ADDENBROOKE’S CHARITABLE TRUST

EVALUATING THE IMPACT OF RESEARCH FUNDING

A report prepared by Dr Jenny Longmore PhD FBPharmacolS

Overview

Medical research in a clinical setting is essential if patient care and treatment is to be further improved. Through funding research awards and fellowships¹, ACT provides significant support for clinical research at Addenbrooke’s and the Rosie hospitals, fuelling the public domain with new knowledge to facilitate the translation of research into tangible patient benefit. Between 2007 and 2013, ACT granted 117 research awards (totalling £2,707,547) and supported more than 200 researchers at CUH and connected organisations.

In 2013 it commissioned an independent evaluation of the impact of this funding. The investigation highlighted the following:

- While many of ACT’s awards were small they were of high strategic value, investing in people, extending CUH research capabilities and adding value to leverage external funding for more extensive, longer term research projects.

- ACT-supported research provided opportunities for patient and public involvement through participation in clinical studies and/or the use of patient tissue and blood samples.

- Naturally, given CUH’s research strengths, cancer projects accounted for approximately half of ACT research funding. Other healthcare categories included reproductive and child health, oral and gastro-intestinal, cardiovascular, stroke, mental health and neurology. Specifically, research was directed at better understanding biological alterations that cause disease and developing new methods for detecting and diagnosing disease but also covered the discovery and clinical testing of new treatments, clinical management and health service research.

- Fuelling the public domain with new knowledge facilitates the translation of research into tangible patient benefits in the future. Ninety five original research papers were published acknowledging ACT alongside other funders, demonstrating that ACT-funded research is embedded in a wider body of knowledge and collaboration.

¹ An independent evaluation of ACT’s Cambridge Clinical Research Fellowships can be found at: www.act4addenbrookes.org.uk/researchfellowships
• ACT-funded research resulted in high value successes, delivering immediate patient benefits by changing hospital policy and guidelines, informing staff training, and exerting influence in the East Anglia region and beyond.

Overall the evaluation demonstrated a successful track record of ACT supporting research at CUH and recommended the next steps to work strategically and in partnership with the NIHR\(^2\) Cambridge BRC and other supporters, to enhance the availability of funding for high quality research of relevance to CUH patients and the wider NHS.

\(^2\) National Institute of Health Research
Background

Addenbrooke’s Charitable Trust (ACT) is the independent registered charity for Cambridge University Hospitals NHS Foundation Trust (CUH), which includes Addenbrooke’s and the Rosie hospitals. Its mission is to provide support for the care, research and education provided by CUH, achieving benefits for patients over and above those that can be achieved through mainstream funding alone.

ACT trustees make available medical research awards to support innovation, pump-prime new initiatives and bridge gaps in grant funding. In 2013, ACT commissioned an independent evaluation of past research funding as a means of reporting to donors and with the objectives to assess:

- impact - towards public and patient benefit and transforming healthcare
- positioning – within the wider context of CUH research and research funding in the UK.

*Addenbrooke’s Charitable Trust (ACT) deeply appreciates the generosity of members of Cambridge University Hospitals’ (CUH) Research Advisory Committee, in particular its Chair, Dr John Bradley, in providing expert peer review and the NIHR Cambridge Biomedical Research Centre for co-funding some research awards.*

Key findings

**How ACT supported CUH research**

Between 2007 and 2013, ACT supported more than 200 scientists, applying funding flexibly in response to opportunities to add value and invest in people. Projects were of one year duration or less. This approach, coupled with regularly granting numerous small value awards (i.e. 77 awards were of £25,000 or less), had substantial impact and was a high value strategy.

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<tr>
<th>ACT research awards</th>
<th>2007</th>
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<td></td>
<td>£469,986 (16)</td>
<td>£307,300 (14)</td>
<td>£446,522 (15)</td>
<td>£402,774 (21)</td>
<td>£220,899 (12)</td>
<td>£561,536 (23)</td>
<td>£298,530 (17)</td>
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**GRAND TOTAL: 117 awards made to the value £2,707,547**

Different types of research awards addressed different purposes. Detailed evaluation of the sub-set of awards granted 2010-2013, showed pilot and bridge awards were the mainstay across this period (47% and 24% respectively). The purpose of pilot (or pump priming) awards is to support innovation and generate pilot data towards more extensive

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3 The majority (92%) were researchers from CUH or the University of Cambridge; the remainder were collaborations with University College London, University of Newcastle, Papworth Hospital or Luton and Dunstable NHS Trust.

4 Other types of research award were: Infrastructure – e.g. equipment dedicated to research; training e.g. using new equipment or techniques; supplementary - high value opportunities to extend research funded by others.

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grant applications for external funding and bridge awards fill temporary gaps between major funding awards (from external organisations) allowing research to continue, preventing disintegration of valuable research teams or providing short term support for researchers new to CUH.

"Support from ACT has been invaluable in enabling our group to initiate important experiments designed to investigate the safety and effectiveness of a novel drug for improving outcomes after kidney transplantation. This work now forms part of a more extensive research programme and, when completed, will allow us to proceed with the next stage of drug testing and ultimately benefit transplant recipients."

Mr Kourosh Saeb-Parsy University Lecturer and Honorary Consultant Transplant Surgeon

Pilot and bridge awards are intended to leverage follow-on funding. Assessing leverage (or the multiplier effect) is difficult, although external funding decisions that such awards feed into are in the public domain, the grant applications themselves (containing information about supporting pilot/bridge studies) are confidential. Nevertheless a detailed snapshot of 21 of the 33 ACT research awards granted in 2010/2011 showed substantial success, with some investigators reporting follow-on funding with a 10:1 leverage ratio.

Below are two examples of researchers who received ACT funding and later went on to secure follow-on grants:

1) **Adding value** - Dr Richard Sandford (awarded an ACT grant of £19,700):

Primary biliary cirrhosis is a chronic liver disease and many patients do not respond well to treatment and require a liver transplant. This award helped understand which genes are associated with the more severe forms and strengthened collaborations with other universities, broadening the research into a UK-wide Primary Biliary Cirrhosis consortium.
of researchers which, in 2013, received an MRC Stratified Medicine Grant (£1.6m apportioned to Dr Sandford, University of Cambridge)\(^5\).

2) **Investing in people** – Dr Jane Goodall (awarded an ACT grant of £15,091):

This ‘between grant’ support for Dr Goodall focused on the role of IL23, a key immune hormone, in causing inflammation in arthritis and other pathological immune responses and the potential of interfering with this biochemical pathway as a new therapeutic approach. The award helped Dr Goodall secure a Senior Fellowship from Arthritis Research UK (£800,261) and an MRC grant (£226,108)\(^6\).

"ACT funding allowed me to submit an application to secure a Senior Fellowship from Arthritis Research UK. From this position I have now secured more research funds and a position as a Senior Lecturer with the Division of Cardiovascular Medicine at the University of Cambridge. ACT support was vital to my career progression and my ability to continue my work in clinical research".

**Dr Jane Goodall, Senior Lecturer, University of Cambridge**

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<th>Leverage: the multiplier effect</th>
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<td>No. awards</td>
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<td>21 (of 33 awards granted 2010/2011)</td>
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ACT provided pivotal support to clinical academic researchers at CUH. In addition to the dedicated Cambridge Clinical Research Fellowship scheme (providing short term support at the entry point into clinical academic research training - separately evaluated\(^7\)), ACT awarded a small number of fellowships to bridge gaps around the scarcity of external funding at the intermediate point in the training pathway (immediately following PhD qualification).

Below are two examples of researchers who received ACT fellowships to facilitate transitions in the clinical academic training pathway:

1) **Investing in people** - Dr Michael Chapman (awarded an ACT grant of £79,091):

This research focused on the role of genetic mutations in multiple myeloma and supported the transition of Dr Chapman to an independent clinical academic researcher helping him secure a Wellcome Trust Intermediate Fellowship (£972,933)\(^8\).

2) **Investing in people** – Dr Matthew Murray (awarded an ACT grant of £56,517):

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\(^{5}\) [http://www.medschl.cam.ac.uk/mrc-award-for-primary-biliary-cirrhosis-research/](http://www.medschl.cam.ac.uk/mrc-award-for-primary-biliary-cirrhosis-research/)


\(^{7}\) [http://www.med.cam.ac.uk/blog/arthritis-research-uk-senior-fellowship_awarded_to_jane_goodall/](http://www.med.cam.ac.uk/blog/arthritis-research-uk-senior-fellowship_awarded_to_jane_goodall/)

\(^{8}\) [See evaluation summary and full report at: http://www.act4addenbrookes.org.uk/researchfellowships](http://www.act4addenbrookes.org.uk/researchfellowships)


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This award allowed Dr Murray to continue his research on the regulation of cancer-promoting proteins in malignant germ cell tumours which usually occur in the testis or ovary. Dr Murray received the prestigious ‘Young Investigator of the Year 2012’ from the Royal College of Paediatrics & Child Health and SPARKS and was appointed as Academic Consultant Paediatric Oncologist at Addenbrooke’s Hospital.

The research supported and how it was positioned
Of ACT’s grants awarded 2010-2013, 62% supported cancer research. There are a number of reasons for this, including:

- CUH’s cancer researchers are embedded within Addenbrooke’s, which is a large regional hospital, and are influenced by the needs of their patients
- there is a wealth of cancer research expertise and technologies accessible within the Cancer Research UK Cambridge Institute
- there is a dedicated cancer research fund. This is not mirrored across all disciplines.

Non-cancer areas, similar to national trends (Luengo-Fernandez et al 2012), are under-represented in ACT’s portfolio to date, however there were valuable successes in terms of influencing clinical practice and patient guidelines at CUH, the East Anglia region and internationally (see below).

The evaluation deployed the Health Research Classification System (HRCS) showed ACT-funded research (whether cancer related or non-cancer related) focused on two main types of research activity:

- the development of new methods for detection, screening and diagnosis of disease
- aetiological research aimed at better understanding the biological alterations that cause disease.

This reflects the strengths of CUH research and the substantial funding for aetiological research which CUH receives from major national funders such as the Medical Research Council, the Wellcome Trust, Arthritis UK and Cancer Research UK. Importantly there is a clear link between the purposeful ACT pilot and bridge awards with external grant making bodies.

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9 http://cuh.org.uk/addenbrookes/news/2012/april/cambridge_childrens_doctor_scoops_prestigious_prize.html
10 Health Research Classification System HRCS was developed by the UK Clinical Research Collaboration http://www.hrcsonline.net/rae to analyse funding made available by Research Councils, NIHR and large and small charitable funders. UK Health Research Analysis published by UKCRC in 2006 and revisited in 2009/10; ‘From Donation to Innovation – An analysis of health research funded by medium and smaller sized medical research charities’ published by UKCRC in 2007.

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Benefits – generation and dissemination of new knowledge
Crucially the independent evaluation demonstrated that the goal of generating new knowledge of relevance to patients and the NHS was fulfilled. There was extensive dissemination ensuring the research findings allow others to develop concepts further. Between 2008 and 2013, 95 published research papers (acknowledging ACT support alongside other funders) were published, showing that ACT research is embedded and contributes to a wider body of knowledge.

The publications mainly fell into three types of research activity (with approximately half related to cancer research and one quarter to cardiovascular, oral and gastrointestinal research and reproductive health and childbirth research):

- aetiology research
- developing new methods for screening, detection and diagnosis
- clinical evaluation of new treatments and interventions.

Researchers made presentations at local, national and international meetings including scientific conferences and patient support groups, and some received prizes for scientific excellence.
Top five influential research publications
(acknowledging ACT alongside other funders)

from Google Scholar

(this may change due to less frequent citations of more recent papers)

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<th>No. citations</th>
<th>HCRS code</th>
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*The paper reports on the role of interleukins in regulating the immune response and how alterations in this system may increase the susceptibility of some patients with autoimmune diseases to some types of infection. It is a robust addition to a growing body of evidence.


*The study reported on a family of genes encoding for Forkhead Box proteins (FOX genes - which are binding proteins that regulate transcription of DNA) and showed that mutations in FOX genes are involved in some rare forms of congenital malformations that are lethal in neonates. Since this publication knowledge of the role of mutations in FOX genes has been extended and in the US a laboratory offers a service for analyses for genetic alterations of the FOXF1 gene which is of use in genetic counselling (Sen et al 2013).

| KHAN FZ, VIRDEE MS, PALMER CR, PUGH PJ, O’HALLORAN D, ELSIK M, READ PA, BEGLEY D, FYNN SP, DUTKA DP. 2012. Targeted left ventricular lead placement to guide cardiac resynchronization therapy The TARGET study: a randomized, controlled trial. J Am College Cardiol 59, 1509-1518. | 87 | 6 |

Benefits for patients

A NIHR survey reported 9 out of 10 people would participate in research if they were diagnosed with a medical condition or disease\(^\text{11}\). Between 2010 and 2013, 80% of ACT-supported research provided opportunities for patient and public participation either through clinical studies or through the use of, tissue samples / organs or patient data.

Linking medical research to policy and clinical practice is essential for patients and the NHS to realise benefits, however, tangible benefits often lie in the future and there are recognised difficulties with ‘attribution’ as to which funders supported the resulting research. This applies to ACT-funded research, given the distribution towards early stage research. However, a number of important immediate benefits arose and detailed analysis of the 2010/11 subset of awards showed some low cost yet high impact awards resulting in immediate benefits for CUH patients through changed hospital and regional practice.

Dr Marcus Redley (£22,778), for example, undertook the challenging topic of assessing and improving the quality of care and treatment given for individuals with learning disabilities at Addenbrooke’s Hospital. The wide and targeted dissemination of his study findings raised awareness, stimulated discussion and formed the basis of staff induction and training. This was achieved through multiple presentations at specialist conferences and patient support groups within Addenbrooke’s Hospital, the East Anglian Region and nationally. The outcomes supported grant applications to other funding bodies.

“The successes of this project, both in terms of its impact within Addenbrooke’s, and the securing of funding from the NIHR’s Research for Patient Benefit Programme can be attributed to a close and amicable collaboration between researchers the university and the staff within the hospital.”

Dr Marcus Redley, Cambridge Intellectual and Developmental Disabilities Research Group

Another example comes from Ms AnneMarie Winstone and Dr Christopher Verity (£6,558) who developed a pocket guide on Fetal Alcohol Syndrome for midwives and new and expectant mothers. This was distributed to 13 NHS Trusts and included on the Public Health England website. Ms Winstone’s team raised awareness and provided training to organisations local to Cambridge, nationally and internationally including media interviews for national TV and radio news.

“This midwifery research project meant I made many new connections with health care professionals, fantastic parent and carer support groups, as well as children affected by Fetal Alcohol Syndrome. Fetal Alcohol Spectrum Disorders are 100% preventable and pregnant women need to be made aware that the safest way to avoid these disorders is by not drinking any alcohol in their pregnancies.”

Ms AnnMarie Winstone, Research Nurse Addenbrooke’s Hospital

Next steps
The evaluation showed a successful track record of ACT supporting research at CUH. It recommended that ACT continues with its impact evaluation and for ACT to work strategically and in partnership with the NIHR Cambridge BRC and other supporters, to enhance the availability of funding for high quality research of relevance to CUH patients and the wider NHS.

Acknowledgements
We are grateful for the expert advice and input from ACT (Julia Brown, Louise Conway, Stephen Davies, Anne Jackson, Marie Janson, Mark Olivier and Samantha Sherratt) and CUH (John Bradley, Denise Chapman, Carol Hatfield, Isla Kuhn, Carol Tabor).

Bibliography
- RAND Europe 2006. Reviewing the returns of research: capturing payback from funding by the Arthritis Research Campaign.
Some examples of potential patient and healthcare benefits emerging from ACT funded research

<table>
<thead>
<tr>
<th>Cancer research (including anal, blood, brain, breast, colon, germ cell, lung, ovarian, pancreas, prostate, renal, thyroid and urethral):</th>
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<tbody>
<tr>
<td>- new ways to diagnose cancer and monitor its progression and response to treatment</td>
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<td>- new treatments tailored to the patient – e.g. using differences in the biology of the same type of cancer in children and adults to develop age-specific treatments or treating subtypes of breast cancer in different ways</td>
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<td>- identifying factors that increase risk of more aggressive cancer progression including ways to screen and monitor higher-risk patients and develop alternative treatment pathways.</td>
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<tr>
<th>Non-cancer (including cardiovascular, oral and gastrointestinal, reproductive health and childbirth, inflammation and immune system, mental health, neurology):</th>
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<td>- knowing how risk factors (such as genes and autbodies) predispose to a particular disease and incorporating this information into clinical management strategies, improved monitoring of patients at higher risk for their disease worsening</td>
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<td>- biomarkers as new approaches for diagnosis, predicting and monitoring patient responsiveness to treatment, (e.g. using information about the biological consequences of infection or brain injury)</td>
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<td>- enhanced reliability of blood tests</td>
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<td>- refinement of existing treatments or developing less invasive surgical / diagnostic techniques</td>
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<td>- new treatments including ways to lessen side-effects and long-term patient follow-up of the impact of treatment</td>
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<td>- improvements in controllable factors influencing patient response to treatment or care (e.g. modifying doctors shift change procedures)</td>
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