OHE Consulting
A division of the Office of Health Economics

Consulting Report

Exploring the Interdependency between Public and Charitable Medical Research

Report for Cancer Research UK

20 April 2011

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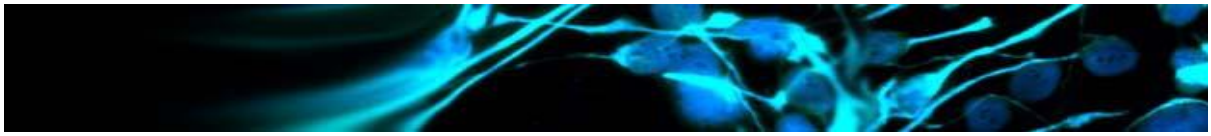

A Report for Cancer Research UK

Exploring the Interdependency between Public and Charitable Medical Research

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Executive Summary

- In its Spending Review released in autumn 2010, the UK Government announced its plans for reducing public expenditure to help cut the fiscal deficit. The Government recognised the large and positive contribution of scientific research to the UK economy; the science budget was not hit as badly as budgets for other sectors. However, given the financial pressure faced by the government now and for the foreseeable future, Exchequer support of health research is likely to remain under scrutiny. This is true for both the health and economic return on investment and the interplay with other sources of funding, specifically charitable funding. The last concern is the focus of our study.

- The objective of this study was to explore the interdependence between publicly-funded and charity-funded medical research[1], and what impact changing levels of public funding might have on medical research and, more broadly, on the UK economy as whole. We assess whether a reduction in public funding for medical research would, or would not, be expected to result in disproportionate damage to the UK. In other words, would a cut of £X million of public funding of medical research cause more than £X million of damage?

- We conducted a literature review of peer-reviewed economic papers and other relevant papers and reports available in the public domain (the grey literature). Our intent was to investigate whether government and charity funding of medical research complement or substitute for one another. In parallel, we undertook an interview programme involving key funders and stakeholders directly involved in the UK medical research system. The focus was on understanding the differences in research activities currently funded, how various stakeholders make funding allocation decisions, and the value of joint funding. In addition, we organised and facilitated a workshop that provided an element of peer-review, a check on the validity of our preliminary findings by key experts.

- We found substantial benefits, both financial and qualitative, from the existence of a diversity of funders for UK medical research. These include:

    - Sharing costs and pooling risks for research programmes. This enables high cost studies that might not otherwise be funded, and permits each funder to diversify risk across a wider portfolio of projects;
    - Providing a stable flow of financial support for medical research in the long term;
    - Building an environment more conducive to research in the UK, by drawing on the differing skills and know-how of funders and through the complementarity of research funding across this diverse group of funders;
    - Creating a competitive research environment that has the potential to increase research quality.

- The UK offers a high quality, internationally respected, scientific research base that relies on support from a mixture of public, for-profit and charitable funders. A key strength of this environment is the existence of the critical mass necessary to enable research to be conducted efficiently and successfully. In particular, regional clusters of universities, institutes, hospitals

[1] Throughout this report the term "publicly-funded" applies only to funding by the Exchequer, i.e. ultimately from taxation. It does not include charity funding.

and private companies work together to create an environment with substantial research synergies.

- Any future reduction in the level of government financial support for medical research is likely to cause disproportionate damage to the UK as a whole because of the negative impact on:

    - The UK economy, as it would discourage private investment in the life sciences sector with a consequent loss in UK GDP;
    - The ability of medical research charities to raise funds. Withdrawal of government funding from an area of research risks being interpreted by the general public, and particularly by investors in research, as a downgrading of the importance of that research. Public spending on medical research is expected to stimulate additional private donations to charities. This is known as the "crowding-in" effect and implies that a cut in government funding would lead to a decline in charity income;
    - The charitable sector's contributions to research, as charity funding for medical research also relies on the research infrastructure provided by government. In the long term, charities might be forced to shift some resources away from direct research activities and/or to redirect part of their research funding outside the UK in order to achieve the greatest return on their research spending;
    - UK patients' healthcare. An active research environment has a positive impact on the standard of care; fewer clinical trials in the UK could lead to a decline in UK patients' health outcomes.

- Reducing public funding for medical research would cause short-term damage that would take a long time to repair. Short-term consequences of reduced public funding include missing the opportunity to exploit economies of scale and leaving costly infrastructure (fixed costs that are unavoidable in the near term) under-employed.

- A short-term interruption in investment in research can also have long-term consequences on research capacity in terms of the research work force. A degradation of career prospects now could not only cause members of the existing specialised research workforce to be made redundant, leave the country, or divert permanently to other career paths, but may also dramatically reduce the supply of new researchers.

- We suggest areas where the collection or generation of UK-specific evidence would be valuable in filling current gaps in knowledge, including:

    - Scoping the extent of the "crowding-in" effect that public funding has on the level of private contribution to charities for UK medical research, including the extent to which public expenditure affects the ability of charities to raise funds. Current evidence is mainly from outside the UK;
    - Developing case studies to test the consequences on charitable and other research of removing specific government research funding streams.

1. Introduction

1.1 Context

In its autumn 2010 Spending Review, the UK Government announced its plans for reducing public expenditure to help cut the fiscal deficit. However, the Government recognised the large and positive contribution of scientific research to the UK economy. As a result, the science budget was not as badly hit as those for other sectors. In particular, the medical research budget was maintained in real terms (GDP deflated) and large investments in research infrastructure previously planned, such as the UK Centre for Medical Research and Innovation (UKCMRI) at St Pancras, were confirmed.

Prior to the Review, press reports indicated that consideration had been given to the withdrawal of public funding from cancer research. This highlights concerns that the full extent of the consequences of reduced government spending on medical research are not yet understood by policy-makers, particularly in terms of the impact on charity-funded research.

Given the financial pressure faced by the UK Government at present and for the foreseeable future, Exchequer support of health research is likely to remain under scrutiny. This is likely to be particularly true for: (i) the health and economic return on the resources invested; and (ii) the ability of other sources of funding to substitute, specifically charitable funding.

Evidence of the positive and substantial health economic return of public and charitable research spending, specifically in the areas of cardiovascular disease and mental health, is provided in a 2008 study by OHE with Brunel University and RAND Europe: "Medical research: what's it worth?" – commissioned by the Medical Research Council (MRC), Wellcome Trust and Academy of Medical Sciences (HERG et al., 2008). This report, however, did not investigate the benefits that co-existence of public and charity funders can bring to medical research. This is the focus of the current report.

1.2 Terms of Reference

Cuts to public funding for medical research in the UK, were they to occur, would likely have negative effects not only on direct health, scientific and economic gains, but also on the productivity of research funded by other organisations, including Cancer Research UK (CR-UK). OHE Consulting has been commissioned by CR-UK to explore the relationships between publicly-funded and charity-funded medical research, with particular reference to the UK and cancer research. Specifically, answers are sought for the following questions:

- What are the similarities and differences between the ways in which medical research funds are allocated by the UK Government and by charities? This includes the criteria applied, the relative weights attributed to different criteria and the types of research activities they respectively support;
- What are the knowledge and skills offered by the different funding bodies?
- Does publicly-funded research yield spillovers that benefit charity-funded research and vice versa?

- Do medical research activities that are co-funded by public and charitable funders yield a higher (or lower) rate of return[2] as compared to single-funder programmes?
- Are public/CR-UK collaborative projects different from single funder (non-collaborative) projects in ways that imply different consequences if public funding for them were to be cut?
- Are there significant economies of scale and/or scope in medical research?

These initial questions might be summarised as asking whether a reduction in public funding for medical research would, or would not, be expected to result in *disproportionate* damage, i.e. would a cut of £X million in public funding of medical research cause more than £X million of damage to the UK economy? As our study progressed, we also uncovered evidence of the likely impact of a reduction in public medical research spending on charities' abilities to fund research.

Our work brings together in one place a concise, coherent economic analysis of the benefits of having public funding available alongside charitable support of medical research[3]. In so doing, we highlight areas where empirical evidence is robust, limited, or not available, thereby identifying areas that would benefit from further research.

1.3 Method

Our work involved the following tasks:

1. Searching for and reviewing grey and peer-reviewed literature that examine the respective roles of charitable and government support for medical research, including whether public and charitable support for medical research complement or substitute for one another.

2. Conducting interviews with key experts including clinicians, publicly-funded bodies and other health research funders (including CR-UK) to ascertain:
    a. The type of activities currently funded in England and the approaches adopted by different stakeholders to allocate their funds;
    b. The value of joint funding;
    c. The potential impact of changes in the level of public funding;
    d. The existence of additional evidence available in the published and unpublished literature.

3. Organising and facilitating a workshop prior to submitting the final report to present our preliminary findings and test them with key stakeholders. An independent academic expert on the economics of research participated to provide an external challenge.

This report is organised as follows:

- Section 2 explains the roles of key research funders, how they interact, and the pros and cons of co-funding;

[2] By 'rate of return' we mean the increase in the national income per unit of additional financial support to research expressed as a percentage. It represents the impact of research funding on the national economy. We discuss this aspect in more detail in Section 3.
[3] It is perhaps worth stressing that the subject of this report is *not* partnerships and collaborations between individual researchers, but rather the impact of having both government and charity funding sources.

- Section 3 presents and discusses the adverse consequences that a reduction in public funding in research could create, including the impact on the level of private contributions to charities, economic losses, and standard of healthcare;

- Section 4 outlines our key messages, the level of evidence supporting them, and identifies a research agenda based on the information gaps identified in our study. Additional research can better inform the debate about the role of public spending in medical research and help maximise social benefits generated by the current research system;

- Appendices 1 and 2 provide details of the literature review and of the interview programme.

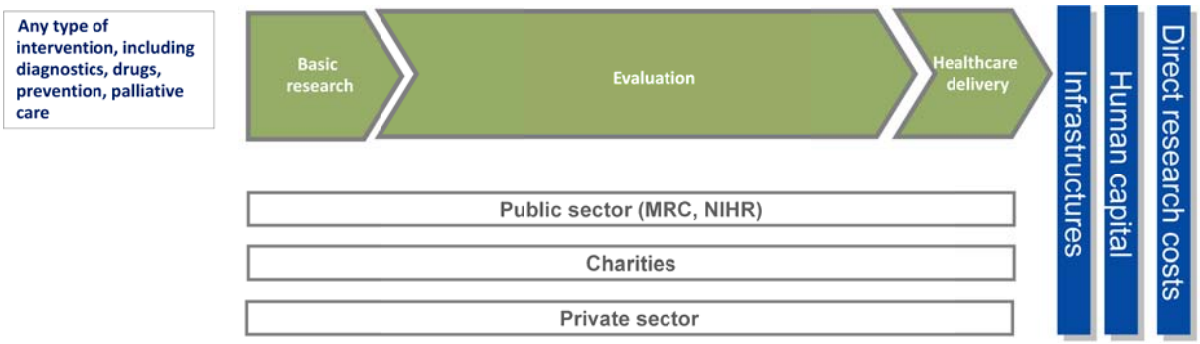
Throughout this report we use the term "publicly-funded research" to mean research supported by the Government using taxpayers' money. We use the term "charity research" to mean research supported by voluntary donations from the public to charities.

2. Multiple Funding Sources in Medical Research

2.1 The Medical Research Pathway

The starting point of our analysis is a simplified representation of the medical research pathway, used in our interview programme to elicit experts' views (see figure 1 below). The purpose of this exercise was not to provide a comprehensive mapping of the funding structure in England, which entails a variety of funding and research bodies and networks, but to identify key characteristics of the system that are relevant to our economic analysis on the complementarity or substitutability of public and charity medical research funding (e.g. key stakeholders, their roles and financial capabilities, the incentives and hurdles they face).

Figure 1: Simplified medical research funding pathway in the UK



In figure 1, the first row shows the innovation pathway that health interventions, including diagnostics, pharmaceuticals, vaccines, and health programmes, generally follow.

The second stage, "evaluation", involves the development/refinement of the intervention and a wide range of other activities, depending on the type of intervention and its regulatory requirements (i.e. efficacy and safety standards that new interventions may have to fulfil in order to be used in patients). For example, in the case of pharmaceuticals, new or existing lines of research emerging after basic research must go through a series of studies to identify valid drug candidates and then test them in laboratories and in patients. These include Phase I, II, and III studies.

From a funder perspective, the key differences between earlier phases, particularly basic research, and later phases, such as phase II and III trials for pharmaceuticals and vaccines, are:

- Objectives. Early research is principally driven by a desire to advance scientific knowledge. While this often has a disease focus, benefits may apply to more than one disease area and may not have an immediate commercial use. Many fundamental biological or genetic investigations can have an impact on the understanding of more than one disease. For later research, the objectives are more strongly disease-focused and, in some cases, more clearly linked to public health goals;

- Time span before potential benefits, measured for example in terms of patients' health gains, accrue. This is much longer for early research as benefits can take more than a decade to identify, develop and introduce into clinical practice as a new intervention. HERG et al. (2008) identified an average lag of 17 years;

- Scientific risk is greater in earlier stages, particularly for novel strands of research; where the chances of success may be low but the potential benefits are great. As the opportunity cost of investing in basic research initiatives can be very high, the public sector, charities and other non-commercial organisations are usually the main source of funding for this phase. In addition, given their expertise and experience, charities might be better placed than public funders with wider research portfolios to select the scientists and the projects to support research related to 'their' specific disease areas;

- Number of funding partners. As a project progresses along the research pathway, more funding streams become available and more parties can be involved. For example, at the Gray Institute, which is co-funded by the Medical Research Council (MRC) and CR-UK, the bulk of financial support for basic research comes directly from those two bodies; clinical research may also involve foreign funders, including biopharmaceutical companies;

- Infrastructure need. The infrastructure required to conduct basic research is centred in universities with life sciences departments and institutes. Later-phase clinical trials involving patients are hosted by universities and conducted in the NHS (with NHS Trusts providing infrastructure support in hospitals and other specialist health services).

2.2 The Key Research Funders

The bottom three rows of figure 1 show the key medical research funders in England, namely the public sector through the MRC, funded by the Department for Business Innovation & Skills (BIS) and the National Institute for Health Research (NIHR), funded by the Department of Health (DH); charities, with CR-UK, the Wellcome Trust and the British Heart Foundation (BHF) being the largest organisations in the sector; and the private sector, including biopharmaceutical companies. Similar funding streams operate in all four nations of the UK. Grant and infrastructure funding for clinical research is provided by the individual departments of health (in Scotland, this is in collaboration with the Chief Scientist's Office) and infrastructure funding for university research is directed through higher education funding council equivalents in each nation. Therefore, while this section focuses on England, our conclusions are valid for the rest of the UK because of the similarities in research funding and support systems.

Interviewees from five organisations providing research funding (CR-UK, Wellcome Trust, NIHR, MRC, and a pharmaceutical company – see appendix 2 for a complete list), pointed out that their organisations were involved, to a greater or lesser extent, in a full range of research activities from basic research to clinical research and the delivery of healthcare interventions. The UK Clinical Research Collaboration (UKCRC) has mapped the research portfolios of the 11 largest UK-based funding bodies (public, charity and private) using the Research Activity Codes based on the Common Scientific Outline (CSO), which is a cancer-specific classification system (UKCRC, 2006). Research areas are grouped into the following categories: Underpinning Research, Aetiology, Prevention, Detection and Diagnosis, Treatment Development, Treatment Evaluation, Disease Management, Health Services.

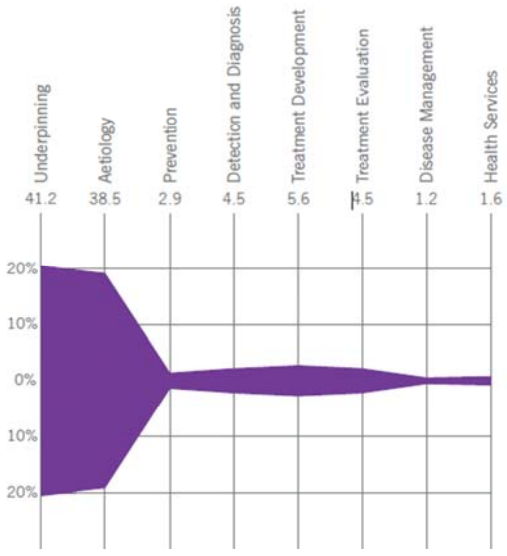
Figure 2a (where "England" represents the DH spending), 2b, 2c, 2d and 2e compare the distribution of key funding bodies' resources across research activities, considering only the direct costs of research and not indirect costs, such as those incurred for maintaining and building infrastructure. The diagrams illustrate that the MRC and Wellcome Trust direct most of their resources to the earliest stage of research (underpinning); the DH is more concentrated on later stage activities, such

as treatment evaluation and health services; and the two disease-specific charities (CR-UK and BHF) inject a greater proportion of their funds into aetiology.

Figure 2a

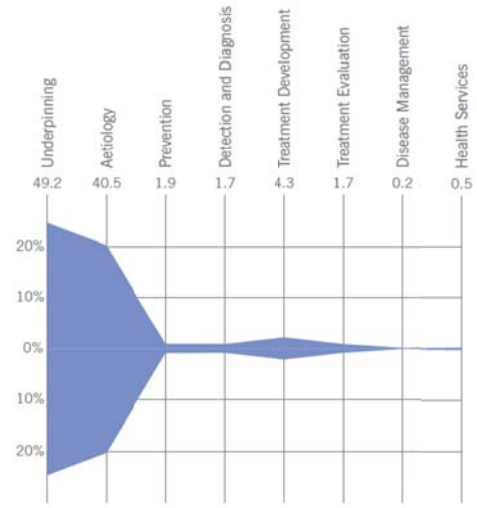
England

Figure 2b



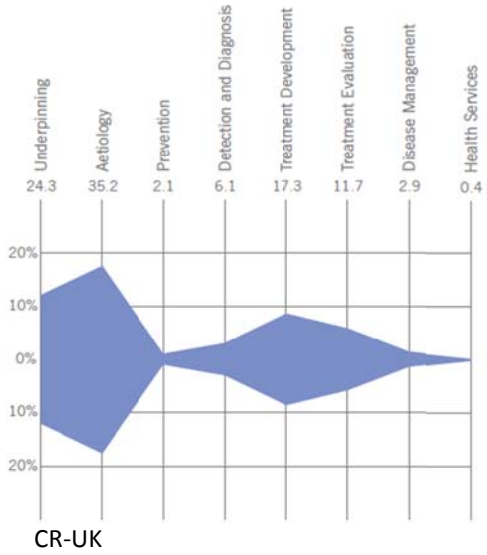
MRC

Figure 2c



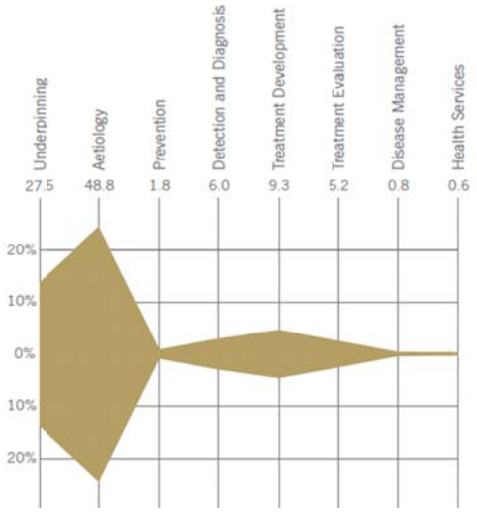
Wellcome

Figure 2d



CR-UK

Figure 2e



BHF

Proportion of combined total spend on the Database

- Greater than 25%
- 16% – 25%
- 5% – 15%
- Less than 5%

Source: UKCRC, 2006

With regards to the approach used to allocate resources, our interviews suggested that the criteria and processes adopted by large funders of medical research are similar, whether public sector or charity. All have funding committees, peer-review processes and other governance procedures to ensure that the selection system is fair and transparent (see Schroter et al., 2010 for a discussion of grant review processes for biomedical research by funding organisations internationally). In some cases, some duplication of effort could occur, for example, when the grant review committees of different organisations have overlapping membership. In some cases, however, the process has been streamlined and co-funders rely on a single, highly-recognised, peer-review process. For instance, CR-UK applies a dispensation to some elements of peer-review when this has already been carried out by public sector funders such as the MRC or NIHR. Smaller charities also sometimes choose to follow other funders' procedures, including the peer-review and selection process.

2.3 Cost Structures

2.3.1 Direct and indirect costs

A key element in the research funding system, represented in the right-hand side of figure 1, is the distinction between indirect costs of research, comprising general research infrastructure such as facilities, staff salaries and other overheads; and direct costs of research, which include any expenses that can be attributed directly to a specific research initiative. Indirect costs cover resources to build capacity that is shared by different users for different activities and purposes. Direct costs (as described in UKCRC, 2006) are direct funding for peer-reviewed research that has a specific set of objectives such as training awards, projects, programmes, institutes and unit awards.

Our interviews indicated that the costs to build and maintain infrastructure for research are substantial in absolute terms, but in proportion to the overall costs of research. This is valid both for basic research, where university buildings, laboratories and other technical equipment (e.g. sequencers) must be in place; and clinical research, where clinical trial sites and processes to recruit patients need to work effectively. The levels of investment required to undertake and sustain

research activities are called “fixed costs” as they do not vary with the level of research activity (in the short term).

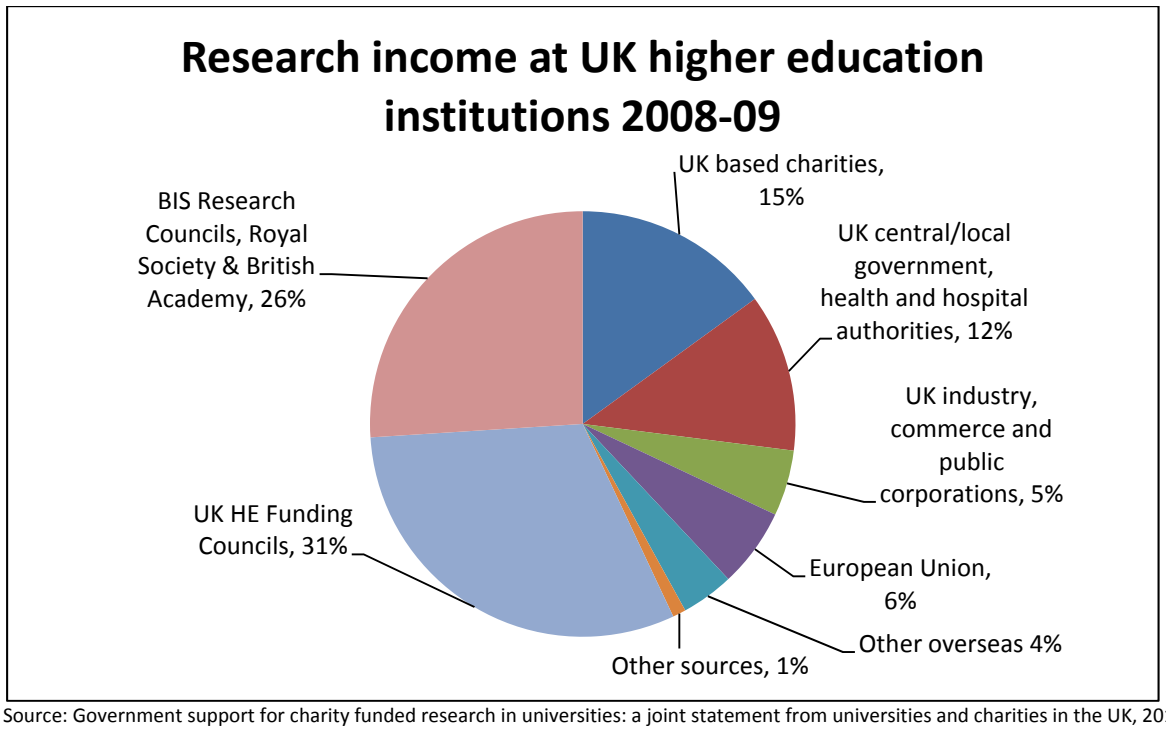
2.3.1.1 Universities

Our interviewees indicated that the distinction between direct and indirect costs is particularly important for research undertaken in universities. The English academic research base is funded through the “Dual Support System”, under which grants from the Higher Education Funding Council for England (HEFCE), funded by BIS, support the research infrastructure, while grants for specific projects and programmes are provided by research councils, such as the MRC, charities, government departments, the EU and industry. The Quality Research (QR) block grant from HEFCE is allocated to universities to build and maintain their research capacities on the basis of quality. In addition, HEFCE includes an additional element of QR funding based on the amount of charitable funding received by universities to support the indirect costs not covered by charitable grants. This additional funding is known as the “charity support” element of QR funding, or the Charity Research Support Fund (CRSF).

A large proportion of charities’ funds directed to universities operate through fellowships to individual investigators, which support career development for individual researchers, or through grants for two-to-five year projects (that can be extended to over ten years for clinical trials). In this funding model, costs directly attributable to specific research programmes are covered by charities and some of the infrastructure and general running costs are provided by the CRSF.

Grants awarded by research councils such as the MRC can cover up to 100% of the full economic costs of research activities, including direct and indirect costs.

Figure 3: Sources of financial support of UK universities



Source: Government support for charity funded research in universities: a joint statement from universities and charities in the UK, 2010.

Figure 3 shows the key sources of research income at UK universities in 2008-2009, where higher education funding councils, including HEFCE, represent the largest share, accounting for 31%.

2.3.1.2 Institutes

Large charities, such as the Wellcome Trust and CR-UK, can contribute to indirect costs through capital awards that fund new laboratories and new equipment and create institutes. The Wellcome Trust provides funding for two institutes (Wellcome Trust Sanger Institute and the Gurdon Institute, jointly funded with CR-UK). Around 30% of the CR-UK budget (CR-UK's Research Strategy Report, 2009/10) is currently devoted to its five institutes, located throughout the UK, which conduct multi-disciplinary and highly innovative research in cancer. Grants to these institutes cover the full economic costs of research.

Consistent with economic theory, since infrastructure and overheads are non-excludable because of the impossibility of preventing their use by other, non-disease/non-health-specific research, charities mainly support the direct costs of university research programmes/investigators that are directly linked to their objectives. On the other hand, they do cover both direct and indirect costs in their institutes where the full benefits of their infrastructure funding is captured by researchers devoting their efforts to specific projects aligned with the charities' objectives.

2.3.1.3 Hospitals and clinical trials

Clinical research studies funded by organisations such as CR-UK that are conducted in the NHS are supported by infrastructure funding that is provided largely through the NIHR. This covers elements of the indirect costs, including hospital buildings and maintenance, administrative costs and specialised staff. The NIHR also has its own programmes of funding for specific research projects within the NHS.

One path for channelling this funding from the NIHR is through both disease specific and comprehensive local clinical research networks. These networks have played an important role in strengthening the research base by providing infrastructure to support clinical studies. For example, the National Cancer Research Network (NCRN), developed and funded by the health departments of the four UK nations, has contributed to the increase in the number of patients in cancer trials in the UK. Since its establishment in 2001, the proportion of UK patients participating in global clinical trial programmes in oncology has risen from 4% to 18%, currently the highest figure worldwide (Cameron et al., 2010).

Costs of non-commercial research studies in the NHS are attributed in three ways:

1. Research costs are the direct costs of the research itself. They include the costs of data collection and analysis and other activities needed to answer the questions that the research is addressing. Funding for these costs usually comes directly from research funders;

2. NHS support costs include the additional patient-related costs associated with the research, which end once the research study stops, even if the patient care continues. These costs cover items such as extra patient tests, extra in-patient days, and extra nursing attention. Funding for these costs is from the NIHR;

3. Treatment costs are the patient care costs that would continue to be incurred if the treatment under investigation were to be provided after the research activity had stopped. This includes, for example, a study that delivers an experimental treatment or a service provided in a different location from normal practice. The difference between standard costs and additional treatment

costs is known as the “excess treatment cost”. Funding for these costs is currently included in the commissioning budget that is allocated to Primary Care Trusts.

2.4 Interdependency and Co-Funding in Medical Research

The research funding flows that originate from different organisations, including the public sector, charities and others, theoretically may be used in the following ways:

- Self-sufficient and independent initiatives that are funded by a single body and do not have any connection with other research initiatives;

- Single-funded initiatives that are interdependent with activities or centres funded (at least partly) from other sources – for example, a university unit and a research institution that are supported by different funders can benefit from collaboration and cross-fertilisation of ideas; or a study supported by a grant from one funder may benefit from infrastructure support provided by another;

- Jointly-funded initiatives with two or more (“multiple”) sponsors and explicit links among groups of researchers.

Wholly independent and self-sufficient medical research initiatives are rare. Arguably all research activity depends, to a greater or lesser extent, on other parts of the total medical research “ecology” in the UK, and in many cases, internationally. For example, universities conducting charity-funded projects also receive infrastructure support from the public sector through QR and the CRSF.

Numerous studies and government reports attest to the interdependence of the many different parts of the medical research landscape (see for example, Academy of Medical Sciences, 2003; BIGT, 2003; and Department of Health, 2004). Thus, category 1 above is negligible in practice. Consequently, changes to one part of the research landscape, e.g. a reduction in publicly-funded medical research, will have knock-on effects on the rest of medical research activity in the UK, including that funded by charities and industry.

One necessary condition for engaging in collaboration is the presence of a shared interest among partners. Individual funding organisations have specific mandates for which they are accountable. Charities are constrained by their publicly stated charitable purposes, i.e. those purposes for which they exist and for which they raise and disburse funds. A cancer research charity, for example, would not be likely to switch all its resources to non-research activities or to invest in non-cancer research. While CR-UK directs some funding towards facilities and staff to support general research and basic research grants, both of which may produce benefits in other disease areas *in addition to* cancer, their primary focus always will be on cancer research.

Public bodies generally are bound to meet public health goals and are accountable through Parliament for the use of taxpayers’ money. Collaborations enable public funders to identify common ground with other organisations and maximise the combined returns from investment in research. As we explain below, when working in partnership, sponsors either contribute to the overall financial burden or cover specific cost elements of research.

Supportive funding also can be directed towards driving collaboration across different research sites. CR-UK is in the process of developing 20 "virtual centres" across the UK. The centres are intended to facilitate local partnerships principally involving NHS Trusts, universities and the charity. The objective of these virtual centres, such as the one involving the University Hospitals Birmingham NHS Foundation Trust and the University of Birmingham, is to provide stable funding to develop a joint collaborative approach in selected research locations. The main purpose is not to build physical facilities, but to maximise research synergies among centres and other organisations operating nearby, e.g. by facilitating knowledge transfer from laboratories to clinical settings and vice versa.

2.5 The Value of Co-Funding and Collaborations

From a funder perspective, the key advantages of co-funding partnerships are both financial and qualitative, such as the opportunity to share knowledge and expertise. This section is based primarily on evidence provided by our interviewees.

The financial factors are:

- Overall resources available (cost-sharing). Without multiple funders, large and expensive studies would be less likely to be funded. Even large charities such as CR-UK would not be able to undertake, on their own, a screening trial that can cost over £10 million. From the individual funder's perspective, then, contributing to initiatives with multiple co-sponsors injecting significant resources means high investment leverage; any financial input used in conjunction with other resources can generate a higher return than a financial input invested in isolation;

- Risk pooling. Given the uncertainty about the eventual benefit of any research investment, particularly during the earlier stages of the innovation pathway, funders can share the risk of research with other co-funders and allocate their resources to a variety of initiatives, rather than concentrate on just one or only a few initiatives;

- Stability of financial support in the long term, which has an important role in the development of an environment conducive to research. In particular, the government commitment to fund research on a large scale provides a key signal to external investors internationally. A stable research environment also can attract talented scientists from other countries by creating a secure environment for research;

- Complementarity of funding. Under the traditional funding structure, the public sector provides resources to maintain and create infrastructure and cover the running costs of universities and NHS facilities. Other funders, such as charities, then can offer grants covering only the costs directly attributable to specific projects or researchers. Although large charities have increasingly invested in institutes, government support of public infrastructure that can be used by different parties for different purposes remains a key element of the national research base; it could not be replaced easily by charities.

The qualitative factors are:

- Opportunity to share experiences and expertise. Multiple funders bring different assets and skills into a research programme. For example, charities bring disease-specific expertise, in-depth knowledge of the relevant scientific community and strong networks of supporters;

public sector bodies bring in their own particular expertise including knowledge of the NHS and how to facilitate the implementation of new discoveries in clinical practice;

- Creation of a competitive research environment that can raise the overall quality of research outputs; when funders' expectations are high and scientists are highly motivated;

- Increased transaction costs and delays. One of the challenges of a system of multiple funders is an increase in transaction costs and delays because of the need to co-ordinate across organisations. For example, while a trial funded solely by CR-UK might be reviewed and funding approved within six months, a co-funded trial can take up to 18 months to achieve funding approval. Although responsibility for expenditure makes it appropriate for each funding body to conduct its own peer-review process for grants, in some cases anticipated delays resulting from internal bureaucracy, particularly in the public sector, may deter some funders from entering into such partnerships. Industry, for example, sees speed and efficiency as a key criterion for involvement in partnerships because unnecessary extensions to the duration of trials can reduce the commercial (on-patent) life of the product under investigation. It is important to note that such time delays are separate and in addition to those that result from regulatory and governance processes for initiating clinical trials.

Bibliographic methodologies provide some evidence that papers with multiple authors have a greater impact than those with a single author; we did not find empirical evidence demonstrating that the same applies for co-funded studies as compared to single-funded studies.

3. Potential Impact of Hypothetical Changes in the Level of Public Funding of Medical Research

Given the benefits arising from initiatives co-funded by different stakeholders, including government and charities, we discuss here the likely consequences of a hypothetical change – a reduction in the level of public contribution to medical research. We do not distinguish between cuts affecting the MRC's budget and those of the government health departments. Given the similarities in the research funding system among the four UK nations, we will refer in this section to the effects of public cuts on the UK as a whole.

In the next sections, we discuss the negative impact on:

- The fundraising ability of charities, known in the economic literature as "crowding-in" and "crowding-out" effects;
- Economies of scale and labour supply issues;
- The national economy, including any losses in national income and "economic rent" if medical research moves out of the UK or is not initiated in the country;
- Health-related effects, potentially implying a decline in the health outcomes of UK patients because of decreased involvement of NHS hospitals in clinical trials and the loss of government influence in shaping the research agenda of charitable and commercial organisations.

3.1 "Crowding-In" or "Crowding-Out"?

Government involvement in funding research entails a cost to the economy in terms of deficit financing, excess tax and administrative burden. Voluntary donations by private individuals to support research are therefore an important alternative source of funding. The overall ideal mix of public and private research funding is determined by the trade-off between the benefits and costs of government intervention, in conjunction with resources available from charity fundraising.

Changes in government funding flows can affect charities' funding flows and vice versa. If, for example, government funding of medical research decreases (increases) and this causes donors to increase (decrease) their own contributions to medical research charities, then government funding and private donations are substitutes. This effect is identified in the literature as "crowding-out". If, however, decreases (increases) in government funding lead to decreases (increases) in private contributions to charities, then the two sources of medical research funding are complements and there is a "crowding-in" effect.

Whether crowding-out or crowding-in applies has important policy implications. If government funding has a crowding-in effect, then reducing government support would reduce charities' abilities to continue to invest in current and new initiatives.

A full discussion of the economic literature tackling this question can be found in appendix 1. We report here the key findings of our review of the literature.

Theoretical arguments support both crowding-out and crowding-in effects. The three main drivers that can generate crowding-in effects are: signals of the quality of research, economies of scale and matching grants.

In practice, government funding for research acts as a "quality signal" for public institutions or charities; government funding can therefore crowd-in private contributions. In addition, if government grants allow charities to exploit economies of scale, then government grants can crowd-in private contributions because charities can provide greater output at lower cost, thereby making contributions more effective. The presence of funding complementarity identified in the literature as matched grants, where government supports infrastructure and other indirect costs and charities cover direct costs, are another plausible cause of the crowding-in effect.

Empirical evidence specific to the UK medical research environment is scarce. The existing relevant study (Khanna and Sandler, 2000) provides evidence of crowding-in of charitable funds as the result of public funding in the "UK health sector" (not clearly defined). However, the estimates provided are not statistically significant and are dated (1983-1990). Some evidence from the US suggests that whether crowding-in or crowding-out prevails depends on the nature of the activity undertaken by the charity. One study (Payne, 2001) shows that government funding crowds-in charity contributions to research universities as opposed to non-research universities. However, owing to the major cultural, institutional and economic differences between the US and the UK, these results should be interpreted with caution.

We conclude that a reduction in government funding for research can also reduce the ability of charities to raise funds. Therefore, policy-makers cannot assume that a drop in government funding for medical research could be replaced, on a pound-for-pound basis, with charity funding. A crowding-in effect in the UK seems likely given that:

- Charities have an incentive to ensure that their resources are used in high quality institutions, increasing the value of the research they fund. This has the potential to increase the efficiency of turning contributions into outputs, thereby increasing the charities' ability to raise funds. Thus, for example, HEFCE's Quality Research (QR) grant, which signals the quality of universities, can result in a crowding-in of private donations when charities decide to fund in QR-funded institutions;

- Clinical research networks, such as the NCRN, provide the necessary infrastructure and research staff to conduct clinical research successfully. The NCRN therefore has the potential to crowd-in private donations to those charities funding clinical trials not only by increasing the efficiency of turning contributions into outputs, but also by signalling the quality of clinical trials to donors.

More generally, government under-investment in research infrastructure, e.g. buildings, equipment, technical staff, IT, libraries and information resources, can reduce the productivity of charity medical research funding. This clearly affects charities' efficiency in turning contributions into output, potentially compromising the ability to raise funds in the future.

3.2 Economies of Scale and Labour Supply Issues

When fixed costs are large, some economic advantages accrue from "being big": as the scale of production increases, the cost of producing an additional unit decreases. This is known in economics as "economies of scale". In the context of medical research, where fixed costs are generally significant, a cut in Exchequer funding would lead to a reduction in research projects (which represent variable costs) and leave costly infrastructure underemployed. In the short run, when fixed costs have already been incurred, a cut in variable costs will translate, effectively, into an increase in the average cost per unit of research. In the long run, if government decreases its support of fixed costs, this could have a crowding-out effect on charity contributions because the cost of producing research would increase (as charities would not be able to exploit economies of scale).

A cut also is expected to have other adverse effects in the long run on the expensively-trained scientific workforce, including scientists and other specialised staff, that has been built over time. Career progression for younger researchers would disappear, causing them to divert permanently to other career paths, and the supply of new talented researchers would be interrupted. It takes years to rebuild the pipeline of a specialised labour workforce if it is temporarily interrupted. The UK medical research base has a high international reputation built up over decades; cutting funding could undermine that reputation in a short time.

3.3 Impact on the UK Economy

The UK currently provides a high quality, internationally respected, scientific research base that can rely on financial support provided by a mix of public and not-for-profit organisations as well as private industry. As indicated by our interviewees, the key strengths of the UK research environment are:

- Strong capability in the field of health research, based on the development of a highly skilled work force and a scientific community of talented researchers;
- Capacity, mainly consisting of clinical trial infrastructure and other research facilities.

In other words, the UK has created the "critical mass" required to conduct research in an effective and successful way. Compared to other countries, the UK is highly ranked in terms of the quality of its universities. For the life sciences, two British universities are in the global top ten, and five are in the global top 20 (QS World University Rankings, 2010). Given the fixed costs incurred over time, in particular since the 1990s, to build capacity and capability in the country, UK funders now can exploit substantial economies of scale and undertake additional research at lower unit cost. The networks and centres involving government, academia, hospitals, not-for-profit and private companies operating in the same geographic area (such as Oxford) are regional "clusters" of innovative activities that encourage research synergies.

However, in recent years the global competition among countries as locations for medical research has increased significantly. Emerging countries (for example, in Eastern Europe and Asia) have become progressively more attractive to international investors because of their lower-cost infrastructures and easy access to patients. In order to improve access to new treatments, Asian countries such as Taiwan are introducing policy incentives for encouraging pharmaceutical companies to undertake research there.

In this context, we examine the possible economic consequences of a reduction in public support for medical research in the form, for example, of cuts in funds allocated to research councils. In other words, is there any advantage for the UK economy in retaining or improving the current system of publicly supported medical research?

3.3.1 The private sector

The first element to consider is the role of publicly-funded research as a stimulus for privately funded research and development (R&D). The empirical studies published in the literature all are based on US data, but the principles underpinning the model might well be valid in the UK context.

Toole (2007) estimated the marginal impact in the long term of an increase in publicly-funded (mainly by the National Institutes of Health [NIH]) basic research on privately-funded pharmaceutical industry R&D. He calculated that, in the US, an extra $1 spent by the public sector on basic medical research leads to an additional $8.38 in private spending on R&D. When considering the impact on clinical research, Toole found a smaller impact for public spending, i.e. a $1 increment in public support of clinical research stimulates an additional $2.35 in private R&D.

Another study based on US data (Ward and Dranove, 1995) provides an overall estimate of the elasticity of private spending relative to public spending on medical research, including basic and clinical research. They estimate that a 1% increase in NIH spending leads to a 2.5% increase in private pharmaceutical industry R&D spending.

These estimates depend to some extent on the scale of both public and private spending on research in the US, which is much higher than in any other country in the world, and the level of research spending by the industry as compared to the public sector, which in the US is 4.96 times as great (Toole, 2007). However, they do provide evidence of economic benefit spilling over from public spending on medical research in terms of retaining and attracting additional investments in the sector from organisations outside and suggest that those investments create additional value for GDP.

Another strand of the economic literature shows that additional financial resources devoted to research are likely to have a strongly positive impact on the national income of the country where the investment is done. This usually is identified by the literature as the “social return” to private R&D investment. This includes not only the direct benefits realised by the organisation that made the original investment, but also any other benefits, including enhanced knowledge, technological advances and new processes, of which external organisations can take advantage (known as research “spillovers” in economic jargon). It has been shown that the social rate of return (i.e. the return to the national economy as a whole) is much greater than the private return accrued by the original investor, and is likely to be around 50%. This means that for each £1 extra invested by the private sector this year, the gains for the UK’s GDP would be £0.50 every year thereafter (PICTF, 2001; Garau and Sussex, 2007).

In the case of the UK, we have argued that these benefits would be lost if public funding for medical research were to be cut because private investment in R&D could lessen and possibly some of the existing industry R&D would be driven abroad (see HERG, OHE and RAND Europe, 2008). The factors underpinning this scenario are:

- The direct impact on infrastructure: Research capacity and capability could be seriously undermined by a short-term interruption to funding. The labour force could be damaged if career prospects worsened; members of the existing labour force might leave the country or turn to other work; new entrants could be discouraged. A key study on the economics of clusters (Abramovsky et al., 2007) indicates that there is a positive correlation between the location of R&D-performing organisations and the presence of high quality university departments relevant to their research activities. This pattern is particularly evident in the pharmaceutical/chemical sector;

- The quality/reputational signal to organisations worldwide: public cuts, even if minimal, may be seen as a decline in government commitment to research and a consequent degeneration, in the medium or long term, of the research environment in the country as whole.

From our interviews, it was clear that charities, even those with significant financial capabilities, could not replace the public sector in building and sustaining a strong national research base, for two main reasons: first, the scale of the overall investment in fixed (indirect) cost required and, second, because the non-excludable nature of infrastructure means that it may have multiple users who do not always match the individual charity's remit.

The available evidence does not analyse the potential effects on private investment in R&D or GDP of a reduction, as opposed to an increase, in public spending on medical research. However, we can argue that if the Government cuts its research spending, this has an impact on the research base and on the reputation of the UK as a high-quality research location, as explained above. Published evidence (PICTF, 2001; Garau and Sussex, 2007) shows that even if the resources currently employed in medical research are re-used in another productive sector of the economy (in their best alternative use), they at best would produce less GDP than in the medical sector. In other words, medical research generates what economists call "economic rent".

3.3.2 The charitable, not-for-profit sector

The published literature does not analyse the impact of changes in the level of public expenditure on the outputs of research by charities and philanthropic organisations. Decreased public investment in the research base may prompt these organisations to reduce their research investment and focus on other activities or, in a more extreme scenario, move their research efforts to more favourable locations outside the UK.

Charitable organisations are not-for-profit and so in this regard have objectives similar to those of the public sector. Both types of funders assess the available investment options (which can be specific projects or programmes, but also fellowships and longer-term types of funding) based on their expected return measured as a contribution to science (knowledge advancement) and, ultimately, impact on patients' health outcomes.

Charities are similar to private organisations in that they are interested in maximising return on investment, albeit not measured in terms of profits. Particularly in cancer, where a number of charities and patient groups are active in the research arena, each organisation faces competition for fundraising and needs to prove to donors it is delivering high-quality and high-impact research outputs in a cost-effective way. This means that financial support for university research units based on quality and productivity, and initiatives to establish new, independent institutes near those universities and other public R&D laboratories where opportunities to share, access and exploit scientific knowledge abound. If the quality of this environment is damaged, as a result, for example, of a decrease or a stagnation in public support for medical research, charitable organisations have the following options:

- Continue to fund project-specific grants to universities (covering direct/variable costs) and start providing financial support for infrastructure as well (indirect/fixed costs) in order to maintain the current research base;
- Focus exclusively on independent, self-funded initiatives such as institutes;
- Gradually move part or all (depending on the scale of the cuts) of their research outside the UK to countries offering a more favourable research environment.

The first option is not entirely viable for charities because, given their disease-specific remit, they cannot devote a large part or all of their available assets to support and develop infrastructure that can have multiple uses. Although they would be able, as they currently do, to support part of the infrastructure that is required for their projects/programmes, their resources would be insufficient to fill all the gaps generated by public cuts.

The second option might be difficult as well since the location of institutes completely funded by charities is influenced by the presence of good university centres, which would be damaged by government cuts (fewer trained researchers and key opinion leaders/scientists would be available). Also, this option may not allow charities to diversify risk across different approaches as they do now. As a result, the support of high-risk projects would need to be balanced by a larger number of projects with a more immediate and less uncertain pay-off (e.g. patient information, advocacy). For example, the BHF has stated that they would consider funding more non-research activities.

It is worth noting that the first two options would be not be feasible for small charities as they do not have the financial capabilities to invest in infrastructure or create and maintain independent institutes. Therefore, a reduction of public spending in research would seriously damage and compromise their activities.

The third option represents the most extreme scenario that charities might be forced to consider. We understand that neither CR-UK nor other charities have a plan to shift a proportion of their research efforts overseas, so we consider this option here only as a hypothetical scenario. Still, charities presumably are more concerned about achieving patients' health improvements and less about the potential losses to the domestic economy. Therefore, a case might be made for them to move part of their research activities abroad if the UK science base were to depreciate in future. In particular, non-context-related research, such as basic research, can be conducted in other locations with a minimum impact, if any, on UK patients.

On the other hand, it would be much more difficult to move clinical research overseas because of the need to have UK populations in trials in order to obtain results relevant to UK patients. In

essence, charity funding of medical research is internationally footloose only to the extent that it does not reduce the ability to conduct UK-relevant research.

3.4 Impact on UK Patients' Health Outcomes

The interview programme highlighted the idea that national healthcare systems involved in medical research, especially clinical studies, can capture indirect benefits that would be lost if research was conducted somewhere else. The assumption is that healthcare institutions such as hospitals that are actively involved in research are likely to deliver better quality care than those that are not.

This argument relates to the economic concept of absorptive capacity, according to which conducting research can help healthcare systems assimilate and exploit knowledge generated locally and elsewhere. This emphasises that doing medical research can have a positive impact in transferring new knowledge across different parts of the national/local healthcare system (from university laboratories to NHS hospitals, for example) and implementing it in daily clinical practice. A literature search on this topic was beyond the remit of our study. However, an informal paper circulated by Professor Peter Selby (former co-director of the NIHR Clinical Research Network)[4], who has been particularly active in the field, cited some research showing a correlation between involvement of healthcare providers in clinical research and better patient outcomes generally (Dubois et al., 2005; Karjalainen and Palva, 1989; Mujumdar et al., 2008).

The argument about the presumed benefits of the involvement of the NHS workforce, mainly clinicians, in other types of medical research is weaker. It is based on the assumption that people engaged in research tend to be more intellectually stimulated and more receptive to innovation in clinical practice. However, no published evidence was found to support this[5].

Another dimension to consider when assessing the effects of cuts in public funding of medical research is the consequent decline in the Government's influence in shaping the R&D agenda of private and not-for-profit organisations. Through co-funded initiatives, research councils and government departments can play a role in the selection of research programmes undertaken across the country, guiding them toward public health priorities.

[4] Summary report of Lyon workshop on "Clinical research and healthcare outcomes" available at: http://www.crncc.nihr.ac.uk/OneStopCMS/Core/CrawlerResourceServer.aspx?resource=cc350d58f3d142b9b6d175afe71daf6f&mode=link&guid=e8f869abd6a84969a3132dfdc8eb4e86

[5] Professor Richard Sullivan (King's College London, Chairman of the European Cancer Research Managers Forum) is undertaking research in this area, as yet unpublished.

4. Conclusions

Charities are major funders of medical research in the UK. With the public and private sectors, charities enable and contribute to a richly varied, successful and internationally renowned medical research sector in the UK.

There have been many initiatives to strengthen the UK's medical research base, not least in areas of direct and indirect relevance to cancer research, including the creation of more infrastructure, trained research staff, processes and systems to facilitate medical research. Cutting public funding could threaten all this: the deeper the cut, the greater the possible damage.

Both the public sector and charities are involved in all stages of the innovation pathway, from basic to clinical research, and have established similar approaches to making fund allocation decisions via rigorous peer-review processes. However, distribution of the costs of research amongst different funders is uneven; infrastructure and other fixed costs, which represent a large proportion of the total costs, are predominantly sustained by the public sector.

Each funding body offers its own skills and know-how. In particular, medical research charities can provide specific expertise in a defined disease area and access to a network of both experts and supporters; public sector bodies bring in their own particular expertise including knowledge of the NHS and how to facilitate the implementation of new discoveries in clinical practice.

Based on our interview programme with a variety of key stakeholders, we identified financial and qualitative benefits from co-funding medical research. Financial benefits include the possibility of sharing both the costs and risks associated with a research enterprise (which can also lead to better investment leverage); providing a stable flow of financial support for research in the longer term; and the opportunity for "matching" funding, where the public sector provides the infrastructure and other indirect costs and other profit and non-profit funders cover costs directly attributable to specific projects.

Qualitative benefits include the opportunity to share experience and expertise among the funders and the creation of a competitive research environment, possibly increasing research quality.

The key challenge of partnerships is an increase in transaction costs and delays as activities are co-ordinated across organisations.

Suggestions of possible future reductions in the level of UK government support for medical research are worrying. Such cuts, we believe, would cause disproportionate damage to the UK for the reasons described in this report. Most importantly:

- Impact on GDP gains. Empirical evidence based on US data shows that public spending on medical research stimulates additional investment in R&D by the private sector. This, in turn, leads to significant social return (as compared to other sectors) in the form of increases in the nation's GDP. Therefore, it is likely that a reduction in UK public spending on medical research would discourage private investment in the UK with a consequent loss of those beneficial economic spillovers.
- Government funding can increase the efficiency of charities' operations because it allows them to take advantage of economies of scale, significant in research given the high fixed

costs associated with the infrastructure required. In the short term, cuts in public funding of medical research will lead to a reduction in the number of research initiatives funded (regarded as variable costs) and, as a result, costly infrastructure will be underemployed. A short-term interruption in investment in research also can have longer term consequences. Degrading career prospects now not only may cause members of the existing specialised research labour force to be made redundant, leave the country or divert permanently to other career paths, but also may reduce the supply of new researchers. The flow of new researchers cannot be turned off and on again without lasting damage.

- Impact on the ability of charities to raise funds. Our literature review reveals that public funding may have a "crowding-in" effect on charitable funds. In particular, economic theory predicts that government funding of a particular research area or institute/university provides a signal of importance and quality; this can enhance the ability of charities to attract private contributions for those activities and institutions. In addition, the fact that government funds complement other sources of funding (what the literature identifies as "matching grants") increases the efficiency of charities' activities, which can act as another "pull" factor for fundraising from the general public and from private research investors. These results suggest that a reduction in the level of government support can reduce the ability of charities to raise funds and, therefore, in the long run, reduce the overall resources available for research.

- Impact on the charitable sector contributions to research. Given the need of charities to pursue their objectives in the most cost-effective way, the reduced public funding of medical research might prompt charities to reduce or relocate part of the research effort currently undertaken in the UK. In particular, early stage research, which does not normally generate context-specific knowledge, might be relocated to other countries with a stronger science base.

- Impact on UK patients' healthcare. Some evidence demonstrates the indirect benefits of undertaking research in a specific location/health site on patient outcomes. Healthcare institutions such as hospitals that are actively involved in research are likely to deliver better quality of care than those that are not research active.

4.1 Research Agenda

During the course of our work for this report we identified some evidence gaps that would benefit from further research:

- UK-specific data is needed on the crowding-in (or crowding-out) effect discussed in Section 3.1. Existing evidence is largely non-UK. Investigating the relationship between specific UK public funding directed towards research (e.g. HEFCE, NIHR and MRC support of cancer-specific initiatives) and the level of private contributions to charitable organisations such as CR-UK would be valuable. This would test the extent to which public support for research can improve the ability of charities to raise funds. Different approaches could be employed, including regression analysis, surveys and a discrete-choice experiment among key groups of donors.

- An econometric approach to assessing the impact that public spending on medical research has on charitable funding of research in essence could reproduce the US statistical analysis

by Toole (2007), adapted for the UK and using UK data. This would be an empirical test of the relationship between public and charitable spending on research, i.e. assessing the extent to which public expenditure stimulates charitable spending on medical research.

- Developing case studies to test the consequences if government funding were no longer provided in specific circumstances. This would illustrate the adverse consequences of Exchequer cuts (e.g. damage to the labour force) on UK research.

- The economies of scale and complementarity of research funding between charities and the public sector needs better definition. Research would comprise an activity-based breakdown from an economic perspective of how charities' funds are used in research, e.g. distinguishing among: staff salaries, capital costs, materials and other costs in institutes and other centres; expenditure in facilities in the UK and overseas; and self-sufficient initiatives as opposed to those dependent on co-funders.

- Quantitative evidence on the benefits of funding in partnership would assess the relationship between the research impact and the presence of multiple sponsors.

- Assessment of the economic return to public and charitable research spending in the area of oncology, replicating the HERG et al. (2008) study but using cancer-specific data. We understand that a feasibility study is being considered in this area.

- Exploring the benefits to NHS patients of conducting trials in NHS health institutions, identifying and reviewing the key factors driving the improvements in standards of care that are generated by an active research environment. We understand that NCRN is conducting quantitative work on this. The suggested study could build on that and provide a qualitative analysis of the underlying economics.

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Appendix 1. Literature Review

Objectives

The objectives of the literature review were to:

- Identify the economic principles underpinning charity and government contributions to medical research or research in general;
- Investigate whether government and charitable funding of medical research or research in general, complement and/or substitute each other within the UK science funding system.

Method

We did an initial search using Google and Google Scholar. This process provided a general overview of the most cited articles from the grey and the peer-reviewed literature and formed the basis for a more focused literature search using EconLit and PubMed.

The initial general search included the use of keywords and/or combinations of these keywords. The selection of those keywords was based on our experience in previous literature reviews on this topic, and what in our view were most likely to identify relevant literature. Keywords used included:

"Charity" (*or "Non Profit", "Philanthropic"*), "Contribution" (*or "Private Contributions", "Public Contributions"),* "Donations" (*or "Private Donations"*), "Crowding-In", "Crowding-Out", "Economic" (*or "Economic Analysis", "Economic Complementarity", "Full Economic Costing", "Economic Effects", "Economic Partnerships", "Economic Welfare"*), "Funding" (*or "Charity Funding", "Government Funding", "Philanthropic Funding", "Private Funding", "Public Funding", "University Funding"*), "Goods" (*or "Public Goods"*), "Health" (*or "Health Benefits", "Health Department", "Health Project", "Health Sector"*), "Risk" (*or "Risk Allocation", "Risk Diversification", "Risk Spreading", "Financial Risk"*), "Research" (*or "Basic Research", "Biomedical Research", "Clinical Research", "Health Research", "Medical Research", "Research Councils", "Research Partnership", "Research Project", "Research Spillovers"*).

In general, the number of hits using a keyword or combinations of keywords was always very high. For instance, using the combination "Charity Medical Research Crowding In" resulted in approximately 14,300 Google hits and 16,600 Google Scholar hits. For this reason, we restricted our attention to the results appearing in the first six Google and Google Scholar outcome pages. This strategy comprised the screening of an approximate 120 total hits for each keyword or combination of keywords. The approach used to screen and identify relevant literature was the following:

- Phase 1: Initial screening of hits using the short Google description appearing in each hit item.
- Phase 2: Second level of screening by reading introductions, abstracts, executive summaries and conclusions of selected phase 1 literature.
- Phase 3: Generate additional search by:
    - Searching references appearing in the articles selected in phase 2;
    - Searching for literature that citied papers selected in phase 2;
    - Exploring relevant websites where possible.

- Phase 4: Third level of screening by reading introductions, abstracts, executive summaries and conclusions of papers selected in phase 3.

We also did a search in EconLit and PubMed using the following keywords:

"Charity", "Crowding in", "Crowding out", "Economic Welfare", " Medical Research ", "Research Funding ", "Private" (*or "Private Donation" "Private Provision "*)," Public Goods". We note that most of the relevant literature identified here already had appeared in the "General Search" stage.

To identify relevant keywords and select papers, we used the same approach applied for the Google and Google Scholar search. The number of hits varied substantially for each keyword and combination of keywords used. For instance, using together Econlit and PubMed databases, the keywords "Medical Research" produced 5,302 hits, but "Charity Medical Research" produced no hits.

Results

After performing the search and screening process, we selected a total of 65 documents. Out of the total, 24 were classified as "key" because they directly addressed the review objectives. The remaining articles were classified as "relevant" because we used them to set the economic context. The complete list of both key and relevant papers is provided at the end of this appendix.

The following sections present the key findings of the review of the "key peer-reviewed literature" (list C at the end of the appendix).

Government involvement in funding research entails a cost to the economy in terms of deficit financing, excess tax and administrative burden. Voluntary donations by private individuals to support research are therefore an important alternative source of funding. The overall ideal mix of public and private research funding should be determined by the trade-off between the benefits and costs of government intervention and the resources available from charity fundraising. Policy-makers need to understand:

- The determinants of charities' ability to raise funds;
- Whether charity research funding substitutes (crowd-out) or complements (crowd-in) government funding.

The determinants of levels of charities' fundraising

The model by Dominiguez and Weisbrod (1986) assumes that the level of individual private contributions reflects the importance to the individual of the output measured in terms of quantity and/or quality of research delivered by the charity. The key factors determining the level of private contributions are:

- Efficiency of the charity in transforming contributions into outputs. The more that is achieved per pound donated, the higher the level of individual contributions;

- The level of advertising expenditure. Advertising can increase the individual's understanding of what a charity can deliver. It follows that increased expenditure in this area can positively

affect the demand for a charity's output when it signals the quality, quantity and social benefits of the charity's output. Andreoni (2006) provides a model showing the importance of signalling quality to raise funds. This is particularly true for charities producing complex goods or services, such as research, which have strong incentives to advertise the characteristics of their outputs even if it this is costly (Vesterlund, 2001). However, advertising expenditure can decrease the efficiency of contributions because less is allocated to produce output, perhaps then decreasing the level of contributions; at the same time, advertising provides useful information for donors, thus potentially increasingly the level of contributions.

Table A1.1 displays the results of the two key articles testing this model, i.e. empirical evidence on the extent to which private contributions to charities are responsive to efficiency and advertising expenditure. The figures in the table show the percentage variation in the level of private contributions in response to a 1% increase in the variables measuring efficiency and advertising expenditure.

Table A1.1: Relationship between private contribution, efficiency, and advertising expenditure

Evidence	Data	Efficiency	Advt. Exp.
Dominguez and Weisbrod (1986)	"Scientific Research" (US)	0.8	0.95
Khanna and Sandler (2000)	"Health Sector" (UK)	0.4	0.25

Dominiguez and Weisbrod (1986) use US data and find that increases in efficiency and advertising expenditure are associated with increases in the level of private contributions to charities involved in "scientific research". The magnitudes of these effects are statistically significant at a 10% level or better. Khanna and Sandler (2000) also find similar effects for charities involved in the "health sector" using UK data for years 1983 to 1990. Here, the magnitudes of these effects are statistically significant at a 5% level; much lower compared to the US analysis.

Crowding-out and crowding-in effects

Changes in government funding flows can affect charities' funding flows and vice versa. If, for example, government decreases (increases) funding to medical research and this causes donors to increase (decrease) their own contributions to medical research charities, then government funding and private donations are substitutes. This effect is identified in the literature as "crowding-out". If, however, decreases (increases) in government funding lead to decreases (increases) in private contributions to charities, then the two sources of medical research funding are complements and "crowding-in" effect exists.

In a time when policy-makers are debating whether charities can replace government support for science, whether crowding-out or crowding-in applies has important policy implications. If government funding has a crowding-in effect, then reducing government support would reduce charities' ability to continue to invest in current and new research initiatives.

The economic literature in this area can be divided into theoretical and empirical approaches, although many articles provide both types of analysis.

From a theoretical perspective, government grants include all income that charities receive from the government either directly or indirectly. For instance, in England, government grants provide indirect support to charity-funded research activities in universities through the CRSF. The theoretical models presented in the next section abstract from specific funding arrangements. As a result, these models hold in the context of both direct and indirect government support to charities, for example, via provision of infrastructure.

However, the empirical evidence discussed is based on US and UK data so it needs to be interpreted cautiously owing to the major cultural, institutional and economic differences between these countries. For instance, it may well make a difference in terms of the impact of a government grant to fund research if it is allocated directly, as it can be the case in the US, rather than indirectly to a charity. In the UK major charities involved in medical research do not receive direct grant funding from the Government.

What does the theoretical literature say about the crowding-out and crowding-in effect?

Table A1.2 summarises the theoretical literature on crowding-out and crowding-in of charity funding resulting from changes in the level of government funding and vice-versa.

Warr (1982) and Roberts (1984) construct theoretical models where increased government grants to charities crowd-out private contributions one-to-one. The assumption is that private contributors only care about the overall level of funding and not the source of funding, making the sources of funding perfect substitutes. According to Warr's and Roberts's models a cut in government support would lead to an equal increase in funds available to charities to replace the funding previously provided by the government.

Andreoni (1990) develops a model where individuals receive a "warm glow" from their giving, so that although increased government grants crowd-out private contributions to charities, one dollar more of government funding leads to a less than one dollar fall in charity funding, i.e. public and private contributions are imperfect substitutes.

Andreoni and Payne (2003) and Heutel (2009) predict a crowd-out effect. However, Andreoni and Payne (2003) note that this is because charities tend to reduce their fundraising efforts when they receive a government grant. Heutel (2009) predicts the converse crowding-out effect, so that governments reduce their grants in response to an increase in private donations to charities.

Table A1.2: Theoretical literature on crowding-in and crowding-out effects

Theoretical	Crowding-Out	Crowding-In
Warr (1982)	Only care about levels not source (1-1)	
Roberts (1984)	Only care about levels not source (1-1)	
Bergstrom et al (1986)	"Warm Glow" effect (<1)	
Rose-Ackerman (1986)		Economies of scale Matching Grants
Andreoni (1990)	"Warm Glow" effect (<1)	
Khanna and Sandler (2000)		Reputation Monitoring
Payne (2001)		Quality Signal (University)
Andreoni and Payne (2003)	"Strategic Response"	
Heutel (2009)	"Strategic Response"	Quality Signal (Source of Funding)

A large body of theoretical literature also examines when government grants can be expected to crowd-in private donations.

Rose-Ackerman (1986) explains that "matching" grants are likely to spur an increase in donations. In addition, if charities' activities exhibit economies of scale and government grants allow charities to exploit these economies of scale, then government grants can crowd-in private contributions. This is because charities can then provide more output at lower cost, thereby making contributions more effective. Khanna and Sandler (2000) explain that crowding-in can result when government, in addition to grants, provides official monitoring, and when those grants effectively signal the good reputation of the charity involved.

Payne (2001) shows that if government grants to universities act as a signal of public institutional quality, crowding-in can overcome crowding-out effects. Heutel (2009) also explores the role of a "quality signal", showing that with imperfect information (uncertainty about the quality of the output provided by charities), one source of funding may act as a quality signal and crowd-in the other source of funding.

What evidence is there to support crowding-out or crowding-in?

Empirical evidence on crowding-out and crowding-in effects is varied. Most is related to the US, with only a small proportion based on UK data. Table A1.3 shows summarises the literature.

The evidence presented in the literature is highly contingent on the nature of the charities' activities, on the actual relationships between government and charities, and on the econometric model and techniques employed. Hence, evidence must be interpreted with a high degree of caution.

Table A1.3: Empirical literature of crowding-in and crowding-out effect

Evidence	Crowding-Out			Crowding-In		
	Health	Research University	Others	Health	Research University	Others
Khanna and Sandler (2000)				**(✓)** (UK)		✓ (UK)
Payne (2001)			✓ (US)		✓ (US)	
Andreoni and Payne (2003)			✓ (US)			
Heutel (2009)			**(✓)** (US)			✓ (US)

(✓): The statistical relationships are not statistically significant.

Khanna and Sandler (2000) use data from 1983 to 1990 to study the determinants of voluntary donations for four UK charity cohorts: health, overseas aid, religious and social welfare. Their study shows that government grants are associated with crowding-in effects for all cohorts except overseas aid. However, evidence of crowding-in for charities involved in the "health sector" (not defined) is not statistical significant at a 10% level, and only the crowding-in effect for the social welfare cohort is statistically significant.

Payne (2001) explores the effects of government funding on private donations to research universities, non-research universities (defined as universities whose highest degree granted is a master's) and liberal arts colleges in the US. Results suggest that public funding and private donations are positively correlated for research universities and negatively correlated for non-research universities and liberal arts colleges. On average, she finds that increasing federal research funding by one dollar increases private donations by 65 cents for research universities, but decreases them by 9 cents for non-research universities, and by 45 cents for liberal arts colleges.

Andreoni and Payne (2003), using US data for arts and social service charities, find that government grants cause significant reductions in funds raised, i.e. crowding-out.

Heutel (2009) uses US data to test for crowding-out and crowding-in in either direction. He finds strong evidence that government grants crowd-in private donations, consistent with his quality signalling model. Regression point estimates indicate that private donations crowd-out government grants, but they are not statistically significant. An important caveat to his study is that it fails to incorporate data for research charities.

Conclusions

Theoretical arguments support both crowding-out and crowding-in effects. The three main drivers that can generate crowding-in effects are: signals of the quality of research, economies of scale and matching grants.

In practice, this means that government funding for research acts as a "quality signal" for public institutions or charities, therefore "crowding-in" private contributions. In addition, if government

grants to charities allow them to exploit economies of scale better, then government grants can "crowd-in" private contributions because charities can provide greater output at lower cost, thereby making contributions more effective. Matched grants, where government supports infrastructure and other indirect costs and charities cover direct costs, are another plausible cause of a "crowding-in" effect.

The empirical evidence specific to the UK medical research environment is scarce. The one relevant study provides evidence of crowding-in of charitable funds by public funding in the UK "health sector" (not defined clearly). However, the estimates provided are not statistically significant and are dated (1983-1990). Evidence from the US suggests that crowding-in or crowding-out prevails depending on the nature of the activity undertaken by the charity. One study (Payne, 2001) shows that government funding crowds-in charity contributions for research universities, but not for non-research universities. However, owing to the major cultural, institutional and economic differences between the US and the UK, these results should be interpreted with caution.

We conclude that a reduction in government funding for research also can reduce a charity's ability to raise funds. Policy-makers should not assume, then, that a decrease in government funding for medical research can be replaced, on a pound-for-pound basis, with charity funding. A crowding-in effect in the UK seems likely given that:

- Charities have an incentive to ensure that their resources are used in high quality institutions, thus increasing the value of the research they fund. This has the potential to increase the efficiency of turning contributions into outputs, which in turn increases the willingness of donors to give to the charity. For example, HEFCE's Quality Research (QR) grants have the potential to signal the quality of universities, thereby crowding-in private donations for charities that decide to provide grants to QR-funded institutions.

- Local clinical research networks, such as the NCRN, provide the necessary infrastructure and research staff to conduct clinical research successfully. NCRN thus has the potential to crowd-in private donations to charities that fund clinical trials not only by increasing the efficiency of turning contributions into outputs, but also by signalling the quality of clinical trials to donors.

Government under-investment in research infrastructure – buildings, equipment, technical staff, IT, libraries and information resources – can reduce the productivity of charity medical research funding. This clearly affects charities' efficiency in turning contributions into output, potentially compromising their ability to raise funds in the future.

List of Papers

A. Key Grey Literature:

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Appendix 2. Interview Programme

Objectives and methods

We conducted an interview programme involving key experts in the field. Our objective was to explore differences in research activities, discover how they may complement one another, understand how different stakeholders make funding decisions, and gauge the value of joint funding. Although the remit of the study was not restricted to cancer, the interview programme concentrated on this disease area, providing a variety of examples relevant to CR-UK.

We contacted people directly involved in research initiatives that are either co-funded or exclusively funded by charitable bodies. Interviewees were drawn both from charities (mainly CR-UK), the public sector (Department of Health and Medical Research Council), and the private sector; and from academic units performing the funded research, i.e. professors in leading academic departments and research centres. Given the focus of the study, interviewees were sought mainly from the English research environment, with the exception of one representative of a US based philanthropic organisation and one from an NGO. The latter two did not reply to our request for an interview.

We contacted 18 people in total and conducted interviews with eleven. Table A2.1 below lists the roles and the affiliations of the interviewees.

Table A2.1: Types of interviewees

Role	Affiliation	Number
Funder/charity	CR-UK	3
Funder/charity	Wellcome Trust	1
Funder/government	MRC	2
Funder/government	NIHR	1
Funder/industry	AstraZeneca	1
Academic/clinician	Gray Institute/ University of Oxford	1
Academic/clinician	University of Southampton/Southampton centre	1
Academic/clinician	University of Birmingham/ Birmingham centre	1

Semi-structured interviews were conducted either by phone or in person. The terms of reference of the study and a questionnaire were sent in advance to interviewees. The list of questions aimed at:

- Understanding the UK medical research funding structure from an economic perspective;
- Understanding the ways in which medical research funds are allocated by the UK Government and by charities;
- Assessing the value of co-funding research initiatives;

- Assessing the impact of changes in the level of funding for medical research;
- Measuring research outputs.

Results

The interview programme conducted for this study has shown that:

- Several types of research initiatives are co-funded by the public and charity sectors in the UK, ranging from basic research to clinical research and the delivery of healthcare interventions. The infrastructure needed for these activities varies. For example, for clinical studies partnerships and networks to facilitate patient recruitment.

- Substantial benefits are generated when initiatives involve multiple funders. These are both financial and qualitative, the latter being less tangible, such as the opportunity for sharing experiences and expertise. Funding partnerships also may entail costs, due primarily to time delays in approving and starting the programme. Although no estimates are available, it emerged that in most cases the benefits of co-funding partnerships are considered to exceed the costs;

- A cut in research spending would have a disproportionately negative impact on the UK research system; worst would be a cut in government funding of research, a key element in attracting international investors and researchers;

- Research outputs can be measured in a variety of ways, combining qualitative and quantitative indicators. No evidence was found directly linking the number of sponsors with research impact.