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# Mental Health Retrosight

Understanding the returns from research  
(lessons from schizophrenia)



EUROPE

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(lessons from schizophrenia)

## **POLICY REPORT**

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PREPARED FOR THE ALLIANCE OF MENTAL HEALTH RESEARCH FUNDERS

RR-325-GBF



The cover image shows “Fish Schizophrene” © Bryan Charnley.

Bryan Charnley (1949–1991) intended his work to show the common humanity of the sufferer and how the artist can transform the most negative situations into the basis for creative inspiration. He trained at Central School of Art in London but had to leave in 1969 following a breakdown, which was later diagnosed as resulting from schizophrenia. From 1982 onwards his work began to address his inner life, dreams and mental states, particularly the nature of schizophrenia. In 1984 four of his paintings were purchased by the Bethlem Royal Hospital for their permanent collection.

The painting on the cover was one of a series, images of which can be seen with his other work on the web at [www.bryancharnley.info](http://www.bryancharnley.info). The Self Portrait Series was painted as he experimented with varying dosages of medication. The 17 portraits show graphically the terrible suffering of mental illness. In July 1991 Bryan Charnley committed suicide. Subsequently the Self Portrait Series was exhibited at the National Portrait Gallery in 1992.

The project described in this report was supported in Canada by the Graham Boeckh Foundation, Alberta Innovates Health Solutions, and the Canadian Institutes of Health Research; in the UK by the National Institute for Health Research; and in the USA by the National Institute of Mental Health.

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## Preface

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Mental Health Retrosight was a three-year international project that aimed to investigate the translation and payback from mental health and neuroscience research, with a particular focus on schizophrenia. It looked at the development of research over a 20-year period in Canada, the USA and the UK.

The project was supported in Canada by the Graham Boeckh Foundation, Alberta Innovates Health Solutions, and the Canadian Institutes of Health Research; in the UK by the National Institute for Health Research; and in the USA by the National Institute of Mental Health. It was the first project funded through the Alliance of Mental Health Research Funders, a joint initiative between the Graham Boeckh Foundation and RAND Europe. The network was established as a 'think tank without borders' that would undertake research and analysis into mental health research funding.

This report presents the key observations from the study and a summary of the methods involved. The full methodology is set out in an accompanying report (Guthrie et al., 2013b). There is also a briefing note on the study and two further vol-

umes containing the case studies of research and perspectives on advances in treatment (Pollitt et al., 2013a; Pollitt et al., 2013b).

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# Contents

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Preface .....	iii
Table of figures .....	vi
Table of tables .....	vii
Summary .....	ix
Acknowledgements .....	xv
CHAPTER 1	
<b>Context and Background</b> .....	1
CHAPTER 2	
<b>Methods</b> .....	9
CHAPTER 3	
<b>Observations and policy provocations from the analysis of 18 case studies</b> .....	19
CHAPTER 4	
<b>Observations and implications from analysis of six perspectives</b> .....	41
CHAPTER 5	
<b>Findings, caveats, contribution and future research questions</b> .....	53
References .....	61



## Table of figures

---

<b>Figure S.1.</b>	Study findings, policy provocations and research agenda .....	xii
<b>Figure 1.1.</b>	Schizophrenia is a neurodevelopmental disease with a long premorbid phase .....	2
<b>Figure 1.2.</b>	The forward- and backward-tracing approaches to learning from the past .....	5
<b>Figure 2.1.</b>	Conceptual overview of the study .....	10
<b>Figure 2.2.</b>	Methodological stages of the two streams of work .....	10
<b>Figure 2.3.</b>	The Payback Framework .....	12
<b>Figure 2.4.</b>	A diagrammatic overview of the initial steps of analysis .....	17
<b>Figure 3.1.</b>	Distribution of broader social and economic benefits for mental health and cardiovascular research .....	21
<b>Figure 3.2.</b>	Correlations between knowledge production and the other four payback categories .....	21
<b>Figure 3.3.</b>	The mean impact scores of different types of research across the five impact categories .....	23
<b>Figure 3.4.</b>	Researchers working in a cloud that show interests in other field(s) have a higher impact and those that are focused on a single topic have a lower wider-societal impact .....	27
<b>Figure 3.5.</b>	Research clouds which include researchers involved in more than one stage of the translational pathway have a higher impact .....	28
<b>Figure 3.6.</b>	Research clouds that had a researcher who spanned boundaries had a higher impact .....	29
<b>Figure 3.7.</b>	Researchers working in clouds that are motivated by patient need have a higher wider-societal impact .....	33
<b>Figure 3.8.</b>	Researchers working in a cloud whose motivation was curiosity focused had a lower impact .....	33
<b>Figure 3.9.</b>	The majority of case studies were funded from multiple sources and types of funding .....	34
<b>Figure 3.10.</b>	No association between number of funding sources and impact was detected among the case studies .....	35
<b>Figure 3.11.</b>	No association was detected between type of funding sources and impact (except for knowledge production) .....	36
<b>Figure 3.12.</b>	Among the case studies the setting of research does not appear to affect the impact .....	37

# Table of tables

---

<b>Table S.1.</b>	Definitions of payback categories .....	x
<b>Table S.2.</b>	The six interventions examined .....	xi
<b>Table 2.1.</b>	The payback categories .....	12
<b>Table 2.2.</b>	Case study research cloud topics .....	14
<b>Table 2.3.</b>	Previous studies using the Payback Framework .....	15
<b>Table 3.1.</b>	Impacts in each payback category with selected examples .....	20



# Summary

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## **The problem: how does basic research translate into clinical application?**

There is a common perception that mental health research has been poorly translated from bench to bedside (Gould & Manji, 2004; Insel, 2009). The past two decades have seen tremendous advances in basic sciences – the human genome has been decoded, molecular biology is unravelling the basic structure of how cells function, new imaging technologies are unveiling the intricate functions of the brain. But how does basic research translate into clinical application? This question seems to come into particular focus in the field of mental health research where, despite significant advances in the biomedical understanding of mental health and brain function, these are yet to have much practical impact on the diagnosis and treatment of schizophrenia. Still there are no diagnostic blood tests, imaging is not clinically valuable or routine, treatments are chosen largely on a trial-and-error basis, and there are no objective biochemical markers to follow (Grant & Wooding, 2010).

## **Our aim: identifying where and how mental health research has translated into advances in schizophrenia treatment**

This project forms part of the growing field of ‘the science of science’ and seeks to identify success in research translation and impact, and to understand how that success occurred and how it might be replicated (Grant & Wooding, 2010). It is no longer enough simply to campaign for more funding for science. At a conceptual level, we need to understand what attributes lead to research success. For example, what kind of science, what kind of scientists, what kind of settings and what kind of funding mechanisms are most effective in promoting discovery and translating the most promising research findings from bench to bedside?

This project aimed to identify where translation of mental health research has occurred, with a particular focus on schizophrenia. We set out to:

- identify the long-term clinical benefits or ‘payback’<sup>1</sup> that arise from the translation of mental health research into practice;
- identify attributes that are associated with the successful translation of research to produce different types of ‘payback’;
- provide insights to inform funding policy.

## **Our approach: using retrosight to identify attributes of successfully translated research**

The word ‘retrosight’ in the project’s title refers to the idea that we can learn from the past to inform our current and future practice in science and funding policy. Clearly today’s research questions are different from those of the past, but there has been less radical change in the funding and governance of research, and in the social structures of science and their interactions with healthcare and society.

In this project we both followed forwards from research carried out around 20 years ago and traced backwards from current interventions to understand their origins – often over an even longer period. In tracing forwards we focused on research in three countries – Canada, the UK and the USA – thereby providing ourselves with a variety of national contexts in which to explore the development and adoption of research.

---

<sup>1</sup> We define ‘payback’ to mean those academic, health, social and economic benefits of research as commonly used in research impact assessment and defined by Buxton and Hanney (1996) in the development of the ‘payback model’. We do not imply a numerical estimate of the return on investment, as sometimes used in economic analysis.

### Forward-tracing case studies

We selected 18 pieces of research for the forward-tracing case studies, evenly distributed across the three countries and distributed across basic, clinical and interventional research. We picked research that was considered important at the time, by selecting papers that were highly cited in the five years following their publication. We then contacted the corresponding authors of these papers and interviewed them to construct the ‘research cloud’ around each paper. As defined in more detail in Box 3 (Chapter 2), a research cloud is a body of research carried out by a particular research group that corresponds to a particular discovery, advance or insight. The concept of research clouds seeks to align the unit of analysis in this study with researchers’ conceptions of the nature of their work.

Having identified a research cloud, we then constructed a case study tracing the development of the research, its impacts and the individuals involved through to the present day. This involved interviews with researchers and those who used the research, a review of published papers, an examination of archive material and a bibliometric analysis. To structure these case studies, we used the Payback Framework (Buxton & Hanney, 1996) – widely used to examine research impact. The Payback Framework provided both a logic model to structure the narrative of the case study and five categories into which we classified the various impacts of the research: knowledge production; research targeting and capacity building; informing policy and product development; health and health sector benefit and broader economic benefits (Table S.1).

To ensure the accuracy of our case studies, both the investigators who carried out the research and those who had acted as interviewees reviewed the drafts. The case studies were then independently peer reviewed by two researchers with knowledge of the field, one from the same country and one from another country to provide international context.

Having identified the impacts arising from each of the 18 research clouds, we asked a nine-member international panel comprising researchers, research funders, practitioners and patient and family representatives to provide a numerical rating of the extent of impact for each case study in each payback category. Using these ratings we identified case studies of high and low perfor-

**Table S.1.**  
**Definitions of payback categories**

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**Knowledge production:** publication of papers and reports.

---

**Research targeting and capacity building:** (i) better targeting of future research; (ii) development of researcher skills, research infrastructure, etc

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**Informing policy and product development:** (i) improved information bases on which to take policy decisions; (ii) informing product development

---

**Health and health sector benefits:** (i) health or quality of life gains; (ii) cost reduction in the delivery of services; (iii) qualitative improvements in the process of service delivery and effectiveness of services

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**Broader social and economic benefits:** (i) wider economic benefits from, e.g., increased employment or commercial exploitation of research; (ii) social benefits from societal change, e.g., attitude change

---

mance in each category. Because we used five different measures of impact, it was possible for cases to have high impact in some areas (e.g. knowledge) and low impact in others (e.g. health).

We then compiled a list of attributes that might influence the translation of research – characteristics of the research, the researchers and the research setting. These were identified from our previous research, from the research of others and through an initial examination of the case studies in this project.

In the final stage of analysis we examined in detail those attributes that occurred more often in high-impact than in low-impact case studies in particular payback categories. Taking these attributes, we returned to the case studies to check consistency and tease out their meaning in more detail, alongside reviewing the literature available on the area to place our observation in context.

### Backward-tracing perspectives

To provide a supplementary source of data to look at the question of research translation in mental health, we selected the six interventions (Table S.2) to trace backwards from clinical advance to the antecedent research. We identified the interventions through the combination of a survey, a comparison of clinical guidelines over time and across the three countries of the study, and the input of our subject-expert advisors.

Having selected the interventions, we then tried to develop narratives for each through a

**Table S.2.**  
**The six interventions examined**

- The use of **cognitive behavioural therapy**, a form of psychosocial or ‘talking’ therapy, as a treatment for schizophrenia.

---

- The recognition of the value of **early intervention** in schizophrenia and the realisation that treatment was often delayed.

---

- The use of **supported employment** as a way to help people with schizophrenia gain and maintain employment.

---

- The development, introduction, removal and reintroduction of **clozapine**, the first of the second-generation antipsychotic drugs.

---

- The recognition of, and moves to address, the **metabolic side effects of second-generation antipsychotics**.

---

- The recognition of the role of **cognitive deficits in schizophrenia**, and efforts to develop drugs to address them.

combination of telephone and face-to-face interviews, review of archived material and literature reviews. As we developed these, it became clear that the scope of the subjects covered and the contested nature of the fields meant it was not feasible to construct a single, definitive narrative for each intervention. Instead we concentrated on consulting a variety of sources and establishing a balanced perspective. This is why we refer to these narratives throughout this report as ‘perspectives’ rather than as narratives or case studies.

To analyse the perspectives we took a narrative approach, in which a researcher not involved in compiling the perspectives read and reviewed them, taking an iterative approach to extracting and describing the important attributes that appeared to have either promoted or hindered translation.

In the final stage of our analysis, we took the conclusions emerging from both the case studies and the perspectives and looked at how they reinforced and complemented one another to draw up a list of our overall findings and conclusions from the study.

### **Strengths and weaknesses of these methods**

The approach we have taken, as with all approaches in the science of science, brings with it its own strengths and weaknesses (Guthrie et al., 2013b). The strength of our approach lies in its ability to uncover details about the process of research and

translation into patient benefit. The weaknesses lie particularly in the relatively small sample size, which we attempted to mitigate through stratified selection for the forward-tracing case studies and expert-guided selection for the backward-tracing perspectives. The robustness of our conclusions depends on the accuracy with which we have been able to construct our case studies and perspectives and the fidelity with which we have been able to distil the essence of these, through quantifying the impacts in the case studies, identifying the attributes that might drive translation, and extracting the key insights from the perspectives. To enhance the solidity of our findings we attempted to insulate the study observations from our conscious and unconscious biases, through randomising forward-tracing case study selection, using an external panel to rate the impact of the case studies, using an objective approach in shortlisting our attributes and through combining a series of inputs to select topics for our perspectives.

### **Our findings and their potential implications for policymakers**

The diagram (Figure S.1) presents the complete list of findings of this report, colour coded to indicate the research strand from which they are derived, and links them forwards to the policy provocations they raise. We use the term ‘provocation’ rather than ‘recommendation’ because of the relatively small sample size of this project. Below we describe each of the top four ‘headline’ findings and give an assessment of the strength of the evidence supporting them. Reflecting this remaining uncertainty, we have also presented in the diagram the key questions alongside the provocations, as an emerging research agenda.

### **Headline findings**

**Headline Finding 1: The case studies and perspectives support the view that mental health research has led to a diverse and beneficial range of academic, health, social and economic impacts over the 20 years since the research was undertaken.**

The forward-tracing case studies captured a wide range of impacts across the five payback categories from knowledge production through health benefits to economic impacts. The backward-tracing perspectives also demonstrated the role of research

FIGURE S.1

HEADLINE FINDINGS

- The case studies and perspectives support the view that mental health research over the past 20 years has led to a diverse and beneficial range of academic, health, social and economic impacts
- Clinical research has had a larger impact on patient care than more basic research has over the 20 years since the research was undertaken
- Those involved in mental health research who work across boundaries are associated with wider health and social benefits
- Committed individuals, motivated by patient need, who effectively champion research agendas and/or translation into practice are key in driving the development and implementation of interventions

FINDINGS

- Personal interactions between researchers, whether through the convening of conferences and meetings or through more informal events, allow the sharing of research ideas and implementation experience and are often key in sparking collaborations
- The development and adoption of interventions is affected by broader trends such as the rising emphasis on evidence-based medicine and the recovery movement
- The uptake of new practices then allows further practice-based and epidemiological research
- There are country-specific differences in research and uptake, which may be associated with health system organisation, with national culture and/or with disciplinary perspectives
- Non-academic stakeholders such as regulators, funders, professional and healthcare organisations, industry and the media can play a large role in affecting the rate of adoption of new interventions and ideas
- The publication of research findings and reviews of the evidence in the international research literature is important in supporting the progress of research

KEY

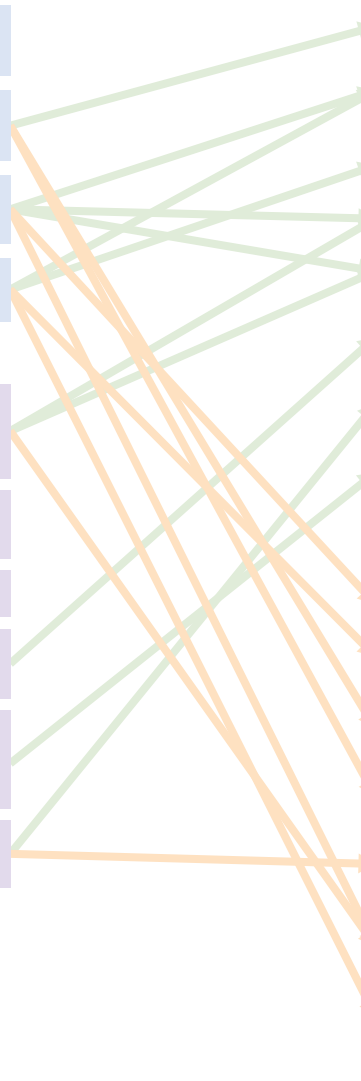
- Findings emerging from the perspectives
- Findings emerging from both the case studies and the perspectives

POLICY PROVOCATIONS

- Funders aiming to make a difference in patients within 20 years should focus on clinical research
- Support individuals who work across boundaries – both disciplinary boundaries and stages of translation pathway – possibly by providing soft ‘expenses’ type accounts and facilitating networking activities
- Identify and support researchers who are motivated by patient need
- Develop opportunities for networking across disciplinary and translational boundaries
- Support face-to-face meetings, workshops and conferences
- Improve learning across different countries and different contexts through systematic comparative analysis
- Support open publication of all research results
- Reach outside the research funding arena to work collaboratively with other organisations in the mental health policy and care community

RESEARCH AGENDA

- Investigate ways to develop and nurture the boundary-spanning potential of researchers
- Unpick the role of motivation in driving the impact of researchers and research teams
- Work to develop more nuanced classifications of basic research and understand the different impacts of these types of research
- Investigate the distribution of impacts across basic research
- Investigate the role of open-access publication in promoting the translation of research into patient benefit
- Map the importance of face-to-face interactions in an increasingly virtual scientific world and the relative strengths of different virtual environments
- Investigate ways to inspire researchers to pursue patient needs
- Investigate the correlation between academic and wider societal impacts more widely



in improving health as well as demonstrating the breadth of research types that contributed to these benefits.

**Headline Finding 2: Clinical research has had a larger impact on patient care than basic research has over the 20 years since the research was undertaken.**

The analysis of case studies and the long time lags between research and impact seen in our backward-tracing perspectives suggests that clinical research has a larger payback than basic research in terms of health, social and economic benefit over periods up to 20 years.

This finding aligns with our previous case study research that has shown clinical research having a larger health, economic and social impact than basic research over shorter timescales – 10 years for arthritis, 15 years for cardiovascular research.

There are two ways in which we could be wrong about this conclusion – in other words, two ways in which basic research could be having a larger impact than clinical research over a 20-year timescale which we don't see in the data that we have examined: the impact of basic research may come from a small number of large successes, which we are less likely to have included; or basic research may be having impacts that we cannot trace or are too diffuse for us to follow. It is also possible that basic research may be necessary as the foundation of future clinical research, or that basic research may go on to have a larger impact than clinical research over longer timescales. This study does not address either of those possibilities.

**Headline Finding 3: Those involved in mental health research who work across boundaries are associated with wider health and social benefits.**

Our analysis of both the perspectives and the case studies shows that individuals with broad disciplinary breadth and/or the ability to bridge the gap between the research world and the policy and care spheres (or the reverse) were frequently key in driving change forwards. They often did this by getting directly involved in the implementation of their research findings. Likewise the analysis of case studies showed that researchers who worked across disciplinary boundaries were associated with research that had a higher impact. This suggests that funders should support individuals

who work across boundaries – both disciplinary boundaries and stages of the translation pathway – possibly by providing soft 'expenses' type accounts and facilitating face-to-face networking activities.

**Headline Finding 4: Committed individuals, motivated by patient need, who effectively champion research agendas and/or translation into practice are key in driving the development and implementation of interventions.**

The analysis of case studies tentatively suggests that the motivation of researchers to improve the lives of patients may be more important than funding mechanism or research setting, but as noted this needs further investigation. The examples of committed individuals from the perspectives also tended to be motivated by patient needs in driving either the research agenda or the incorporation of advances into routine practice. Funders may benefit from giving priority to the support of researchers motivated primarily by patient need, although the identification of such individuals may not be straightforward.





# Acknowledgements

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We should like to start by acknowledging all those scientists who were willing to act as participants for this study, particularly the investigators of the 18 forward-tracing case studies and our interviewees for the six backward-tracing perspectives. The study would clearly have been impossible without them.

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## **The Mental Health Retrosight team**

Jonathan Grant, Steven Wooding and Alexandra Pollitt devised the methodological approach and carried out the analysis, with input from other members of the research team. Alexandra Pollitt and Steven Wooding managed and coordinated the project, supported by Sophie Castle-Clarke and Gavin Cochrane.

The forward-tracing case studies were carried out by Stephanie Diepeveen, Susan Guthrie,

Molly Morgan Jones, Siobhán Ní Chonaill, Stuart Olmsted, Alexandra Pollitt and Dana Schultz. The backward-tracing perspectives were written by Stephanie Diepeveen, Susan Guthrie, Marcela Horvitz-Lennon, Molly Morgan Jones, Siobhán Ní Chonaill, Alexandra Pollitt and Dana Schultz. Bibliometric analysis for the study was carried out by Vincent Larivière.

Shitij Kapur (Institute of Psychiatry) and Harold Pincus (Columbia University) provided expert advice and guidance for the project.

The report was drafted largely by Steven Wooding, Alexandra Pollitt and Jonathan Grant, edited by Claire O'Brien, and designed by Paul Barrett Book Production.

## **Quality assurance**

Tom Ling, Chris Henshall, Saba Hinrichs and Sarah Ball acted as our quality assurance reviewers and provided thoughtful, constructive and timely criticism.

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Four babies were born to members of the project team during Mental Health Retrosight: Daniel Peter Wooding (13 November 2010), Rosalind Eleanor Guthrie (30 November 2012), Aoibhe Mary Lawton (16 March 2011) and Joseph Ellis Lawton (20 June 2012).



# Chapter 1 Context and Background

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## Introduction

This chapter sets the scene for the research project starting by outlining the burden of mental health problems. It then focuses on the burden of schizophrenia and the progress of research to address that, highlighting how much more there is to do. The research to address the remaining needs requires as efficient and effective organisation as possible, and the second half of the chapter considers how we can collect the evidence to enable that to happen.

## The health, social and economic burden of mental-health problems and schizophrenia

This project focuses on schizophrenia, one of the major causes of morbidity and mortality owing to brain disorders. However, given the interconnected nature of different disorders, and possible similarities in underlying mechanism, our focus when looking at research topics necessarily spreads outwards to include more general research on mental health and cognitive processes. Over the past ten years mental health has increasingly been seen as of equal importance to other causes of death and disability (Department of Health (England), 2011; World Health Organization, 2005). Estimates suggest that up to 14% of the global burden of disease is due to mental health disorders, but because of the interactions between physical and mental health this is likely to be an underestimate (Prince et al., 2007). Within the area of mental health, the disorders with the greatest burdens are depression, substance abuse and schizophrenia.

Schizophrenia is a chronic, severe and disabling disorder. It is characterised by symptoms such as hallucinations, delusions, disordered thinking,

movement disorders, social withdrawal and cognitive deficits. Today, schizophrenia affects approximately 1% of the population worldwide. Schizophrenia reduces life expectancy by between 10 and 20 years – mostly as a consequence of suicide (Andrew et al., 2012; Rössler et al., 2005). The burden of schizophrenia is amplified by its chronic nature, the relatively early age of onset of the disease (15–35 years) and the limited effectiveness of treatment. It has been estimated that, while the best current treatments are cost effective (Andrew et al., 2012), they leave approximately two-thirds of affected individuals with persistent but fluctuating symptoms, and only alleviate one-quarter of the burden of disease (Andrews et al., 2003).

## The burden of schizophrenia is felt across the world

In 2008 the World Health Organization estimated that schizophrenia is the third most important neuropsychiatric cause of disability and death in Canada, the UK and the USA, leading to over 600,000 ‘Disability Adjusted Life Years’ per year. Across the world as a whole, schizophrenia ranks as the fourth most significant cause of neuropsychiatric disability.

Other estimates counting ‘Years of Life Lost’ have suggested schizophrenia is the most significant neuropsychiatric condition across the world (Lopez et al., 2006). These estimates also place schizophrenia as the eighth most significant cause of ‘Years Lost to Disability’ for all diseases for low- and middle-income countries; schizophrenia does not however rank in the top ten diseases for high-income countries.

In addition to the burden of schizophrenia on those who suffer from it directly, schizophrenia places a huge – though difficult to quantify – burden on the families of sufferers and those who care for sufferers (Awad & Voruganti, 2008).

Overall, schizophrenia places a large burden on society. The total economic burden was estimated for Canada in 2004 and found to be CAN \$6.85 billion (Goeree et al., 2005). At the same time Knapp and colleagues surveyed previous estimates of the national burden of schizophrenia across the world and concluded that, although the estimates varied widely, they all demonstrated the ‘heavy societal burden of schizophrenia’ (Knapp et al., 2004). Two recent estimates place the economic burden of schizophrenia on UK society at over £11 billion per year (Andrew et al., 2012; Fineberg et al., 2013).

### A brief outline of current understanding of schizophrenia and developments in treatment

The opportunities for improving the lives of patients and families have inspired generations of researchers to tackle schizophrenia. It is now increasingly recognised that schizophrenia is a neurodevelopmental disorder, the foundations of which may be laid many years before the clinical symptoms appear (Insel, 2010). It also appears that the disorder is a heterogeneous concept, potentially consisting of a number of overlapping syndromes that any one conceptualisation struggles to explain in full (Keshavan et al., 2011). We show a simplified version of the neurodevelopmental model suggested by Lieberman et al. (2001) in Figure 1.1. According to this model, there may be a long initial

asymptomatic, or premorbid, phase during which there may be some mild cognitive, social and motor impairments; however, these are not reliable indicators of later schizophrenia (see, for example, Erlenmeyer-Kimling & Cornblatt, 1987). This phase develops into a prodromal phase where changes in behaviour are first seen – and there is active debate about whether predictive symptoms can be identified in this phase (see, for example, Gottesman & Erlenmeyer-Kimling, 2001).

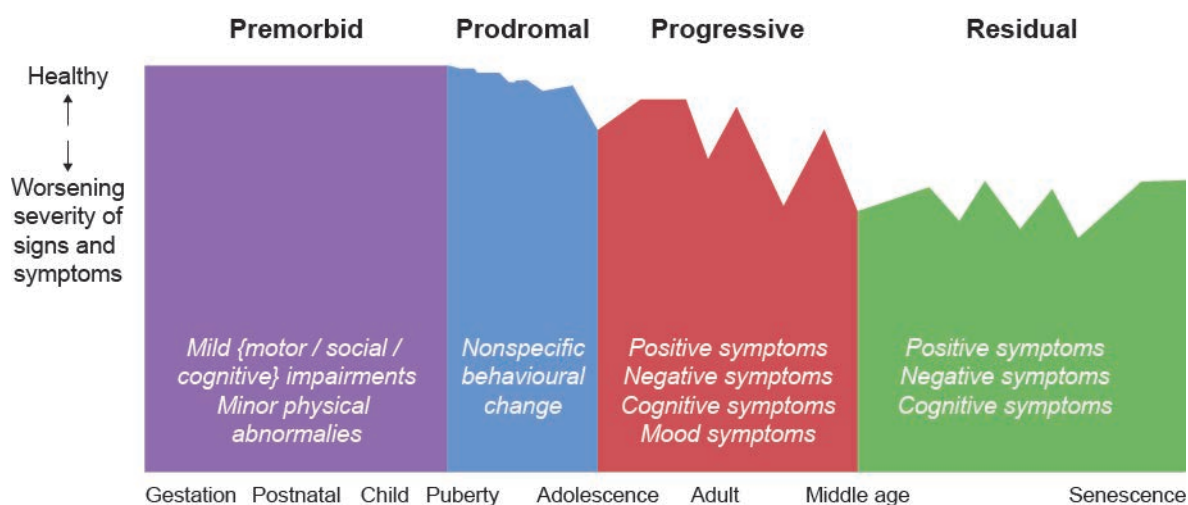
The start of formal first-episode schizophrenia is identified as the point at which the first psychotic episode is experienced. Most people recover symptomatically from this, but the majority will then experience one or more subsequent psychotic episodes, from which some proportion will fail to recover to their previous level of functioning (Lieberman et al., 2001).

After five to ten years in the progressive phase many people experience stabilisation, but at a lower level of functioning than originally (Lieberman et al., 2001).

### Schizophrenia treatment

As the causes of schizophrenia are still unknown, current treatment focuses on reducing the symptoms of the disease using antipsychotic medications and psychosocial interventions (National Institute of Mental Health, 2007). There were no effective treatments for schizophrenia at all until chlorpromazine was discovered in the early 1950s. The first-generation antipsychotics (FGAs) enabled patients to leave mental hospitals and

**Figure 1.1.**  
Schizophrenia is a neurodevelopmental disease with a long premorbid phase



function moderately well in society at large (Saha et al., 2005). However, the first generation of ‘typical’ antipsychotic medications could cause side effects such as rigidity, persistent muscle spasm, tremors and restlessness.

In the early 1990s a second generation of ‘atypical’ antipsychotics with fewer initially apparent side effects was developed. These were seen at the time as a new dawn in pharmacological therapy. Unfortunately, over time it became clear that they had their own set of side effects that, although taking longer to develop, could be quite problematic – including weight gain and metabolic disorders such as diabetes and hypercholesterolemia.<sup>2</sup> Trials such as the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study<sup>3</sup> have now questioned the clinical superiority of the second-generation antipsychotics (SGAs). In fact, there have been suggestions that the mortality rate for individuals with schizophrenia has increased over the past several decades, with the side effects of these drugs potentially being among the contributing factors (see, for example, Goff et al., 2005).

In parallel with pharmacological treatments, a number of psychosocial interventions have been developed to treat schizophrenia. These include supported employment, family psycho-education, cognitive behavioural therapy (CBT), assertive community treatment, peer-support programmes and skills training, to name only a few (Keyser, et al., 2008; NHS Centre for Reviews and Dissemination, 2000). Over the past few years the nature of research on psychosocial interventions has been changing, including expectations that studies should resemble randomised controlled drug trials and that a more standardised process of care should be developed which assesses fidelity in the implementation of the intervention. Practice guidelines, such as those from the National Institute for Health and Care Excellence (NICE) and the Veterans Administration, also increas-

ingly expect that pharmacological and psychosocial interventions will be combined in a package.

Despite significant advances in the biomedical understanding of mental health and brain function, these are yet to have much practical impact on the diagnosis and treatment of schizophrenia. It is still not possible to diagnose schizophrenia, or follow the effectiveness of treatments, using biochemical markers, blood tests or imaging. This means that individualised treatment has to be selected largely through trial and error. Few truly innovative treatments have been developed, and several promising new treatments, including SGAs, have had disappointing results when disseminated into practice.

There have been steady improvements in treatment over the past 20 years, although these have largely consisted of the improved implementation of existing evidence-based treatments in routine practice. Alongside this there have been breakthroughs in terms of research methods – with brain imaging studies, the identification of key signalling receptors and extensive genetic analysis. However, the kind of treatment breakthroughs that have been seen in some other therapeutic areas are generally absent from this field.

At the same time, the global burden of disease resulting from psychiatric disorders looks set to increase, which will entail significant social and economic costs in both developed and developing economies. Three areas of activity lie ahead for this research field. First, there is a need to develop novel treatment approaches and interventions. Secondly, there is a need to optimise and better understand existing treatments. Finally, there is a need to learn how best to make these treatments widely available and accessible.

## The science of science

Given the large burden of schizophrenia and the need for research to address it, the next challenge is how best to organise and support that research. The Alliance of Mental Health Research Funders (previously the Science of Science Mental Health Network) has played a significant role in developing this field in the area of mental health.<sup>4</sup> The

<sup>2</sup> The presence of high levels of cholesterol – a form of lipid/fat – in the blood.

<sup>3</sup> The CATIE study, funded by the National Institute for Mental Health (NIMH) from December 2000 to December 2004, is a US nationwide public-health-focused trial comparing the effectiveness of old and new antipsychotic medications used to treat schizophrenia. It is the largest, longest and most comprehensive trial ever carried out to examine existing therapies for this disease. <http://www.mentalhealthamerica.net/go/research/catie> (as of 19 March 2009).

<sup>4</sup> <http://grahamboeckhfoundation.org/projects/alliance-mental-health-research-funders-formerly-sos>

network, through the leadership of the Graham Boeckh Foundation, has brought together an international collection of funders (including the US National Institute of Mental Health [NIMH], the Canadian Institutes of Health Research and Alberta Innovates Health Solutions, and the UK National Institute for Health Research) to share expertise and experience in commissioning mental health research. In addition, the network has funded this study as well as another to map mental health research over the past 30 years using bibliometrics (Larivière et al., Forthcoming).

There are four overlapping reasons to examine how research produces knowledge and other benefits to society – to analyse the science of science. These are the four As of advocacy, allocation, accountability and analysis (Guthrie et al., 2013a). Each of the reasons requires a different emphasis in terms of data collection and analysis. First, if the value of research can be demonstrated, it is important to make the case for it to be supported. Currently the emphasis of such studies is often on demonstrating the economic value of research at a macro-economic level. An example of such a study is ‘Medical Research: What’s it worth?’, covered in more detail in Box 1. This estimated that public-sector research in the mental health field had had a 37% rate of return – demonstrating that, as a whole, mental health research is good value for money. This finding played an important role in maintaining the level of support for biomedical research in the UK Comprehensive Spending Review 2007.

Secondly, once the funding for research has been secured, it must be allocated to programmes, institutions, projects or individuals. The science of science can provide evidence for how this may be carried out most effectively and provide methods, such as bibliometrics, that can supplement and enhance the information available for decision making (Ismail et al., 2009).

Thirdly, once funding has been allocated, good governance requires that the recipients of public funding should be able to account for their decisions and spending. One plank of such accountability frameworks can be provided by ‘science of science’ endeavours that provide a way to catalogue the diversity of impacts arising from research while minimising the burden placed on researchers. One example is ResearchFish, a survey tool that descends from the Medical Research Council’s e-Val and Arthritis Research UK’s RAND/

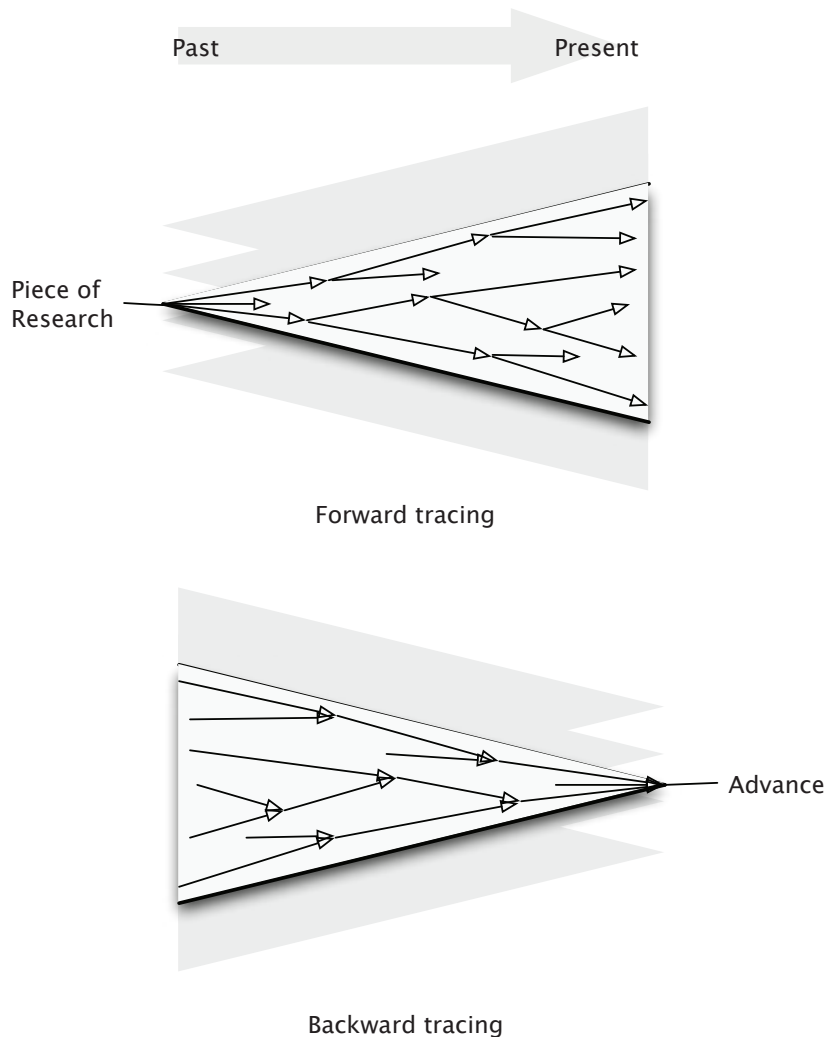
ARC Impact Scoring System (RAISS) (Research-Fish Ltd, 2013; Wooding, et al., 2009).

Finally, through analysis we can start to learn how to organise the endeavour of science to achieve most effectively and efficiently the progress in patient care and understanding that medical research funders desire. It is to this area of analysis that this report seeks to contribute. Understanding how research contributes to improvements in the lives of patients requires an understanding of the processes of research, from the genesis of the ideas of researchers and clinicians, through funding decisions and the research itself, and on to the translation and implementation of those initial ideas. Many of the ideas will fall by the wayside during the process, but we need to understand how best to organise the research enterprise to find and implement the successful ones. In outline, the analysis thread of the science of science is aiming for a better understanding of research performance and, more importantly, the drivers of improved performance. At a conceptual level, we need to understand what attributes lead to research success. For example, what kind of science, what kind of scientists, what kind of setting and what kind of funding mechanism are most successful in promoting the translation of research from bench to bedside?

To be grounded, these approaches will inevitably need to learn lessons from the past – a field which we have surveyed in Marjanovic et al. (2009). This raises an inherent question about whether it is possible to apply historical analyses to contemporary science policy. Some would argue that the science of the past is so fundamentally different that lessons cannot be learned, while others would counter that if the focus is on the administration of science rather than the science itself, such lessons may be valid. That said, we acknowledge that such an approach may restrict the opportunity for innovation because by evaluating past activity one inevitably draws lessons from existing practice and may narrow the options available to a research funder.

We use the term ‘retrosight’ to refer to the idea of learning from past experiences in research to improve current policy. The term is derived from two landmark studies in science policy. The first – Project Hindsight (1967) – was a study sponsored by the US Department of Defense that examined the incremental advances of various technologies

**Figure 1.2.**  
The forward- and backward-tracing approaches to learning from the past



(Sherwin & Isenson, 1967). The second was Julius Comroe's book, *Retrospectroscope: Insights into Medical Discovery* (1977). Comroe examined new life-saving advances in medicine and how they had come about. At the same time, in a more or less direct response to Project Hindsight, he worked with Robert Dripps to trace the research antecedents of clinical advances in cardiovascular medicine. This study was described in an article in *Science* (Comroe & Dripps, 1976).

Hindsight and *Retrospectroscope* are both examples of tracing back from an advance to look at its history and research antecedents (shown as **Backward tracing** in Figure 1.2). The second approach, which we have used in our previous Retrosight studies, is to trace forwards from research carried out in the past that has (or has

not) translated from bench to bedside (shown as **Forward tracing** in Figure 1.2). This approach relies on carefully selecting case studies of research to enhance the transferability of the findings within mental health research and potentially to other fields and by taking a number of steps to reduce the likelihood of investigator biases. The case studies bring together a range of data sources including key informant interviews, document and literature reviews, and bibliometrics. These case studies are then systematically compared, first to differentiate between those that have measurably high impact and those that do not. Then they are qualitatively coded to identify attributes that may be associated with high impact. Finally, we systematically examine each factor to see if it appears to be associated with high impact and



develop actionable policy recommendations based on this evidence. This methodological approach was successfully used to evaluate arthritis and cardiovascular research funding (Wooding et al., 2004; Wooding et al., 2011). The main findings of these studies are set out in Box 2. Indeed, one of the motivations for undertaking a Retrosight anal-

ysis in the field of mental health research was to see whether there was agreement between – and thus potential transferability of – the key observations arising from the previous arthritis and cardiovascular studies (i.e. whether a finding observed in one can be applied to another field without additional analysis).

**Box 1:**  
**Estimating the economic benefits from medical research in the UK**

A recent study carried out by a consortium involving Brunel University, the Office of Health Economics and RAND Europe focused on measuring the returns from investment into research in cardiovascular disease and mental health over 17 years between 1975 and 1992. Cardiovascular disease was chosen because much is known about how therapies and diagnostics affect health and lifespan; and mental health was selected because, conversely, there is less understanding of such effects.

Developing a methodology to work out the health and gross domestic product (GDP) gains from investing in these two areas, the researchers aimed to address a raft of questions, including these:

What proportion of global cardiovascular disease / mental health research may be attributed to the UK?

What is the time lag between research expenditure and its impact on health?

What were the key treatments and interventions over this period and how many people used them?

Data were gathered from UK research funders, including the Medical Research Council, the Department of Health and the Wellcome Trust, to work out total investment in the two chosen disease areas. Evidence-based clinical guidelines were used to estimate the UK's research contribution to interventions in these fields, including those from NICE. Evidence on 46 different combinations of cardiovascular diseases and interventions to treat or prevent them was analysed – for example, aspirin, beta blockers and smoking cessation – while the study for mental health used evidence on six such combinations. Quality Adjusted Life Years, estimated by NICE to have an opportunity cost value in the NHS of £25,000 each, were used to measure the quantity and quality of life gained from a health intervention.

The researchers estimated that the health and GDP gains from UK public and charitable investments in cardiovascular disease research over the

study period were equivalent to an annual rate of return of around 39% for cardiovascular disease and 37% for mental health research. Thirty per cent of the gains reflected a common estimate of the economic benefits to the UK economy, and the remaining 9% for cardiovascular disease and 7% for mental health research represented the opportunity cost value of the gains from new treatments or preventative measures.

The findings emphasised that public and charitable funding of medical research encouraged greater investment from the pharmaceutical industry, a spill-over effect. One example of this is that public investment in universities generates skilled graduates, new ideas, networking opportunities and high-quality libraries. The report points out that it is no coincidence that high-tech firms choose to base themselves near top-quality universities. Each £1 of extra public/charitable investment in UK medical research was shown to yield £2.20 to £5.10 of extra pharmaceutical company investment, which taken together earned an extra £1.10 to £2.50 GDP per year for the UK economy.

The study also estimated a time lag between research expenditure and eventual health benefits of around 17 years. This raises further questions, such as whether the measured returns on investment are specific to the time frame studied. Do returns differ depending on the area of research funded? These uncertainties also apply to the time lag between investment and benefit in different disease areas. More research is clearly needed to answer these questions and expand upon the insights gained from the study.

The researchers point out that the study was not intended to be viewed as a one-off exercise, but rather as an opening into a new research field that will lead to even more robust studies in future. However, the results do provide the first real quantitative estimates of the economic benefits of UK public and charitable investment in medical research.

## Box 2: Previous Retrosight studies

We have carried out two previous studies with close parallels to this work, using the Retrosight method. The first, for Arthritis Research UK, examined 16 research grants awarded in the early 1990s and traced their development up to 2003. The second examined cardiovascular and stroke research funded in the late 1990s and traced its impacts through to 2009. This study was supported by an international consortium of funders and examined 29 case studies across three countries.

The key findings of 'The returns from arthritis research' were as follows:

**Individuals translate research** – Human interaction, rather than funding mode or publication impact, is the key factor in driving effective translation of research into practice.

**Short, focused project grants seem to provide value for money** – Smaller project grants may offer similar payback to that identified for larger programme grants.

**There was a diversity of research payback** – The broad definition of research benefits used by the payback model revealed that each of the research projects examined yielded a much richer range of outputs and outcomes than expected.

**Intended or unintended flexibility in funding is used to the benefit of the funder's mission** – Therefore, a case may be made for building a degree of flexibility into scientific funding.

**Referees' contributions to the peer-review process are of variable benefit** – The studies with the most negative peer-review comments were the ones with most impact, but they were funded.

**The Payback Framework was likely to be suitable for use operationally to monitor the impact of research as it developed.**

The key findings of 'Project Retrosight – Understanding the returns from cardiovascular and stroke research' were as follows:

**The cases revealed a large and diverse range of impacts arising from the 29 grants studied.**

**There were variations between the impacts derived from basic biomedical and clinical research.**

**There was no correlation between knowledge production and wider social and economic impacts.**

**The majority of economic impacts identified came from a minority of the projects.**

**Factors associated with high and low impact could be identified.**

## Organisation of this report and supporting reports

This report is divided into five chapters. Chapter 2 briefly describes the methods we employed in the study, with significantly more detail set out in the accompanying methodology report (Guthrie et al., 2013b). We used both forward-tracing case studies and backward-tracing perspectives, covering 20 years of mental health research. Chapter 3 describes four headline observations and the policy provocations arising from the case studies. For each observation we set out the evidence from this study and outline that from previous related research. We also consider the caveats that should be borne in mind and draw up initial provocations for policymakers. Chapter 4 provides a summary

of the six perspectives and describes the observations arising from our analysis of them – setting each observation in the context of previous literature – and where appropriate considers the implications for policy. The final chapter considers how the observations from the perspectives and case studies can be brought together as findings, draws out relevant policy provocations and identifies questions for further research. The chapter also reviews the caveats that should be borne in mind when considering the research, and discusses the contribution of this work to the field of the science of science. The full case studies used to support our analysis are available in the case study report (Pollitt et al., 2013b), and the perspectives are published as the perspectives report (Pollitt et al., 2013a).



## Chapter 2 Methods

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### Introduction

This chapter provides an overview of the methods used in the study. We begin by providing a brief conceptual overview of the study, before explaining how the case studies and perspectives in the two parallel streams of work were selected, carried out and analysed. A more detailed account of the study's methods has been published as a separate report (Guthrie et al., 2013b).

Through this research we tried to identify attributes of the research – of the researcher, the setting and the research itself – that are associated with larger benefits to patients and society. By examining in our case studies and perspectives how these attributes appear to have affected translation, we make judgements about whether their importance may be generalised. We then test those insights within the wider literature to strengthen our confidence in our conclusions. One of our key concerns was to try to minimise the potential for our preconceptions and biases to affect our findings and conclusions; we have therefore used a variety of algorithmic techniques to distance ourselves from key decisions within the project. These methods included stratification, randomisation, consensus scoring and calculations of likelihood, all of which are mentioned below and covered in more detail in the methods report (Guthrie et al., 2013b).

### Conceptual framework

This study combined two approaches previously applied in the science of science:

- ‘forward-tracing case studies’, which start from a piece of research carried out in the past and follow it forwards through time, documenting

its influence on future research, policy, practice and wider outcomes;<sup>5</sup>

- ‘backward-tracing perspectives’, which start from a clinical advance and work backwards through time to identify its research antecedents and other influences on its development.

We chose to combine these approaches in this study because, while important advances in basic science have greatly expanded our knowledge of the brain, we have yet to see the full benefit of these in terms of understanding and treating mental illness. These uncertainties led us to add to our established methodology the backward-tracing part of the study: an analysis of clinical developments which *have* impacted on mental health-care, with the aim of identifying the research and other events that contributed to this.

These two complementary streams of work are illustrated in Figure 2.1.

The following sections describe the main elements that made up these two aspects of the study – the case studies (tracing forwards from research) and the perspectives (tracing back from advances). Figure 2.2 provides an overview of the various steps involved in each of these.

### Forward-tracing case studies

Our aim in using a case-study approach in the forward-tracing strand of the research was to identify the range of impacts produced by a particular

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<sup>5</sup> We use the shorthand of 20 years as a conservative description of the timeframe of the forward-tracing case studies; in many cases the timescales are longer than this. The case studies are all based on research that gave rise to papers between 1985 and 1990 (between 22 and 27 years ago), but in some cases continued past this date. This means that some of the research had been completed by this date and therefore was probably funded five to ten years earlier.

Figure 2.1. Conceptual overview of the study

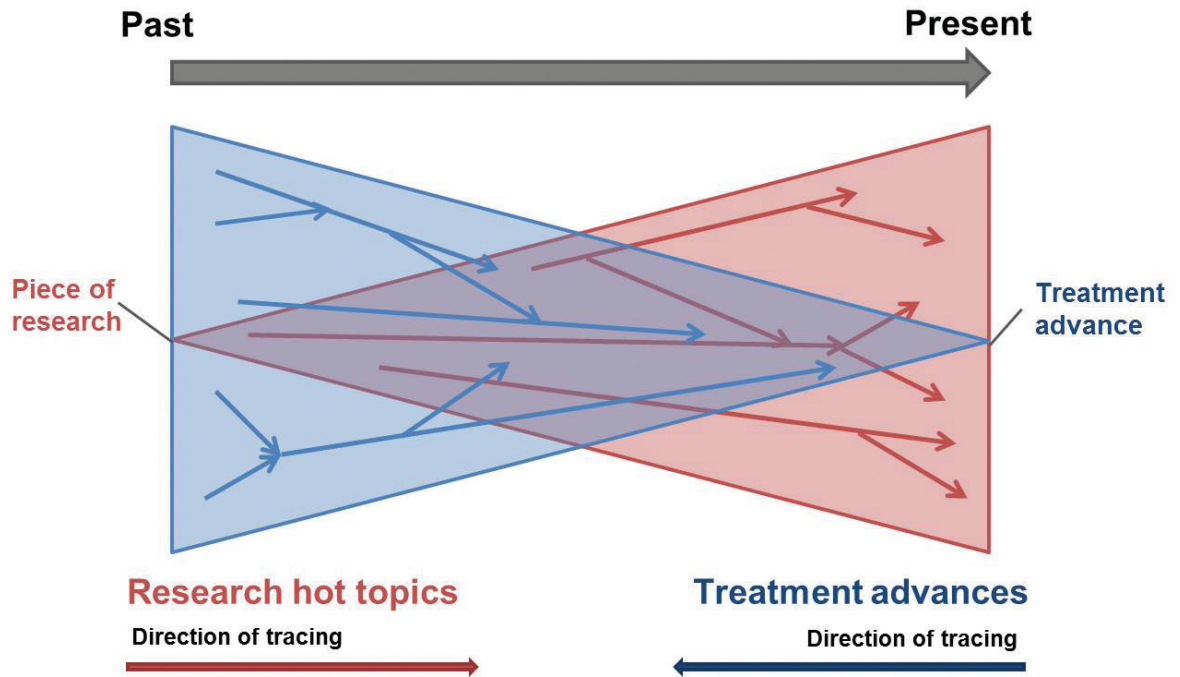
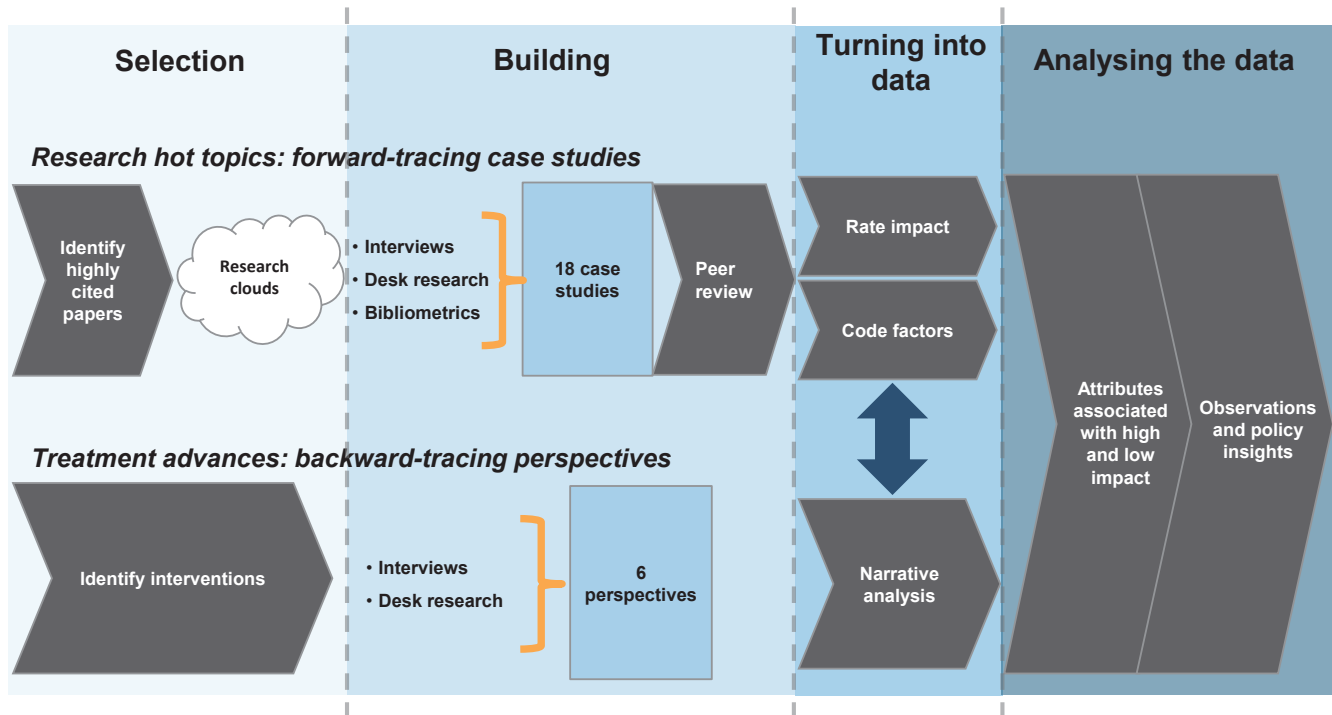


Figure 2.2. Methodological stages of the two streams of work



piece of research and to explore the reasons why impacts did or did not occur. While our previous studies have built such case studies around individual research grants, in this instance we focused on a concept we termed a ‘research cloud’, as we define in detail in Box 3. Our aim in doing this was to capture a key section of a stream of

research, a unit of analysis akin to the way that researchers think about their own work. The research clouds we identified (in discussion with the researchers) tended to be supported by multiple funding sources and produced a number of papers, but held together conceptually as a single, coherent body of work.

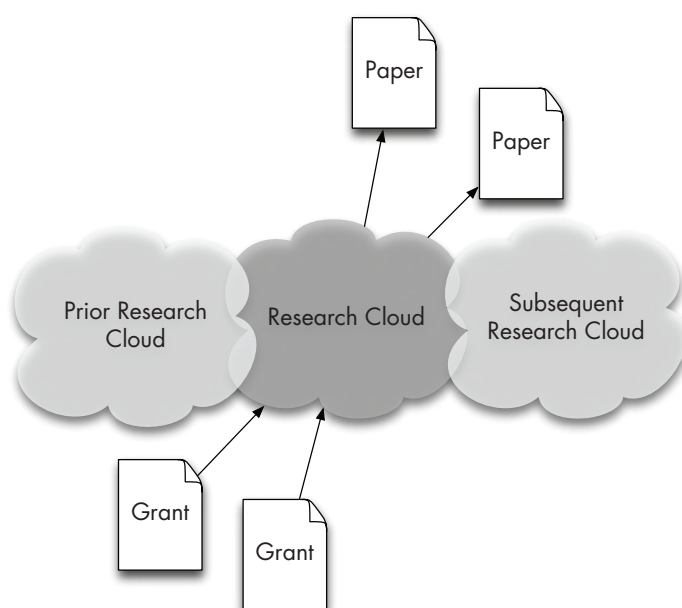
### Box 3 Defining research clouds

Research clouds are a unit of analysis that embraces that idea that the process of research cannot be separated cleanly into discrete units. Unlike the units of papers or research grants, the idea of the research cloud seeks to capture how science works in practice and how researchers think about their work, while identifying units of research for analysis.

Through the interviews in our previous work it became clear to us that researchers tend to see their work developing incrementally and to see the steps as spanning a range of grants and/or other funding sources. They may identify a receptor responsible for physiological function and then move on to investigate its signalling, or learn and apply a new technique to a problem before moving to apply that knowledge in a different experimental system (Wooding et al., 2004; Wooding et al., 2011). Both of these examples contain two successive research clouds in the story of the research on a particular topic. We chose the term ‘clouds’ to reflect the idea that each may have somewhat diffuse boundaries. In practice we found

that although adjacent clouds may have some overlap, on most occasions we could define a workable delineation between them. This approach to defining the unit of analysis is akin to approaches that define research ‘events’ or ‘breakthroughs’ (e.g. Sherwin & Isenson, 1967; Illinois Institute of Technology, 1968) – although we focus more on the stages in research activity than on the outputs/outcomes. As illustrated in the figure below, each research cloud may be supported by a number of research grants and may produce more than one research paper.

Research clouds have the advantage of an approach not focused solely on grants or publications – they seek to embrace the activities of science itself: the inspirations, the experiments, the collaborations, the chance meetings and the unexpected. Explicitly acknowledging the diffuse and contestable nature of the boundaries of the research clouds provides us with a framework to consider this in the case studies and ensures that we remain sensitive to the difficulty of defining boundaries in research.



## The Payback Framework

A number of approaches have been developed to describe and capture the impacts of research, ranging from individual case studies, through logic models, to econometric modelling (Hanney et al., 2007; Boaz et al., 2009; UK Evaluation Forum, 2006; Committee on Science Engineering and Public Policy et al., 1999). These methods vary in the range of impacts they consider and the extent to which they attempt to understand how they arise. In this study, we used the Payback Framework, which takes a wide definition of research impact running from the generation of new knowledge in academic papers through to societal and economic benefits (Buxton and Hanney, 1996; Hanney et al., 2004). These impacts are categorised into

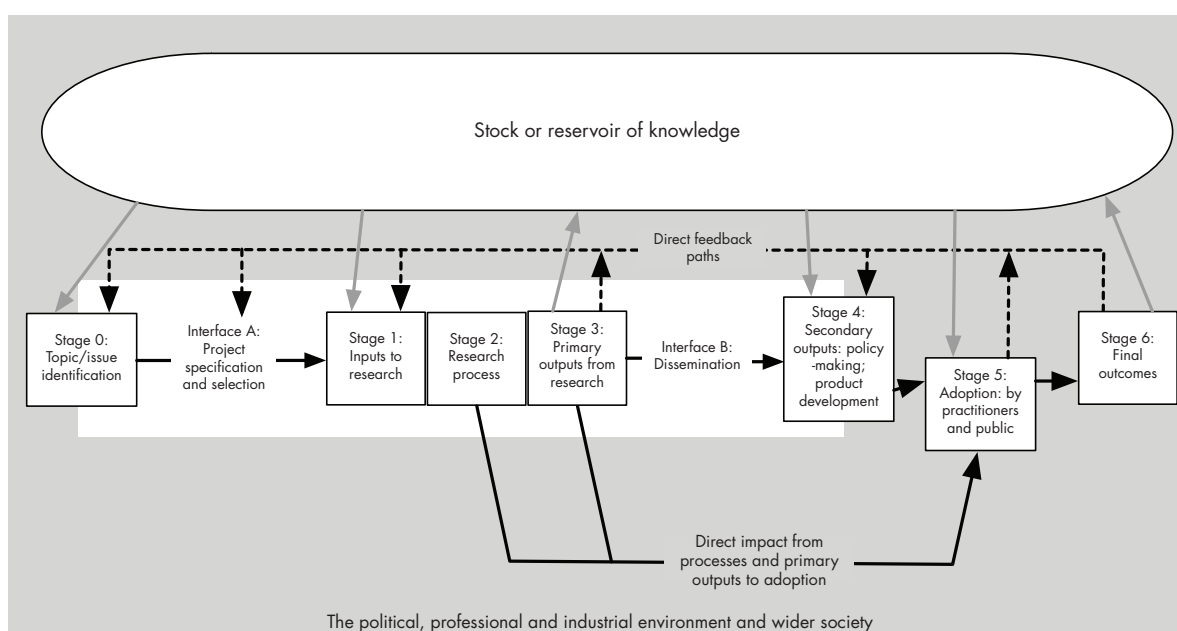
five payback categories (shown in Table 2.1). We consider the first two categories to correspond to impacts within the research system ('academic impacts'), and the final three to impacts on society more widely ('wider impacts').

Crucially, and unlike many other approaches, the Payback Framework develops a number of plausible hypotheses ('if-then' statements) about how different stages of research and its impacts may be causally connected, and thus provides a useful basis from which to categorise evidence to understand the research process better. This is done through a second component of the framework: the logic model (as illustrated in Figure 2.3). The model provides a common structure for examining why the researchers first undertook a

**Table 2.1.**  
The payback categories

<b>Academic impact</b>	<b>Knowledge production:</b> publication of papers and reports.  <b>Research targeting and capacity building:</b> (i) better targeting of future research; (ii) development of researcher skills, research infrastructure, etc
<b>Wider impact</b>	<b>Informing policy and product development:</b> (i) improved information bases on which to take policy decisions; (ii) informing product development  <b>Health and health sector benefits:</b> (i) health or quality of life gains; (ii) cost reduction in the delivery of services; (iii) qualitative improvements in the process of service delivery and effectiveness of services  <b>Broader social and economic benefits:</b> (i) wider economic benefits from, e.g., increased employment or commercial exploitation of research; (ii) social benefits from societal change, e.g., attitude change

**Figure 2.3.**  
The Payback Framework logic model



particular piece of research; what they hoped to achieve; how and why it was funded; the research process itself, including collaborations, use of shared resources and so on; research outputs (e.g. publications); how those outputs influenced subsequent research topics and careers; how the research was subsequently translated into 'secondary outputs' through influencing clinical policies or product development; and how the research then translated into improvements in health and broader social and economic benefits.

The Payback Framework has the advantage of covering a wide range of the paybacks from research, and allowing cross-case comparisons by providing a uniform classification of paybacks and narrative structure. When used to structure case studies, as for this study, it allows in-depth exploration of the circumstances and context of the research, as well as nuanced treatment of issues such as the contribution of research to particular paybacks (Croxon et al., 2001; UK Evaluation Forum, 2006).

The framework has also shown itself to be suitable, with slight modification, for use in a range of research contexts from basic biomedical research through health services research, including social science and research in the arts and humanities (Wooding et al., 2004, 2005, 2007; Hanney et al., 2007; Levitt et al., 2010).

### Selecting the research clouds for the case studies

Selection of our 18 case studies was shaped by a number of specific aims: we wanted to examine a diverse range of research, the research needed to be drawn from across the three study countries, the research should have taken place long enough ago for findings to have been translated, and we wanted to focus on lines of investigation seen as promising at the time.

While previously we have selected case studies based on research grants awarded, in this study we decided to use scientific papers to identify research clouds, as described above. We decided to work in this way in part because reliable records of funding were not readily available across the study countries and time period, but also because a bibliometric method seemed more appropriate in meeting the various aims outlined above. The first step in selecting our case studies was to define a dataset from which to draw individual papers. Using

a combination of journal classification and Medical Subject Headings (MeSH) assigned to individual papers (more detail on which is provided in Guthrie et al., 2013b) we defined an initial set of 283,836 papers published during the period 1985–1990. Making an assumption that the number of citations a paper receives in the five years following its publication is a reasonable proxy for its interest at that time to other researchers, we identified a subset of highly cited papers to act as starting-points for establishing the wider research clouds. These papers were sorted into a selection matrix by country (Canada, UK, USA) based on the affiliation addresses of the authors, and research type (basic, clinical and interventional, the last of which was further subdivided into pharmacological, psychosocial and service delivery). Within each cell of the matrix, papers were selected randomly as the basis for case studies.

The wider research cloud associated with each paper was subsequently delineated in consultation with the researchers involved. The number of papers in each cloud varied from 2 to 22. The topics of the final set of 18 case studies are listed in Table 2.2.

Using a bibliometric method in selecting the topics for the clouds for the case studies brought a number of strengths and weaknesses to the study. Unlike the grant-based selection of our previous studies, it allowed for the inclusion of industry-funded research and studies supported solely by discretionary or 'soft' funding from the host institution. Indeed our sample included research clouds with both of these funding sources. The data-driven selection method also minimised 'cherry-picking' of research, ensuring that we did not focus solely on work seen with the wisdom of hindsight to be particularly interesting or exceptional.

However, the method was not without its challenges. With only contact details from 25–30 years ago, it was not possible to contact all of the researchers named on the papers selected. Additionally, the classification of the research into basic, clinical and interventional categories was based solely on the initially selected paper. In some instances, the research cloud as a whole was focused slightly differently, and so at the analysis stage we reclassified the case studies as described in Box 4. We did not consider this need to reclassify a serious limitation of the methodology because



the aim of our selection framework was to ensure that a range of research was selected, not that the sample was necessarily equally distributed across these research types.

**Table 2.2.**  
**Case study research cloud topics**

Neurotransmission of dopamine and the plasticity of the brain
Testing the effects of dopamine on calcium currents in rat pituitary
The use of in-situ hybridisation to locate all 13 GABA-A receptors in the brain
Demonstrating the existence of 5-HT <sub>3</sub> receptors in the central nervous system, in different species and using several techniques
Using PET scanning to understand the pathophysiology of the human brain in patients with schizophrenia
The molecular neurochemistry of the human brain, particularly related to neuropsychiatric and neurodegenerative illnesses
The use of electrophysiological measures (P300) to detect and quantify brain dysfunction in psychiatric illness and to compare in different diagnoses
The hypothesis that elevation (i.e. increased density) of dopamine receptors is important in schizophrenia and, more generally, the dopamine hypothesis of schizophrenia
An epidemiological study of patients with first-episode schizophrenia, looking at levels of expressed emotion among relatives and its association with relapse in Chandigarh, India
First-episode schizophrenia, particularly in relation to the Northwick Park cohort study
Identifying the frontal lobe as an area of functional and neuropsychological deficits in the schizophrenic brain
The use of childhood home movies to understand characteristics of preschizophrenic children and neuromotor deficits
Investigating the role of calcium in schizophrenia and looking at the use of verapamil in the treatment of schizophrenia
The implications of lateralisation in the dopaminergic brain
Developing a service model for family psycho-educational interventions, in particular investigating the effects of educational interventions with families living with schizophrenic relatives
Characterising the relationship between schizophrenia and depression in a long-stay hospital population
The role of gender in a clinical trial of an inpatient family intervention
Understanding the interactions and effects between dosage of antipsychotics and family psycho-educational intervention

## Building the case studies

In building the case studies we aimed to meet two objectives. First, we needed to catalogue accurately the impacts arising from each research cloud. This was done using the five payback categories. Secondly, we wanted to produce a structured and comprehensive narrative, which would allow us to examine the contextual attributes that might have influenced the impacts produced. By using the same detailed structure for each case study, based around the Payback Framework, we ensured as far as possible that the same information was available for each research cloud and that the case studies were comparable in the subsequent analysis.

The central aspect of data collection for each case study was interviews with the researchers involved. These interviews were essential in revealing the interests and motivations of the research teams and the development of their ideas. Interviews were also carried out with collaborators, competitors and other key people in the field – a total of 48 people across the 18 case studies. This was supplemented by reviews of the literature (both the papers forming the research cloud and more widely) and a bibliometric analysis tracing the citation level and characteristics of the research in question. Building the case studies was an iterative process: interviewees would highlight new lines of enquiry in the literature, which in turn raised further questions or indicated others to whom it would be useful to speak.

The major strengths of this approach were in using an established framework, which ensured comparability across the set of case studies, and in the level of detail we were able to include, particularly from the interviews. However, this latter point also meant that the case studies were resource intensive to conduct, with the result that we were limited in the number of cases we were able to include. While the balance between detail and sample size is always an issue in qualitative research of this nature, this study generally compared favourably with other similar projects. Table 2.3 lists other studies that have used the Payback Framework in exploring research impact, and the number of case studies in each.

A final and crucial step in building the case studies was their review, both by the researchers involved and other experts in the field. The objective of this peer review was to verify the historical accuracy of the narrative, to verify whether the

**Table 2.3.**  
**Previous studies using the Payback Framework**

Author	Year	Title	Number of case studies
Wooding et al.	2011	Understanding the returns from cardiovascular and stroke research	29
Levitt et al.	2010	Assessing the impact of arts and humanities research at the University of Cambridge	4
Oortwijn et al.	2008	Assessing the impact of health technology assessment in the Netherlands	5
Nason et al.	2008	Health research – making an impact	8
Peckham et al.	2008	Assessing the impact of the NHS Service Delivery and Organisation Research and Delivery Programme	11
Kalucy et al.	2007	Primary health care research impact project	4
Hanney et al.	2007	An assessment of the impact of the NHS Health Technology Assessment Programme	16
Nason et al.	2007	Policy and practice impacts of research funded by the Economic and Social Research Council: a case study of the Future of Work Programme	4
Wooding et al.	2004	The Returns from Arthritis Research	16
Buxton and Schneider	1999	Assessing the 'Payback' from AHFMR-funded research	7
Buxton et al.	1999	Assessing the Benefits from North Thames Research and Development	19
Buxton and Hanney	1997	Assessing Payback from Department of Health Research and Development	18

science was suitably described and, importantly, to ensure that impacts had been correctly attributed to the research cloud on which the case study focused.

The full set of case studies has been published as a separate volume alongside this report (Pollitt et al., 2013b).

### Generating analysable data from the case studies

Once the 18 case studies were complete, we needed to turn the case-study narratives into a suitable form for inclusion in a systematic and rigorous analysis. This involved two separate tasks: rating the impacts catalogued in each of the five payback categories, and distilling a set of research characteristics and influencing attributes from the detailed narratives.

An international panel of experts – comprising scientists, practitioners, family and patient representatives, and policymakers – carried out the rating of impact. As explained in more detail in the methodology report (Guthrie et al., 2013b), panel members individually scored each research cloud's impact on a nine-point scale (0 no impact,

9 highest impact within set of case studies) in each of the payback categories before meeting as a group for a two-day discussion workshop. The aim of this workshop was not to reach consensus, since there are legitimate differences in subjective valuations of different impacts, but instead to reduce differences that were due to misunderstanding or misinterpretation. Following the workshop, each panel member was given the opportunity to rescore each case study and a final set of impact scores was compiled.

That these scores showed broad agreement (but not consensus) suggests that our approach to quantifying impact was successful, while the fact that the case studies that the panel scored most highly differed by payback category demonstrates the value of using a framework that considers multiple definitions of research impact. We should acknowledge, though, that while the scoring workshop was valuable in strengthening the panel's understanding of the various case studies, in drawing on the collective judgement of a panel it is impossible to control completely for, or gauge the extent of, the influence of individual members on one another's assessments.

The second element of turning the case study narratives into analysable data involved coding their content against a series of ‘attributes’ – that is, characteristics of the research itself, the researchers who carried it out, the institution they were based in, the funding they received and the wider context within which the events were situated. These attributes were derived in part from those explored in our previous studies, but this initial list was also supplemented throughout the study by emerging ideas from the research team. Case studies were each coded by two researchers, and the use of an iterative process allowed attributes only emerging at the coding stage then to be examined across the full set of case studies. The result of this exercise was not only binary data indicating the presence or absence of each factor in each case study, but also a catalogue of all of the references coded to each factor, allowing a more nuanced examination of the role of each.

While it is inevitable that some occurrences of attributes will have been missed in the coding, this was minimised through the coding of all case study narratives by two researchers independently, and we believe that remaining instances are likely to have occurred randomly. Additionally, the iterative approach of returning to the text coded to each factor in order to check its consistency meant that any incorrectly coded text was also detected (although there were very few instances of this).

### **Analysing the case studies**

Having created two sets of data from the case studies – the impact scores and catalogue of attributes – our next step was to combine these in an analysis of attributes which appeared to be associated with either high or low impact. First of all we needed to define high- and low-impact groups. This was done by simply sorting the median impact scores for each category from high to low and allocating the top third to a high-impact group and the bottom third to a low-impact group. This use of a relative definition of impact level was considered appropriate because for each individual category the impact scoring was carried out within set, rather than on an absolute and externally anchored scale.

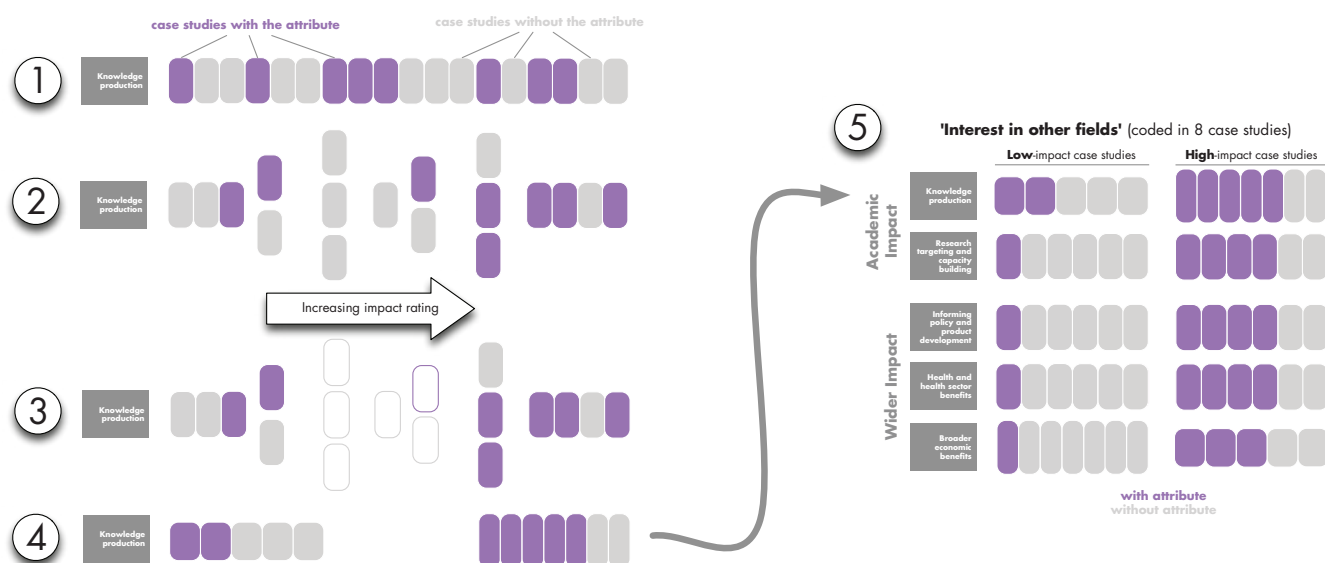
To explore the association of the various attributes with research impact, we looked at the distribution of its occurrence between the research clouds considered high and low impact in each

payback category. As an example, of the eight case studies coded for the attribute ‘researcher interest in other fields’, five were rated as high impact in the knowledge production category and two as low impact (the remaining one being in the mid-impact group). This example is illustrated in graphical form in Figure 2.4. While not using the mid-impact group at this point in the analysis meant that we did not use the full data we had available, we considered this necessary to ensure clear separation between the high- and low-impact groups.

In all, our codebook contained 162 different attributes, and we examined the association of each of these with each of the five payback categories. We then used a numerical method to identify a manageable number of associations that appeared to merit attention. We used the Fisher Exact Test as a means of calculating the likelihood of associations occurring by chance, as it makes no assumptions about distributions and can easily be applied across a large number of comparisons (Cochran, 1954; Namey et al., 2007). As the aim was to select a manageable number of associations for more detailed analysis – that is, the likelihood was only one contributor to the evidence of an association – we chose our threshold of likelihood to give us around 30 associations to examine. This led us to use a threshold of 25% chance. We could have used our judgement to select the 20 associations we found most interesting, but we wanted to insulate the analysis process from our preconceptions as far as possible. Making a large number of comparisons in a relatively small dataset introduces the likelihood of spurious associations, but this stage was intended only to act as a high-level initial screen to guide a subsequent in-depth qualitative analysis. In this stage we re-examined all the text coded to each factor and considered possible confounding or complementary attributes. We also situated the apparent association in the context of previous research findings and theoretical debate. In doing so we looked at the causal plausibility of the relationship – that is, whether there was a credible causal chain given what we know about how research translation occurs, and also whether any previous research findings were consistent with the observation. We did this for each of the attributes that our numerical ‘likelihood scan’ highlighted.

While a number of apparent relationships that initially appeared interesting were not considered

**Figure 2.4.**  
A diagrammatic overview of the initial steps of analysis



To identify the groups of case studies for analysis we worked through the payback categories one by one. In the diagrams each case study is represented by a rounded rectangle – where the attribute was identified the case is shaded purple, and where it was absent, grey (1). Starting with knowledge production, we sorted the case studies into ascending order of impact, taking notice of ties in the rankings (2). We then split the case studies into roughly equal thirds – a high, medium and low group – and dropped the mid-group from the initial analysis. We could not split exactly into thirds because of ties in the ratings (3). Different ties occurred for different categories, hence the number of case studies in each group varies slightly across the categories. To allow the diagrams to show the fraction of case studies with a particular attribute and enable easy comparison across categories, we changed the width of the rounded rectangles to take into account the number of case studies in each group – so where there are five case studies the rectangles are wider than where there are seven (we adjusted the height to ensure that each case study still occupies the same area) (4). Finally, we collected the case studies with the attribute to the left of each group and those without attribute to the right and displayed all the categories alongside each other (5).

relevant upon a more detailed exploration of the case studies and wider evidence, those relationships which were most robust and from which useful policy observations could be derived are presented in Chapter 3, where we discuss the study's key findings.

### Backward-tracing perspectives

Perspectives looked backwards in time from treatment advances made in recent years, exploring the research that contributed to their development, as well as other barriers and facilitators to their adoption into practice. The perspectives were intended to supplement the data collected through our case studies, particularly providing examples of successful translation which we were concerned we might not find in the forward-tracing case studies.

### Selecting the perspectives

In selecting our six perspectives we aimed to identify recent advances that had resulted in substantial benefits to patients, or where there were clear indications of potential to change care. In order to investigate a suitable range of advances we developed a set of criteria to aid our selection. In summary, we wanted to consider the following:

- A balance of pharmacological and non-pharmacological interventions.
- Some treatments that had been adopted in a similar way across the study countries and some for which implementation was more variable.
- Some advances that focus on the individual and others that focus more on their environment (family, community, etc).

- Advances that were at different stages of translation – from ‘on the cusp’ of entering practice to treatments that had reached mainstream use.

Our initial approach to selection was to conduct a Delphi-like survey of various mental health stakeholders (including clinicians, researchers, service users and service providers) to generate a broad list of possible advances. Two immediate candidates emerged from this exercise: cognitive behavioural therapy (CBT) and early intervention in treatment for schizophrenia. However, a poor response rate for the survey prevented the clear identification of other advances and led us to supplement this information with a review of clinical guidelines in the three study countries and consultation with the project’s expert advisors.

As the survey had broadly suggested a focus in the area of community or family interventions, we reviewed the relevant recommendations listed on clinical guidelines and discussed final selection with our expert advisors. Using criteria of interventions that were both well enough defined to form the subject of a case study, and feasible in terms of scale and data availability, we decided that the third perspective should focus on supported employment.

The initial survey had also suggested various pharmacological treatments, but there had been little specificity or clarity on particular areas of focus. In order to balance pharmacological and non-pharmacological advances, we wanted to select three perspectives in this area. One of our selection criteria was to explore interventions at different stages of development, so – having consulted clinical guidelines and our expert advisors – we decided to focus on: clozapine; addressing the metabolic side effects of SGAs; and the development of drugs to address cognitive deficits associated with schizophrenia.

### **Building the perspectives**

Perspectives were built up through a combination of desk-based research and interviews with some of the key figures in each of the three study countries. This was an iterative exercise as new influences came to light, and the process involved exploring the early influences providing inspiration, the development of the intervention itself,

and its subsequent dissemination and adoption into practice. Each perspective consisted of a detailed historical narrative, a table of key events and a ‘historiograph’ showing the influence of these events on one another.

We use the term ‘perspective’ to describe these narratives, since it became clear to us that the story of progress in the field is often contested – in terms of the key events and how they were interconnected – and it was beyond the resources of the study to identify a single clear narrative that was universally approved and agreed to capture the understanding of all stakeholders. Therefore, each perspective offers a view on the developments in a particular area that aims to reflect the range of views of researchers and other parties consulted in the production of the narratives. As far as possible, we have constructed detailed and balanced accounts. However, we do not claim that they offer a full and definitive picture of the development of a particular intervention or potential intervention as understood from all viewpoints. Therefore, they remain ‘perspectives’. While this is clearly a limitation of our approach (along with the fact that the resource demands limited the number of perspectives we could undertake), they do provide useful examples of effective translation in the later stages of the translation pathway.

The six perspectives have been published in full in a separate volume (Pollitt et al., 2013a).

### **Analysing the perspectives**

We carried out a thematic analysis of the six perspectives to assess the attributes that contribute to, or hinder, developments in mental health research and the implementation of interventions. This analysis used an inductive approach to coding and identification of themes. Starting from a blank sheet of paper, one member of the research team carried out a first reading of the narratives, noting all attributes that appeared relevant to successful translation. These were then clustered into a long list of potential themes. The long list of themes was then refined through discussion with other members of the research team. Finally, the data were recoded by the researcher who initially coded the perspective according to the agreed themes, and the evidence for each theme was analysed across the six perspectives.

## Chapter 3 Observations and policy provocations from the analysis of 18 case studies

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In this chapter we describe the four observations from our analysis of the 18 forward-tracing case studies. For each observation we set out the evidence derived from our analysis, and then compare this with previous studies and the academic literature; alongside considering the caveats to our analysis. From this we draw out initial policy provocations and future research questions. The next chapter considers the backward-tracing perspectives and how they supplement our evidence base, and our final chapter brings together the two sources of evidence to present our overall findings.

The four observations are as follows:

- 1 The case studies support the view that mental health research has led to a diverse and beneficial range of academic, health, social and economic impacts over the 20 years since the research was undertaken.** Wider societal impacts<sup>6</sup> were less common but had a stronger correlation with academic impact than observed in other disease areas.
- 2 Clinical research has had a larger impact on patient care than more basic research over the 20 years since the research was undertaken.** This relationship holds regardless of the approach used to classify 'clinical' and 'basic' research.
- 3 Mental health research conducted by researchers who work across boundaries resulted in greater academic and wider societal impacts.** This includes individual researchers and teams whose work spans stages

in a translational pathway or more than one discipline.

- 4 Researcher motivation to address patient need seems to be a key driver in determining whether mental health research has an impact.** Motivation may be more important than funding characteristics or research setting.

**The case studies support the view that mental health research has led to a diverse and beneficial range of academic, health, social and economic impacts over the 20 years since the research was undertaken.**

### Summary

In line with our previous work, the in-depth retrospective case-study approach used in this study captured a wide range of impacts across the five payback categories. Case studies were selected through highly cited papers, so all had an academic impact. Other papers in the research cloud also tended to be highly cited. Wider societal impacts were fewer in number, but the rating panel still considered the majority of research clouds to have had health, social or economic impact. The impacts identified in this project by no means reflect the full range of advances made over the time period, but provide useful examples of success stories that may be able to inform and inspire future research efforts.

### Case study analysis

As noted previously, there is a perception that mental health research has been poorly translated into clinical application (e.g. Gould & Manji, 2004; Insel, 2009). There may be relatively few

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<sup>6</sup> As shown in Table 2.1., we define academic impact as being the first two payback categories (knowledge production, and research targeting and capacity building) and wider societal impact as being the subsequent three payback categories (informing policy and product development, health and health sector benefits, and broader social and economic benefits).

**Table 3.1.**  
**Impacts in each payback category with selected examples**

Payback category	Total contribution and examples
<i>Knowledge production</i>	<p>All 18 case studies were rated as having impact in this category:</p> <ul style="list-style-type: none"> <li>• 170 papers in 18 clouds               <ul style="list-style-type: none"> <li>– 17,714 citations (108/paper)</li> <li>– 402 self-citations (2%)</li> <li>– 553,648 second-generation citations</li> <li>– 7,755,240 third-generation citations</li> </ul> </li> <li>• Identification of the expression of mRNAs for GABA-A receptor subunits in the brain</li> <li>• First study to show that the duration of untreated psychosis was associated with poorer outcomes</li> <li>• Demonstrated that expressed emotion was associated with differences in outcomes in schizophrenia across cultures</li> </ul>
<i>Research targeting and capacity building</i>	<p>17 case studies were rated as having impact in this category:</p> <ul style="list-style-type: none"> <li>• Early research on dopamine receptors and schizophrenia helped to promote interest in schizophrenia and dopaminergic system</li> <li>• Development of various techniques, e.g. microdialysis, in-situ hybridisation, use of PET scanning in studying mental disorders</li> <li>• Many examples of career progression including PhDs, promotions</li> </ul>
<i>Informing policy and product development</i>	<p>14 case studies were rated as having impact in this category:</p> <ul style="list-style-type: none"> <li>• Citation of the original papers in at least 14 clinical guidelines including UK NICE, US PORT and APA, Cochrane Collaboration reviews, and DSM-IV Sourcebook</li> <li>• Related stream of work led to clinical development of ondansetron and alosetron</li> <li>• Examples of researchers providing consultancy advice to pharmaceutical companies</li> </ul>
<i>Health and health sector benefits</i>	<p>12 case studies were rated as having impact in this category:</p> <ul style="list-style-type: none"> <li>• Part of a wider body of evidence that influenced the treatment available to long-stay patients returning to the community</li> <li>• Contributed to the justification for family intervention, and training programmes for carers of people with schizophrenia</li> <li>• Informed dosage strategies for FGAs, including the demonstration that intermittent dosage should not be used</li> </ul>
<i>Broader social and economic benefits</i>	<p>11 case studies were rated as having impact in this category:</p> <ul style="list-style-type: none"> <li>• UK NICE guideline estimates that family intervention resulted in cost savings of £2,634 per schizophrenia patient</li> <li>• Contributed to shift in attitudes away from the concept of schizophrenogenic families</li> <li>• Key researcher played important role in the early intervention movement in the West Midlands, which was critical in the implementation of early intervention in the UK</li> </ul>

examples of research travelling the length of this continuum, but when we consider at a more granular level some of the phases within this pathway we find that there are examples of important advances and that a variety of research impacts may be identified, both in our case study research clouds and more widely in literature discussing progress in the field. Our 18 case studies revealed a diverse range of impacts across the five payback categories, as summarised in Table 3.1.

### Comparison with existing evidence

As found in our previous studies on cardiovascular and arthritis research, the detailed case study approach enabled us to identify a wide range of research impacts. Other techniques, such as bibliometrics, would have identified knowledge pro-

duction only. The distribution of these impacts across case study research clouds was also similar to that observed previously: wider societal impacts were *not* found in all the research clouds. Despite this pattern being consistent with previous studies, the skew in wider societal impacts was less extreme than observed in the cardiovascular case studies (Figure 3.1).

The fact that the distribution of wider societal impacts was less skewed in the current study is consistent with the greater correlation between knowledge production and wider societal impact than we have observed previously. As illustrated in Figure 3.2, knowledge production scores correlated well with impact in research targeting and capacity building, and although there was a lesser correlation with other categories, there is still a

Figure 3.1. Distribution of broader social and economic benefits for mental health and cardiovascular research

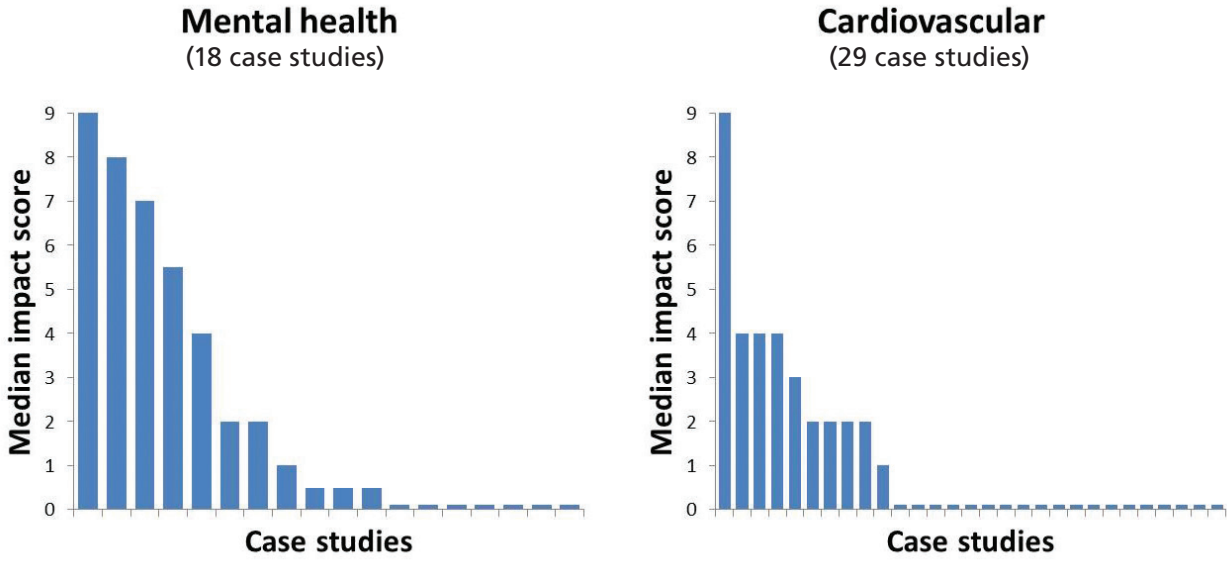
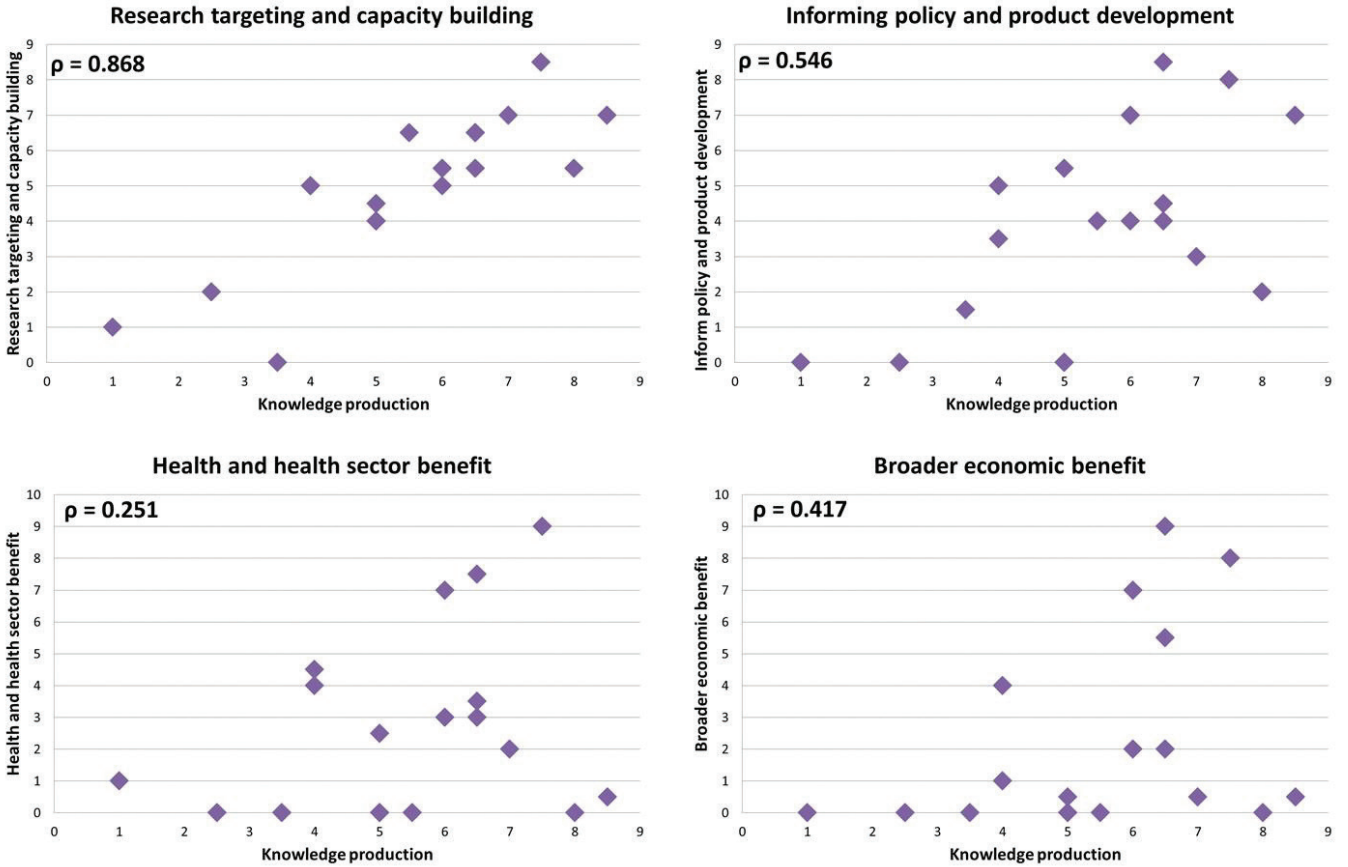


Figure 3.2. Correlations between knowledge production and the other four payback categories ( $\rho$  indicates Spearman's rank correlation coefficient)





stronger association than we found in our cardiovascular study.

### **Caveats and future research directions**

Unlike in our previous assessments, case studies were selected through the identification of highly cited papers (rather than, say, research grants), which then acted as a starting-point from which to establish the broader research cloud. Given this method of selection, it comes as no surprise that all research clouds generated knowledge, and the correlation established in previous work between ‘knowledge production’ and ‘research targeting and capacity building’ (Wooding et al., 2011) suggests that we would also expect a fairly high level of impact in this latter category. The reasonably strong correlation found between ‘knowledge production’ and the wider societal payback categories – something we had not observed previously – merits further investigation to establish whether this is a feature of the mental health field more generally (i.e. research uptake is driven by academic publication), a characteristic of our sample, or merely an artefact of some aspect of our methodology. For example, in this study we looked back over a longer time period (20 years) than we have in our previous work, and it may be that this has allowed more of the downstream impacts to be realised.

### **Policy provocation**

From a policy viewpoint the diverse and beneficial range of impacts identified in the case studies illustrates that there is a return from mental health research – both in terms of academic and wider societal impacts – but that this return may take a long time to accrue and that it may often be incremental rather than paradigm-shifting. This supports the continued funding of mental health research, although funders need to manage expectations about the time it takes for that research to translate into impacts outside the research system. Indeed this analysis suggests further emphasis may be needed on translational research along the lines currently occurring in many countries, such as the Canadian TRAM network discussed later in this chapter.

## **Clinical research has had a larger impact on patient care than more basic research over the 20 years since the research was undertaken**

### **Summary**

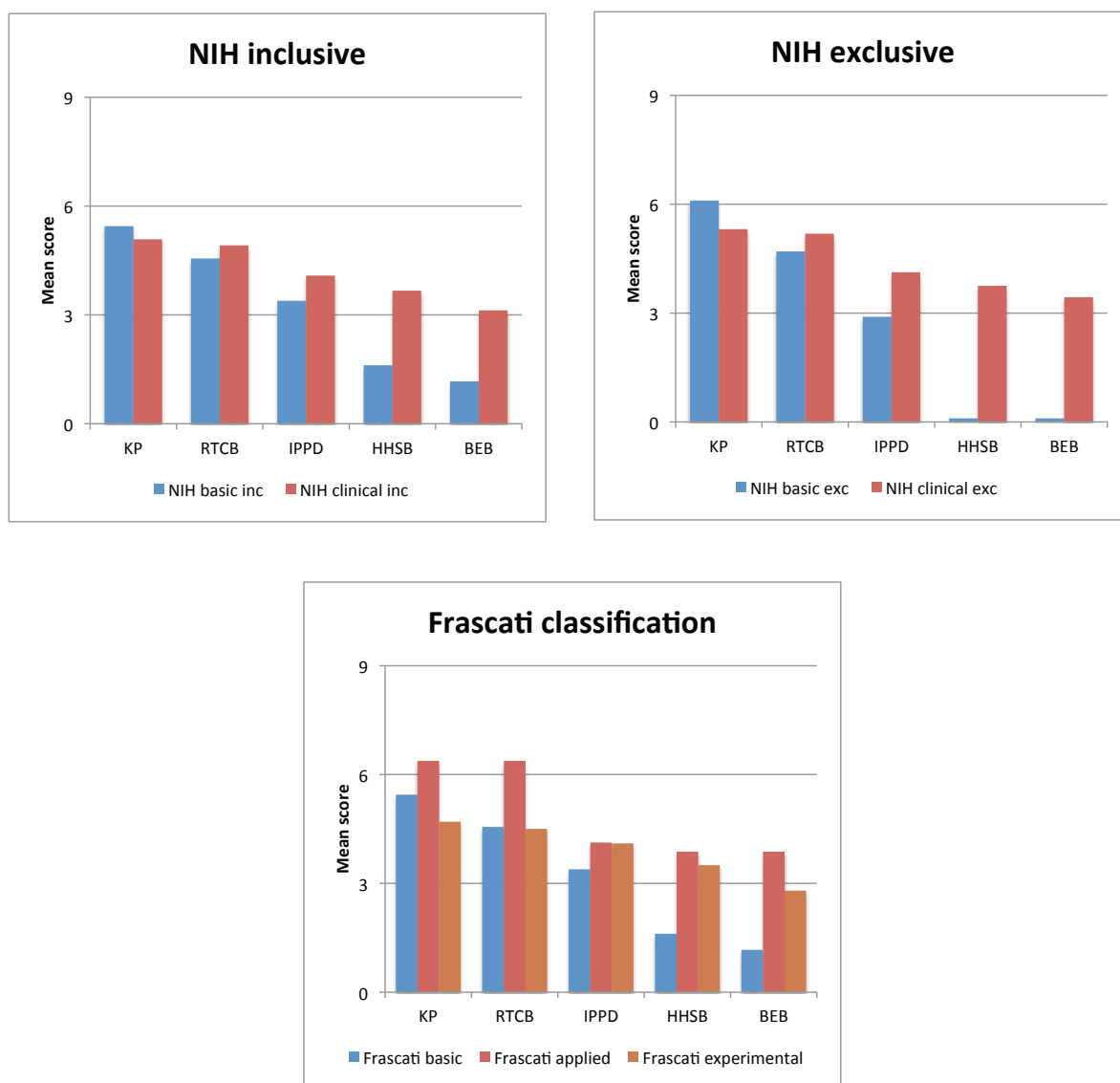
Potentially the most provocative observation arising from our analysis is that, over a span of observation across 20 years, clinical research has had greater health, social and economic impact than basic research. This is the third time that we have made such an observation (now across 63 case studies), with each analysis deliberately going further back in time: 10 years in arthritis research, 15 years in cardiovascular research and 20 years in mental health research. We are aware that this challenges the orthodoxy in biomedical science policy, where basic research is seen as the foundation for clinical advances. From a policy perspective this would suggest that research funders may need to invest proportionally more into clinical and applied research if they wish to achieve wider health, social or economic benefits within a 20-year period.

### **Case study analysis**

There is a long-running science policy tradition of classifying research into applied and basic categories, or in the biomedical field the broadly similar clinical and basic categories. Unfortunately, there are a number of different definitions for the two categories and the clinical/basic distinction is not necessarily mutually exclusive (for more details see Box 4). However, we found that the case studies were classified in a largely similar manner regardless of which of the definitions we used (for more details see the methodology report, Guthrie et al., 2013b). Importantly, both definitions gave us a spread of case studies across the types of research.

When we examined the mean impact ratings for each case study research cloud for these classifications, we saw a similar profile for all the comparisons. That is, research closer to application had a higher impact in the categories of health and social or economic benefit across all the classifications over the study timescale of 20 years, irrespective of the definition we used (see Figure 3.3). We were concerned that different mixes of research within the basic and clinical categories might drive these differences in impacts but, as discussed in detail in the methodology report, this proved not to be the case (Guthrie et al., 2013b).

**Figure 3.3.**  
**The mean impact scores of different types of research across the five impact categories**  
 (for discussion of the distribution of scores between raters and within groups see Guthrie et al., 2013b)



### Comparison with existing evidence

We have made a similar observation about the relative impacts of clinical and basic research in our previous studies. In the arthritis research study, which was conducted over a 10- to 15-year timescale, we noted that ‘possibly due to these timescale issues, the clinical research studies appear to have the largest amount of payback [across all categories]’ (Wooding et al., 2004). In cardiovascular research we noted that ‘basic biomedical and clinical research produce a wide range of benefits, but within a time period of 15–20 years

it is likely that basic biomedical research will produce more of the traditional academic impacts, and clinical research will produce more wider societal impacts on health policy, health gain and broader economic benefits’ (Wooding et al., 2011). In this study we see a similar pattern over a 20-year timescale. These observations suggest that the time lag to application for basic research is long (i.e. over the order of 20 years). Indeed, looking at the perspectives (Chapter 4) underlines the length of the time lag between research – of all types – and changes in treatment. Most of the narratives

#### Box 4. Classifying basic/clinical research

There are a number of ways of classifying research that differ in the criteria they use for classification. We chose to focus on two sets of definitions, the Frascati definitions used for compiling international research and development statistics and those used by the US National Institutes of Health (NIH) as the largest funder of biomedical research in the world.

The Frascati definition is intended to be used across all fields of research and is based on the purpose of the research. It defines basic research as that undertaken ‘without any particular application or use in view’. It defines two categories of directed research: applied research which is ‘directed primarily towards a specific practical aim’ and interventional research, the aim of which is ‘producing new materials, products or devices, to installing new processes, systems and services, or to improving substantially those already produced or installed’.

The NIH clinical definition focuses on the research subject, covering more or less all research that is carried out on identifiable living human subjects. By

contrast, the NIH basic definition is similar to the Frascati definition and concentrates on the motivation for the research.

Because of these differences, we use three methods of classification for our analysis:

- The Frascati definition, which applies across all areas of research, not just biomedical research.
- The NIH definitions of clinical and basic research. In this case the definitions of clinical and basic research are not mutually exclusive, so we ended up with two classifications:
- NIH inclusive, where we count any case study classified as both clinical and basic in both categories;
- NIH exclusive, where we count only case studies classified as clinical or basic.

We did not use the original definitions that we used to select the research papers, because that system was tied to journal publication and we now wanted to classify bodies of research by their content.

contain research, often involving patients, which occurred more than 25 years before the widespread adoption of new treatment approaches. A broader survey of time lags in biomedical science reveals that on average lags are around 17 years (Morris et al., 2011).

Almost since the beginning of science policy literature, right up to the present there has been a lively debate between the advocates of applied and basic research (Bush, 1945; Collins, 2012; Nathan & Schechter, 2006). A trio of the earliest studies contested this issue. Project Hindsight was funded by the US Department of Defense to examine, among other things, the relative contribution of applied and basic research to 20 advances in military technology. It did this by building a family tree of the key events that enabled each advance; tracing back an arbitrary 20 years, the study concluded that 75% of events were ‘applied science’ (Sherwin & Isenson, 1967). Two further studies were carried out in response to Hindsight: TRACES, which looked at a range of innovations (Illinois Institute of Technology, 1968), and a study by Comroe and Dripps specifically examining advances in heart-disease treatment (Comroe

& Dripps, 1976). These studies took a similar methodology but traced back further in time, in the case of the former 50 years and in the case of the latter up to 220 years. The two studies that looked over a longer timescale found a higher contribution of basic research. These results are all consistent with the observation that basic research has a longer time lag to application.

Assuming that the relative contributions of clinical and basic research can be fairly measured (see caveats section for discussion), the key arguments are:

- i. whether basic research has a larger eventual impact, and hence is worth the wait;
- ii. whether basic research is necessary as the foundation for applied research; and
- iii. whether there are other types of impact that are necessary and cannot be provided by applied research.

It is often assumed that basic research has a larger eventual impact through ‘breakthrough’ discoveries or paradigm shifts. However, most discussions depend on anecdote (Collins, 2012) and we could

not find any examples that attempted to address this question systematically. The corollary to these suggestions is that there is much to learn through relatively simple observational clinical research that could lead to major improvements in patient care, improvements that can often be quickly put into practice (Rothwell, 2006). In fact the difference between the impacts of clinical and basic research does not need to be this stark – if clinical research has a shorter lag to impact than basic research, it gains a ‘headstart’ in achieving impact. By the time the basic research starts to have an impact, the clinical research will already have accumulated impact. Therefore to have a larger impact, basic research needs to have impact at a faster rate than the clinical research for its overall impact to overtake the clinical research impact. Equivalently, if basic research has an impact for a longer period than the clinical research it may end up having had a greater impact overall.

The second argument is that basic research is necessary as the foundation for applied research. Put another way, there are two questions: whether basic research is needed to sustain effective applied research and to what extent applied research is independent of basic research. There are a number of counter-examples that provide instances where applied research has preceded, and indeed inspired, basic research. A clear example is general anaesthesia, where the mechanism of action was only identified in 2008, around 150 years after general anaesthesia entered use (Bahnasi et al., 2008). Rosenberg, who suggests that ‘the normal situation in the past, and to a considerable degree also in the present, is that technological knowledge has preceded scientific knowledge’ provides a good catalogue of examples from engineering-based disciplines. Rosenberg’s examples include that of the science of thermodynamics, which was developed in response to, rather than in anticipation of, the steam engine. However, all these examples are anecdotal, effectively demonstrating that it is possible for applied research to lead basic research. They do not directly show which type of research has the greatest impact. Hopefully the identification of the anaesthetic receptor will lead to better anaesthetics and the development of thermodynamics will lead to better engine design – although it is possible that it would be more effective or efficient to develop new anaesthetics or better engines through trial, error and

perceptive observation than through application of understanding of the mechanism gained from the basic research. The supported employment perspective in Chapter 4 shows the potential for treatments to be developed without recourse to basic research not involving patients – as the intervention originated directly from work with patients and social research in community settings. Similarly the early-intervention perspective demonstrates the ability of health-services research to direct improvements in care without recourse to basic research.

Finally, it is possible that there are important impacts from basic research that are not provided by applied research. Although the Payback Framework aims to capture a wide range of the benefits that accrue from research, there are potential benefits that are probably less well captured – for example, the importance of basic science in attracting new recruits into the scientific profession, the relative rate of economic spillovers between different types of research, and the value of a diverse research base in allowing rapid absorption and contextualisation of new published research from elsewhere.

### **Caveats and future research directions**

There are two key reasons why we may have been unable to measure the relative contribution of clinical and basic impacts fairly:

- i. The distribution of impacts from basic and clinical research may be different, in that the probability of impact may be less for basic research. If this is true, then our small sample size is less likely to include one of the basic projects with impact than to include a number of smaller impacts from clinical research – hence unfairly disadvantaging basic research, although in this situation if we include one of the basic research successes, basic research will be unfairly advantaged.
- ii. Because of the longer time lags and possible different nature of impacts, it may be harder to trace and catalogue the impacts of nonclinical research. We have endeavoured to address this issue by compiling comprehensive case studies, but cannot fully defend ourselves against this possibility. It is also likely that the case studies we have

examined (even over a 20-year timescale) will continue to develop and to have further impacts, which could benefit the basic cases if these yet-to-be-realised impacts are larger than those that accrue to the clinical/applied cases.

Finally, it is worth remembering that these measurements of relative impact occur in a complex system of research in which basic research has influences on applied/clinical research and vice versa. This means that, although they are valid observations of the research system as it was and is set up, they may be different in a research system with a radically different mix of types of research. For example, not only are there ‘feedback loops’ (Klein, 1985) in terms of applied research inspiring basic research as outlined above, but others have suggested that, in the field of technological development, basic research and applied research have been known to interact throughout the innovation process, enabling greater innovation than would have been possible with either basic or applied research alone (Yoshida et al., 2009).

### Policy provocations

Our case studies suggest clinical research has a larger payback in terms of health, social and economic benefit over periods of up to 20 years. From a policy perspective this raises the need to think about the aims of funding and suggests that organisations aiming to make a reliable difference to patients within a decade or two should focus on clinical research. Organisations with a longer-term perspective should look to support a balance of clinical and nonclinical research.

## Mental health research conducted by researchers who work across boundaries resulted in greater academic and wider societal impacts

### Summary

The strongest observation coming from the cross-case analysis is that those research clouds that had a researcher who was working across basic/clinical research, clinical research/policy or disciplinary boundaries tended to have higher impact for all of the payback categories. From a policy per-

spective, such an observation would suggest that funders might want to favour individuals or teams who work at these interfaces or, as described in the management literature, are ‘boundary spanners’.

### Case study analysis

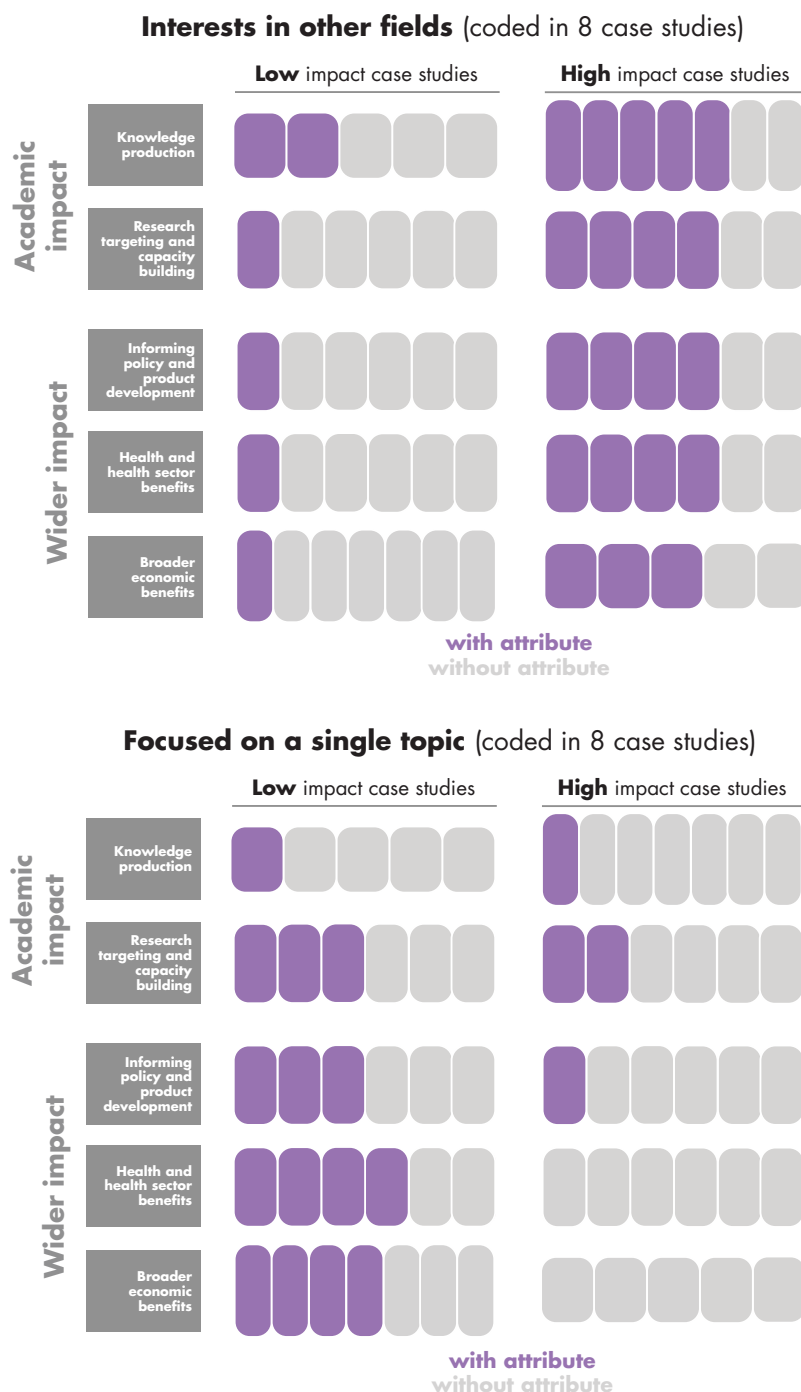
A recurrent theme identified from our qualitative analysis of the case studies was the positive influence of those who have the ability and willingness to work across the research-to-practice continuum or across research topics. This ability often became more apparent as their careers developed, as illustrated by the following verbatim quotes from our interviewees:

- *It became very obvious that in order to change systems you had to change policy ... so that's what I had to learn: what is policy, how do you deal with policy, how do you create policy, how do you change policy-level frameworks that then will lead to effective plans and interventions. So I learned it.*
- *It's interesting the influence that [this] has had on me because I have spent the last few years straddling the research/clinical gap and here they probably see me as an academic clinician. So I tend to lead on service evaluation, and those kinds of things, and always have. I also constantly alert my colleagues to the latest research evidence to keep them informed. A lot of the work I have done for which I have an international reputation has been in translating research into practice.*

However, it is worth noting one voice dissenting from this analysis: ‘*basically, I was a monomaniac about D2*’.

This relationship with boundary crossing is further investigated in Figure 3.4, which shows that researchers working in clouds that show ‘interests in other field(s)’ have a higher impact and those that are ‘focused on a single topic’ have a lower impact. Of the eight case studies (2 basic, 6 applied) that were coded for research ‘interest in other fields’: five were in the high-impact group for knowledge production; four for research targeting and capacity building, informing policy and product development and health and health sector benefits; and three for broader economic benefits. By contrast the respective number of low-impact case studies was 2, 1, 1, 1 and 1. Those clouds that had a researcher who ‘focused on a single topic’ had no

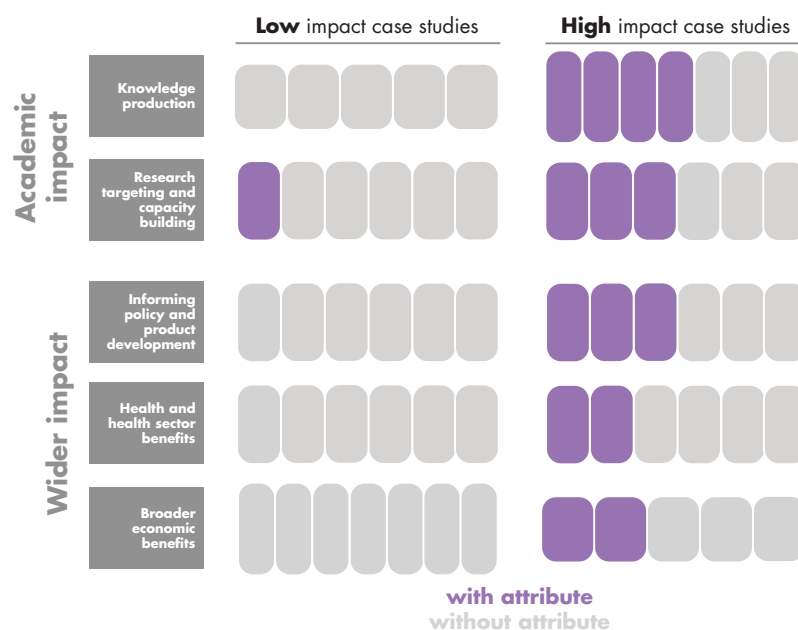
**Figure 3.4.** Researchers working in a cloud that show interests in other field(s) have a higher impact and those that are focused on a single topic have a lower wider-societal impact



association with impact for the first three payback categories and a negative association for health and health sector benefits and broader economic benefit. Of the five case studies (2 basic, 3 applied) that were coded for ‘focused on a single topic’, four were low impact for these later two categories and

there were no high-impact case studies. There was one case study that was coded for having researchers working in the cloud that showed both ‘interests on a single topic’ and ‘research interest in other fields’ and six case studies that were not coded for either characteristic.

**Figure 3.5.** Research clouds which include researchers involved in more than one stage of the translational pathway have a higher impact (coded in 5 case studies)



Another way of examining a related issue is to see whether researchers working in a cloud are ‘involved in more than one stage of the translation pathway’. The translation pathway is a way of conceptualising the route through barriers (or ‘gaps’) at different points in the research-to-practice continuum.<sup>7</sup> T1 often refers to the first translation gap to be crossed – that is, the capacity to translate the results of discoveries generated by basic biomedical research in the laboratory to the bedside as well as to commercialise health discoveries successfully. T2 refers to the second translation gap and addresses the capacity to synthesise, disseminate and integrate research results more broadly into healthcare decision making and clinical practice and policy.<sup>8</sup> As illustrated in Figure 3.5, five case studies (1 basic, 4 applied) were coded as involving researchers who worked across these translational

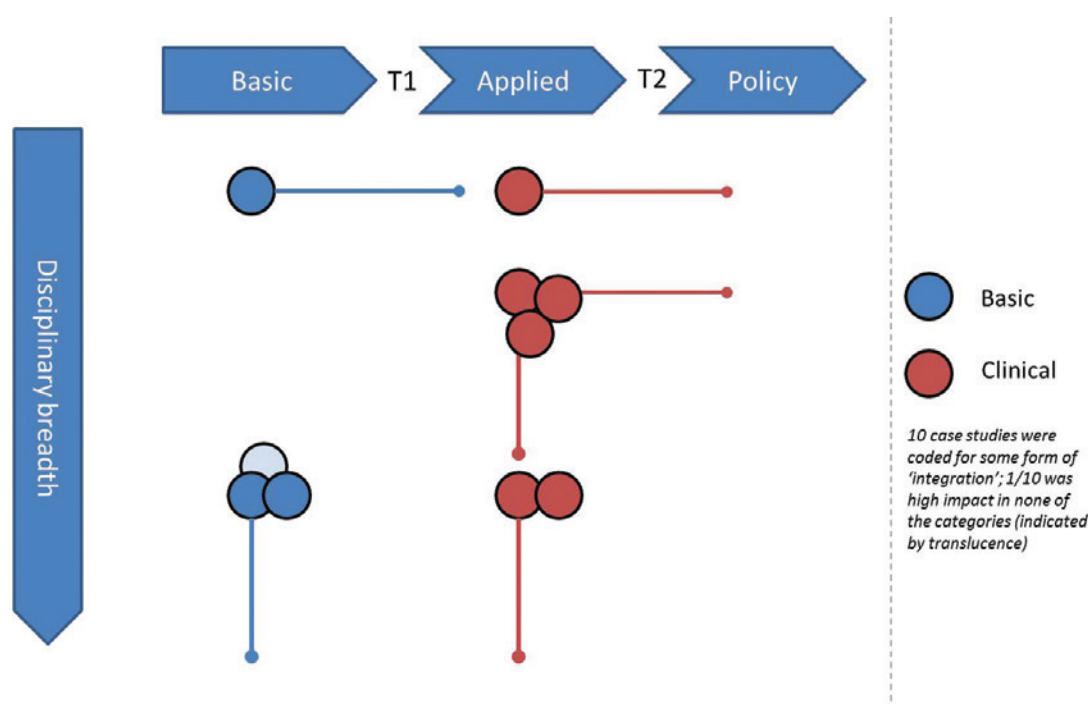
phases. For knowledge production four case studies were coded as being high impact (none as low impact). Likewise we also detected an association between working at more than one stage of the translation pathway and high impact in improving policy and product development (with 3 case studies coded as high impact and none as low impact) and broader economic benefit (with 2 case studies coded as high and none as low).

We then combined these two analyses as conceptualised in Figure 3.6. In this figure we have plotted the ten case studies (indicated as circles, coloured blue for basic and red for applied) that were coded for either type of integration – i.e. ‘interest in other fields’ along the vertical axis and ‘involved in more than one stage of the translation pathway’ along the horizontal axis. Of the ten case studies that were coded for either of these characteristics, nine were high impact for at least one of the payback categories, as illustrated by the darker shading in the figure. The direction of the integration is indicated by the line that is coming from the case study. So, for example, if you take the top left-hand circle (coloured dark blue), there is a horizontal line that crosses the T1 (basic → applied) gap. Using this combined coding, we then assessed

<sup>7</sup> See Trochim et al. (2011) for a review, as well as Woolf (2008). Note that different authors use a different number of stages and different nomenclature.

<sup>8</sup> Some further disaggregate the T2 gap and add on T3 and T4 phases, with T3 involving dissemination and implementation research and T4 addressing the predictors of research outcomes and how these will be interpreted by decisionmakers.

**Figure 3.6.**  
**Research clouds that had a researcher who spanned boundaries had a higher impact**  
 (coded in 10 case studies)



the association between high- and low-impact case studies, as illustrated in Figure 3.6. As demonstrated, we observe that there is a positive association with researchers working in clouds that integrate – either vertically or horizontally – and those clouds that are high impact, and this holds across all five payback categories. Of the ten case studies (4 basic, 6 applied), six were high impact for knowledge production (2 were low impact), five were high impact for research targeting and capacity building and improving policy and product development (2 and 1 were low impact respectively), four were high impact for health and health-sector benefits (1 low) and three were high impact for broader economic benefits (1 low).

In other words, based on the analysis of the case studies, we conclude that research clouds that had a researcher who spanned boundaries tended to have higher impact for all of the payback categories.

### Comparison with existing evidence

The observation that mental health research resulting in an academic, health and social or economic impact is associated with researchers who work across boundaries by spanning a translational

pathway or more than one discipline resonates with (but is not identical to) conclusions we made in our previous studies of arthritis research and cardiovascular research. For example, in our analysis of 16 case studies of research grants funded by the UK Arthritis Research Campaign (ARC) between 1990 and 1994, we concluded that when research resulted in a development of practical value to patients it largely occurred due to the conviction, effort and personal networks of a particular investigator, and was not associated with the type or mode of the funding stream (Wooding et al., 2004). This led us to recommend to ARC that they introduce two new types of awards: translation awards would be topic focused and aim to translate previous ARC-funded research directly; partnership awards would be people focused and provide resources to ARC-funded researchers to develop networks with potential users of research.

Similarly, in our international study of 29 cardiovascular research grants funded between 1989 and 1993, we noted that all high academic (5/5) and wider impact (5/5) case studies on basic biomedical research demonstrated a clinical motivation, compared to 2 out of 6 low academic impact case studies, and 3 out of 6 for low societal impact.



Similarly all high societal impact (5/5) case studies on clinical research had evidence of strategic thinking by the principal investigator, compared to 1/4 low wider impact case studies. This led us to conclude that when seeking a high impact, funders should encourage and support clinically motivated basic biomedical research as well as focus clinical research funding on principal investigators who think strategically about translation into clinical practice.

Finally, in an earlier study on diabetes research, Hanney et al. (2006) explored methodological approaches for assessing the impact of health research through a case study of a single research leader in the UK. One of the side observations of this work was how the subject benefited from undertaking a wide range of research studies across a broader portfolio of research projects.

These observations echo a broader body of management literature concerning 'boundary spanners' which dates from the 1970s. The term was initially used to describe a role which connects organisations to their external environment, serving as a source of new knowledge regarding environmental contingencies and conditions (allowing decisionmakers to adapt to significant external changes) as well as a form of external representation (Leifer & Delbecq, 1978; Aldrich & Herker, 1977; Keller & Holland, 1975; Dollinger, 1984).

In relation to biomedical and health research, the notion of 'boundary spanning' has been referred to as the process of brokering 'relationships across networks (e.g. scientific and commercial)' and the facilitation of the 'transfer of knowledge across contexts' – particularly various translational gaps or disciplinary boundaries (Swan et al, 2007). With this in mind then, 'boundary spanning' in this context is primarily concerned with the sharing of knowledge through either collaborative networks or individuals operating across various disciplines or research areas, as opposed to environmental data gathering. The notion that biomedical and health research can benefit from disciplinary or sectorial collaboration is not new. For example, the importance of collaboration between basic and applied research has been demonstrated by Lander & Atkinson-Grosjean (2011), who undertook a single large case study of a Canadian network of scientists and clinical scientists studying pathogenomics of immunological disorders and concluded (underlining added for emphasis):

*The project, which began in the clinic and moved first into the clinician scientist's research lab, and then into the university laboratory, was based on studying an 'experiment of nature'. As such, it grounded scientific research in the patient's needs. Translational science helped to bring new ideas to both the clinic and basic science. Through laboratory research, the ... project was able to conduct tests that were not possible in the clinical setting and ultimately developed a diagnostic assay. Further, by beginning with a clinical question rather than a scientific question, the project was able to move beyond current scientific theories. Throughout this process, ideas, artefacts and individuals crossed boundaries, moving from the clinic to the research lab and back to the clinic again. Within this process clinician scientists appeared to act in a key role as boundary-spanners between the clinic and the lab.*

Moreover, Swan et al. (2005) have advanced a theory of 'Knowledge Integration' which 'emphasises the combination and deployment of knowledge drawn from different domains in order to achieve specific innovation outcomes (e.g. the development of a new product or process)'. The concept builds upon Owen-Smith et al.'s (2002) work on integrative capability, which is defined as 'the ability of innovators to move back and forth from basic research to development, and thus to facilitate the translation of basic research into innovation' (Swan et al., 2005) – a concept previously advanced by Henderson (1994). The concept of Knowledge Integration extends this idea and encompasses the 'integration of knowledge and expertise across a wider spectrum of actual and potential involves and stakeholders, i.e. scientists, regulators, physicians, patients etc.' as well as recursive links between different stages of the innovation process. Swan et al. (2005) postulated that the intensity of knowledge sharing between upstream science (e.g. scientific research) and downstream application (e.g. clinical practice) differs depending on how clearly defined the pathway to translation is. For example, an 'intense interaction' will occur when clinicians know they are likely to use a new product or treatment practice. In order for this collaboration to work successfully Swan et al. (2005) state: 'What is required are individuals who have worked across different professional, if not disciplinary domains, and so can translate and integrate knowledge.'

What we can add to these findings is that this boundary-spanning activity is associated with not only scientific and translational impact but also, within the confines of our analysis, wider health, social and economic impacts. Given that the ability of project-team individuals to work across networks and domains facilitates effective translation, it is perhaps not surprising that the work of these individuals is also associated with wider societal impacts. Nevertheless, to our knowledge this is the first time that such an observation has been empirically derived and thus it is a novel and important conclusion. However, the current literature and the nature and role of boundary spanners provides a much more nuanced assessment (Williams, 2010) that would need to be applied to future ‘science of science’ projects. For example, it is important to locate the role of the boundary spanner in the interlocking forces of structure, agency and ideas (Hay, 1995), differentiate between boundary-spanning teams and boundary-spanning individuals (Marrone, 2010), and have a better understanding of the roles and competencies of boundary spanners (Williams, 2002).

### Caveats and future research directions

The analysis we present in this section is subject to the caveats identified in our discussion of the strengths and weaknesses of our approach (see Chapters 2 and 5). In addition, as noted above, the key characteristics that we have looked at – ‘interest in other fields’, ‘focused on a single topic’, and ‘involved in more than one stage of the translational pathway’ – were coded in only eight, five and five case studies respectively (although when we combined the two integrating characteristics it was coded in ten case studies). That said, we have strong corroborating evidence from our previous work and from theoretical and empirical support from the management literature giving us confidence in our analysis and associated observations. In terms of future science of science, the role of the boundary spanner needs to be explored in the context of biomedical and health research (as Lander & Atkinson-Grosjean (2011) have done) and more specifically in mental health research. And in undertaking such studies it will be important to unpick and develop a more sophisticated understanding of the actual activities of boundary spanners, whether they are more effective (in the context of research translation) working as indi-

viduals or as teams (or both), and how the wider institution and system context impacts on their performance.

### Policy provocation

Based on the evidence derived from Mental Health Retrosight, our previous analysis of the arthritis and cardiovascular research, and the broader literature on boundary-spanning activities, we would conclude that individuals or groups who span different research communities are key in successfully translating research into subsequent academic, health, social and economic outcomes. That being the case, research funders need to reflect on how they will identify, develop and support such individuals – or groups of individuals. At a research-systems level it is important that incentives are aligned that promote and reward translation research activity. In the UK, for example, the new Research Excellence Framework will in part be assessing the research performance of universities on their social and economic impact from 2014.<sup>9</sup> Over a five-year period over £1 billion of research funding will be based on this assessment of impact. Currently such a macro-level system for rewarding translational activity is not in existence in the USA or Canada. However, several countries have recently introduced initiatives that are focused on bridging various translation gaps and a number of these have a specific mental health focus. For example, the Graham Boeckh Foundation and the Canadian Institute of Health Research (both of whom co-funded this study) recently established Transformational Research in Adolescent Mental Health (TRAM), which is a patient-oriented research-to-practice network.<sup>10</sup> What seems to be missing from this policy mix for all three countries is a focus on supporting boundary-spanning activities at an individual level. A policy provocation would therefore be to identify researchers who are spanning various boundaries and then to offer them, in effect, a soft ‘expenses’ type account to support and facilitate their networking activities.

<sup>9</sup> <http://www.ref.ac.uk/>

<sup>10</sup> <http://www.tramcan.ca/>

## Researcher motivation to address patient need seems to be a key driver in determining whether mental health research has wider societal impact

### Summary

An interesting observation, which resonates with our previous studies, is that researcher motivation seems to be more important than instrumental policy interventions, such as the funding characteristics or research setting, in determining whether research successfully translates from bench to bedside. From a policy perspective, this would suggest that funders need to understand better a researcher's motivation for undertaking different projects and put more weight on that in determining funding decisions. From a science-of-science perspective, it also suggests that further work is needed to understand researcher motivation, with perhaps less emphasis being put on funding mechanisms.

### Case study analysis

A number of our interviewees indicated the importance of focusing on patient need in their research and said this was one of their driving motivations for pursuing a research career and their specific projects. This is best illustrated in the verbatim quote below:

- *I couldn't have done any of this research if I didn't see patients, because I had this corpus of learning that had been given me and then I saw the people who I was working with and these things did not compute ... – they weren't the same thing.*

This is confirmed empirically in Figure 3.7. Researchers working in clouds that were 'motivated by patient need' had a higher wider-societal impact (and no association with academic impact). Of the nine case studies (1 basic, 8 clinical) that were coded for this characteristic, five out of six were high impact for informing policy and product development, four out of six for health and health sector benefits and three out of five for broader economic benefits. By contrast, the number of low-impact case studies for these three payback categories were one, none and one. It should be noted, however, that this observation

may be confounded by the larger number of clinical case studies in this analysis.<sup>11</sup>

Interestingly, the converse was also partly true: that is, researchers whose 'motivation was curiosity focused', in those 13 (5 basic, 8 clinical) case studies where such a characteristic was coded, tended to have a lower impact, as illustrated in the following two quotes:

- *I think my effort is more long term. I contribute to the literature, and I hope that people that are more at the translational process will be able to see some of those principles that they can adapt.*
- *I was fascinated by how this system worked. I wanted to know how this thing operated. I [didn't care] if there [was] any application.*

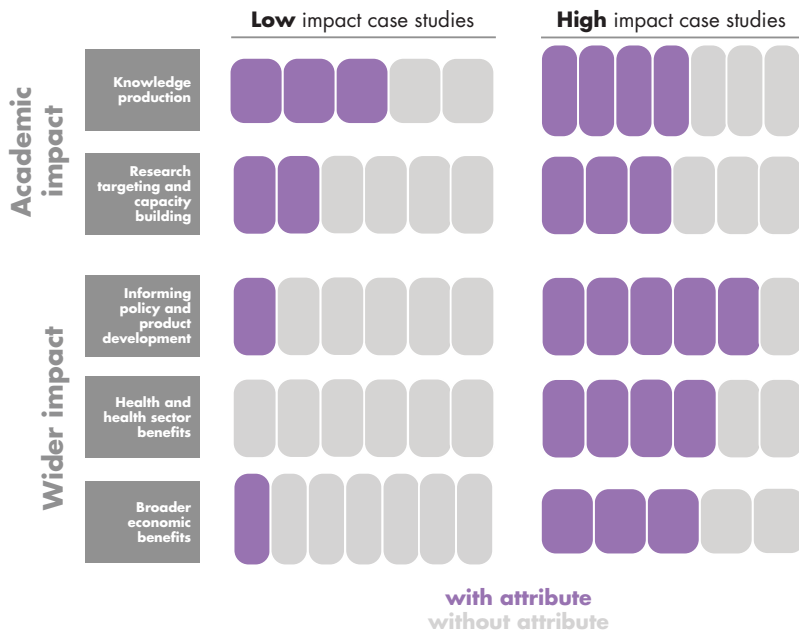
This is emphasised in Figure 3.8, where for research targeting and capacity building all six low-impact case studies were coded for having a researcher working in the cloud whose 'motivation was curiosity focused', compared to three out of six for high-impact case studies. Likewise for health and health-sector benefits and broader economic benefit, all the low-impact case studies had this code compared to three out of six and two out of five for the high-impact case studies respectively.

As described in more detail below, the primacy of researcher motivation resonates with our previous studies, although it is important to note that in all the studies researchers were describing their motivations retrospectively. In the arthritis project we concluded that research translation 'is largely due to the conviction, effort and personal network of a particular investigator, and is not associated with the type or mode of funding'. For this reason we went on to investigate here whether there was any association between funding characteristics or research setting and concluded that there was not.

As illustrated in Figure 3.9, 10 out of the 18 case studies were funded from multiple sources of funding and eight had a single source. Four of the eight sole-funded case studies were intramurally funded – that is, the researchers were employees

<sup>11</sup> We tried to test this by grouping the clinical-only case studies into three groups of high, medium and low impact but were constrained by the very small numbers; that said, when we did this the relationship did fall away; hence, as discussed in the caveats section, there is a need to treat this observation with some caution.

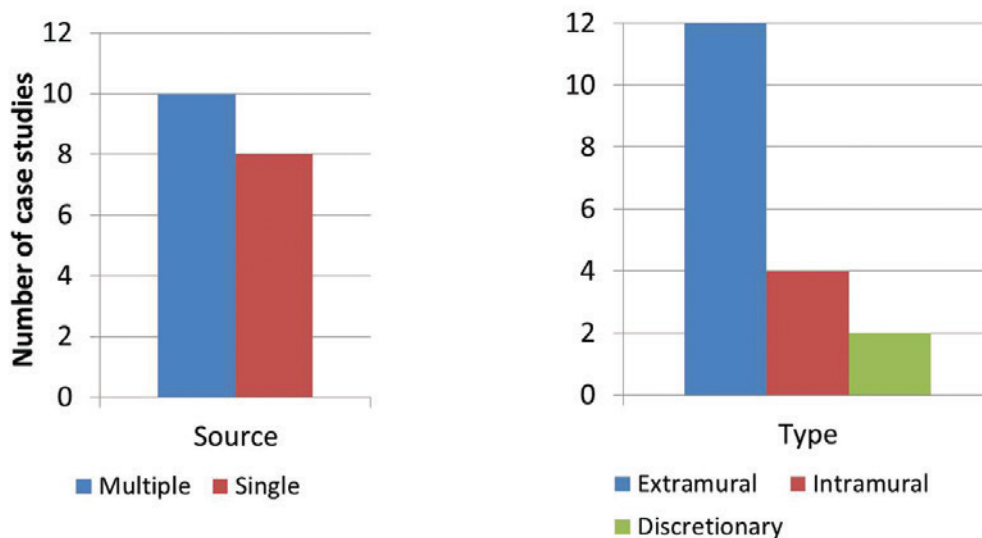
**Figure 3.7.**  
**Researchers working in clouds that are motivated by patient need have a higher wider-societal impact (coded in 9 case studies)**



**Figure 3.8.**  
**Researchers working in a cloud whose motivation was curiosity focused had a lower impact (coded in 13 case studies)**



**Figure 3.9.**  
The majority of case studies were funded from multiple sources and types of funding



of the funding organisation. Twelve of the 18 case studies were extramurally funded (4 of which were sole sourced) – that is, they were funded through a competitive peer-review process. Two case studies were supported by ‘soft’ or discretionary funding – that is, there was no formal review process.

In Figure 3.10 and Figure 3.11 we have compared the number of funding sources and the mechanism of funding by the level of impact for the five payback categories. As may be seen, there is only one category across these two figures where an association is apparent, and that is knowledge production for intramurally-funded research. In this category four out of the intramurally funded case studies were high impact and none was low impact (the remaining 1 case study was mid-impact).

We undertook a similar analysis of the setting in which the research occurred. However, as demonstrated in Figure 3.12, there is no association between the level of impact and the setting of the research across any of the payback categories.

### Comparison with existing evidence

As noted above, the observation that researcher motivation (as opposed to funding characteristics or the setting of the research) seems to be a key driver in determining mental health research impact resonates with our previous studies. In the arthritis study we concluded that individuals translate research and we could not identify any association with the mechanism of funding.

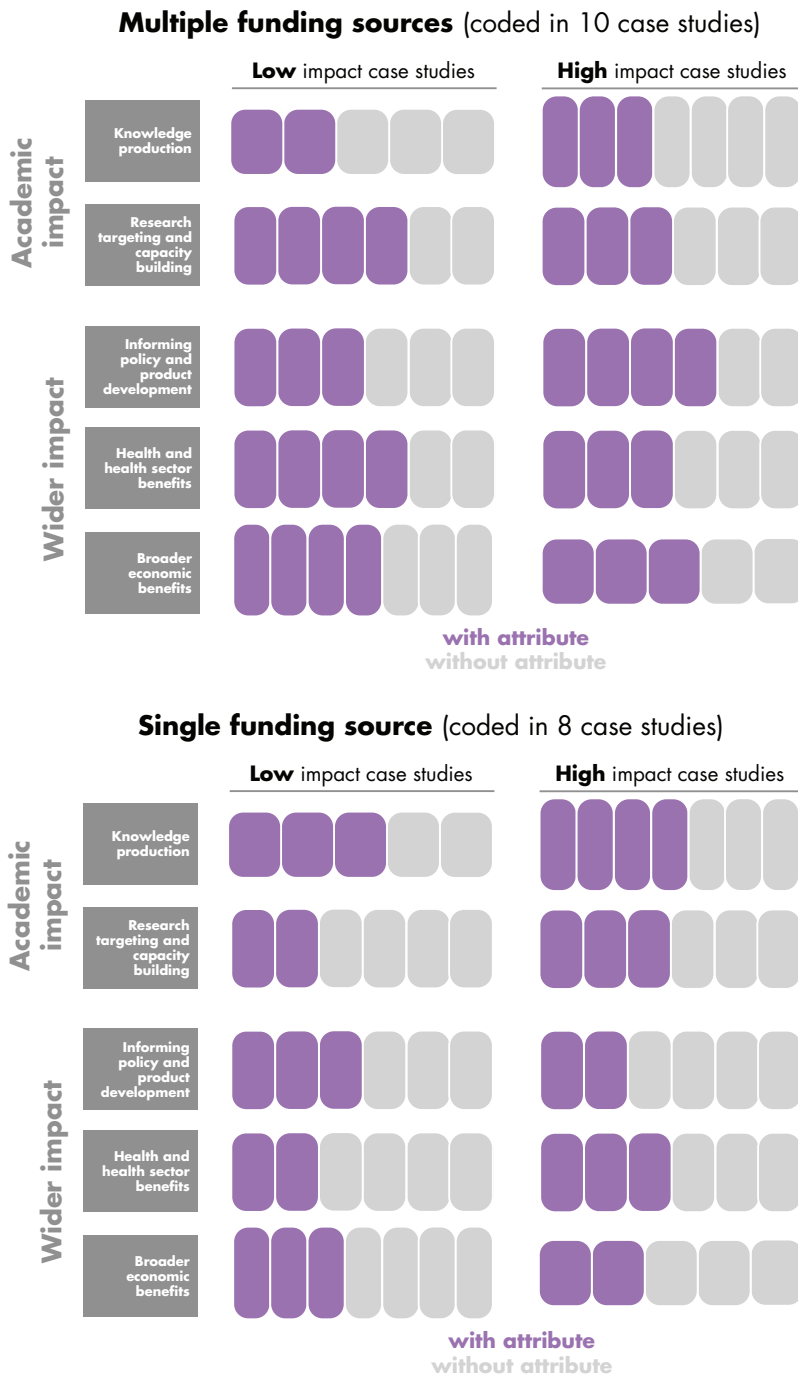
In the cardiovascular study we concluded that basic biomedical researchers with a clear clinical motivation had a higher academic and wider societal impact and that likewise strategic thinking by clinical researchers was associated with high wider-societal impact (the details of this are discussed in more depth above). However, in contrast to the current study, we also concluded that setting mattered: the co-location of basic biomedical research in a clinical setting was associated with a high wider-societal impact. From our sample of 29 cardiovascular research grants, the majority (4/5) of high wider-impact case studies on basic biomedical research were conducted in a clinical setting compared to 2 out of 6 low societal-impact case studies.

When looking at the wider academic literature we could not identify any studies that concluded that the motivation of researchers was more important than funding characteristics or research setting in terms of research impact. Indeed, we could not identify any study which examined both motivation and funding or setting. However, there is a body of literature that finds that neither funding mechanisms nor research settings are associated with impact, and a separate collection of studies that explores the importance of various types of motivation in scientific innovation. The first selection of studies includes Herbertz & Müller-Hill’s (1995) study on the effect of funding mechanisms on international research output in molecular biol-

ogy. The results indicated that the four institutions with the highest percentage of highly cited papers were divided equally between those supported mainly through grants and those receiving block institutional support. Less clear cut was an analysis of the US National Cancer Institute that evaluated the impact of both research setting and funding

mechanism on the 13 most important advances in cancer research (Narin, 1989). The study concluded that research setting (large vs small institutions, universities vs medical schools and location) did not have a major impact on the occurrence of the advance. It also concluded that National Cancer Institute (NCI) support mechanisms

**Figure 3.10.**  
**No association between number of funding sources and impact was detected among the case studies**

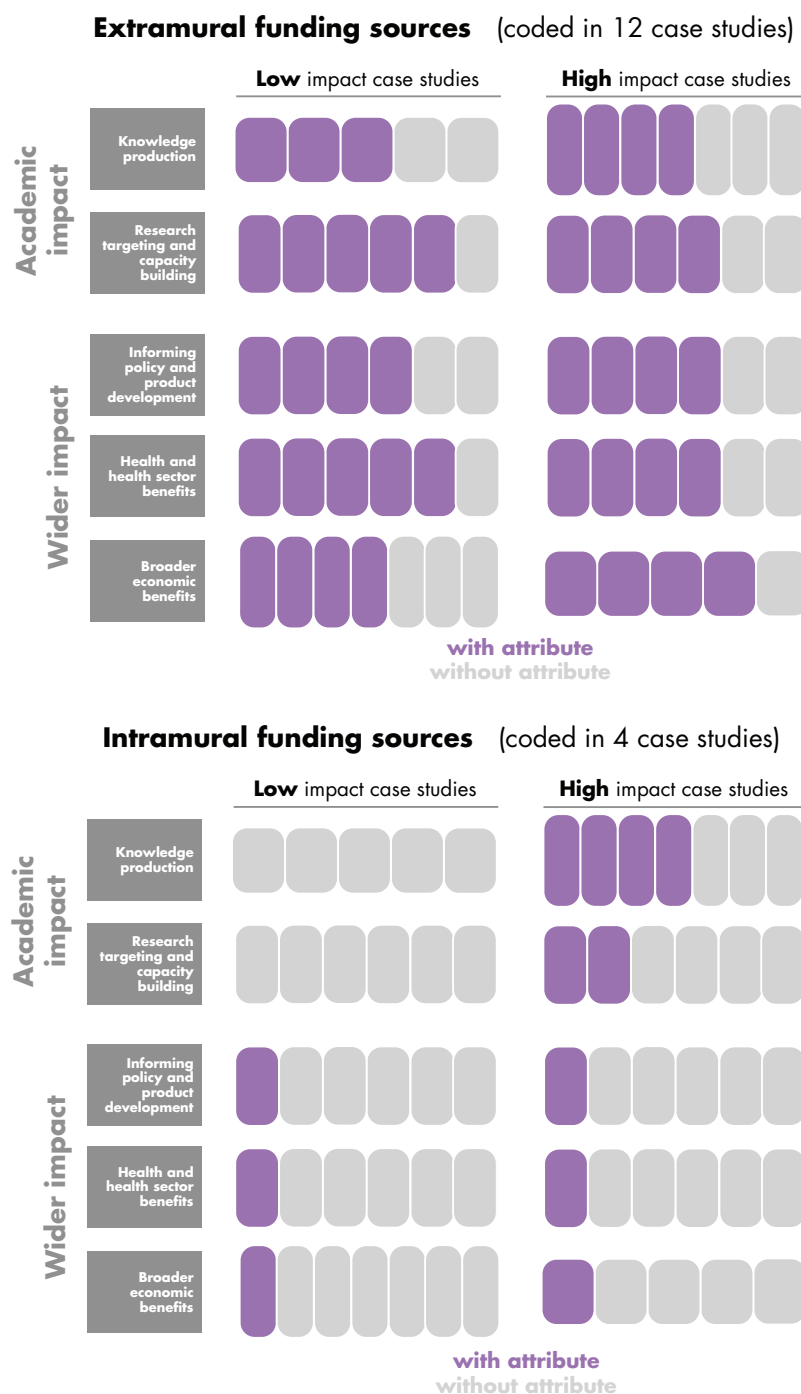


contributed significantly to the advances, with two mechanisms – project grants and intramural support – performing especially well.

There are also studies which have found that the impetus for the research has had a tangible impact on the research outcome – although this

impetus may not necessarily align with researcher motivations. In the 1960s Project Hindsight studied the effect of research type (basic vs applied) and research setting on the development of 20 selected weapons systems over two decades. The study concluded that most innovations arose from

**Figure 3.11.** No association was detected between type of funding sources and impact (except for knowledge production)



**Figure 3.12.**  
**Among the case studies the setting of research does not appear to affect the impact**





mission-oriented research conducted in government laboratories. The contribution of basic and university science was small (Sherwin & Isenson, 1967).

In exploring researcher motivation, Sauermaun & Cohen (2010) draw on psychology literature in distinguishing between intrinsic and extrinsic motives (Amabile et al, 1994; Ryan & Deci, 2000):

*Individuals are extrinsically motivated if they seek to obtain benefits that are provided by some environmental entity such as a market, a superior, or a body of peers upon an evaluation of effort or performance. Extrinsic benefits do not result directly from engaging in the task but are separable and indirect task outcomes ... individuals are intrinsically motivated if they seek to obtain benefits that originate from within the individual or the activity itself – not the environment – and often reflect an interaction between particular characteristics of the activity (e.g., particular problem area) and of the individual (e.g., interest in that problem area).*

Within the context of this analysis then, those motivated by curiosity are intrinsically motivated and those motivated by patient need are extrinsically motivated. Sauermaun & Cohen's (2010) study assesses how far various motivations (both intrinsic and extrinsic) affect the quantity of effort (measured in hours worked) and the character of effort (measured via intermediate activities and cognitive processes) as well as performance (measured in the number of patent applications). They found that there is a 'robust, strong positive association between individuals' patent applications and their preferences for income, intellectual challenge, and independence'. The positive relationships between innovative output and these motives persist even when performance is measured in the number of patents commercialised – 'which better reflects valuable innovations' – or if salary is used as a broader measure of researchers' preferences. The study also found that individuals with 'strong desires for challenge and independence have a stronger "taste for science" and interact more intensively with the scientific community outside their employing organisations ... which in turn may give them access to productivity-enhancing external knowledge'. However, the study did not find significant effects of the motives of contributing to

society or advancing one's own career. Therefore, the study provides a different view from the results presented in this paper, whereby researchers who were motivated by intellectual curiosity produced research with less impact than those motivated by patient need. However, this difference could be due to the difference between the impact of basic research and its 'translation' compared with patent applications.

Finally, it is worthy of note that, in terms of extrinsic motivation, recognition is cited in a wide range of literature as the primary motivation for scientific research (Crane, 1965; Cole & Cole, 1967; Dasgupta & David, 1994). However, this has been contested, given that only a minority of scientists gain recognition (Gustin, 1973), and recognition was not found to be a major driver in this study. However, in relation to this it is important to acknowledge that the scientific elite dominate the field (known as Lotka's law) and as a result it has been argued that funding mechanisms evolve to match the incentives of researchers rather than researchers adapting their behaviour in response to funding agencies (Auerswald & Branscomb, 2003). Although this hypothesis requires further investigation, it may provide an answer as to why researcher motivation is more important than funding mechanism, particularly if the researchers involved in this study belong to the scientific elite.

### **Caveats and future research directions**

As indicated in the preceding commentary, the role of researcher motivation and experience, and its interaction with funding characteristics and research setting, is an area that warrants further investigation. In this study we have analysed retrospective, self-reported motivations. We need to understand in detail what the concept that we are reporting as 'motivation' is and how it manifests itself for researchers and research teams.

While the analysis presented above is intriguing and potentially coherent, it needs to be interpreted with some caution, given the nature of supporting evidence. Furthermore, it is notable that this relationship parallels that of the differential pattern between basic and clinical research and there may be a degree of confounding and/or interaction between the motivation for the research and the type of research, as well as between motivation and boundary spanners. In future analyses we need to define and differentiate between different types of

researcher motivation and then see whether like groups of researchers are systematically associated with different types of impact. As such this could involve developing a personality test for scientists, building on the earlier work of Lowe and Taylor (1986). A separate issue that has been core to some of the first and seminal ‘science of science’ studies is the role of funding mechanisms (e.g., the differential impact between research grants and contracts, or large longer-term grants and smaller shorter grants). From a research funder’s perspective this is clearly a central piece of evidence for any research strategy. The fact that 50 years of studies have yet to demonstrate conclusively that one form of funding mechanism is better than another perhaps suggests that this is the wrong question to be asking (Marjanovic et al., 2009). Indeed an interesting hypothesis generated from our analysis is that research motivation seems to ‘trump’ funding mechanism when assessing impact. This definitely needs further examination but could be an important insight for those determining funding policy – that is, focus on the individual characteristics of the researcher rather than on the institutional characteristics of the research funder.

### **Policy provocation**

It would seem that researchers who are motivated by patient need are important in determining whether research has a wider societal impact.

This observation is derived from analysis of this project and our previous examinations of cardiovascular and arthritis research. However, while researcher motivation is covered in the academic literature, it is done in a broader context of aiming to understand the possible influences of the recognition systems within science. Thus from a policy perspective we need to be cautious so we do not overinterpret these results – although a provocation may be that, when seeking to achieve health, social or economic impact, funders should encourage and support researchers who are motivated by patient need. Likewise the supporting evidence for our observation that motivation is more important than funding characteristics is speculative, although it potentially provides an explanation for why funding mechanism does not seem to be an important characteristic associated with impact in the wider literature.

### **Closing comment**

In this chapter we have reviewed the main observations arising from our analysis of the 18 forward-tracing case studies. This analysis resulted in a number of results, hypotheses and policy provocations. In the following chapter we review observations from the six backward-tracing perspectives, and the implications for policy.



## Chapter 4 Observations and implications from analysis of six perspectives

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In this chapter we set out the observations from our six perspectives. Each of these traces the development of an intervention or approach currently used or being developed for the treatment of schizophrenia, setting out the research which contributed to the intervention's development and adoption as well as the other barriers and facilitators that helped or hindered this process (for further details, see below). In addition to allowing us to look at the processes of translation in detail, the perspectives illustrate the many ways in which research has contributed to improving care. Although not all of the ideas for these interventions originated from research on mental health (e.g. supported employment), all of them were developed and improved through research.

The interventions examined were:

- supported employment
- CBT
- early intervention
- clozapine
- addressing the metabolic side effects of SGAs
- cognitive-enhancing drugs.

These interventions were identified through a combination of approaches, which included a survey of mental health stakeholders, a review of clinical guidelines in Canada, the UK and the USA, and consultation with the project's steering committee. One of the aims of the selection process was to cover advances that are at different stages of translation. This led us to select as our three pharmacological advances one which has been in existence for a significant length of time (clozapine), one which has come to the fore in the past two decades (addressing metabolic side effects), and one which has not yet resulted in the development of a new product but is a current focus for drug development (cognitive-enhancing drugs).

The perspectives were then built up through an iterative process combining desk-based research with interviews with some of the key figures in each of the three study countries. We explored the early influences providing inspiration, the development of the intervention itself, and its subsequent dissemination and adoption into practice. Each perspective consisted of a detailed historical narrative, a table of key events and a historiograph showing the influence of these events on one another. Further details about the selection and methodology are provided in Chapter 2 and the accompanying methodology report (Guthrie et al., 2013b), while the full set of perspectives has been published as a separate report (Pollitt et al., 2013a).

In summary, and as discussed further below, our analysis of the six perspectives resulted in the following suggestions.

- 1 The accumulation of research evidence and translation of this evidence into advances in mental healthcare varies in pace but is influenced by a number of factors, including:
  - i. publication of research findings and reviews of the evidence in the international research literature;
  - ii. committed individuals who effectively champion research agendas and/or translation into practice;
  - iii. personal interactions between researchers, whether through the convening of conferences and meetings or through more informal events, allowing the sharing of research ideas and implementation experience;
  - iv. the role of non-academic stakeholders such as regulators, funders, professional and healthcare organisations, industry and the media;
  - v. the uptake of new practices, which then drives further practice-based and epidemiological research;

- vi. broader trends, such as the rising emphasis on evidence-based medicine and the recovery movement.
- 2 There are country-specific differences in research and uptake, which may be associated with health system organisation, with national culture and/or with disciplinary perspectives.

In this chapter we begin by summarising the narratives of the six interventions, the full versions of which have been published separately (Pollitt et al., 2013a). We then present our findings in terms of some of the common factors that appear to have either supported or hindered the development and adoption of each intervention in the three focus countries of Canada, the UK and the USA. These factors were identified by two separate means. First, three members of the research team each coded two perspectives for a range of factors, both those previously explored in the case studies and (through an iterative process) others that emerged during the course of the analysis. Secondly, a fourth member of the research team reviewed all six perspectives and drew out a series of common themes. The team as a whole then met to discuss their findings, and both analyses were combined in developing the observations presented below.

## Summaries of the six perspectives

### Supported employment

Supported employment is a form of vocational rehabilitation which emphasises placing clients in socially integrated work settings followed by training and ongoing support with no time limits (within the bounds of resource constraints), rather than training clients prior to placement.

Vocational rehabilitation in mental health has its origins in early mental hospitals and the work activities patients often undertook in maintaining them, but it was not until the beginnings of the clubhouse movement – a type of programme involving structured, work-related activities that became particularly popular in the 1950s – that rehabilitation became the primary focus of such work (Dew & Alan, 2005; Pratt et al., 2007). The broader concept of psychiatric rehabilitation became increasingly prominent in the mental health field during the 1960s as programmes of hospital closures began and the need for appropriate community care became clear.

The vocational rehabilitation services developed during this period utilised a ‘train–place’ approach. This emphasis on the need for substantial training and preparation before entering employment forms the basis for models such as sheltered workshops, hospital-based work programmes and job clubs.

During the 1980s and early 1990s traditional train–place programmes began to fall out of favour in the USA owing to a lack of convincing evidence of effectiveness and a major shift in attitudes in the field of psychiatric rehabilitation. This changing landscape was characterised by the emergence of the ‘recovery’ movement, the increasing acceptance of psychosocial rehabilitation, and an increased emphasis on consumer choice. This led to the development of a range of different vocational rehabilitation programmes and the emergence of the concept of supported employment, initially most notably in the form of the Choose-Get-Keep model (Danley & Anthony, 1987).

In 1993 the Individual Placement and Support (IPS) model of supported employment was developed at New Hampshire-Dartmouth Psychiatric Research Center in the USA (Becker & Drake, 1993). This simple, clearly defined programme became the subject of numerous randomised controlled trials and demonstration projects. As evidence for its effectiveness mounted, its implementation expanded across the USA and into other countries, including the UK and Canada.

Although there have been a number of barriers to the widespread adoption of IPS – not least some evidence that its effectiveness may depend on factors such as the strength of the local economy and the nature of welfare systems – as well as some resistance to change by practitioners, its use is now recommended by national clinical practice guidelines in both the USA and the UK.

### Cognitive behavioural therapy

Antipsychotic medication has formed the basis of treatment for schizophrenia since the first antipsychotic drug was developed in 1952. Although antipsychotic drugs have brought considerable benefits to many patients with schizophrenia, they have rarely been associated with complete recovery or full remission from the symptoms.

The recognition of the limitations of antipsychotic drugs in the treatment of schizophrenia prompted the search for psychosocial approaches

that might improve patient outcomes. In the UK increasing numbers of mental-health professionals became interested in adapting cognitive approaches and behavioural theory to the treatment of schizophrenia, while in the USA there was a focus on strategies grounded in CBT to help patients better manage and cope with their illness (Mueser et al., 2002). The original form of CBT, rational emotive behaviour therapy, was developed in the 1960s by Albert Ellis to treat neuroses, but the model of CBT that is most commonly practiced today has its origins in the work of A.T. Beck. CBT as a treatment for schizophrenia is part of a wider framework of CBT approaches applied to a range of mental disorders such as anxiety, post-traumatic stress disorder and depression (Tai & Turkington, 2009). It is based on the notion that the cognitive processes implicated in mood and anxiety disorders occur transdiagnostically, meaning they co-occur across psychiatric disorders (Harvey et al., 2004). A number of studies have supported the notion that psychotic symptoms may be understood in relation to normal psychological processes and, as a result, the symptoms can be effectively treated by CBT techniques (Yusupoff & Tarrier, 1996).

The research base and clinical use of CBT for schizophrenia has developed dramatically over the past ten years as the evidence base for its effectiveness in helping people cope with their symptoms has been established. CBT has also been endorsed in national guidelines in the USA, Canada and the UK as a recommended treatment for patients with schizophrenia since the early 2000s.

### **Early intervention for schizophrenia**

Early intervention in schizophrenia may refer to intervention in either the prodromal stage (i.e. to prevent onset of a psychotic episode) or the first episode stage (i.e. focusing on prompt detection and treatment of psychosis). Some studies have associated tailored first-episode interventions with an improvement in treatment response and long-term outcomes, and at the very least these engage people with care at an early stage in order to reduce suffering, but there have been few randomised controlled trials demonstrating a causal link. In the past ten years there have been efforts to reach individuals with early intervention and treatment in the prodromal stage. Although this is still an emerging area, there are some studies, including

five randomised controlled clinical trials, which have demonstrated the potential effectiveness of prodromal interventions. Nonetheless, many argue that the evidence base is not considered strong and there remains debate in the literature and within the schizophrenia research community about the nature and robustness of the evidence base around the effectiveness of both prodromal interventions and first-episode interventions.

In the absence of national research and development strategies during the initial stages of development, many of the key events and initiatives in the development of early intervention services were driven at a local level – for example, the work of Patrick McGorry and Alison Yung in Australia. Their intervention programmes and services for both the prodromal and first-episode stages not only established an initial evidence base, but also brought many researchers together to form an international network which began to establish similar programmes and services in other localities.

Despite locally strong initiatives in different countries, out of our three case-study countries only the UK has evidence of a national research and clinical delivery strategy for intervention in the first-episode stage. There has also been considerable policy and advocacy activity at a national level, although this has triggered extensive debate, particularly around prodromal intervention. The suggestion that an ultra-high-risk group can be identified and treated based on prodromal symptoms is controversial, due to the possibility of ‘false positive’ diagnoses and unnecessary stigmatisation and discrimination. While a ‘risk syndrome’ was initially proposed for inclusion in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), this was subsequently dropped.

Due to the lack of clarity over the strength of the evidence base for the effectiveness of either form of early intervention, the practice guidelines in the USA, the UK and Canada vary in the degree to which they promote early intervention. Although the guidelines generally recognise the importance of providing treatment as early as possible and recommend intervention at the first-episode stage, they do not identify a specific tailored approach for this intervention, and none recommends prodromal interventions.

## Clozapine

Clozapine, a tricyclic drug developed in 1959 by Wander AG, came to prominence because of its atypical pharmacological properties, unique profile of therapeutic effects and serious adverse effects. Despite great clinical promise, clozapine's initial introduction was derailed by potentially life-threatening treatment-emergent effects, and – in the USA – prohibitively high costs.

In the 1960s and early 1970s, widespread scepticism existed about the drug's potential antipsychotic efficacy because it was not associated with extrapyramidal (involuntary motor) symptoms. After empirical studies proved the sceptics wrong, Sandoz launched clozapine in major European markets in the mid-1970s.

However, in 1975 the deaths of Finnish inpatients who had developed serious haematological disorders led to clozapine being removed in many European countries and in the USA, although it remained available through a compassionate need programme. Despite these problems, overwhelmingly positive feedback from patients/families and clinicians, the passion and persistence of Gil Honigfeld (at Sandoz) and academic researchers, and the active collaboration of the US Food and Drug Administration (FDA) eventually led to its approval in 1989 for use in treatment-resistant patients, with the proviso that the company devised a system to minimise haematological risks. To comply with the regulator's terms, Sandoz marketed a highly controversial and expensive bundled product, the Clozaril Patient Management System, which ensured that delivery of the medication was dependent on regular blood testing. By 1991, in the wake of a class-action anti-trust law suit, clozaril was unbundled in the USA, and the following year Sandoz significantly scaled back its marketing resources.

In 1995 Sandoz requested US FDA approval for an antisuicidal indication. Rejection of the request on the grounds that randomised evidence was lacking led the company, now called Novartis, to sponsor the InterSePT study. InterSePT's finding of clozapine's superiority over another SGA in the management of suicidal behaviour paved the way for US FDA approval of the drug's second unique indication in 2002.

By 2003 growing evidence that clozapine and other SGAs were associated with metabolic side effects led the US FDA to issue a warning about

the increased risk of treatment-emergent hyperglycaemia and related adverse events associated with SGA use. Despite clozapine's risks, however, recent evidence not only has confirmed its superiority for treatment-resistant psychosis but has also shown that the drug is associated with substantially lower mortality than all other antipsychotics. This evidence has been recognised by all major clinical practice guidelines, but the drug still has not been broadly adopted.

## Addressing the metabolic side effects of second-generation antipsychotics

Until clozapine, the first of the SGAs, became more widely available in the early 1990s, the only medications for the treatment of psychotic symptoms in people with schizophrenia were agents now known as FGAs. While early research did appear to associate FGAs with metabolic dysregulation, attention shifted away from this with the increase in use of compounds with a higher risk of neurological side effects. When clozapine was introduced, its metabolic effects garnered some attention but this was somewhat overshadowed by the fact that SGAs had markedly reduced neurological side effects. Clinical and pharmaco-epidemiological research aimed at clarifying the association between SGA use and metabolic dysregulation only began in earnest after olanzapine, risperidone and quetiapine entered the market.

Multiple case reports and small case series were published in the 1990s and early 2000s. These studies paved the way for randomised and meta-analytic evidence that was published in the 2000s. Critical contributions to the empirical evidence base also came from analysis of a database maintained by the US FDA containing adverse events voluntarily reported to the agency, and a study conducted by CATIE investigators that focused on prospectively assessed metabolic effects of the antipsychotics used in the trial. This growing body of evidence demonstrated that although SGAs did not lead to the serious neurological side effects associated with FGAs, they were associated with potentially severe metabolic effects, in many cases manifested through chronic conditions such as diabetes, obesity and cardiovascular disease.

The earliest organised response to the emerging empirical evidence occurred in 2001, when researchers attending the Mount Sinai Conference in the USA addressed issues of clinical monitoring

and implications for practice. Regulators also took notice. In 2002 the UK's Committee on Safety of Medicines and the Medicines Control Agency recommended glucose monitoring in patients at risk for diabetes, and in 2003 the US FDA issued a class warning on the increased risk of treatment-emergent hyperglycaemia and related adverse events associated with SGA use. Later that year professional organisations released a consensus statement that ranked antipsychotics by their degree of metabolic risk and recommended metabolic screening and monitoring. Similar recommendations were made in US and UK clinical guidelines shortly after. In addition, a number of lawsuits were filed against pharmaceutical companies over their handling of information regarding side effects.

Despite the empirical evidence, regulators' warnings and clinical guidelines, studies have found generally low rates of metabolic monitoring in current routine practice.

### **Cognitive-enhancing drugs**

Since schizophrenia was first described in 1909, positive psychotic symptoms (e.g. hallucinations and delusions) have been the target of most available treatments. Although important research on cognitive processes among hospitalised patients was conducted in the 1930s in the USA, attention to cognition in schizophrenia was scarce until antipsychotics were introduced in the 1950s, when US researchers began investigating the potential cognitive effects of these drugs. Between the 1970s and the 1990s, teams of investigators – mainly based in the USA – worked on various lines of research. Although this early basic research may have initially appeared somewhat disjointed, it laid the empirical foundation for later research and development efforts on cognitive-enhancing (or procognitive) drugs.

The first concrete effort aimed at promoting research on cognitive-enhancing drugs for people with schizophrenia began in March 2001 with the NIMH decision to develop a programme with this aim. This programme, the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) initiative was launched in 2003. Although the initiative's goal was to construct a pathway to drug approval, the lack of a consensus battery of tests to measure cognitive deficits meant that developing such a tool became the initial focus. In April 2004 the US FDA made the

controversial clarification that drug approval was contingent on concurrent change on a co-primary measure of functional outcome. A month later NIMH funded the Treatment Units for Research on Neurocognition and Schizophrenia (TURNS) initiative, which aimed to select and test potential cognitive-enhancing drugs. At the final MATRICS meeting, held in 2004, discussions focused on the need for research aimed at evaluating animal models for the MATRICS cognitive domains and at measuring cognition in schizophrenia drug discovery more precisely. These discussions paved the way for another NIMH-sponsored initiative, the Cognitive Neuroscience Treatment to Improve Cognition in Schizophrenia (CNTRICS).

In January 2009 the European Commission approved funding for Methods leading to New Medications in Depression and Schizophrenia (NewMeds), a programme focused on the discovery of cognitive-enhancing and other psychiatric drugs. Described as a very unusual public–private collaboration, the primary goal of NewMeds is to improve preclinical–clinical translation.

### **Factors affecting the translation of research into patient benefit**

Mental health research, like all medical research, is an iterative process, whereby new research draws upon previous research findings and clinical experience and feeds into subsequent research. While interventions are developed based on research findings, research also depends upon the implementation of interventions, allowing their effectiveness to be assessed and a body of evidence to be built up over time. From our analysis of the perspectives we distilled the following set of factors that appeared to affect the speed at which research progressed and ultimately led to development and implementation of new treatments.

#### **Publication of new research findings and reviews of the evidence in the international research literature**

Our findings suggest that journal publications remain an important medium for the sharing of new research findings, reviewing findings to date and setting out the need for future research. Throughout the perspectives, reference is made to papers that were published and the influence that these had on subsequent research. As an example,



in the Early Intervention narrative, inspiration for the Treatment and Intervention in Psychosis Study in Norway ‘came out of the literature on reducing the duration of untreated psychosis of first episode schizophrenia’ (Pollitt et al., 2013a, Chapter 3). Research publications also directly suggested topics for future research. For example, again in the development of Early Intervention, an early evaluation of the Personal Assessment and Crisis Evaluation Service (PACE), published in 1996, set out areas of focus for future research which were then acted upon.

In some cases, it was not new research that was important, but that a concept was restated at an appropriate time and was influential. In this way, Hyman & Fenton’s article (2003) was ‘a key contribution to the re-conceptualisation of schizophrenia as a syndrome with multiple domains of dysfunction’ (Pollitt et al., 2013a, Chapter 6), in order to rebalance focus toward cognitive symptoms. Another contribution is the publication of special issues of journals focusing on a particular topic, which can have considerable influence. For example, a special issue of the *Psychosocial Rehabilitation Journal* pulled together the contemporary knowledge (in 1987) on supported employment, and some cited this as the beginning of widespread uptake of such programmes.

In some circumstances the lack of access to publications is reported to have slowed the uptake of research and implementation. For example, CBT is reported to have had an impact in Canada only after it had been tried in the USA, despite much previous work in the UK, owing to US journals being more readily available to (or more commonly read by) Canadian researchers than UK journals. Similarly, many early studies on clozapine were published solely in German, making them less accessible to the international research community and potentially limiting early interest.

The significance of publications in driving further research has been discussed within wider debates on knowledge generation in science and the distinction between codified and tacit knowledge. If knowledge is seen as the product of research, this needs to be converted and reduced in an easily communicable manner to become a public good (Dasgupta & David, 1994). More often than not, publications are used as the medium to distribute this codified knowledge.

In a study on why companies publish in refereed scientific journals, Hicks (1995) also suggests that ‘publications signal the existence of tacit knowledge and other unpublishable resources, thus building the credibility needed to find partners in knowledge exchange’ (p. 421).

The analysis of our perspectives, alongside evidence from the existing literature, supports the importance of publishing scientific findings. It follows that research funders should look to ensure the publication of all research findings in publicly accessible literature. A logical extension of this finding is the argument that the benefits of publication might be maximised by ensuring that articles are as widely accessible as possible. In this respect, it may be worthwhile to explore the advantages and disadvantages of open-access publishing.

### **Committed individuals who effectively champion research agendas and/or translation into practice**

In five of the six perspectives, particular individuals were highlighted as important in driving the research agenda in a particular direction. These were people who were pioneers in their research fields and in many cases also active clinicians, those who focused their research on areas they felt were promising, and those who advocated particular treatments. For example, in the case of early intervention, Patrick McGorry and Alison Yung at the Early Psychosis Prevention and Intervention Centre and PACE clinic in Australia began their work locally but became a driving force in the field internationally, building a foundational evidence base and bringing together researchers. The development of CBT for people with psychosis was championed by a small number of clinical researchers based in the UK and ‘the sustained commitment of these researchers to devote research to developing a cognitive model of schizophrenia ... emerges as a key factor in the evolution of CBT techniques for schizophrenia and a major contributor to the evidence base upon which current treatment approaches to schizophrenia have been drawn’ (Pollitt et al., 2013a, Chapter 2).

Similarly, in the clozapine case study, a small but passionate contingent of advocates – including researchers and clinicians who saw the benefit for their patients, a key industry representative (Gil Honigfeld) and patient advocates – are suggested

to have facilitated the development and adoption of clozapine.

Key individuals were also important in the translation of research findings into practice. For example, in the field of cognitive-enhancing drugs for schizophrenia, Wayne Fenton, a practising psychiatrist and researcher, as well as an NIMH employee, is cited as ‘the individual who demonstrated extraordinary leadership within the National Institute of Mental Health by translating these ideas into effective Institute initiatives’ (Pollitt et al., 2013a, Chapter 6).

A discussion of the role of key individuals may be found in wider literature on the characteristics of successful innovation. Early work in this field, such as Schon’s (1963) article on radical military innovations, states that ‘a new idea either finds a champion or dies’ (p. 84). The contention that innovation is closely related to the presence of committed individuals has been found in a number of case studies (e.g., Roberts, 1968; Rothwell et al., 1974; Rubenstein et al., 1976; Burgelman, 1983; Ettl et al., 1984).

For example, Rubenstein et al. (1976) argue:

*It appears from our results that organisations don’t make R/D/I projects successful, individuals do. ... For those who believe that organisational structure, control mechanisms, formal decision-making processes, delegation of authority and other formal aspects of a so-called well-run company are sufficient conditions for successful technological innovation, we can say with confidence that this is not so.*

This concept of effective product champions and technological gatekeepers being essential to successful innovation has also been built on within management literature. While agreeing with the previous literature that champions can play a decisive role in implementing innovations, it is contended that the identification of different types of champions and the distinction between champions and gatekeepers needs to be addressed. Howell and Higgins (1990) argue as follows:

*While both project champions and gatekeepers are involved in communication and information-processing activities, gatekeepers gather and disseminate external information to project groups while champions seek out creative ideas from information sources and then enthusiastically sell them (p. 318).*

While there is substantial evidence both from our study and from the wider literature that key individuals can play an important role in driving the development or dissemination of an intervention or idea, it is unclear how research funders can best identify and utilise such individuals. Further research is necessary to determine whether these individuals are more likely to be researchers, clinicians or other stakeholders.

It does, however, appear that there may be overlap between this finding and our observation on the importance of researchers who are motivated by patient need and work across different stages of the translation pathway. Some of the key individuals identified in the perspectives – for example, in the cases of early intervention and procognitive drugs – clearly spanned boundaries between research and practice, while also being committed advocates for these interventions. It may be that people who are in such positions are better placed to act as champions, either through having access to key decisionmakers in each domain or through having established expertise and credibility in each. There may be particular value in enabling or encouraging individuals with these characteristics to act as champions for their work.

### **Personal interactions between researchers, whether through the convening of conferences and meetings or through more informal events, allowing the sharing of research ideas and implementation experience**

Five of the six case studies noted that physical meetings between researchers, and in some cases other stakeholders, were important for moving the research agenda forwards. These took the form of conferences, networks set up between researchers, and visits between researchers based at different sites.

Conferences were important in galvanising interest in particular research areas (CBT), sharing hypotheses and research findings (CBT), defining research priorities (supported employment), summarising evidence and developing a consensus (metabolic side effects of SGAs, early intervention) and engaging non-academic stakeholders (early intervention).

Meanwhile, more informal engagement was also seen as important. In many research programmes, visiting sites where programmes were

already in place and learning first-hand how these programmes were run were important for implementation and subsequent research. For example, IPS programmes really only emerge in places where people who were implementing the programmes had access to experts (supported employment) (Pollitt et al., 2013a, Chapter 1).

In particular, site visits were considered important for sharing experience between researchers in different countries. UK researchers were introduced to IPS models through visits to Dartmouth in the USA, where supported employment was already implemented. Similarly the establishment of the Birmingham Early Intervention Service by Max Birchwood was aided through his contact with one of the lead investigators of the earlier Northwick Park study and by Birchwood's period of sabbatical spent in Australia, where he had visited Patrick McGorry and learnt about the early intervention programmes established there.

The role of informal engagement and personal interactions between researchers in sharing tacit knowledge and advancing research agendas has been evidenced in wider literature. Kraut et al.'s (1988) study of the patterns of contact and communication in scientific research considers the impact of physical proximity on both collaborative relationships between researchers and their research outputs. However, this study, like many others in the literature, deals with more formal conceptualisations of collaboration, such as co-authorship. The difficulties in defining collaboration to encompass more informal interactions has been discussed by Katz and Martin (1997), who argue that the nature of research collaboration as a social convention means that 'there is little consensus on where other, less formal links between scientists "end" and collaboration begins' (p. 26). Further research is needed on these informal links, as Subramanyam (1983) states: 'a brilliant suggestion made by a scientist during casual conversation may be more valuable in shaping the course and outcome of a research project than weeks of labour-intensive activity of a collaborating scientist in the laboratory' (p. 35).

The idea that face-to-face meetings between researchers are important would suggest that there is value in research funders encouraging the organisation of conferences and meetings, as well as providing funding for researchers both to attend these formal events and to participate in

more informal networking opportunities. This may be particularly pertinent at a time when the economic climate in many countries is causing research funders to reduce the resources available for such activities.

Further research is needed to determine what kinds of meeting are most valuable and whether they are of particular benefit to certain types of researcher. While technological advances are making it easier for researchers in different locations to communicate, the effectiveness of 'virtual' meeting in comparison to face-to-face contact remains unclear. Future research may wish to explore how new technologies can be most effectively used in encouraging collaboration and the sharing of ideas, as well as in identifying occasions where physical meeting might be particularly important.

### **The role of non-academic stakeholders such as regulators, funders, professional and healthcare organisations, industry and the media**

The academic community is influential at many levels in the research process, from advising on research policy through to carrying out the research and influencing its dissemination. A key way in which non-academic stakeholders were seen to influence the uptake of research was through policies on research funding. This included public sector funding, for example from the NIMH in the USA, and that from smaller charities or foundations or the pharmaceutical industry. A positive relationship with funding agencies was suggested to be important in developing supported employment programmes in British Columbia, whereas in the case of cognitive-enhancing drugs the decision across the pharmaceutical sector to cease funding for drug-discovery research in schizophrenia may have hindered research.

A further positive role of non-academic stakeholders, working together with academic and clinical experts, came from the publication of government policy documents, and guidelines produced by professional and healthcare organisations such as the American Psychological Association and the UK's NICE. In the UK, government reports promoted the IPS model, while clinical practice guidelines were important in driving more widespread monitoring of metabolic side effects of SGAs, as well as the uptake of clozapine and early intervention for schizophrenia.

Decisions of regulatory agencies such as the UK Medicines and Healthcare products Regulatory Agency (MHRA) and the US FDA were seen to have an effect on implementation, and hence furthering research, in the perspectives relating to pharmacological interventions. In the case of clozapine, cognitive-enhancing drugs and addressing the metabolic side effects of SGAs, regulatory agencies had both positive and negative effects through their role in the drug-approval process. With regard to metabolic side effects of SGAs, regulators recommended the monitoring of metabolic indices of those receiving antipsychotic therapy and required the addition of warnings to product labelling, making further understanding of metabolic side effects a high priority.

In two of the pharmacological perspectives, the media were also suggested to have an effect on research. First, in the case of metabolic side effects of SGAs, a press release suggesting links between olanzapine and diabetes received wide coverage and increased awareness of the scope of the problem. Secondly, in the case of clozapine, an article in the *Wall Street Journal* on side effects led to further review and discussion of studies claiming non-bioequivalence of a generic clozapine product with the original.

In the wider literature the role of non-academic stakeholders is considered in the Triple Helix model by Leydesdorff & Etzkowitz (1998), which is concerned with how university–industry–government relations are an essential component of national innovation strategies, and explores the network of communications and expectations that influence institutional arrangements across stakeholders. There are also studies that argue that innovation can be understood as a collective process, drawing on an innovation system in which multiple actors are networked and can bring useful knowledge and information together and in which firms have a more important role to play in enhancing innovation (Lundvall, 1988; Nelson, 1993).

Consoli & Mina (2009) note the significance of engaging firms within health research:

*Firms are top investors in R&D in an industry where competition typically is innovation-led. Moreover, while the merits of product discovery are often shared with academic research, firms have distinctive – and often global – capabilities*

*in product development, the management of the regulatory process for the approval of new drugs and devices, and the marketing and distribution of innovations (2008, p. 307).*

Another strand of literature considers the role of patients or end-users in healthcare research. Crawford et al.'s (2002) systematic review of research that has engaged patients in the planning and development of healthcare concludes that 'patients have contributed to the planning and development of services across a range of settings, but the effects of this process on the quality and effectiveness of services are unknown' (p. 4).

The fact that stakeholders other than researchers often appear to be influential in the development and adoption of new interventions suggests that it may be valuable for research funders to encourage collaboration outside the research community. However, the most appropriate approaches to engaging these different stakeholder groups in the research process may vary. There remain gaps in the evidence base around how to engage the various non-academic groups best, how to involve patients and families in research better, and at what point this engagement can be most effective.

### **The uptake of new practices, which then drives further practice-based and epidemiological research**

As is clear from the points made previously, the speed of research can be driven or limited by the speed of implementation of new practices. According to interviewees, in some instances delays in drug approval reduced the drive for further research, whereas the entry of SGAs to the US and UK markets in the 1990s, and the concomitant surge in utilisation, led to further studies on glucose and lipid dysregulation among SGA users.

The organisation and financing of the mental health system in the USA (compared with, say, the UK) may have hindered the dissemination of CBT in routine practice, which in turn may have limited US research in this field. Meanwhile, in the case of supported employment a simple, clearly defined programme of IPS (with, for example, accompanying toolkits) was thought to facilitate implementation and allow randomised controlled trials to be conducted.

Some models of translational research have implied the significance of practice as a driver of

further research. Westfall et al. (2007) proposed a multiphase model of translational research, which differs from previous models (see Sung et al., 2003) as it involves ‘a bi-directional dynamic translational process with practice influencing research and vice versa’ (Trochim et al., 2011, p. 3). They suggest that this practice-based research can help identify the reasons for the gap between recommended care and actual care, demonstrate whether treatments are effective and sustainable in everyday care, and provide a ‘laboratory’ in which to test system improvements (Westfall et al, 2007).

This symbiotic relationship between research and practice has also been highlighted in the economics of innovation literature. In their article on the evolution of medical know-how and practice, Nelson et al. (2011) discuss how new practices can drive further research and say that advances in technology in different areas, or what has been learned in clinical practice, are the stimulus for medical progress’ (p. 1340).

The observation that the introduction of interventions into practice often drives further research highlights that, particularly in the case of behavioural interventions, it is not generally possible to develop an intervention in isolation from mental healthcare delivery. While it is clearly important to have sufficient safety and ethical evidence before a particular intervention is routinely implemented, it may not be possible to determine conclusively the most effective way of implementing without the ability to evaluate effectiveness both on a large scale in practice and in a ‘real world’ situation.

### **Broader trends such as the rising emphasis on evidence-based medicine and the recovery movement**

Research and uptake of new interventions is also influenced by prevailing beliefs about the subject area and wider trends in health and society more broadly. In two perspectives, supported employment and early intervention, interviewees noted the increasing emphasis on evidence-based medicine as a factor driving research forwards in areas where previous practice had not been informed by rigorous evidence. Meanwhile, more specific changes affected individual interventions. Closure of mental health inpatient wards is thought to have increased the need for, and hence accelerated the development of, supported employment services (among other community-based services).

In the case of cognitive-enhancing drugs, the unitary model of schizophrenia (i.e. considering it as a single disease entity with one cause, one diagnosis and one treatment) may have acted as a barrier to early research. The ‘neuroleptic dogma’, that extrapyramidal side effects were an essential feature of an antipsychotic agent, is suggested to have hindered interest in clozapine when the compound was first discovered, as these side effects were not found to be present.

The rising emphasis on evidence-based medicine observed in the case studies is reflected in wider research on its significance in medical research. Sackett’s (1997) influential article defines evidence-based medicine as ‘the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients’ (p. 71). Within mental health research, the evidence-based medicine approach has been seen as a way of bridging the gap between research and practice as well as essential for engaging non-academic stakeholders (Geddes et al., 1997).

In a review of research on CBT, Compton et al. (2004) found a considerable evidence base to support the efficacy of problem-specific cognitive-behavioural interventions and that ‘CBT is consistent with an evidence-based medicine perspective that values empirically supported problem-focused treatments’ (p. 957).

The concept of recovery is also relatively new in the field of mental health, despite its being quite commonplace in research on physical illness and disability (Wright, 1983). Within mental health research it was not until the late 1980s that recovery-oriented practice began to gain momentum (see Deegan, 1988; Anthony, 1993; McDermott, 1990). This shift in focus meant that both the types of interventions developed and the outcomes considered to be meaningful and desirable changed (Davidson et al., 2009).

### **Country-specific differences in research and uptake, which may be associated with health system organisation, with national culture and/or with disciplinary perspectives**

We found some differences between the USA, the UK and Canada in terms of research and implementation. Country-specific factors were particularly noted in the three case studies relating to psychosocial interventions. One interviewee

suggested that CBT for schizophrenia may have developed first in the UK due to the multidisciplinary, collaborative nature of research in this country and the earlier acceptance of psychosocial treatments as appropriate for schizophrenia. Similarly, collaboration between industry and academia is not straightforward in the USA (Geyer, 2010), and an interviewee pointed to the existence of more opportunities for collaboration between academics and industry in Europe, suggesting that this may have enhanced research into cognitive-enhancing drugs.

Differences in funding models and the funding available are reported to have caused variability in research and uptake between the countries. According to interviewees, funding for CBT research was more readily available in the UK than the USA, allowing more CBT research in the UK, whereas the higher propensity for research to be investigator driven in Canada than in the UK allowed researchers to focus on areas which they saw as promising, which included supported employment.

Differences in health systems also affected the direction of research. Traditionally, psychologists in Canada do not work directly with mentally ill patients in the public sector, reducing the capacity to practice CBT on an individual basis with people with schizophrenia. This led to more focus on the

development of CBT treatments in a group setting in Canada. Meanwhile, in the USA early intervention services are fewer in number and more varied in their delivery than in the UK, possibly due to the centralised nature of the healthcare system in the UK, which enables more rapid and wider dissemination of new practice. Finally, differences in healthcare systems have in turn driven further research. Differences between the US and UK health systems have led to the call for US-specific research on CBT for schizophrenia, to assess its effectiveness in the US context. Meanwhile, there is ongoing work in Canada to understand the IPS model of supported employment in the Canadian context (for example with respect to differing benefits systems and responsibilities for mental health and social care), exploring potential similarities to and differences from the US model.

### **Closing comment**

Following the discussion of our forward-tracing case studies in Chapter 3, this chapter has reviewed the main observations arising from our analysis of the six perspectives, providing insights primarily into the later stages of the research translation process. In the following chapter we combine the two sets of observations to develop a set of findings, as well as policy provocations that stem from them.



## Chapter 5 Findings, caveats, contribution and future research questions

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In this study we have explored how mental health research has been translated, or not, into improvements in understanding, diagnosis and patient care in the field of schizophrenia. We have tried to identify the attributes of the research, the researchers and the setting where the research was carried out that are associated with effective translation. Our aim was to suggest possible ways in which research funding could promote better translation.

In this chapter we summarise our findings, discuss the general caveats that should be borne in mind when examining them, and consider our contribution to understanding the translation of research. (We discussed the specific caveats relevant to particular findings in Chapters 3 and 4.) Below we also suggest questions for a future research agenda as illuminated by this study.

### Findings

By considering our six perspectives on treatment advances and the 18 case studies on research clouds we can draw together the observations into a set of findings about the mental health research system and make suggestions/policy provocations for how to improve its effectiveness in the future. As noted in the caveats section below, at the outset of the project we had anticipated that the backward-tracing perspectives and the forward-tracing case studies would overlap, allowing us to triangulate our observations. However, there was less overlap between the two types of narrative than we had anticipated: the observations from the perspectives were more focused on the mental health research and care systems, while those from the case studies were more on the detail of research-funding policy. Consequently we have ended up with some findings drawn from just the perspectives and some that draw on both sets of data,

although often in subtly different ways. The latter comprise our four ‘headline findings’.

In the rest of this section we present the findings, set out in an order that combines the strength of the available supporting evidence, their significance in terms of potential for change and their novelty. Inevitably, all of these criteria require the exercise of judgement on our part.

### Headline findings

**Headline Finding 1: The case studies and perspectives support the view that mental health research has led to a diverse and beneficial range of academic, health, social and economic impacts over the 20 years since the research was undertaken.**

The forward-tracing case-study approach used here captured a wide range of impacts across the five payback categories, from knowledge production through health benefits to economic impacts. As case studies were selected through highly cited papers, it was unsurprising that knowledge production occurred in all case studies; indeed, other papers in the research clouds also tended to be highly cited. Wider societal impacts were fewer in number, but the rating panel still considered the majority of research clouds to have had health, social or economic impact.

The backward-tracing perspectives also demonstrated the role of research in improving health as well as demonstrating the breadth of research types that contributed to these benefits.

Because of the relatively small sample size the impacts identified in this project are not likely to reflect the full range of advances made over the time period, but provide useful examples of success stories that may be able to inform and inspire future research efforts.



**Headline Finding 2: Clinical research has had a larger impact on patient care than more basic research has over the 20 years since the research was undertaken.**

Our case studies and our previous work in the area, along with other work examining time lags, suggests that clinical research has a larger payback than basic research in terms of health, social and economic benefit over periods up to 20 years. It suggests therefore that organisations looking to make a reliable difference to patients within 20 years should focus on clinical research, leaving those organisations with a longer-term perspective to support a balance of clinical and basic research. This finding leaves open the question of which type of research has the larger eventual impact over timescales longer than 20 years.

This finding emerges directly from the analysis of our 18 case studies, but is also supported by the long time lags between research and impact seen in our backward-tracing perspectives. It aligns with our previous case-study research that has shown clinical research having a larger health, economic and social impact than basic research over shorter timescales – 10 years for arthritis, 15 years for cardiovascular research.

There are two ways in which we could be wrong about this conclusion – in other words, two ways in which basic research could be having a larger impact than clinical research over a 20-year timescale which we don't see in the data that we have examined. First, the distribution of impacts from basic research might be very different, with a smaller number of studies having a larger impact. In that case our small sample of studies means we are more likely to include clinical successes (which would be more common) than basic successes (which would be rarer). Secondly, it is possible that basic research provides benefits that we cannot trace or that are too diffuse for us to identify, hence we undervalue the impact of basic research.

As mentioned above, this study does not address the related, but separate, question of whether basic research has a larger eventual impact. There are two particular reasons why this might be the case. The impact of basic research, although slow to develop, could eventually be larger and/or longer lasting. Secondly, it may be that basic research is irreplaceable as the foundation for clinical research. Although it is clear that

current clinical research draws on previous basic research, the counterfactual is hard to test: we do not know what knowledge and breakthroughs could have been provided by additional clinical research over the same timescale.

All of these issues suggest the need for further research to understand better how best to classify research and to investigate the differing contributions of basic and clinical research in a more nuanced way.

**Headline Finding 3: Those involved in mental health research who work across boundaries are associated with wider health and social benefits.**

Our analysis of both the perspectives and the case studies shows that individuals with broad disciplinary breadth and/or the ability to move from the research world into the policy and care spheres (or the reverse) were frequently key in driving change forwards. They often did this by getting directly involved in the implementation of their research findings; this lends support to current efforts to build capacity in implementation science. Likewise the analysis of case studies showed that researchers who worked across disciplinary boundaries were associated with research that had a higher impact. There is also a body of management literature that supports this observation, although little of it is based on biomedical research. This suggests that funders should support individuals who work across boundaries – both disciplinary boundaries and stages of the translation pathway. One approach could be providing soft 'expenses' type accounts and facilitating networking activities. An intriguing question is whether and how these skills can be developed and nurtured. A later finding suggests that networking opportunities might be most effective if held face to face.

**Headline Finding 4: Committed individuals, motivated by patient need, who effectively champion research agendas and/or translation into practice are key in driving the development and implementation of interventions.**

The analysis of case studies tentatively suggested that the motivation of researchers to improve the lives of patients may be more important than funding mechanism or research setting, but as noted in

the research agenda below this needs further investigation. The committed individuals identified in the perspectives also tended to be people who were motivated by patient needs in either driving the research agenda or incorporating advances into routine practice. Our previous work supports the idea that motivation to help patients is associated with higher impact. The wider literature suggests that motivation and commitment are important in outcomes of scientific research – although the literature we identified tended to define motivation in broader terms, reaching beyond the biomedical field. Funders could benefit from giving priority to the support of researchers motivated primarily by patient need, although the identification of such individuals may not be straightforward.

## Other findings

**Finding 5: Personal interactions between researchers, whether through the convening of conferences and meetings or through more informal events, allow the sharing of research ideas and implementation experience and are often key in sparking collaborations.**

Although publications were found to be important in spreading information, it was notable in the analysis of the perspectives that often face-to-face meetings appeared to inspire new approaches or start new collaborations. This would suggest that the support of such research events could provide a relatively cheap and cost-effective way to improve the mental health research system, implying that research funders should continue, or indeed enhance, support and funding for face-to-face meetings, workshops and conferences. The importance of boundary spanners, identified earlier, suggests that some of these meetings should aim to bring people together across disciplinary and translational boundaries.

**Finding 6: The development and adoption of interventions is affected by broader trends such as the rising emphasis on evidence-based medicine and the recovery movement.**

It is clear from our perspectives that wider societal changes in the perception of and approach to mental health have affected the progress of research and improvements in care. Research funders therefore need to be sensitive to these wider changes in planning their strategy. However, while it may be

valuable to support further changes it is likely to be beyond the scope of research funders to drive such change.

**Finding 7: The uptake of new practices then allows further practice-based and epidemiological research.**

Both the perspectives and the case studies show the value of well-considered experimentation in treatment and care. Given the complexity of mental healthcare it is important to test interventions with patients in the community. Complexity and sensitivity to context also makes it important to incorporate research, evaluation and learning elements into care programmes.

**Finding 8: There are country-specific differences in research and uptake, which may be associated with health system organisation, with national culture and/or with disciplinary perspectives.**

In our assessment of the perspectives, country-specific differences associated with national culture, health system organisation and disciplinary perspective seemed to influence research agendas and the effectiveness and speed of translation. Similar effects could be seen in the case studies – but as different case studies were influenced by different aspects and each country's systems had strengths and weaknesses, 'country differences' did not emerge as a factor associated with high or low impact. This suggests that research funders should systematically develop ways to share and compare practice with the aim of improving the effectiveness and speed of translation from bench to bedside through systematic comparative analysis.

**Finding 9: Non-academic stakeholders such as regulators, funders, professional and healthcare organisations, industry and the media can play a large role in affecting the rate of adoption of new interventions and ideas.**

Research funders are part of a wider system that operates internationally and nationally with the goal of delivering improved patient outcomes derived from research. The analysis of the perspectives illustrated the importance of well-designed and timely collaborations between both researchers and funders that could catalyse progress in a field, or set a strategic direction. However, there were contextual differences in the three countries

studied that seemed to influence the translational pathway.

As pharmaceutical interventions moved closer to patient use, regulators and the ways in which they interacted with other stakeholders could be crucial. Therefore, research funders should develop a better understanding of the national and international mental health research system and the roles of the various stakeholders within it, and look to enhance collaborative working with the aim of facilitating effective and accelerated translation for research from bench to bedside.

**Finding 10: The publication of research findings and reviews of the evidence in the international research literature is important in supporting the progress of research.**

Our analysis of the perspectives showed that publication of original research in the peer-reviewed serial literature and the synthesis of this research into reviews was a key way in which information spread through fields. The role of open access in facilitating and accelerating this discussion needs further investigation. Research funders should require the publication of all funded research and consider the role of open access in improving scientific discourse in mental health research.

**Methodological contribution, strengths and weaknesses**

In this study we set out to show how research carried out 20 years ago has developed to affect patient care in mental health. We also sought to trace back from some advances in schizophrenia care to understand the research antecedents of these changes and the key barriers and facilitators to their development and adoption into practice.

We have shown that it is feasible to trace research forwards over this timescale, and that research clouds are a valuable unit of analysis that accord with the way that researchers see their work. By contrast, we have shown that it is much harder to build an agreed narrative when working backwards in time, and that such undertakings are very resource intensive, although they may provide useful insights into the development of care and the role that research plays in this.

Building on our previous work, we have refined our techniques for distilling the meaning from qualitative case studies and quantifying the

impacts produced using a scoring panel. In this study we showed that a relatively diverse panel of mental health stakeholders has a reasonably consistent view of the value of research impact within the five categories defined in the Payback Framework.

Through this study we have also developed the concept of research clouds. We believe that this is a significant advance on using papers or research grants as the unit of analysis because it allows a more nuanced consideration of the boundaries of pieces of research, and it appears to align better with the way in which researchers consider their work. Research grants and papers are specific elements (inputs and outputs respectively) of the research process, but may not effectively capture the overall activity taking place. In this respect, both grants and papers are markers of research activity but at different points, and both risk missing parts of the research process that may be important in influencing the impact the research ultimately has. Specifically, focusing on a grant award may fail to capture the motivations, related work and other influences that led the researchers to apply for that funding, while choosing a particular paper suggests a later and narrower-still focus for the analysis. By contrast, our sense was that using research clouds in this study made it easier for researchers to reflect on their work and retrospectively identify and untangle some of the influential context.

These advances provide a foundation for us, and others, to build on in understanding the processes by which research has an impact on care in mental health.

The retrosight approach allows a unique insight into the details of research translation, but brings with it a set of limitations that must be borne in mind when interpreting the findings of the study. In summary, these characteristics fall into four areas: issues around sampling; the accuracy of the perspectives and case studies; how well we can distil the essence of the narratives, both in terms of quantifying impacts and identification of the key attributes present in each case; and, finally, how we develop our conclusions from the distilled data and the full narratives. Each of these is discussed below, along with the steps we took to minimise their impact on our study.

**Sampling**

The case-study approach allows us to capture detailed and nuanced narratives, which are the

key to understanding the research translation process, but because of the effort required to construct them our sample size was necessarily limited – which poses challenges to being able to generalise from our findings. Although 18 case studies is already a large collection by the standards of the field, to strengthen our ability to generalise we used stratified random selection – stratification to ensure variety, and randomness to limit our biases and misjudgements. Using publications, rather than research grants, as the starting-point for identifying research clouds allowed us access to all published research – which includes that carried out ‘in the margins’ of an academic lab without specific funding, and some industry research for which funding records may not be available.

Sampling highly cited research papers did increase our chances of oversampling research clouds with high academic impact, as these are likely to have produced greater numbers of highly cited papers. Given that we found some correlation between knowledge production and wider impacts, we may also have skewed our sample towards research producing health, social and economic benefits, but as we set out to include at least some examples of successful research translation this could be seen as an advantage, at least for this study.

One of the key strengths of our approach is that we have traced pieces of research and the story of innovations over a long time period – over 20 years for the case studies; and 40 years or more in the case of the interventions explored in the perspectives. This has the advantage of allowing time for new ideas to develop and mature into practice, possibly along a meandering or tortuous pathway. However, it has the disadvantage that interviewees’ recall may be fading or they may no longer be available for interview. As discussed above, we have attempted to mitigate this problem by drawing on multiple sources and documentary evidence, although looking so far back also means that less documentary evidence has survived. Because of the study’s timeframe, on 14 occasions we were unable to contact the researcher initially selected or they declined to take part. In these instances, an alternative paper (and associated research cloud) was selected.

For the perspectives we used expert guided selection, supported by analysis of clinical guidelines to ensure that we selected a diversity of cases

across intervention type (pharmacological/non-pharmacological), focus (individual / wider environment), extent of use in each country, and stage of the translation pathway.

### Accuracy

For both the case studies and the perspectives much of our information comes from in-person interviews with those involved. This has the advantage of allowing us access to many of the nuances and context of decisions and events; but has the disadvantage of providing a potentially biased viewpoint, even if not intentionally, and making us reliant on interviewees’ recall. We have mitigated those issues through using multiple sources and attempting to confirm key events through documentary evidence.

For the case studies we then took further steps to ensure the accuracy of the narratives, both by reviewing our write-ups with the researchers involved and through external review by independent experts in the relevant field. In recruiting these experts, we aimed to identify experts both within the country in which the research took place and internationally.

To improve the consistency of case studies between researchers on the team we used structured interview protocols, three face-to-face full-team meetings to review developing narratives and regular telephone-based updates. We also ensured that two researchers worked on each narrative and then arranged these pairs to ensure overlap between researchers.

A challenge of using research clouds was identifying accurately the level of research support – in terms of grants, infrastructure and other investment they received. The approach we devised was to ask case-study authors to estimate pairwise comparisons between the resources for each cloud and then combine these to produce an overall division of clouds into three groups (large, medium and small). However, regardless of whether research clouds or individual grants are considered, it is important to note the difficulty of estimating the resources consumed by research carried out in an academic environment (for more detail on how we estimated the size of research clouds see Guthrie et al., 2013b).

For the perspectives it became clear to us that, with the resources we had available, it was not likely to be possible to draft one narrative that

encompassed all the diverse, and at times controversial, viewpoints. If we had added an additional review stage it would simply have had the effect of introducing another viewpoint. As a result we based our narratives on a synthesis of a range of interviews, covering a variety of viewpoints and review of the documentary evidence.

### Data distillation

To analyse our case studies we depended on a number of techniques to distil our data. We used a scoring panel to identify which case studies were most and least successful in producing various types of impact, and we extracted the occurrences of text describing particular attributes to explore their relationship with impact, focusing on a subset which appeared to be of most interest and most robust. These techniques help distance the conclusions from our biases and preconceptions and make the analysis more structured, transparent and manageable. By returning directly to the source data when refining our factor analysis we hope to have achieved a sensible compromise.

### Developing our conclusions from distilled data and full narratives

Although this study draws on a large body of evidence, it is divided into only 18 case studies and 6 perspectives, limiting our ability to apply statistical tests of the strength of associations. Further compounding this, we have examined the effect of many possible attributes that could drive research impact. Because of this the strength of our conclusions is based primarily on a hierarchy of judgment and expertise, drawing on both the data we have collected in this study and previous research in this area and on similar concepts elsewhere. For the case studies we also tried to insulate ourselves from our biases through the use of scoring and the transparency of case-study coding.

One of the analytical challenges we faced was integrating the findings emerging from the forward-tracing case studies and the backward-tracing perspectives. We had initially decided to carry out the perspectives because of our concern that our case studies might not have had health and economic impacts. In fact, although none of our case studies led to a major breakthrough, we did see a range of smaller health and economic impacts. Combining the findings from the two approaches was complicated for a number of reasons.

The two strands had very different scales due to the nature of the starting-points – an individual research cloud and a broadly defined intervention. This meant that the attributes and factors emerging from the two strands were often at different levels. Attributes emerging from the case studies tended to be micro-level characteristics of the research environment, whereas the factors emerging from the perspectives tended to be system-level characteristics.

Finally, the two streams of evidence often spanned different parts of the translational spectrum – it proved challenging to trace our perspectives back to research-funding decisions and the factors that initially influenced researchers, and often (as in the case of supported employment) much of the initial research was interwoven with service delivery in another field (of physical disability in the case of supported employment). This was both an advantage and a disadvantage, as it made it harder to integrate the evidence, but ensured that the project had a view across the full translational spectrum from discovery to widespread use.

### Research agenda

We have shown that it is possible to identify attributes that are associated with increased research impact and factors that may accelerate the development and adoption of new interventions; however, in many cases further work is needed to look at their generalisability, significance, relative importance and interactions. It would also be valuable to move from observational studies to examining some of these attributes and factors in an experimental setting.

In this section we discuss some of the specific areas we feel are the most important to investigate further.

### Correlation of impacts

In this study we saw a correlation between the level of academic impact and that of wider societal impact, something we have seen only weakly in previous studies. Whether this relationship exists affects how research should be evaluated. Can academic impact be used as a proxy for or predictor of wider societal impact? In some or all areas of research? And are there specific types of academic impact that are better predictors than others? These are important research policy questions.

## Understanding the impacts of basic research

We have shown that over a 20-year period clinical research has larger wider societal impact than basic research, using a variety of definitions. Two particular caveats remain: whether basic research produces impacts that we have not accounted for, and whether the distribution of impacts from basic research disadvantages it in this type of comparison (e.g. there may be fewer successful impacts from basic research). Further work to investigate these issues would be valuable in helping funders set the relative priorities of basic and clinical research.

We also think it is likely that not all basic research is created equal. There may be categories of research – for example, that carried out by those motivated by patient need or inspired by clinical problems – that out-perform other types of basic research in terms of wider societal impact. We see only fleeting indications of this in our data and suggest that it is an area ripe for further investigation.

## The role of boundary spanners in biomedical and health research

We have highlighted the importance of ‘boundary spanning’ – both disciplinary and translational – in generating wider societal impact, but it is unclear which forms of spanning are most productive, whether the spanners should be individuals or can be constructed through teams, and, finally, how the institutional and funding context can most effectively support and develop such individuals, teams and activities. All of these are promising areas to investigate where there is some literature from spanning in other contexts, but they need to be investigated and understood in the context of mental health research. If boundary spanning turns out to be as important as it initially appears, then it will be important to determine if researchers can be developed into spanners through training, or inspiration, and how to provide fertile ground in which boundary-spanning teams can grow.

## The role and manifestation of motivation

In trying to unpick the effect of researcher motivation on impact, it appears that it may be more important than other attributes such as funding

mechanism or research setting. To strengthen this conclusion it will be important to refine our definitions of motivation, understand whether it is particularly vulnerable to recall bias and tease apart the direction of causality. For example, it may be the case that researchers motivated by patient need carry out work likely to affect patients; but, equally, researchers whose work affects patients may develop a desire to focus on this aspect.

If such work confirms that motivation is a key factor in driving wider societal impact, the question of how this information can be used remains. Can research applicants be screened for motivation? Can funders inspire patient motivation among researchers? Can it be done through building teams?

## Committed individuals

Parallel to our observations about motivation from the case studies, it is clear from the perspectives that committed, well-connected individuals or champions can be important for moving interventions into practice and catalysing new progress in research fields. This raises a similar question to that about motivation and boundary spanners: whether you can effectively train and inspire people to be those individuals, or whether you can only identify and support them.

## The importance of personal interactions

Our perspectives highlighted the importance of direct personal interactions – at conferences and through visits – a theme that was also echoed in some of the case studies. Personal interactions also appeared important in translating research into practice and driving the dissemination of research findings beyond the research community.

In the increasingly connected world of research it may be that such face-to-face interactions are now of less importance. In a world with so many virtual connections it would be valuable to know whether the alternative of physical presence is still the most effective method of germinating new ideas and collaborations.

## The importance of non-academic stakeholders

Given the highlighted importance of non-academic stakeholders such as funders, regulators, professional and healthcare organisations, industry and the media in driving progress forwards,

what are the most effective ways to bring together those organisations to support change, while avoiding conflicts of interest?

### **The importance of open-access publication**

Although our perspectives have highlighted the importance of publication in the peer-reviewed literature, it was hard to tease out the importance of open-access publication as it was much less common in the era examined. It may be that the increased availability provided by open access would accelerate progress; alternatively, the quality thresholds imposed by classical publication models may be a key factor in helping manage information flow. This is an important area for investigation.

### **Perspectives**

Although our perspectives are quite detailed accounts of six advances, their very diversity means that in any one area we have considered only one or two examples of interventions. With a larger number focusing on, for example, drug development or community interventions, there are probably conclusions that could be drawn in each of these specific areas that do not emerge from our diverse sample in this study. It should be possible

to take our perspectives and use them alongside new perspectives to examine particular areas of mental healthcare interventions in more detail.

### **Concluding thoughts on evidence-based practice in research funding**

Other areas of public policy are increasingly embracing the need to base action on evidence of what has worked in the past. Unfortunately, the evidence base on what works in research funding is fragmentary and incomplete – this report provides one piece of the puzzle. We believe it is an important piece – in terms of methodological development, emerging conclusions and pointers to future research – but it is nonetheless only one relatively small piece. We need to start assembling the rest of the puzzle and figuring out which bits are missing. To do that we urge research funders to make clear the evidence on which new funding initiatives are based and, where that evidence is lacking, carry out changes in ways that make evaluating their effects as easy as possible. By sharing such evaluations publicly we can continue to build the evidence base for improving how we fund science.

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This report examines the impacts arising from neuroscience and mental health research going back 20–25 years, and identifies attributes of the research, researchers or research setting that are associated with translation into patient benefit, in the particular case of schizophrenia.

The study combined two methods: forward-tracing case studies to examine where scientific advances of 20 years ago have led to impact today; and backward-tracing perspectives to identify the research antecedents of today's interventions in schizophrenia. These research and impact trails are followed principally in Canada, the UK and the USA.

The headline findings are as follows:

- 1** The case studies and perspectives support the view that mental health research has led to a diverse and beneficial range of academic, health, social and economic impacts over the 20 years since the research was undertaken.
- 2** Clinical research has had a larger impact on patient care than basic research has over the 20 years since the research was undertaken.
- 3** Those involved in mental health research who work across boundaries are associated with wider health and social benefits.
- 4** Committed individuals, motivated by patient need, who effectively champion research agendas and/or translation into practice are key in driving the development and implementation of interventions.

This report provides an overview of the methods and presents the full set of findings, with the policy provocations they raise, and an emerging research agenda. It has been written for funders of biomedical and health research and health services, health researchers, and policymakers in those fields. It will also be of interest to those involved in research and impact evaluation.

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