network, comprising residents of Big Local areas has been set up to achieve this type of involvement. The network works in partnership with researchers and practitioners to further the accessibility and quality of research [5].

An output resulting from this collaboration is a neighbourhood audit tool designed to increase the understanding about features of areas where people spend their time. In developing and testing the tool, input from the people who live in the respective communities has been instrumental [5]. In the area covered by West End, Morecambe's Big Local, researchers engaged members of the community through locally trusted organisations, existing community groups working with young people, as well as traditional dissemination methods such as flyers and word of mouth [6]. A series of four workshops was used to gather the insights of selected young people from the community. The participants were positive about being able to provide their input and opinions towards the development of the tool. The researchers also found this process valuable, highlighting the importance of local knowledge in its development; meetings to further assess the tool are envisaged [6].

The overall evaluation consists of two phases. Phase 1, which started in January 2014 aimed at identifying early learning about effective ways to support community empowerment and control in disadvantaged neighbourhoods; develop methods for evaluations of complex area-based initiatives and assess the feasibility of Big Local on health and wellbeing. Phase 1 of the evaluation also established baseline datasets and a typology of Big Local areas [3]. Phase 2, which started in October 2015, is concerned with the identification of health and social impacts of Big Local [4]. These findings are now being used to advance learning for the communities as well as professionals from the public health and third sector. In the words of the Local Trust's Chief Executive, 'SPHR have shared with us publicly available data – benchmarking for the communities – regarding education, health and employment. So we learned a bit and the communities can access that as well. We now have that data by postcode which we did not have previously' [7]. Knowledge gathered through this evaluation is also being disseminated in the form of academic articles [8][9].

Interestingly, even at this early stage, the National Institute for Health and Care Excellence (NICE), in its communication on the Guidelines on Community Engagement, identifies research springing from this evaluation as relevant for future updates of this guideline [10].

While the NIHR SPHR's evaluation of Big Local is ongoing, the evaluation of the West End, Morecambe project demonstrates involvement of the public in the development, conducting and disseminating of research. Recognition by NICE of the potential of this research to contribute to future guidelines is indicative of the breadth of impact this programme will have upon its completion.

## Evidence

[1] National Institute for Health Research. 2015. School for Public Health Research – Advisory Board Meeting 23 Oct 2014. As of 2 May 2016: <http://sphr.nihr.ac.uk/wp-content/uploads/2015/04/SPHR-23rd-Oct-2014-Adv-Board-Notes-web.pdf>

These are the minutes of the meeting of the 2014 Advisory Board meeting, which highlight the developments of the school in the past year.

[2] World Health Organisation. 2016. The Ottawa Charter for Health Promotion. As of 2 May 2016: <http://www.who.int/healthpromotion/conferences/previous/ottawa/en/>

The international document setting out principles for health promotion in 1986.



[3] School for Public Health Research. 2014. Health inequalities research programme: Evaluating an initiative to put communities in control of neighbourhood improvements. As of 2 May 2016: <http://sphr.nihr.ac.uk/wp-content/uploads/2014/11/27-sphr-asm-2014-hi-programme.pdf>

The poster presents an overview of the progress of the evaluation, focusing on Phase 1.

[4] School for Public Health Research. 2016. About the Communities in Control study. As of 2 May 2016: <http://sphr.nihr.ac.uk/health-inequalities/about-the-communities-in-control-study/>

Webpage on the Communities in Control study.

[5] School for Public Health Research. 2016. Public engagement. As of 2 May 2016: <http://sphr.nihr.ac.uk/health-inequalities/public-involvement/in-partnership-with-practice-and-communities/>

Webpage on the Communities in Control study looking at partnership with practice and communities.

[6] Local Trust. 2015. Recruiting and training young people as community researchers: National Institute for Health Research and West End, Morecambe. As of 2 May 2016:

<http://localtrust.org.uk/news/blogs/community-researchers#sthash.wJy4vzs7.dpuf>

This piece presents insights from the researchers and young people who were selected from the community vis-à-vis the development of the audit tool.

[7] School for Public Health Research. 2016. Pioneering new approaches to public health research: Insights from the NIHR School for Public Health Research. London: NIHR. As of 2 May 2016: [http://sphr.nihr.ac.uk/wp-content/uploads/2016/02/Pioneering-New-Approaches-SPHR-NIHR-A4-Web-download-vesion-r1\\_single-pages-2.pdf](http://sphr.nihr.ac.uk/wp-content/uploads/2016/02/Pioneering-New-Approaches-SPHR-NIHR-A4-Web-download-vesion-r1_single-pages-2.pdf)

This brochure describes a series of case studies from the School for Public Health Research, among which ‘Does giving residents control over decisions about their neighbourhoods improve their health?’

[8] Ponsford R, Collins M, Egan M, Lewis S, Orton L, Salway S, Townsend A, Halliday E, Whitehead M, Popay J. 2015. Development of a framework for identifying and measuring collective control as a social determinant of health: Findings from an evaluation of a natural policy experiment in empowerment. *Lancet* 386: S64. doi:10.1016/S0140-6736(15)00902-2

The research presents the findings from the developed and applied contextually specific framework for exploring collective control in the early stage of a UK area-based community empowerment initiative. The research found that the conceptual framework helped identify shifts in collective control capability that appeared as a result of the introduction of the intervention.

[9] Halliday E, Orton L, Egan M, Lewis S, Powell K, Townsend A, Tyrrell R, Whitehead M, Popay J. 2015. Understanding area-based community empowerment initiatives as events in systems and the implications for evaluating their potential to affect health inequalities. *Lancet* 386: S41. doi:10.1016/S0140-6736(15)00879-X

The research provides insights into how and why the intervention adapts over time as communities develop new capacities and learn from early implementation.

[10] National Institute for Health and Care Excellence. 2016. NICE Public health guideline on Community Engagement (NG44): Relevant ongoing NIHR research: February 2016. As of 2 May 2016: <https://www.nice.org.uk/guidance/ng44/resources/nihr-research-2368402381>

Among the literature that could inform future updates of the NICE guideline, the document mentions the project titled Communities in Control study phases 1 and 2: An evaluation of a natural policy experiment in community empowerment.

### *11.1.8. Speeding up access to vital clot-busting stroke therapies via operational research*

#### *Case study*

Patients with acute ischemic stroke – caused by a blood clot in the brain – have a critically limited time to receive clot-busting (‘thrombolytic’) drugs if they are to avoid suffering permanent brain damage. In urban environments, hyper-acute stroke research centres provide an expedited route to specialist centralised care, with NIHR-supported research in these units helping to improve patients’ timely access to these drugs. In dispersed rural environments, such factors as longer ambulance travel times to hospital add considerable complexity to local decisions around how to provide the best possible stroke care. NIHR-funded researchers at the Peninsula Collaboration for Health Operational Research (PenCHORD) have used advanced computational modelling to inform these decisions and achieve measurable improvements in the numbers of patients receiving life-saving thrombolytic treatment in the south-west of England [1].

Supported through the NIHR Collaboration for Leadership in Applied Health Research and Care (CLAHRC) South West Peninsula, PenCHORD was set up to model healthcare services and predict the impact of changes to patients’ care, before making decisions that impact on their health [2]. To address the challenge of how to provide early thrombolysis to patients with acute ischemic stroke, the team created a detailed working model of patients’ care pathway, from the initial signs and symptoms of a stroke, to first contact with paramedics, to when patients arrive in hospital and begin treatment [3]. They then used this model to run computer simulations of different ‘what if’ scenarios, such as the impact of increased pressure on radiology services (which would act to delay patients receiving a brain scan required to diagnose ischemic stroke) and the speed of communication among different actors in the care pathway (such as paramedics, triage nurses and on-call stroke physicians) [4].

The simulation provided information on improving patient care at virtually no cost, such as paramedics calling ahead to specialist stroke care units, allowing the units to prepare for the patient before the patient’s arrival. Initially working in collaboration with the Royal Devon and Exeter Hospital, in 2011 the PenCHORD team began to apply these changes, with dramatic results. Within a year and a half, the number of patients who were receiving thrombolysis was comparable to those treated in the most specialised urban hyper-acute units (an increase from 4.7% to 11.5% of patients with stroke). In parallel, the average time patients had to wait for this treatment nearly halved (from 58 to 33 minutes). More recent results indicate that thrombolysis treatment rates are at comparable levels to those of large specialised urban centres (14%), representing many more patients likely to have significantly improved outcomes thanks to their receiving clot-busting therapy [3].

Following its initial successes, the PenCHORD team has since extended its modelling work to other hospitals in the region. Making best use of the value of the NIHR CLAHRC's role as a bridge between research and clinical practice, the team is working closely with the Strategic Clinical Network to partner with acute stroke staff in seven local trusts. Each case requires them to feed detailed information gathered from routine clinical care into their simulation, while involving appropriate staff in the hospital, who, ultimately, are responsible for implementing any changes [5].

The NIHR's investment in PenCHORD, through CLAHRC South West Peninsula, is allowing healthcare staff to make small, but significant, improvements to the care they provide, based on innovative models that take a novel approach to analysing local healthcare data. In the case of stroke survivors who receive vital clot-busting therapy at a point before they suffer potentially permanently disabling brain damage, this work is having a profound impact on patients' lives.

### Evidence

[1] Collaboration for Leadership in Applied Health Research and Care South West Peninsula, NHS England. n.d. PenCHORD. As of 5 May 2016: <http://clahrc-peninsula.nihr.ac.uk/research/penchord-redesigning-stroke-pathways-at-the-royal-devon-exeter-hospital>

Overview of PenCHORD's efforts to model and improve stroke care services in the south-west of England.

[2] Collaboration for Leadership in Applied Health Research and Care South West Peninsula, NHS England. n.d. Research and Projects. As of 5 May 2016: <http://clahrc-peninsula.nihr.ac.uk/penchord>

Description of PenCHORD's remit and activities.

[3] NIHR PenCLAHRC. Improving Stroke Care (homepage). As of 5 May 2016: <https://penclahrc.exposure.co/improving-stroke-care>

Website describing features and outcomes of PenCHORD's stroke modelling study.

[4] Monks T, Pitt M, Stein K, James M. 2012. Maximizing the Population Benefit From Thrombolysis in Acute Ischemic Stroke. A Modeling Study of In-Hospital Delays. *Stroke* 43: 2706-2711. As of 5 May 2016: <http://stroke.ahajournals.org/content/43/10/2706.long>

Paper describing the results of PenCHORD's modelling study and recommendations for reducing in-hospital delays.

[5] National Institute for Health Research. 2014-2015. Collaboration for Leadership in Applied Health Research and Care South West Peninsula (PENCLAHRC). London: NIHR. As of 5 May 2016: [http://clahrc-peninsula.nihr.ac.uk/uploads/attachments/Projects/Annual%20Report%202014-15\\_Stroke%20Pathways.pdf](http://clahrc-peninsula.nihr.ac.uk/uploads/attachments/Projects/Annual%20Report%202014-15_Stroke%20Pathways.pdf)

Further summary of the PenCHORD stroke services modelling study, detailing recent impacts and plans for further work.

### *11.1.9. Meeting the needs of older people by involving them in the design of local care*

#### Case study

The NIHR supports community-driven research that engages service users in the development of improved policy and practice for their region. A project conducted in four English regions, with involvement from elderly people from each region, helped to establish user- and carer-centred approaches to care transitions for older people.

Transitions between services have the potential to negatively affect the health and well-being of older people. This is a serious concern given the frequency with which many older people – particularly those with complex needs – move between services [1]. In order to address this concern, the NIHR Services and Delivery Organisation programme funded a study in Solihull, Leicester, Manchester and Gloucestershire to pioneer systematic engagement of service users – in this case elderly people – at every stage of the research in order to identify user-centred approaches to care transitions for each region. Within this overall objective, there were projects focused on people with dementia and on older people from ethnic minorities. In each region, older people with recent experience of care transition were trained in social research methods and brought in to the project as co-researchers. In addition, at each location the research team worked in partnership with the voluntary and statutory sector organisations expected to put the study's findings into practice. By involving local stakeholders, the study aimed to better understand experiences of care transitions.

The study's findings highlighted the significance of the social and psychological needs of elderly people during care transitions [2]. Among the needs identified were consistent relationships with those involved in care, considerate treatment from service providers, informal support networks, and planning and coordination on the part of service providers [1][3]. The study also demonstrated the value of participatory methods in service reviews, particularly with respect to marginalised groups, such as people with dementia [4].

These findings have impacts on policy and practice, both within the four regions where research took place and more widely. Within the study regions, the study informed Solihull's dementia strategy [5][6] and Leicester's adult social care strategy [7] and led to work with carers in developing a carer policy for Gloucestershire [2]. At the national level, policymakers from the Department of Health's Care Quality Commission, the Royal College of Nursing and the Royal College of Social work attended a seminar and participated in discussions on incorporating the study's findings into policy [2]. These policy changes have been accompanied by changes in commissioning. Examples include funding being dedicated to initiatives in Solihull, including dementia outreach provided by the Alzheimer's Society [2]. In addition, the study has influenced the organisation of care, including the role of a Mental Health Support Reablement Team in Solihull and improved coordination between in-patient and community services in Leicester [2].

An example of the study's impact on practice is the increased provision of information to people with dementia. In Solihull, co-researchers helped to develop information packs for people recently diagnosed with dementia, and in Gloucestershire, additional information has been produced to help patients understand care pathways and transitions [2]. Additional changes to practice can be expected through the

study's impact on the training of social workers and reablement staff in Solihull and through staff training on considerate treatment of patients in Gloucestershire [2].

Finally, the study's use of participatory methods has had an impact on the research agenda going forward. For example, in Manchester, a member of the research team has worked with the Manchester City Council Programme Manager for Integrated Community Provision to design an infrastructure and training programme for co-researchers, with the aim of establishing this as a permanent resource at the local level [2]. At the national level, a DVD in which co-researchers describe their participation [8] has been shown at national conferences and been made available as a teaching resource for health and social work students [2]. Members of the research team also worked with INVOLVE, a national group supporting public involvement in the NHS, on a seminar on participatory research to be presented at the Economic and Social Research Council's Festival of Social Science. INVOLVE has used the study's findings in its own work on service user engagement in research [9].

## Evidence

[1] Ellins J, Glasby J, Tanner D, McIver S, Davidson D, Littlechild R, Snelling I, Miller R, Hall K, Spence K. 2012. Understanding and improving transitions of older people: A user and carer centred approach. London: NIHR Service Delivery and Organisation programme. Final report. NIHR Service Delivery and Organisation Programme. As of 14 May 2016:  
[http://www.netscc.ac.uk/hsdr/files/project/SDO\\_FR\\_08-1809-228\\_V01.pdf](http://www.netscc.ac.uk/hsdr/files/project/SDO_FR_08-1809-228_V01.pdf)

Report outlining care transition and older people's experiences.

[2] Research Excellence Framework. 2014. Care transition experiences: Developing a user and carer centred approach. [Case study 38873.] As of 5 May 2016:  
<http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=38873>

Research Excellence Framework case study on experiences of care transitions.

[3] Tanner D. 2011. Identity, selfhood and dementia: Messages for social work. *European Journal of Social Work* 16 (2): 155-70. doi:10.1080/13691457.2011.611795

Journal article on identity in dementia.

[4] Tanner D. 2012. Co-research with older people with dementia: Experience and reflections. *Journal of Mental Health* 21 (3): 296-306. doi:10.3109/09638237.2011.651658

Journal article on research with older people with dementia.

[5] Factual statement provided by Service Manager, Solihull Metropolitan Borough Council.

[6] Factual statement provided by Business Transformation Directorate, Solihull Metropolitan Borough Council.

[7] Leicester City Council Adult Social Care Vision, Priorities and Delivery Summary, 2012–13.

[8] Co-researcher experiences DVD (recorded at Economic and Social Research Council's Festival of Social Sciences event). As of 2 May 2016: <http://www.birmingham.ac.uk/schools/social-policy/departments/health-services-management-centre/news/2012/09/older-peoples-experiences-of-transitions-health-social-care.aspx>

This link leads to a webpage reporting on experiences of care transitions

[9] INVOLVE. 2011. Understanding and improving transitions of older people: A user and cared centred approach. As of 2 May 2016: <http://www.invo.org.uk/posttyperesource/how-to-find-people-to-involve/case-study-one/>

INVOLVE case study on understanding older people's experience in care transitions.

### *11.1.10. Testing non-pharmacological parenting interventions for attention-deficit/hyperactivity disorder*

#### Case study

The NIHR has funded research designed to build an evidence base for the scale-up of community-based innovation. An example is a large-scale, NIHR-funded study assessing the generalisability of existing research findings on a parenting intervention for attention-deficit/hyperactivity disorder (ADHD). Developed in Southampton, it has produced evidence that is expected to influence national guidelines and reach patients nationwide.

ADHD is the most common behavioural disorder in the UK, affecting between 2 and 5 per cent of UK children [1], and it is associated with increased risk of educational failure, interpersonal problems and mental illness [2]. While medication provides a short-term means of controlling symptoms, it has been linked to side-effects, including loss of sleep and restricted growth [3], and many parents prefer to avoid medication [4]. Moreover, the non-pharmacological intervention recommended by the National Institute for Health and Care Excellence (NICE) is a group-based programme, whereas parents generally prefer individualised programmes [5]. The New Forest Parenting Programme (NFPP) was developed in the 1990s in clinics around Southampton to provide an effective alternative to medication for the treatment of ADHD in children. It is an individualised, home-based programme that teaches patients how to modify their child's behaviour.

Three randomised control trials (RCT) of the NFPP have been conducted, producing results that demonstrate positive effects and leading to modifications of the programme [6][7][8]. Building on this work, the NIHR provided funding for a five-year study, known as the Programme for Early Detection and Intervention for ADHD (PEDIA). Led by Professor Edmund Sonuga-Barke of the University of Southampton, the study is designed to establish the relative value of individualised approaches to non-pharmacological treatment of ADHD, as compared with group-based approaches. Evidence from a literature review and stakeholder interviews was analysed to identify target patients for the ADHD study, as well as barriers to uptake and required modifications to the NFPP. This fed in to a large-scale RCT, which assessed the generalisability of the findings from earlier, smaller-scale trials in order to provide evidence for scaling the NFPP up to the national level. Professor Sonuga-Barke has stated that being funded by the NIHR, rather than through research councils or other sources, facilitated the close collaboration between the University of Southampton and clinical partners required to conduct an RCT on this scale [9].

The PEDIA study is expected to have an impact on national-level policy, leading to changes in clinical practice. Findings are expected to be published in time for the next revision of the NICE guidelines on recognition and management of antisocial behaviour and conduct disorders in children and young people.

Professor Sonuga-Barke has indicated that the NICE guideline committee is aware of the study's findings and expects PEDIA to influence the content of the revised recommendations [9]. According to Professor Sonuga-Barke, clinicians attending talks at which emerging findings have been presented have been highly receptive to results regarding the value of the NFPP's individualised approach to non-pharmacological treatment of ADHD [9]. This expected impact – a nationally available alternative to group-based interventions – would represent an example of NIHR research building on local-level innovation to provide people across the nation with treatment that is in line with patient or carer preferences.

## Evidence

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[9] Interview with Professor Edmund Sonuga-Barke (principal investigator, PEDIA), 26 April 2016.





## 12. The NIHR at 10: 100 Activities, 10 Themes, 1 Transformation

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In the past 10 years, R&D funding by and for the NHS has changed significantly as a result of NIHR's formation. Across the 100 case studies in our report, there is strong evidence of substantial impact across patient benefits, the delivery of health and social care, public policy, economic growth and the generation of knowledge. Therefore, transcending the individual case studies presented in this report is the possibility of an eleventh, cross-cutting benefit: the transformative effect NIHR has had, both on itself as a funder for R&D in the NHS and on the wider health research system.

While we have not systematically evaluated NIHR's achievements against the goals in *Best Research for Best Health*, nor against any other document or set of objectives, we can say that among the 100 case studies of impact synthesised in this report, there is evidence of impact that spans the five main goals set 10 years ago. Drawing on just one example out of the 100 for each goal, we find:

- The use of tranexamic acid to prevent clotting, which could benefit more than 1 million people worldwide, is one way in which NIHR-funded research has come to be recognised internationally as world leading.
- The introduction of a leadership development programme for NIHR faculty to manage transformational research demonstrates how capacity building is used as a science policy intervention.
- NIHR's contribution to the testing and roll-out of the World Health Organization's Surgical Safety Checklist, a tool to reduce life-threatening complications now used by 1,790 healthcare organisations worldwide, is helping to improve health and social care.
- The drive to make all research publications open access, in NIHR's case via a Journals Library, as well as introducing multiple initiatives to enable better and improved access to research data, ensures that knowledge is shared and managed in an efficient manner.
- The commitment to 'principles of transparency, fairness and contestability'<sup>7</sup> is affirmed by NIHR establishing a competitive bidding process for its research infrastructure funding, involving international assessment panels in order to ensure that money is spent in a transparent and accountable way for the public good.

The case studies in this report also demonstrate the effects of NIHR's investments in research infrastructure. A significant proportion of NIHR's support for research is in the form of investing in the

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<sup>7</sup> Research and Development Directorate, Department of Health. 2006. *Best Research for Best Health: A new national health research strategy*. London: Stationery Office. P. 32

research infrastructure in the NHS, thereby creating an environment where high-quality research is possible by offering funding that allows for the building of new facilities, acquisition of equipment, financing of staff who are drawn towards research, training of researchers and incentivising of industry to engage in early-stage research. These wide-ranging efforts to support the research infrastructure make NIHR a unique actor that brings together clinicians, researchers and the public to advance research discoveries and improve health and care – an actor that underpins research funded by charities, industry and government departments.

Across the case studies we found evidence that a change in culture and values has occurred. A range of stakeholders, from patient groups to research funders, told us that they now feel that researchers are doing the right type of research, in the right way and for the right reasons. For example, the activities supporting trainees, clinicians and future research leaders have served to build capacity and expertise throughout the clinical career pathway, providing support for clinicians and other healthcare professionals to engage in research. INVOLVE, together with other efforts across the system in patient and public involvement and engagement, have led to a shift in the way that the public and service users are engaged in research. They are an active and integral part of the process, helping to both shape and improve the quality of research that is produced.

Clinical research is also supported and valued in a way that it was not before. We can see evidence of this captured in the impact case studies for the 2014 Research Excellence Framework. A brief analysis showed that nearly 250 case studies – or about 12 per cent of those submitted in the field of life sciences – cited NIHR funding as contributing to health and patient benefits. These findings lead us to conclude that one of the things that NIHR may have helped to achieve is that a higher value is placed on clinical and applied research throughout the sector.

This all suggests that it is the interaction between the physical and the cultural, between the project and the system, between the patient and the researcher that has supported system-level change. NIHR has helped to integrate clinical research across organisational and infrastructural boundaries, thereby creating a virtuous circle of valuing and doing applied and clinical research. NIHR infrastructure allows it to draw in funding from others, including the life sciences industry, charities and research councils. NIHR's nationwide Clinical Research Network supports the use of this infrastructure by the entire system, by finding the right patients to take part in studies. These combined efforts facilitate the translation of research into innovations for the health service, and they facilitate external partners' funding of clinical research. NIHR has helped to create this systemic infrastructure, both technical and knowledge-based, for clinical research. This change is perhaps the most important, and we suggest it has been done in a fashion which is integrated, additive and synergistic with other parts of the wider health and research system. As one interviewee told us, 'NIHR has changed the system for the NHS'; that, 10 years in, seems like it will endure.