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Research Report

'Macro' Evaluation of the NIHR Oxford Biomedical Research Centre

Summary report

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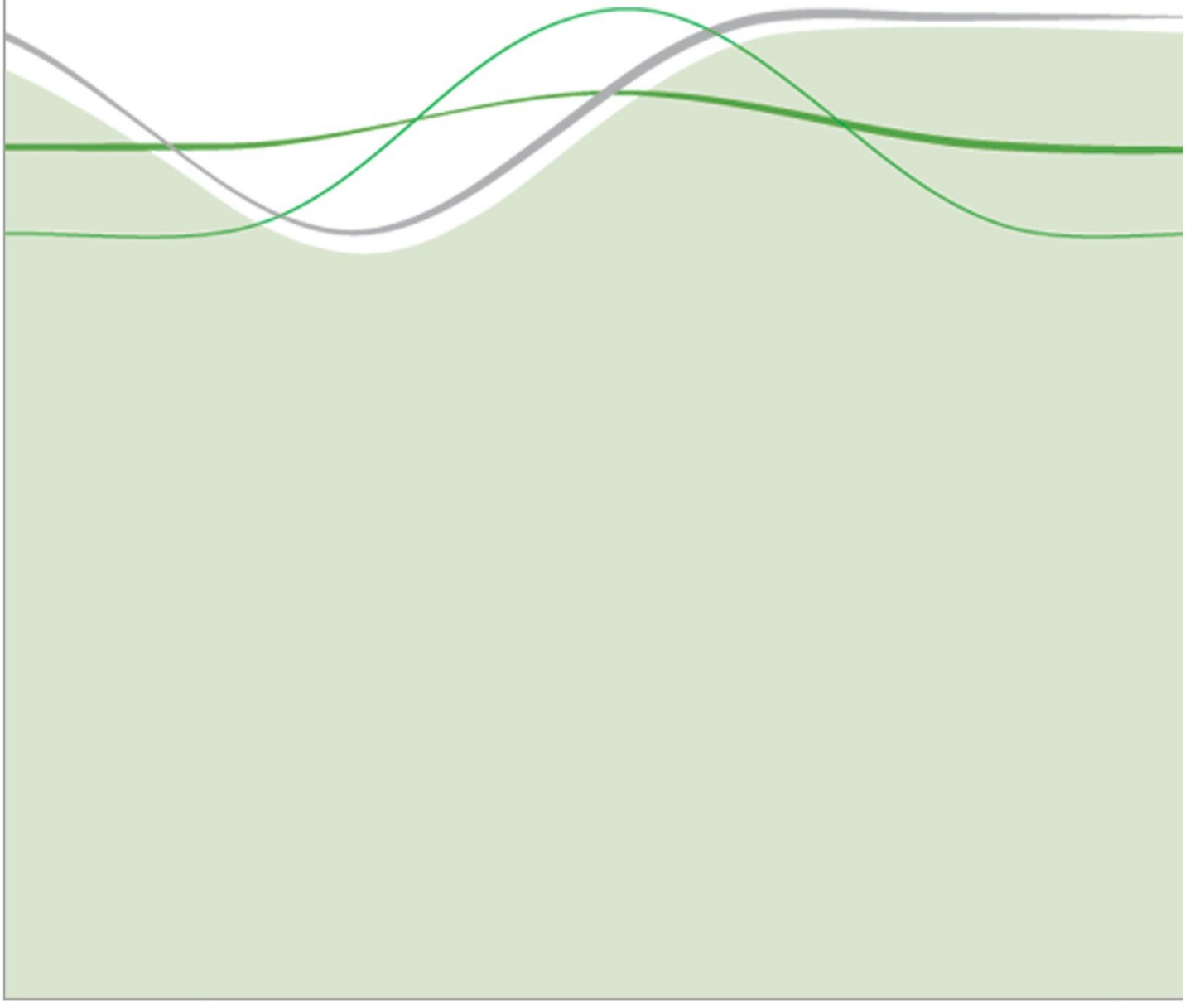

'Macro' Evaluation of the NIHR Oxford Biomedical Research Centre

Summary Report

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1. INTRODUCTION

The Oxford Biomedical Research Centre (BRC) was established in April 2007 with funding from the National Institute for Health Research (NIHR). Oxford BRC is based at the Oxford University Hospitals NHS Foundation Trust (OUH) and is a partnership between the OUH and the University of Oxford, bringing together the research expertise of the University of Oxford and the clinical skills of staff at OUH. This type of knowledge sharing between researchers is thought to significantly increase the efficiency of research and lead to increases in productive efficiency (Adams et al., 2005).

1.1. Evaluating the impact of the Oxford BRC

The Office of Health Economics and RAND Europe were commissioned by the Oxford BRC to undertake a programme of top-down evaluations of aspects of the impact of the BRC. This programme of research has looked at the health, economic and scientific impact of Oxford BRC's research activity, whether achieved directly from the outcomes of the many specific pieces of BRC-supported research, or indirectly due to the BRC's impact on research activity/awareness/culture in health services and industry. The evaluation, conducted from autumn 2015 to mid-2016, consisted of three separate but related studies:

The impact of Oxford BRC on healthcare provision by OUH: This was assessed through a qualitative, interview based study, in which we sought to identify local impacts of the Oxford BRC on healthcare and on OUH. We were interested in both the direct and indirect impacts of Oxford BRC-related research.

The impact of Oxford BRC on industry: This study was based on a survey of companies identified by Oxford BRC and follow-up interviews with a sample of them to build case studies of commercial collaborations.

Bibliometric study: An exploratory bibliometric analysis was conducted to provide quantitative information on changes following the inception of the Oxford BRC in research publications by the University of Oxford and OUH, and on co-authorship collaborations between those organisations, and between them and industry as compared to two comparators.

1.2. This report

A detailed report of the full analysis was provided to Oxford BRC. The present report provides a summary of the research in an accessible form suitable for publication. The next three chapters (2-4) present the approach and findings for each of the three studies. The hospital study (Chapter 2) has also been published as an open access peer-reviewed publication (Lichten et al., 2017). Chapter 5 provides overall conclusions.

2. IMPACT OF OXFORD BRC ON OUH

Full details of the part of the research that is summarised in this Chapter have been published in an open access journal article: Lichten et al., 2017.

It is often assumed that research taking place in a clinical setting not only has benefits for the research itself – for example, by facilitating more effective or efficient clinical trials – but also has a positive effect on the clinical care provided within that institution. A recent major review of the literature did indeed find a positive association between the engagement of individuals and healthcare organisations in research and levels of health

care performance (Hanney et al., 2013). The authors suggested five types of mechanism through which these improvements in performance could occur (Box 1).

Box 1: Mechanisms through which health care improved in research-active settings (adapted from Hanney et al., 2013)

1. Absorptive capacity (most relevant for wider adoption of research in institutions):

    - Changes in the structure of institutions – improvements in infrastructure:
        - Attributes of the setting in which care is delivered, such as accommodation, equipment and personnel, which are brought in to perform research-related activities and may remain in place after the research is completed

    - Changes in human capital:
        - Training/updating staff through research engagement leading to the acquisition and use of new skills, other gains in knowledge and changes in attitudes towards research and research findings
        - Enhancement of group and individual behaviour including more rapid uptake of new treatments, greater likelihood of following clinical guidelines

2. Improvements in the processes of care related to conducting a specific trial:

    - A more rigorous process of defining the standard of care for patients irrespective of their inclusion in the trial
    - Closer monitoring and support
    - Early access to novel technologies

3. Organisational mechanisms within healthcare systems:

    - Example: In the American Veterans Administration system, the whole organisation uses research to improve healthcare. Improvements can occur through conducting research to address known issues in the healthcare system, allowing physicians time to conduct research and thus being an attractive organisation to work for, conducting research to identify best performance targets to set, using research in quality improvement, etc.

4. Collaborative approaches between organisations, teams and individuals:

    - Interactions that improve the relevance of research and policymakers'/managers'/clinicians' willingness to use it
    - Research networks as an increasingly important mechanism

5. Action and participatory research as mechanisms that improve relevance, understanding of and willingness to use research.

This aspect of the overall study aimed to assess the impacts of the Oxford BRC on health care within OUH's hospitals.[1] In doing so we set out to test the prospective application of

[1] John Radcliffe Hospital, Nuffield Orthopaedic Centre and Churchill Hospital, all located in Oxford; and Horton General Hospital, in Banbury.

the list of potential impacts identified by Hanney and colleagues ("the Hanney framework").

2.1. Methods

The main focus of the study was a programme of interviews with key clinicians at the OUH. Throughout we sought to identify the impacts arising *directly* from a research study taking place (e.g. a new surgical technique), as well as the *indirect* impacts, which might be mediated by a range of other aspects, such as staffing, infrastructure, perceptions, training, and so on, including those listed in Box 1.

To prepare for the interviews with the senior clinicians we first interviewed leaders of the Research Themes (RTs) into which Oxford BRC is organised, plus the leaders of three working groups (WGs)[2]. These interviews were also used to inform the design of the Industry study (see Chapter 3).

Next we interviewed senior OUH clinicians (Directors of the clinical Divisions and Directorates[3]) to find out what impacts they had observed. Nineteen of the 23 clinical heads of Divisions/Directorates participated in the interviews and four declined to be interviewed. All interviews were carried out face-to-face at the OUH using a structured protocol to ensure comparability of responses across interviews. Further details can be found in Lichten et al. (2017).

The interviewees' responses were systematically coded and analysed. We discussed the results and emerging themes across questions and also compared and contrasted the perspectives of the two sets of interviewees. Finally we compared the themes which had been identified with the mechanisms outlined by Hanney et al. (2013) (Box 1).

2.2. Results of the RT/WG leader interviews

Based on the responses we received, we were able to group the RT/WG leads' responses to the interview questions into the following main areas (note that some, but not all, of these key areas map to the mechanisms as suggested by Hanney et al. (2013); Box 1):

- **Direct impacts of Oxford BRC research on patient care**: The RT/WG interviewees identified 43 projects or clinical services enabled by Oxford BRC-related projects that they thought had directly impacted the care of OUH patients and/or the organisation of clinical services in the OUH (see Appendix 1).
- Indirect impacts:
    - **Absorptive capacity: infrastructure:** Oxford BRC provides research infrastructure support to OUH by enabling more clinical trials and other research studies to be carried out, and contributing indirectly to the acquisition of equipment used for research[4]. Other forms of Oxford BRC-related improvements to infrastructure at OUH that were cited were:

[2] The Oxford BRC conducts translational research within 14 'Research Themes' and has also established seven 'Working Groups' to address strategic priorities that cross multiple themes.

[3] The OUH is organised into five Divisions, with 18 Clinical Directorates split across these divisions. All 23 of the divisional directors and clinical directors were invited to participate in the interviews.

[4] Interviewees explained that BRC funding cannot be used for capital spending, but Oxford BRC helps contribute to capital acquisitions because Oxford BRC-funded researchers win grants that can be used for capital purchases. For example, in the Genomic Medicine RT, all of the sequencing technology platforms were purchased with funds from research grants. In this case, the equipment subsequently became available for non-research use by OUH staff.

better biobanking, including a tissues database and consent management system, and improved pharmacovigilance and pharmacy support.

- **Absorptive capacity: developing human capital:** The main mechanism through which the Oxford BRC supports human capital development at OUH is funding for staff to do research. This includes paying for medical staff to reduce their clinical hours and devote time to research, funding research fellows and trainees who also do clinical work, and paying for non-medical staff such as nurses to carry out research. Some interviewees felt that, by allowing more staff to do research, Oxford BRC is helping bring about a cultural change through which research is becoming more important in the day to day work of the OUH.
- **Improvements related to clinical trials (enabling more trials or closer monitoring and support):** Interviewees described how the Oxford BRC had helped to increase clinical trials capacity, and enabled more trials to take place. For example, one interviewee explained that in Dermatology, clinical research had previously been undertaken on a relatively small scale and had grown with the Oxford BRC so that now approximately 2,000 patients are recruited for studies each year.
- **Collaborative working:** A commonly stated view across the RT/WG leads was that the Oxford BRC had led to more active collaboration between OUH clinical staff and academic researchers. One way this had been achieved was through the introduction of joint staff appointments with both the University of Oxford and the OUH. Interviewees explained that increased collaboration had made research more clinically relevant and raised the profile of research in the OUH.
- **Patient and public involvement (PPI) in research:** Some interviewees felt that the Oxford BRC has increased the profile of patient engagement in research whilst others were either unsure whether there had been an impact in this area or did not discuss Oxford BRC-related PPI activities. Examples from those who did consider that there had been an impact included training that is run with the Oxford BRC's PPI WG to raise awareness among the researchers and the Open Days held by the Oxford BRC to showcase its work to patients and public.

2.3. Results of the OUH senior clinician interviews

2.3.1. Themes

Our thematic analysis of the full set of interview notes led us to identify ten themes emerging from the discussions with senior clinicians at OUH. Each theme is discussed briefly in turn below (full details can be found in Lichten et al., 2017.) Note that many of these themes link together and overlap with each other.

- **Research activity:** 15 of the 19 interviewees stated that research had affected the NHS work done within their Division or Directorate, either positively or negatively or both, and several also mentioned that they have many research-active colleagues. Responses suggested that there have been increases in research activity at OUH over time and that the Oxford BRC has been part of the reason for this. Interviewees noted that the increase had not been uniform across all OUH Directorates.
- **Formalisation of research roles:** Interviewees explained that increases in research activity have led to increases in research staff. Involvement in research

is now usually formalised with a clear distinction between individuals' roles, and, for each individual, as between the different periods in the working week that are for research versus for delivering care to patients. 13 of 19 interviewees stated that research had changed how personnel are organised; this is part of the third type of mechanism in the Hanney framework: "organisational mechanisms within health care systems".

- **Communication and awareness of research:** 12 of the 19 interviewees stated that ongoing research had raised the profile of research within their directorate or division. Examples of ongoing activities to increase communication and awareness included seminars and discussions to disseminate research, and an activity board to display research posters from conferences. Such changes are part of the 'absorptive capacity' element of the Hanney framework.
- **Reputation:** When asked what the Oxford BRC brings to the hospital and to patient care, four interviewees volunteered that the Oxford BRC improves the reputation and profile of OUH. Linking reputation to other themes, one interviewee felt that that the hospital is more likely to attract funding for improved physical infrastructure because of its high reputation, and another explained that a strong research reputation attracts more and better staff. Reputation is not mentioned as a distinct mechanism in the Hanney framework, although we note it could be be linked to absorptive capacity.
- **Staff recruitment and retention:** Research (including that linked to the Oxford BRC) was identified as a key factor for attracting and retaining high quality clinical staff (including nurses and medical staff) to OUH. However, concerns were also raised that good clinical staff can be attracted away from clinical work to research. These impacts are part of the third item on the Hanney list of mechanisms – 'organisational mechanisms within health care systems' – but we found that the senior OUH clinicians we interviewed gave it more prominence than that placement suggests.
- **Patient benefits from staff involvement in research:** Interviewees were explicitly asked about benefits and downsides for patients of staff being involved in research. 89% agreed that patients benefit from staff having direct involvement in research, and 89% agreed that research has helped OUH patients access novel technologies. These changes overlap with absorptive capacity and improvements in the processes of care related to conducting a specific trial.
- **Access to infrastructure:** Interviewees were asked whether research has meant an increase or an improvement in the infrastructure at OUH that is available for use in clinical care. 74% of interviewees agreed, (examples cited included whole genome sequencing, a digital pathology slide scanner and the clinical trials aseptic unit). This item maps specifically to the first mechanism listed in the Hanney framework.
- **Novel treatments and technologies:** Examples of novel technologies which have become available at OUH due to research include: 1) broader genetic testing; 2) fibroscan testing for liver disease; and 3) a new technique for cardio-resynchronisation therapy using a lead to pace the left ventricle of the heart, which is used to treat patients with heart failure. Note that only benefits of earlier access to novel technologies that are felt by the rest of the hospital's patients *beyond* those taking part in a specific clinical trial are within the Hanney framework as a way in which patient care is improved in a research-active setting.

- **Attitudes to research:** When asked whether staff have changed in their receptiveness to learning from research, 47% of interviewees said yes, and 21% (four interviewees) said no, three of whom elaborated that staff in their part of the OUH have in their view always been receptive to research. This is an aspect of improved 'absorptive capacity'.
- **Collaboration:** 10 of the interviewees mentioned the University of Oxford as a key research collaborator, while four mentioned industry, two mentioned international collaborators and one mentioned Oxford Brookes University. Though RT/WG leads generally shared the view that the Oxford BRC had led to more active collaboration, few OUH clinicians commented on whether there had been a change over time. Collaboration is closely linked to most other themes. It is likely to influence, for instance, the amount of research activity.

2.3.2. Individual projects

The interviewees were asked whether they were aware of any specific Oxford BRC related projects. Twenty-four distinct projects were mentioned unprompted, 12 of which had previously be mentioned by the RT/WG leads (for a detailed list see Lichten et al., 2017).

Next we prompted interviewees about specific Oxford BRC-related projects (selected by the interviewers from the set of 44 projects compiled from RT/WG interviews). In addition to the 12 that had been mentioned unprompted, interviewees confirmed that the projects/initiatives had impact or potential impact in a further 11 cases.

2.3.3. The Hanney framework

Overall, all five types of mechanisms suggested in the Hanney framework were evident in our interviewees' responses.

The first set of mechanisms categorised by Hanney et al. as "absorptive capacity" includes both infrastructure and human capital. The frequency with which each of these kinds of impacts was mentioned suggests it may be helpful to separate them. Furthermore, we identified impacts from research activity which, while clearly connected with infrastructure and human capital, had their impacts on patient care via a more direct route than by increasing the organisation's absorptive capacity. Thus, research activity led to the provision of physical infrastructure or human capital that was then also available for patient care activities (as distinct from research activities) part of the time. Where this was noted, it represents a benefit to patient care that appears to us to be quite distinct from the improved ability of OUH and its staff to also take more advantage of research conducted elsewhere.

We consider that the impact of research activity on OUH's reputation, which in its turn can lead to patient care benefits, is worthy of explicit mention as an additional item in the list of mechanisms. Also, in settings such as this one, impact on staff recruitment and retention may be quite prominent, and may merit more emphasis.

2.4. Cross-analysis of results

RT/WG interviewees spoke in depth about the research they are involved in and often identified a range of positive impacts of that work, including academic impacts. The SCs, who are responsible for managing and delivering clinical services, had a strong awareness of the practical implications of research activity. A summary of the comparison (by theme) is presented in Table 1.

Table 1: Summary of analysis across RT/WG leads and OUH SCs

Theme	Positive changes mentioned (interviewee type)	Challenges and risks (interviewee type)
1. Research activity	Research activity has increased over time (RT/WG, SC). The Oxford BRC plays an important role in enabling research to happen and helps attract additional research funding (RT/WG).	For some, it is unclear how decisions are made about which clinical areas receive Oxford BRC support (SC). The types and topics of research taking place may not fully align with OUH clinical needs (SC).
2. Formalisation of research roles	There has been an increase in the number of medical and non-medical clinical research staff (SC, RT/WG). More clinical staff have time protected for research, which better enables them to engage in research (SC, RT/WG).	Fixed-term BRC-funded research posts can create tension for OUH staff organisation and planning (SC).
3. Communication and awareness of research	Staff awareness of ongoing research and associated opportunities has increased in some clinical areas (SC). Oxford BRC has increased the profile of patient engagement in research through multiple initiatives (RT/WG).	Clinical staff should be better informed about research taking place, opportunities to get involved and findings (SC). External communications could be improved (SC).
4. Reputation	Oxford BRC improves the reputation and profile of OUH (SC, RT/WG).	*[None mentioned]*
5. Staff recruitment and retention	Staff are attracted to the OUH because they believe the Oxford BRC and links to the University of Oxford will create opportunities for research and career development (SC and RT/WG). Research opportunities may encourage staff not to leave the OUH (SC).	High quality staff (especially non-medical staff) may move into research posts and out of clinical work (SC mainly, RT/WG).

Theme	**Positive changes mentioned (interviewee type)**	**Challenges and risks (interviewee type)**
6. Patient benefits from staff involvement in research	Staff are better informed about developments in treatments (SC). Staff reflect more on clinical decisions (SC, RT/WG). Patients interact more with staff; they may receive better care and feel more cared for (SC). Patients gain access to new treatments (SC). Patients report that they enjoy being involved in research and feel they are contributing to the public good (SC, RT/WG).	Patients may feel inconvenienced or overburdened, particularly if study design and communication to patients are poor (SC).
7. Access to infrastructure	Additional, improved or lower-priced infrastructure has become available in some areas because of research (SC, RT/WG).	In other areas, there may be opportunities to share infrastructure which are not being realised (SC). Research activity can put additional pressure on clinical infrastructure (SC).
8. Novel treatments	Many patients have had access to novel treatments and technologies because of research (SC, RT/WG).	*[None mentioned]*
9. Attitudes to research	In some areas staff have become more interested, motivated, and willing to use research findings (SC).† Oxford BRC brought more collaboration between Oxford University and the OUH; it made research more clinically relevant and raised the profile of research in the OUH (RT/WG mainly, SC).	Some perceive a split between the University and NHS; some staff never engage with research and may feel 'outside' of research (SC, RT/WG).
10. Collaboration	Oxford BRC brought more collaboration between Oxford University and the OUH; it made research more clinically relevant and raised the profile of research in the OUH (RT/WG mainly)	*[None mentioned]*

Originally printed in Lichten et al., 2017.

†In some areas, interest and willingness to use findings has been high for a long time, or has increased through a wider shift towards evidence-based medicine.

2.5. Discussion

In conducting the study we found the framework proposed by Hanney et al. (2013) to be useful and relevant for structuring the interview protocol and analysing the responses we obtained. We have highlighted ways in which the framework could be modified for use in the future.

Our qualitative study suffers from inevitable limitations. It does not enable the quantitative estimation of the scale of any net (dis-)benefits on health care at OUH of the Oxford BRC's research activity. In addition, given the long and variable time lags between even translational research – which is the focus of BRCs – and consequent benefits (if any) directly stemming from it, it is too early to detect all impacts at OUH directly attributable to the outputs of research projects related to the Oxford BRC (Hanney et al., 2015).

Finally, we are exposed to the possibility that interviewees' responses are affected by incomplete or biased recall, and also that interviewees were aware we were approaching them for a study funded by a grant from the Oxford BRC, and may have been sensitised to issues about any possible links between research activity and patient care and wished to be supportive as the BRC approached its bid for funding renewal.

Conclusions are presented in Chapter 5 of this report.

3. IMPACT OF OXFORD BRC ON INDUSTRY

This part of our research focused on the impact the Oxford BRC has had on commercial activity. The main aim was to provide quantitative and qualitative evidence about the economic impact that Oxford BRC has had. Oxford BRC retains a list of formal collaborations. Additionally we asked about collaborations, however formal or informal, in the interviews with RT/WG leads and senior clinicians that we described in Chapter 2. RT/WG leaders provided numerous examples of where their research had led to collaborations with industry, and 79% of the senior clinician interviewees stated that research had brought them into contact with companies.

3.1. Methods

This project was split into two main tasks: 1) a survey of all companies identified from Oxford BRC's records as relevant, and 2) a series of follow-up interviews with a sample of them to produce case studies.

The main purpose of the survey was to measure the impact of collaborations between the Oxford BRC and industry, in particular the economic impact. The survey design was based on publications identified from a targeted literature search[5], and also on information shared with us by the Oxford BRC. We also piloted the survey with four respondents from companies and incorporated feedback from Oxford BRC.

[5] We looked for publications that (i) theoretically or empirically analysed the different way that medical research can impact industry, and (ii) assessed the impacts of medical research on industry using a survey. We identified and drew from the following 10 key publications: Bayona et al., 2002; Blumenthal et al. 1996; Downey, 2006; Drucker & Goldstein, 2007; Haskel et al. 2014; SAEI, 2015; HEFCE, 2015; Huggins & Johnston, 2009; OHE Consulting, 2014; UK-IRC, 2013.

3.1.1. Conducting the survey

During the RT/WG leader interviews (Chapter 2), interviewees were asked for examples of research within their RT/WG that may have had economic impacts, and any related contacts. This enabled us to generate a list of 109 companies involved in collaborations with Oxford BRC's RT/WGs.

3.1.2. Selecting and conducting the case studies

Five case studies were conducted to obtain additional information about the impact of the Oxford BRC, beyond that possible from the survey responses. Case studies were selected from the survey respondents, and were chosen to represent diverse ways of collaborating with the Oxford BRC. We selected two Oxford spin-out companies, one company based outside of the UK (Germany) which was contacted by an OUH researcher, one company that contacted Oxford BRC directly, and one company which responded negatively to the survey, suggesting that the collaboration had not gone well.

The case study interviews were semi-structured and based on an interview guide. Questions included some generic questions about the company and collaboration and some tailored questions based on their responses to the survey, for example: You indicated that your company is a spin-out, please could you provide some more information on how your company was formed?

3.2. Results

3.2.1. The survey

The survey response rate was low: only 19 out of 109 contacts (17.4%) responded. As such, these results should be considered indicative rather than conclusive. Sixteen of the 19 respondents (84%) were from the UK (note that a substantially lower 41% of the total 109 invited contacts were from the UK), two from other parts of Europe and one from the US.

3.2.1.1. General information about Oxford BRC-company collaborations

Eleven of the 19 respondents reported they have a single active collaboration with the Oxford BRC; five have had two or more active collaborations; three stated that they did not have any currently active collaboration with the Oxford BRC.

12 of the 19 of participants responded that the collaboration had started through them approaching the Oxford BRC; five were approached by the Oxford BRC and two companies were spin-offs.

The majority of collaborations (12 of 19) were based around seeking advice from academics/clinicians within the Oxford BRC. The development of new products jointly with the Oxford BRC was the second most frequent type of collaboration (8 of 19 respondents).

3.2.1.2. Economic impact of the Oxford BRC and industry collaborations

Economic and commercial value

Based simply on the survey responses received, we estimated:

- Total revenue for industry from completed projects was £15.25million[6]

[6] We asked each company to select an "interval" in which the revenues they received fell. We then took the midpoint of each interval as an estimate of revenue generated.

- Total revenue to date from active collaborations was £2.75million
- Total expected revenue from ongoing projects is £105.5 million.[7]

Two companies reported that active collaborations are already generating revenue, and were therefore asked whether the company could have obtained this revenue in the absence of the collaboration with Oxford BRC. One respondent declared it would have been possible without the BRC but only after a delay; another stated that the revenues would not have been possible without the BRC.

Employment

We also asked about whether any additional employment had been made possible due to collaborations with the Oxford BRC. Eight respondents indicated that they had hired one or more WTE employees. Based on their responses, we estimated that the total employment impact amongst the 19 survey respondents is 30.5 WTE employees hired or retained by companies due to the collaborations with the Oxford BRC.

Investment

Three respondents revealed they have also secured additional investment due to collaborations with Oxford BRC. The estimated total is £16.5million of additional investment secured as a result of the collaborations with the Oxford BRC.

Innovation and its commercial value

Finally, we asked whether the respondent's company had applied for patents, copyrights and/or trademarks as a result of the collaboration with Oxford BRC. Of 17 respondents who answered this question, 15 said "No", and two said "Yes". Of the latter, one was an application for a patent, which was not awarded, and one was an application for a trademark, which was awarded.

3.2.2. Case studies

Of the five case studies carried out, four describe successful collaborations and the fifth an unsuccessful one. The collaborations mainly centred around studies or clinical trials which pursued the validation of a biomedical technology in development. Interviewees suggested that collaborations with Oxford institutions enabled them to win funding, engage new commercial partners, access other BRCs or other potential developers of their products, license their technologies or gain access to pools of early adopters of new technologies and products still in development.

Table 2 shows the full results of the case studies.

[7] To put this into context, the Oxford BRC received in funding from the NIHR for the period 2007-2012, another £95.5m to 2017, and £113.7m for 2017 to 2022. These figures are to provide context only: we are not saying that these revenues could not have been earned without the collaboration between the Oxford BRC and the company; nor are we saying that these are the only revenues earned by industry as a result of the Oxford BRC.

Table 2: Summary of the case studies

	OBS Medical, Ltd.	**TdeltaS**	**Oxehealth**	**Lighthouse Cancer Diagnostics (LCD)**	**Retina Implant AG**
Location	Oxford, UK	Oxford, UK	Oxford, UK	Oxford, UK	Tübingen, Germany
Company background	Spin-out company. OBS Medical has developed *Visensia* in collaboration with Oxford BRC, a technology for early detection of patients' deterioration.	Founded as a spin-out from the University of Oxford (not Oxford BRC).Commercialising ketone ester for treatment of: Alzheimer's, Parkinson's and cancers. 3-4 clinician researchers at TdeltaS are doctoral candidates at University of Oxford.	Spin-out company. Develops software that monitors vital signs with video cameras. Four potential applications of its technology: secure rooms, hospital rooms, home and baby monitoring.	A start-up company founded by two post-doc researchers of the University of Oxford. Company's goal was to develop a cancer diagnostic technology. Piloting the technology in collaboration with Oxford BRC.	Founded in 2003 from a research project carried out at Universitätsklinikum Tübingen (eye clinic) to develop a subretinal implant to restore vision to people blinded due to retina degeneration.

	OBS Medical, Ltd.	**TdeltaS**	**Oxehealth**	**Lighthouse Cancer Diagnostics (LCD)**	**Retina Implant AG**
Type of collaboration	OBS Medical has collaborated with the Institute of BioMedical Engineering (IBME) and the Oxford BRC in two studies: 'CALMS-2' and 'Data Fusion'. Both studies were partially funded by Oxford BRC.	Contact with Oxford BRC but no collaboration was agreed. Company tried unsuccessfully to get funding from the Oxford BRC. Lack of clarity about how to access Oxford BRC funding.	Mainly conducting studies to validate the technology. A 50 patient study in the Kidney Unit of Churchill Hospital. A study to extend vital signs monitoring in the neonatal intensive care unit at John Radcliffe Hospital. Ongoing collaboration: the "Digital Health in a Connected Hospital" project.	LCD directly contacted a member of Oxford BRC to access DNA sequencing clinical labs, clinicians, and clinics in the area. Oxford BRC was "incredibly valuable" in piloting the clinical utility of the technology and giving access to other BRCs for clinical trials. Oxford BRC did much of the hands-on sequencing work, meaning LCD had not yet had to take on additional staff.	Collaboration with the Oxford BRC started in 2009 at a scientific conference. Prof. Robert MacLaren (Professor of Ophthalmology at the University of Oxford and Consultant Ophthalmologist at the Oxford Eye Hospital) initiated contact with Retina Implant AG; collaboration led to a multicentre trial to develop Alpha IMS. The collaboration continued in 2015 with new clinical trials to develop Alpha AMS.

	OBS Medical, Ltd.	**TdeltaS**	**Oxehealth**	**Lighthouse Cancer Diagnostics (LCD)**	**Retina Implant AG**
Impact	Commercialisation of *Visensia.* Reputation: competitive edge was gained from collaboration with Oxford. Access to real data and to an academics-clinicians high level network. Staff were hired and paid with Oxford BRC funding. The company currently employs 13 staff. Collaboration helped in finding commercial partners and investors.	No impact was reported in this case study.	Oxehealth has been awarded £606,000 of funding from 'Innovate UK' for carrying out the 'Digital Health in a Connected Hospital' project. Five licences from ISIS Innovation Ltd. (University of Oxford's research and technology commercialisation company). Oxehealth expects more than £20million of revenue from product commercialisation. Company has grown from 0 to 17 employees since its inception.	LCD and Oxford BRC are applying in partnership for Small Business Research Initiative (SBRI) and Innovate UK funding.	Alpha IMS technology is currently reimbursed in Germany and is generating revenue. Chances to get this technology provided in the NHS have been maximised by the collaboration with OUH, Oxford BRC and Prof. Robert MacLaren. Alpha AMS is expected to generate more than £20m of revenue (UK and rest of EU). Collaborations with OUH and Oxford BRC have been key in securing new investment: £21million of funding in the latter capital round.

3.3. Discussion

3.3.1. Survey

The invitation and the survey itself were designed to encourage responses by explaining in the covering email the survey's importance to the Oxford BRC; by asking closed questions with multiple choice answers; by not requiring compilation of detailed quantitative information; and by restricting the number of questions. Despite these measures, the response rate (17%) was low, limiting the generalisability of the results shown in this chapter.

An issue that inevitably arises from the low response rate is the danger of self-selection bias[8], where mainly those companies who have engaged in particularly positive or negative collaborations with the Oxford BRC choose to complete the survey. We do not extrapolate the results beyond the small set of survey responses for this reason.

Attribution is also an important issue; this is a frequent challenge when estimating the impact of an activity, whatever that may be. Collaborations between Oxford BRC and industry are one element, amongst many others, that may impact industry. A related issue is that we are uncertain to what extent the respondents were able to distinguish the Oxford BRC from other (pre-existing) contacts with Oxford researchers. We therefore cannot be completely sure that all effects reported were specifically due to the Oxford BRC.

Collaborations are likely to take many years, even if successful, to reach the point of generating substantial annual revenues. The existence of such a delay in producing revenues may explain the low number of currently active collaborations that are already generating revenues, the low revenues these collaborations have generated to date, and the high revenues expected for the (higher) number of the currently active collaborations which are yet to generate revenues. Indeed collaborations could generate revenues far beyond the period for which they are "active".

3.3.2. Case studies

The number of case-studies we could undertake was constrained by the funding of the project. They were designed to draw out additional information from interesting and diverse collaborations, as identified from amongst the survey responses. As such they were not a random sample, and were not intended to be representative of all collaborations between industry and Oxford BRC.

3.3.3. Further research

The approach that we took in this study was to go for breadth rather than depth. Future research on the industry impact of the Oxford BRC could be designed for more detailed analysis of a much larger number of cases. These cases could be selected according to the type of collaboration, and could include information collected from the Oxford BRC and the company about the reasons for collaborating and the expected lifecycle of the collaboration, not just its final outcomes. A key element here would be to include some Oxford University spin-off companies.

Conclusions are presented in Chapter 5 of this report.

[8] Note that as we are interested in the impact that the Oxford BRC has generated on industry from its inception, we do not consider sample selection bias (getting a list of all possible contacts from the Oxford BRC) to be an issue.

4. BIBLIOMETRIC STUDY

Given that the Oxford BRC is a partnership that brings together the research expertise of the University of Oxford and the clinical skills of staff at OUH, and that such collaboration is thought to increase the efficiency of research (Adams et al., 2005) and generate opportunities for greater productivity (Lee and Bozeman, 2005), we would expect that the introduction of the Oxford BRC will have had an impact on the quantity and nature of biomedical and health research carried out by related institutions (such as the University of Oxford, NHS hospitals and health centres, and companies[9] located in the Oxfordshire area).

Publication output in peer reviewed journals can be used as a proxy of research performance, and can therefore be analysed to explore any improvements in productivity (Wouters et al., 2015). Bibliometric analysis, based on quantitative indicators of publication output, is one such way to do this. We therefore conducted a bibliometric analysis of Oxford BRC-related biomedical research, with the aim of identifying the effects of the Oxford BRC on research output and collaborations over time.

4.1. Methods

Based on the assumption that most scientific discoveries and research results worthy of note are published in peer reviewed journals, bibliometrics attempts to measure how research in a particular scientific field evolves over time by analysing publications and/or citations. This type of analysis therefore provides quantitative indicators of a key research outcome.

This study aimed to measure:

- The difference (if any) that the Oxford BRC has made to the number of biomedical research publications by the University of Oxford and the OUH;
- The difference (if any) that the Oxford BRC has made to the number of collaborative biomedical research publications between the University of Oxford and the OUH;
- The difference (if any) that the Oxford BRC has made to the number of collaborative biomedical research publications between industry (companies) and the University of Oxford and/or the OUH.

We used two non-London comparator locations without BRCs for some or all of this period (Centre A and Centre B) to assess whether observed impacts on publications were Oxford BRC specific or whether similar trends were observed elsewhere. We selected the two comparators because they were centres in England with a similarly large scale and spread of medical research activity (medical research publications, in this context) at the time this research was conducted. Note that since this research was carried out, both have been awarded BRC status. The comparators that were chosen were considered to the best that were available for this exercise. The purpose of using the comparators was to explore trends that were observed outside of the Oxford BRC, and thus we have not found it necessary to explicitly name the centres in this report.

[9] The company category includes publications from the 72 medical research journal subject categories (JSCs) signed by an author of a private company. Because we use medical research JSCs for this study, companies signing publications in our sample are likely to belong to pharmaceutical and/or health technology production sectors.

4.1.1. Data sources

The analyses were based on bibliographic data from journals and serials published during the period 2000 – 2014 that were processed for the Web of Science (WoS) versions of the Science Citation Index Expanded (SCIE), Social Science Citation Index (SSCI), and Arts & Humanities Citation Index (AHCI) produced by Thomson Reuters. These citation indices cover around 12,000 journals that are assigned to one or multiple fields, called journal subject categories (JSCs). There are 251 JSCs in total.

The Centre for Science and Technology Studies (CWTS)[10] at the University of Leiden was commissioned to identify the publications for this bibliometric analysis. CWTS maintains its own version of the WoS databases which includes a number of enrichments compared to the original Thomson Reuters data. Most importantly, it includes an advanced citation matching algorithm and an extensive system for address unification[11].

4.1.1.1. Data Collection

The data collection process for the analyses was based on the following five steps:

1. Selection of the Medical Sciences Research publications

Each journal in WoS is assigned to one or more JSCs, and publications are classified based on the journal in which they were published. Our analysis includes 72 WoS JSCs, that together cover biomedical sciences and health research.

2. Selection of the Medical Sciences Research publications from the Oxfordshire region and comparator locations published between 2000 and 2014.

Medical sciences research publications with at least one author from the Oxfordshire region were identified. We identified these using the definition of the Oxfordshire region based on NUTS-coding (Nomenclature of Territorial Units for Statistics[12]) at Level 3.

We also collected this data for the two comparator locations: Centre A and Centre B.

3. Assignment of publications to the Universities and the health institutions of considered regions

The Oxford BRC identified the list of health institutions and the university to be included in the analysis for the Oxford area. Selection of health institutions and universities for the two comparators areas were carried out by the OHE based on the Oxford selection. The full list of institutions included in the Oxford region is provided in Box 2.

[10] CWTS studies the dynamics of scientific research and its connections to technology, innovation and society, by analysing research. See www.cwts.nl for further details.

[11] It is important to note that there is delay between the updates of the CWTS version of the WoS database and the CWTS address database. This means that at the time we collected the data for this study, in September 2015, some publications from 2014 may have not been included in the CWTS database; CWTS has estimated this effect to be around a four percent loss of papers. We have identified this effect (in the results section) whenever we consider it may be affecting the results. We also conducted an additional analysis to explore the impact of this limitation on the results by increasing the 2014 figures by four per cent (see full report).

[12] http://ec.europa.eu/eurostat/web/nuts/overview

Box 2: Oxford institutions included in the bibliometric study

Oxford	Centre A	Centre B
University of Oxford	One University	One University
Oxford University Hospitals NHS FT*	Five NHS FTs	Four NHS FTs
John Radcliffe Hospital	One Hospital	Five Hospitals
Churchill Hospital	Companies	One Health Research Centre
Nuffield Orthopaedic Centre		Companies
Horton General Hospital		
Oxford companies**		

*Includes the NIHR Oxford Biomedical Research Centre (Oxford BRC) and the former Oxford Radcliffe Hospitals NHS Trust.
** We group together under the 'company' category all author affiliations belonging to private companies located in each region.

The next step was to identify publications which have at least one affiliation with the University of Oxford, OUH[13] or a company from the Oxford region, and the same for the comparator regions.

4.1.1.2.Analyses

We performed two different types of analyses: 1) before-and-after analyses; and 2) trend analyses. Tests of statistical significance (i.e. t-tests and/or regression analysis) were not considered suitable due to the small number of data points (years).

We assume a delay (or 'publication lag') between the Oxford BRC being established and any subsequent effect on publication output (delays of around three years between the start of funding and publication have been suggested in the literature, for example see Boyack and Jordan, 2011) and as such we use 2010 as the cut off year for the before and after analysis (before period 2007-2010; after period 2011-2014)[14]. Trend analyses were based on the whole period covered by the dataset. For each analysis, we compared total number of publications, collaborations, and share (%) of collaborations among the total publications between both periods.

4.2. Results

We identified 63,187 unique publications from the institutions related to the Oxford BRC during the period 2000-2014. We identified 34,120 publications for Centre A and 42,396 publications for Centre B over the period 2000-2014.

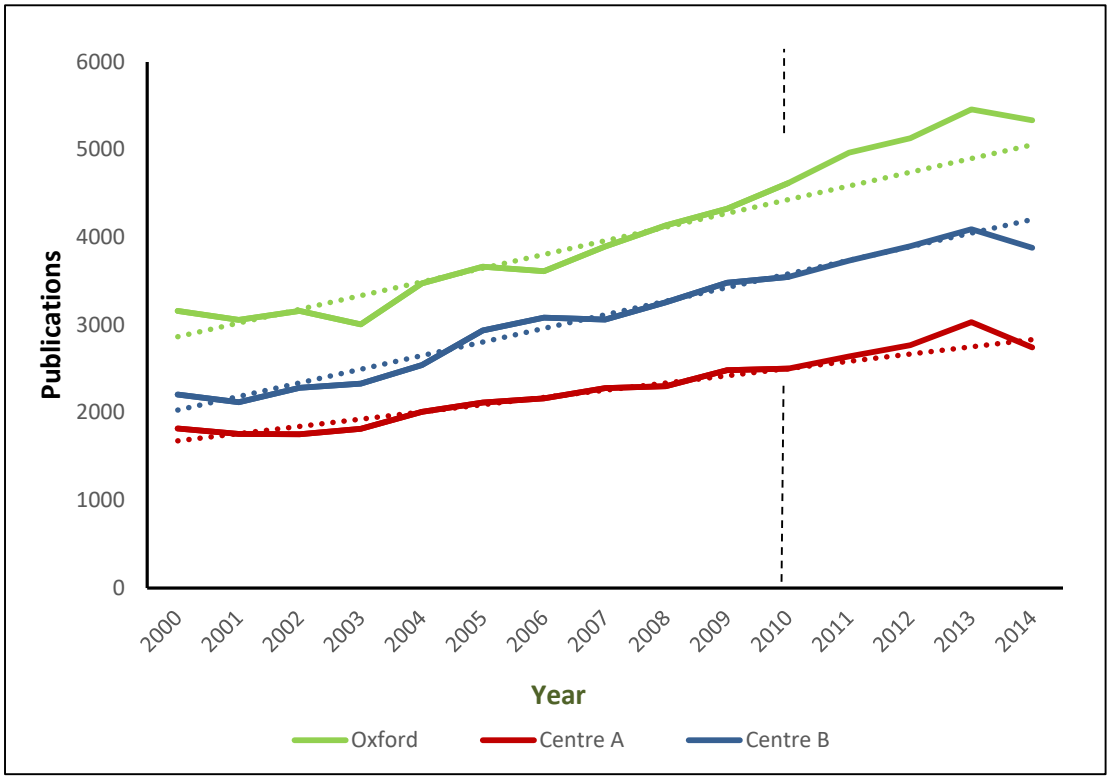
[13]Oxford University Hospitals category includes Oxford University Hospitals NHS FT, John Radcliffe Hospital, Churchill Hospital, Nuffield Orthopaedic Centre and Horton General Hospital. Publications with affiliations to Oxford Biomedical Research Centre and Oxford Radcliffe Hospitals NHS Trust have been homogenised into Oxford University Hospitals NHS FT.

[14]We note that three years is likely to be the minimum lag, and expect that it may be too short for many clinical trials. We chose this based on the available literature and the available data.

4.2.1. Total publications

Figure 1 plots the total number of publications for Oxford, Centre A and Centre B. Trend forecasts (dotted lines) have been calculated based on the 2000-2010 period. The figure shows that Oxford performs better than the forecasted trend after 2010, while no changes in trends are observed for the comparators.

Figure 1: Time series of publications: Oxford and comparators



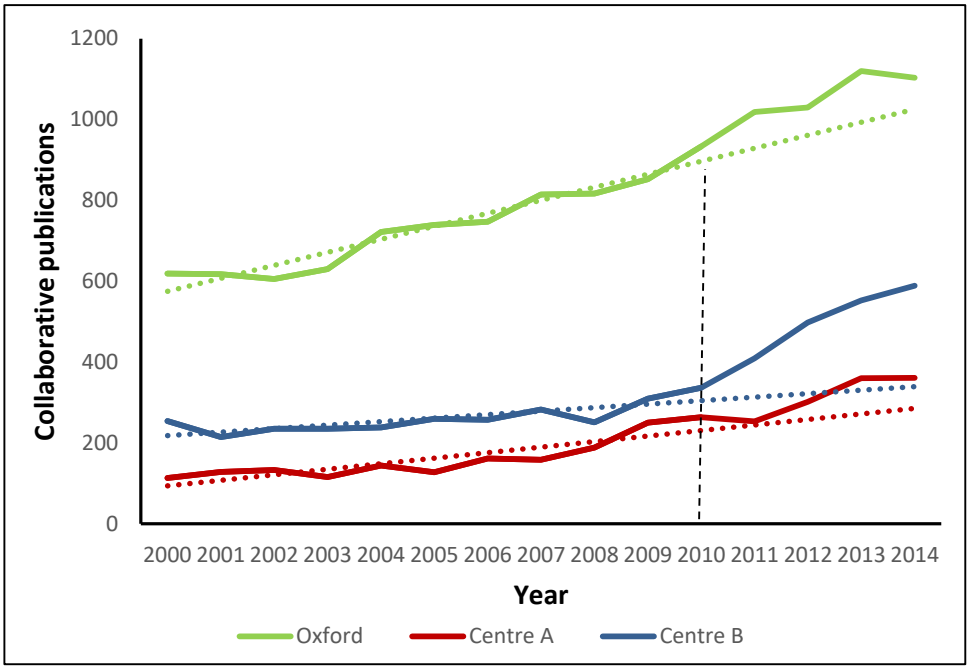
Note: the drop shown by the number of publications in 2014 could be the consequence of the lag in the publications database so it must be interpreted with caution.
Source: CWTS and OHE calculations (2016) based on WoS

4.2.2. Collaborative publications

4.2.2.1. Collaborations between university and hospital

We also conducted analyses of publications of collaborative research between Oxford University and the institutions affiliated to OUH (i.e. at least one author from each), and the same for the comparator locations. Figure 2 plots the trends of collaborative publications for all three locations, including trend lines to forecast the number of their collaborative publications based on the period 2000-2010. The figure suggests that the break in the trend is strongest for Centre B, followed by Oxford, followed by Centre A.

Figure 2: Time series of collaborative publications: Oxford and comparators

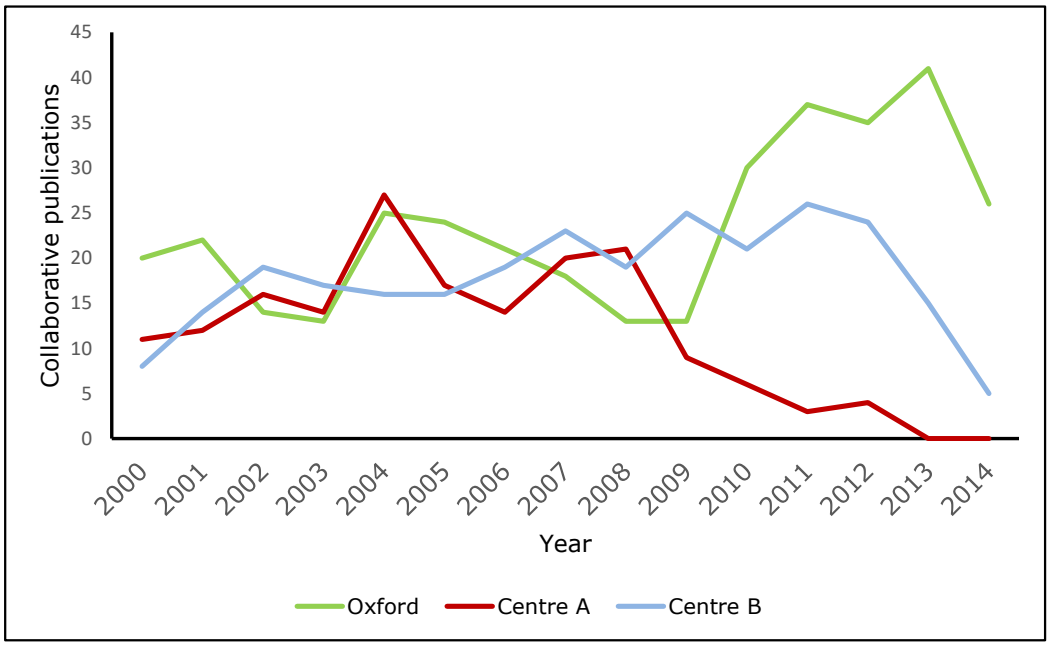


Note: the drop shown by the number of publications in 2014 could be the consequence of the lag in the publications database so it must be interpreted with caution
Source: CWTS and OHE calculations (2016) based on WoS

4.2.2.2. Collaborations between universities and companies

Figure 3 shows the trend of collaborations between universities and companies by location. The figure shows that collaborative publications in Oxford increased after 2009 and that this trend does not hold for the comparator locations.

Figure 3: Company-university collaborations by location

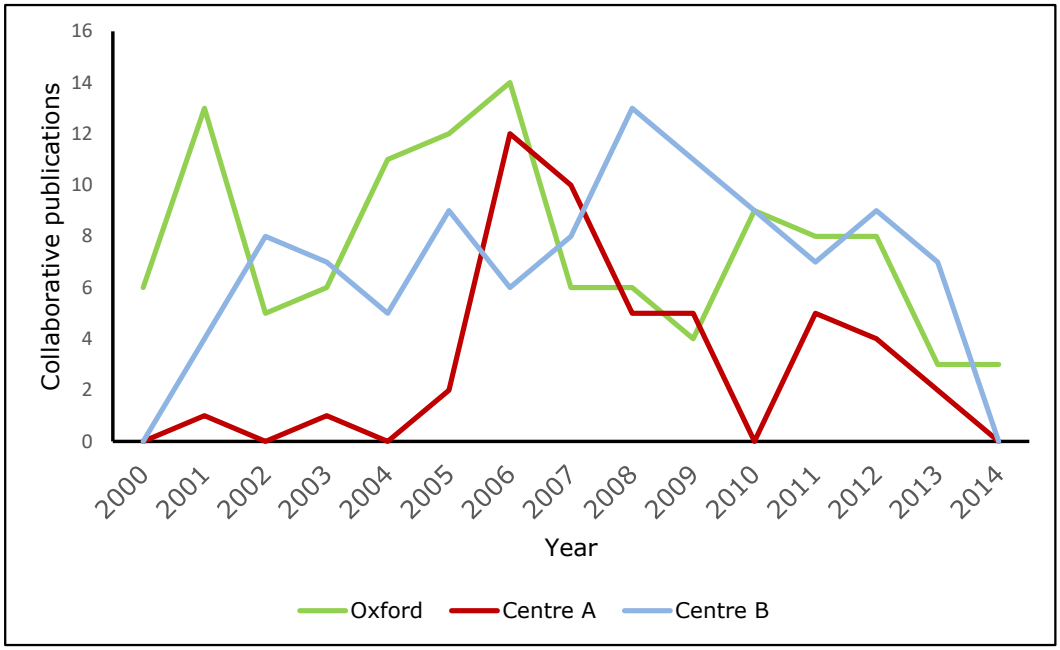


Note: the drop shown by the number of publications in 2014 could be the consequence of the lag in the publications database so it must be interpreted with caution
Source: CWTS and OHE calculations (2016) based on WoS

4.2.2.3. Collaborations between hospitals and companies

Finally, we look at collaborations between hospitals/health institutions and companies for each location. Figure 4 shows the small numbers of papers identified and the variability between years. The figure does not show a clear picture, but we might infer that Oxford has not necessarily performed systematically better than the comparator regions for this type of collaboration.

Figure 4: Company-hospital collaborative publications by location



Note: the drop shown by the number of publications in 2014 could be the consequence of the lag in the publications database so it must be interpreted with caution
Source: CWTS and OHE calculations (2016) based on WoS

4.3. Discussion

4.3.1. Caveats and limitations

Bibliometric data is used to measure research outputs in the form of publications; it does not capture the wider range of impacts that research produces beyond academia. Furthermore, publications and collaborative publications from non-indexed literature (including clinical guidelines) have not been included in the analysis, despite potentially being useful indicators of the impact of medical research.

Another potential limitation is that the datasets used for this study only cover three locations and a 15 year time span. This analysis provides an early indication of changes in publication activity, but further research is needed (see 4.3.2). The numbers of publications and collaborations will also be effected by changes in the structure of the health institutions, hospital Trusts and NHS Foundation Trusts of the three locations over time. We included all publications affiliated to previous names under an institution's current name, but this may not have fully compensated for the changes.

The analysis was conducted using a cut off year of 2010 because research suggests that there are delays between the start of funding and the point when the research outcomes and economic returns take place (see Boyack and Jordan, 2011). Consequently, any impact on the number of publications and collaborative publications expected from the creation of the Oxford BRC would not appear before 2010.

Finally, as mentioned in section 4.1, there is delay between the updates of the CWTS version of the WoS database and the CWTS address database. This means that at the time of data collection and identification for this study, in September 2015, some publications from 2014 may not been included in the CWTS database yet (expected to be around 4% of the total publications from 2014).

4.3.2. Further research

We expect that the Oxford BRC could have had an impact on the quality of research, as well as the quantity. Further research assessing the Oxford BRC impact on quality of medical research and research collaborations between Oxford institutions may provide evidence of an additional impact not explored in this study.

Changes in publication activity could be further investigated with a larger data set and more robust statistical analysis. A wider and more robust statistical difference-in-difference analysis to assess treatment effect of BRC locations versus non-BRC locations throughout the UK would also be interesting. This would explore the overall BRC treatment effect, and may also allow a comparison of Oxford BRC's relative performance compared to other BRCs.

Conclusions are presented in Chapter 5 of this report.

5. CONCLUSIONS

Overall this programme of research has indicated that the Oxford BRC has had a number of positive impacts on health care provided at OUH, through both direct and indirect effects. It is clear that Oxford BRC research plays a major role within the totality of research activity at OUH, with all but two of the OUH senior clinicians noting that the presence of the Oxford BRC has affected the research activities happening within their directorate or division. In particular, Oxford BRC has added positively to the reputation of OUH, and has facilitated collaboration between OUH clinical staff and academic researchers. Patients have also had access earlier to novel treatments and technologies as a result of research activity locally, and research theme leads were able to identify many ongoing BRC-related projects which are expected to benefit more patients in the future (within OUH but also regionally, nationally and internationally). Each of the nine themes that we identified from the interviews with the clinical and divisional directors highlighted positive changes, and some also included remaining challenges.

Oxford BRC has been associated with an increase in the number of publications and collaborations amongst relevant institutions within the Oxford region. The increase in publications was greater than that seen in the non-BRC comparator locations. The effect of the Oxford BRC remained clear for the total number of publications even when we controlled for national tendencies and trends using the comparator locations, but Oxford did not outperform the comparator locations in the trend analysis of collaborative publications (i.e. the number of collaborative publications increased in all locations, yet whilst the numbers were highest in Oxford in all years, the increasing *trend* was not strongest in Oxford – see Figure 2). We also found that collaborations amongst Oxford institutions represent a much greater share of the total medical research performed than in the comparator locations. We conclude that Oxford institutions' performance in medical research has improved since the Oxford BRC was established.

The findings of the hospital study (Chapter 2) and the bibliometric study (Chapter 4) are supportive of each other, with both studies finding that there has been an increase in the

amount of research activity over time. Both studies also indicate that there is significant collaboration between OUH and the University of Oxford. The senior clinician interviewees added that more staff now hold joint appointments (funded by the BRC) between the University of Oxford and the OUH, and it was suggested that the introduction of these joint appointments (together with the Oxford BRC's research nurses) had *'bridged the gap'* between the University and the OUH. Challenges remain however, as the interviewees noted that there was potential for further improvements in the relationship between OUH and the University of Oxford.

Limited evidence also suggests that the Oxford BRC has had a positive effect on commercial activity. The RT/WG leads provided numerous examples of where their research had led to collaborations with industry, and the majority of the OUH senior clinicians interviewed (79%) stated that research had brought them into contact with companies, at least to some extent. These responses were broadly supported by the industry survey (Chapter 3). The survey response rate was low (17%), however, so it was not possible to extrapolate to the whole of the Oxford BRC's industry network. Based on the 19 responses that were received, we estimated that an additional 30.5 WTE employees have been hired or retained, and £16.5million extra investment has been generated by industry collaborations as a result of their collaborations with the Oxford BRC. A total of £17.25million in revenue has already been generated, with an additional expectation of £105.5million future revenues. There were also several intellectual partnerships reported, which did not have an economic focus.

The bibliometric analysis did not reveal an increase in the number of collaborations between OUH and industry. We do not necessarily consider this to be at odds with the findings in Chapters 2 and 3, but rather it could reflect the limitations of our study. For example, there is a lag between the establishment of the Oxford BRC and the subsequent initiation of collaborations with industry, and then there is a further delay during the development/collaboration period and a publication lag. It may be that the increase in collaboration between OUH and industry that was indicated in Chapters 2 and 3 has simply not been expressed through publications yet.

Overall this programme of research has indicated that the Oxford BRC has had a number of positive impacts (both direct and indirect) on OUH patient care, on industry and on research activity. Our work may have been too early to capture important longer-term changes, particularly given that the creation of the BRC was an incremental change in an environment where there was already much academic research. Further research following up on each of these three studies could provide greater insight into the overall 'macro' impact of the Oxford BRC, as has been suggested in Chapters 2-4.

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