The NIHR Invention for Innovation (i4i) programme

A review of progress and contributions to innovation in healthcare technologies

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Preface

The NIHR Invention for Innovation (i4i) programme supports the development of innovative medical technologies for patient benefit. RAND Europe was asked to evaluate the programme, to identify outputs and impacts of i4i projects and to examine the factors influencing performance and progress. This should help inform the future of the programme.

The i4i product development stream supports the '*development of innovative healthcare technologies and their translation into the clinical environment for the benefit of patients*'[1] through funding, as well as business support and scientific advice to medical technology innovators. Projects involve collaboration between at least two partners from academia, the NHS and industry.

The evaluation of the programme used a multi-method approach, including a focused review of background information from i4i, scoping interviews with key informants, a survey of programme participants and case studies of projects representing diverse technologies and health needs.[2]

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[1] National Institute for Health Research (2013).

[2] Selection was done in consultation with NIHR i4i team, by shortlisting from a long list of options provided by the NIHR i4i team.

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Executive summary

Background and context

The National Institute for Health Research (NIHR) Invention for Innovation (i4i) programme supports the development of innovative medical technologies for patient benefit. The i4i product development stream involves collaborative projects between at least two partners from academia, the NHS and industry. Medical technology innovators apply for funding for one to three years, through a peer review-based process that includes presentation to a selection panel.[3] The funding and business advice provided by i4i support the development of early-stage innovations, generally at proof of concept and prototype stages. More specifically, the aims of the i4i product development funding stream are to support the '*development of innovative healthcare technologies and their translation into the clinical environment for the benefit of patients,*'[4] through '*guided progression of innovative medical product prototypes*' and '*provision of business advice to the medical technology professionals it funds*'.[5] Since its inception the product development stream has identified and supported 170 projects, led by 146 principal investigators (PIs).[6]

This evaluation aimed to identify outputs and impacts of i4i projects and to examine the factors influencing performance and progress. This should help inform the future of the programme. The evaluation used a multi-method approach, including a focused review of background information from i4i, scoping interviews with key informants, a survey of programme participants and case studies of projects representing diverse technologies and health needs.[7]

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[3] The presentation to the panel was introduced in 2010.

[4] National Institute for Health Research. http://www.nihr.ac.uk/CCF/i4i/i4i_Flyer_October%202014.pdf (last accessed April 2015)

[5] Society for Research in Rehabilitation (2011).

[6] Our survey analysis was primarily based on responses from PIs on 44 projects. PIs with multiple follow-on projects were asked to focus on their most recent award to avoid survey overload, but were also given the option of completing the survey for each individual project. Some 146 PIs were contacted during the survey by NIHR. Out of 44 project responses in our survey, 27 were on completed projects and 17 on ongoing projects. Source: NIHR i4i Team.

[7] Selection was done in consultation with NIHR i4i team, by shortlisting from a long list of options provided by the NIHR i4i team.

Key findings

Insights on projects

1) **The i4i programme is helping to bridge the 'valley of death' in early-stage innovation. It is supporting projects with diverse starting points, ranging from pre-proof of concept to a completed prototype.** The programme is helping innovators reach a point where they can attempt to attract funding for further downstream development and commercialisation.

2) **The paths travelled by individual projects vary.** For example, some of the projects examined in this evaluation moved from pre-proof of concept to a completed prototype and others started at a proof of concept phase and reached readiness for clinical testing. A minority of projects entered the programme to develop prototypes and progressed to conduct early-phase clinical testing as part of the funded project. According to the survey results: (i) in over half of the cases investigated (64 per cent), a proof of concept was completed; (ii) the majority of projects (88 per cent) completed a prototype during the life of the contract[8]; (iii) over half of the projects (55 per cent) started testing or a pivotal clinical trial; and (iv) the contracts also helped a minority of projects (14 per cent) to get to the stage where they were ready to start testing or start a pivotal clinical trial soon after project completion.

3) **The i4i programme placed innovators in a position to pursue further downstream development after project completion, including further testing and pivotal clinical trials, commercialisation and – in a minority of cases – uptake in the NHS and product placement on the market.** Most commercialisation activity related to the finalisation of intellectual property (IP) arrangements (23 PIs reported this, 52 per cent) and business plans (12 PIs reported this outcome, 27 per cent). Six PIs (14 per cent) also reported starting a company on the basis of i4i-funded work, and an additional seven PIs (16 per cent) noted that another company continued downstream development.[9] In four cases, PIs reported uptake in the NHS (9 per cent) and two PIs (5 per cent) reported placing a product on the market.

4) **Key reported enablers of project progress include the expertise and skills of the project team, the technical and scientific nature of the project, and access to clinicians as a useful source of insights on the usability of an innovation. The adaptability of the grant was also seen as important. Key reported challenges include technical and scientific issues in the project and challenges in product design and usability, as well as regulatory constraints.** Inertia and resistance to change, procurement channels into the NHS and financial challenges to implementing pivotal clinical trials were expected to be key barriers going forward.

Insights on process

5) **i4i is widely seen as rare funder of high-risk early innovation in the medical devices, diagnostics and medical technologies landscape in the United Kingdom. According to interviewees, a number of factors make i4i unique.** These include a willingness to support individuals outside of the 'usual suspects'; an openness to diverse themes and disease areas; and being an adaptable and responsive funding source with a less bureaucratic management approach than some other investors in this space. Some evaluation participants felt that the prestige associated with i4i funding facilitated

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[8] Of which a subset will also have worked on proof of concept.
[9] Source: survey data.

interactions with other stakeholders needed for successful product development and uptake. As one case-study interviewee highlighted: '*When we seek advice from NHS-aligned stakeholders… they are more willing to help you actively if you have got an NIHR grant*'.

6) **The application and selection process for i4i funding helped drive proposal improvements, primarily through feedback on the scientific content but also on business-related advice. The i4i Secretariat is also fulfilling its oversight roles during project life, and performs advisory roles on an as-needed basis. Evaluation participants appreciated i4i's enabling roles.** As illustrated by an interviewee: '*... I was very impressed by the support i4i gave us; we had questions about what i4i wanted around the commercialisation plan and they got back to us on that.... They came to all board meetings and were very positive and gave good suggestions were it was required ...*' Another interviewee highlighted that: '*The i4i Secretariat was instrumental in raising the visibility and the overall impact of the work*'.

Caveats

There are a number of caveats to bear in mind when interpreting the data. First, the survey response rate for PIs was 30 per cent, so we advise caution with the generalisation of findings. Despite this, the variety of projects represented offers useful insights on the nature and impact of i4i funding. Second, despite aiming to target responses on completed projects, the survey responses included a mix of completed and ongoing contracts, the latter of which could require more time for impacts to accrue. Third, a minority of survey respondents, who were identified by the i4i Secretariat as PIs on projects, identified themselves as collaborators or co-applicants rather than PIs (and vice versa). Fourth, it is important to emphasise that the data presented is self-reported, and that an external audit is outside the scope of the current work.

Core recommendations from the analyses

There are a number of areas for policy consideration that emerge from the evaluation evidence (including from interviews, survey and case studies). They relate to programme design and to the role of the Secretariat in facilitating impact and knowledge management. For each area we have identified actions which could help maximise i4i programme impacts. Our intention is not to prescribe specific actions, but rather to raise issues which require careful consideration by i4i programme management.

Programme design

1) **Consider introducing a responsive review mechanism for projects.** In this model, decisions on the amount of funding i4i provides could be phased and determined reactively, following an initial phase of work. To ensure staffing continuity, time-lags between reassessment and work continuation would need to be kept as short as possible.

2) **Encourage applicants to consider adoption, health economic analysis and product design issues at application and selection stages, possibly through the design of the funding application forms.** The i4i programme ultimately aims to achieve patient benefit and some of the challenges to adoption may be mitigated if they are identified and considered in a timely manner. Health economic analysis is increasingly important for product development and uptake but rarely visibly conducted at present by most funded projects. Issues related to product design and usability, and financial obstacles to conducting pivotal clinical trials are examples.

3) **Reflect on the mix of academically, industry and clinically led projects in the portfolio and the roles and levels of engagement by different project partners, throughout the duration of projects.** This current mix may be appropriate, but academically led projects in particular may benefit from active external support in identifying commercialisation and NHS uptake partners.

The role of the Secretariat

4) **Reflect on the scope and scale of business-related guidance and advisory support that the i4i Secretariat can provide.** There are three key areas of additional support which the programme participants we surveyed and interviewed thought would be useful for advancing their projects and maximising prospects for impact:

   a. **Additional engagement in facilitating networks with industry, clinicians and other stakeholders, which could assist product development and uptake.** i4i may also wish to consider funding scoping studies on adoption-related aspects of a project, as they can influence the design of the technical work. This includes considering how to interact with the wider NIHR research infrastructure.

   b. **Awareness raising and information sharing about the i4i programme**, for example through roadshows, showcase events and/or awards recognising leading innovators. Investing in dissemination and publicity were seen as important for downstream investor confidence.

   c. **Providing training in business and entrepreneurship skills.** Some of this training takes place as part of the i4i 'accelerator' programme, but the associated cost can be a barrier.

5) **Consider providing more feedback to applicants, including unsuccessful ones, to help improve future bids.**

Knowledge management and evaluation

6) **Consider how best to track the long-term impacts of i4i projects, after the completion of i4i funding.** This could include follow-up on success rates with downstream fundraising, commercialisation and uptake of projects the programme has supported.

7) **Revisit internal management information systems.** We identified scope for improvement in information management databases and record keeping within i4i (for example updating registers of completed versus ongoing projects or updating information on the roles of key individuals).

Additional points for consideration – participant suggestions

In addition to the recommendations stemming from the evaluation, individuals we interviewed provided some suggestions related to the programme's future for consideration by the Secretariat:

- **Consider the constitution of the i4i selection panel and ways of accessing broader technical expertise.** There could also be scope for more sustained panel engagement throughout a project's life, in an advisory role.

- **Review prospects for engaging with host institutions around IP issues, to coordinate IP management.** IP Management systems and norms within host institutions are not necessarily understood by i4i contract recipients and the Secretariat needs to ensure clarity amongst all parties.

- **Clarify the relative weighting of different technical, social and commercial criteria in the application and selection guidance**, so that applicants have a clearer picture of expectations.

Acknowledgements

Abbreviations

BRCs	Biomedical Research Centres
BRUs	Biomedical Research Units
CLAHRCs	Collaboration for Leadership in Applied Health Research and Care
COPD	Chronic Obstructive Pulmonary Disease
D4D	Devices for Dignity
DeNDRoN	Dementias and Neurodegenerative Diseases Research Network
DH	Department of Health
DPFS	Development Pathway Funding Scheme
EPSRC	Engineering and Physical Sciences Research Council
ERC	European Research Council
FIND	Foundation for Innovative New Diagnostics
GCMI	Global Center for Medical Innovation
HICF	Health Innovation Challenge Fund
HTA	Health Technology Assessment
HTD	Health technology device
i4i	Invention for Innovation
IDRI	Infectious Disease Research Institute
IP	Intellectual property
IRC	Interdisciplinary research collaboration
KII	Key informant interview
MIA	Magnetic immunoassay
MND	Motor neuron disease
MRC	Medical Research Council
NCATS	National Center for Advancing Translational Sciences

NEAT	New and Emerging Applications of Technology
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
PCT	Pivotal clinical trial
PI	Principal investigator
PoC	Proof of concept
PPP	Public-private partnership
RNIB	Royal National Institute of Blind People
SBIR	Small Business Innovation Research
SBRI	Small Business Research Initiative
SHU	Sheffield Hallam University
SME	Small and medium-sized enterprise
STTR	Small Business Technology Transfer
UCL	University College London
UHNS	University Hospital of North Staffordshire
UWE	University of the West of England
VC	Venture capital
WT	Wellcome Trust

1. Introduction

1.1. Overview of the i4i programme

The NIHR Invention for Innovation (i4i) programme supports the development of innovative medical technologies for patient benefit. Since its inception, the programme has identified and assisted projects of critical clinical importance. The i4i programme fills a gap in the innovation finance system, by providing funding at an earlier stage than alternatives such as venture capital. i4i's core funding stream focuses on scientific and technological innovation geared at *product development* of medical devices, diagnostics and medical technologies. i4i also has an *accelerator programme,* which aims to enhance readiness for innovation and help prepare researchers for competitive innovation funding applications. Finally, i4i *challenge awards* are a themed funding stream and focus on innovation at later stages than product development, and on clinical development in particular.

The i4i product development programme is the core focus of this evaluation. It involves collaborative projects between at least two partners from academia, the NHS and industry, who receive funding for one to three years to develop medical product prototypes which can improve patient outcomes, following a two-stage peer review process. i4i builds on the previously established NEAT (New and Emerging Applications of Technology)[10] and HTD (Health Technology Devices) programmes, which aimed to '*accelerate the translation of healthcare ideas into new and innovative products for the NHS.*'[11]

1.2. Aims of the evaluation

RAND Europe evaluated the i4i product development programme. This i4i stream aims to support the '*development of innovative healthcare technologies and their translation into the clinical environment for the benefit of patients*', through '*guided progression of innovative medical product prototypes*', and '*provision of business advice to the medical technology professionals it funds*'.[12]

The evaluation aimed to identify outputs and impacts to date, and to examine the factors influencing performance and progress. This should help to inform the future of the programme.

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[10] This programme no longer exists.
[11] National Institute for Health Research (2011).
[12] Health Research Wales (2015).

The project used a multi-method approach including a focused review of background information from i4i, scoping interviews with key informants, a survey and case studies. More detail on the methods used is provided in Section 2.2.

1.3. Background and context: early-stage innovation finance landscapes for medical devices and diagnostics

Evidence on the impact of various innovation finance and governance models in the medical technology, diagnostics and devices space is scarce, particularly for public financing models and their contributions. Early-stage health innovation (e.g. proof of concept and early prototype phases) is often seen as particularly high risk, and hence less attractive to many investors than both applied and clinical biomedical research and later innovation pathway stages (e.g. clinical testing, manufacturing), where there tends to be a clearer 'division of labour' between public and private sector funders. This leaves a funding gap for early-stage innovators, which is often referred to as the 'valley of death'.[13] Despite business angel and venture capital investors, the relative absence of private investment in very early-stage translational innovation funding makes a compelling case for public involvement. In the United Kingdom, there are few med-tech dedicated Venture Capital funds. This is related to the way medical technology gets developed and exists, the appetite for risk, regulatory pathways, and the time it takes for med-tech to reach a commercial exit (generally a trade exit).[14] Even those that exist tend to specialise in a relatively narrow range of technology types which are perceived to be comparatively more acceptable in terms of a risk-reward profile. As highlighted by one external expert we spoke to: '…*The R&D landscape for med-tech in the UK is much less mature than that of pharma... It is characterised primarily by SMEs [small and medium-sized enterprises] who have been developing interventions in siloes, with limited interaction with patients to understand their needs, and limited interaction with clinicians…[as well as] a lack of understanding of the importance of evidence. This has compromised progress within the sector. The regulatory environment is also different [than for pharma]… with less focus on clinical utility data….*'

Innovation can take a scientific and technological or business model and service form. Different government initiatives tend to tackle these complementary aspects of innovation and various stages of the innovation pipeline, from research through to product and technology development, and service improvement through the diffusion and adoption of innovations in healthcare. For example, the NIHR Research for Patient Benefit scheme aims to support research into everyday practice in the NHS that could benefit patients. NIHR Biomedical Research Centres (BRCs), Biomedical Research Units (BRUs) and the Collaboration for Leadership in Applied Health Research and Care (CLAHRC) schemes focus on applied and clinical translational research which could feed into innovation pipelines, and on implementation science. The Invention for Innovation (i4i) and Health Technology Assessment (HTA) programmes are especially focused on technological and product development for healthcare and patient benefit. They address this from different angles: HTA funds research on the costs, effectiveness and impact of developments in health technology, while the i4i programme directly supports early-stage

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[13] Meslin et al. (2013).
[14] Interview with industry investment expert.

product development. i4i funding seeks to de-risk projects and make them attractive to follow-on funders and investors, ultimately for patient benefit. For the period 2014–2015, the NIHR has allocated £11.4 million to fund i4i projects, across diverse areas of medical and health need, through collaborative working between academia, the NHS and industry.[15] This scheme is discussed in more detail later in the report, focusing on findings from this evaluation.

Other key sources of early-stage translational innovation funding in the UK include the Wellcome Trust Health Innovation Challenge Fund (HICF), Pathfinder Awards and Translational Fund; the Biomedical Catalyst jointly run by the Medical Research Council (MRC) and Innovate UK; as well Innovate UK's Small Business Research Initiative (SBRI) scheme.

The Wellcome Trust Health Innovation Challenge Fund was set up in 2009 as a joint funding partnership between the Department of Health (DH) and Wellcome Trust. Unlike i4i, the fund issues thematic calls for proposals. The focus is on areas of perceived unmet needs in healthcare relevant to the NHS, which can be scaled and integrated with current technology used by the system. Projects funded by the HICF cover the progression from proof of concept to early clinical studies in humans. Similarly to i4i, the HICF accepts applications from NHS organisations and equivalent UK authorities in addition to universities and private companies. While funding of overseas collaborations is permitted (unlike in i4i funding), the lead applicants to HICF contracts must be based in the UK.[16] The Wellcome Trust Translational Fund has existed in its current form since 2012 (although the Trust has funded translational research since 2003).[17] It funds biomedical innovation projects that have already demonstrated proof of principle, and are supported by experimental data in 'strategic highlight areas'.[18] The funding does not have an explicit focus on the introduction of technologies into the NHS. The Wellcome Trust Pathfinder Awards were established in 2012 and explicitly focus on funding applications that would be considered too early for support under the Wellcome Trust's other innovation funding instruments. The ultimate aim of the awards is to kick-start pilot research projects that '*have significant potential to help develop innovative new products in these disease areas, but which may not otherwise be economically attractive to the private sector*'.[19] To this end, the awards also provide dedicated funding for establishing industry-academic partnerships, but require matched funding from industry partners and are capped at £100,000.[20]

The MRC and Innovate UK £180m Biomedical Catalyst, launched in 2012, provides three core types of awards: i) feasibility and concept development awards; ii) early-stage awards; and iii) late-stage awards. It includes the Confidence in Concept awards.[21] Innovate UK administers the awards to business-led applications, while academic-led applications for early- and late-stage awards are primarily administered through the MRC-established mechanism of the Development Pathway Funding Scheme (DPFS). The projects funded through this instrument focus on the pre-clinical stage of development of novel devices and diagnostics. Industry partner involvement is limited to SMEs. However, unlike the Wellcome Trust

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[15] National Institute for Health Research (2013).

[16] In i4i-funded projects, lead applicants must be based in England or Wales. Collaborators may be based outside these areas, but will not be able to receive any funding. See National Institute for Health Research (2015a).

[17] Wellcome Trust (2012a).

[18] Strategic highlight areas are defined in order to encourage more applications in underserved and challenging areas.

[19] Wellcome Trust (2012b).

[20] Wellcome Trust (2012c).

[21] Medical Research Council (2014a).

funding instruments and i4i, it has caps on the proportion of project costs covered and funds between 60 per cent and 80 per cent of eligible costs depending on the award and the type of applicant (business or academia). Projects may apply for co-funding with other organisations outside the MRC, such as other Research Councils.[22]

The UK SBRI scheme has been providing funding for small and medium-sized enterprises (SMEs) since 2009 and is overseen by Innovate UK. Unlike the instruments discussed above, the SBRI is targeted at UK SMEs, and not academic partnerships. It focuses on challenges that are relevant for the NHS and are specified by clinicians and experts. It funds work in three phases along the innovation pathway: Phase 1 feasibility contracts are valued at up to £100,000 and last for six months; Phase 2 & 3 development contracts are worth up to £1 million over one to two years and can take a product to prototype development, pathway testing and validation within a clinical setting. Unlike the Biomedical Catalyst, SBRI covers 100 per cent of the development costs.[23]

Translating biomedical innovation is also included in some international funding programmes, such as the health division of the European Union's Horizon 2020 flagship programme, which has a budget of approximately €1.2 billion. Although it does not have clearly ring-fenced funds for early-stage translational innovation, such projects are also eligible.[24] Since 2011, EU framework funding includes the European Research Council (ERC)'s Proof of Concept Award. This is a follow-up instrument offering translational funding for previous ERC-supported projects, which must be closely linked. ERC grant holders can apply for this additional funding (up to €150,000) to establish the innovation potential of ideas arising from their ERC-funded research projects during the pre-demonstration phase. However, this funding is not ring-fenced for medical technologies and the health sciences exclusively.

As another key international example, one of the main funding instruments for assisting early-stage translational innovation in the United States is the Small Business Innovation Research/Small Business Technology Transfer (SBIR/STTR) scheme. Projects involving small businesses can benefit from stage 1 of the large-scale SBIR program, established in 1982 with the aim of including SMEs in federal R&D funding.[25] Funded through the budgets of federal agencies, this programme supports feasibility research by small businesses, while the STTR supports the same early-stage innovation by partnerships between SMEs and research institutions.[26] US Research Evaluation and Commercialization Hubs have been providing funds to projects in the phases that precede application to SBIR/STTR funding. Established in 2010 and extended in 2015, the six centres funded by this programme work as 'one stop shops': each hub issues calls, selects and provides funding for feasibility studies and access to expertise in areas required for early-stage technology development, including scientific, regulatory and project management.[27] In addition, in 2011, the US established the National Center for Advancing Translational Sciences

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[22] Medical Research Council (2014b); Innovate UK (2014a, 2014b).
[23] SBRI Healthcare (2015).
[24] European Commission (2014).
[25] The program has four objectives: i) to spur technological innovation in the small business sector; ii) to meet the research and development needs of the federal government; iii) to commercialize federally funded investments; and iv) to enhance the participation of women and socially or economically disadvantaged persons in technological innovation. See: SBIR Reauthorization Act 2000 (H.R. 5667 – Section 108).
[26] Small Business Innovation Research (2015).
[27] Foreign Affairs (2015).

(NCATS), a national agency whose work cuts across research domains and specifically focuses on translating medical innovations to market, with a focus on pre-clinical and clinical stages.[28]

Despite examples of supportive initiatives, the overall paucity of both public and private funding sources for early-stage innovation in the medical devices, technologies and diagnostics space makes the case for exploring public-private partnerships (PPPs) as a financing model. Such institutions pool public and private resources, help spread risk and can help broker networks that are needed for successful progression of innovations through the innovation pathway, including networks for access and uptake.[29] For example, in the US, the Global Center for Medical Innovation (GCMI) is funded by federal and industry resources. GCMI was established in 2010 and brings together members of the research, industry and investment community in the medical devices space to help accelerate the commercialization of innovative technologies. Amongst other activities, GCMI supports early stages of innovation, ranging from concept development to prototyping.[30] Other examples can be found in the international development space. The Foundation for Innovative New Diagnostics (FIND) is a PPP that supports the development of diagnostic tests for poverty-related diseases, including both product development and product launch stages, through to market penetration and broad-scale use.[31] The foundation is supported by a series of international donors, including several governments and international organisations, but also private foundations. The IDRI (Infectious Disease Research Institute), established in 1993, supports the development of new diagnostics, drugs and vaccines. It supports the development of diagnostic tools in pre-clinical and clinical phases.[32] But these are rare examples. According to an industry expert we spoke to, PPPs for medical technology development could be more challenging to establish and sustain than those for drugs. In this experts view, medical technology firms differ substantially from pharmaceutical companies: they are not R&D companies but big sales and marketing organisations with completely different organisational cultures, which may make a PPP model less feasible. There are, however, some outliers active in the medical device space, who do also support R&D activity (e.g. General Electric, Johnson & Johnson). An examination of the diverse funding, governance and management models within the existing (and other) PPPs could offer useful insights for the potential establishment of similar institutions at the European level and in the United Kingdom, and help to establish the feasibility of such a model in the medical devices space.

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[28] National Centre for Advancing Translational Science (2015).
[29] Chataway, Fry, Marjanovic and Yaqub (2012).
[30] Global Center for Medical Innovation (2015).
[31] FIND (2015a, 2015b).
[32] Infectious Disease Research Institute (2015).

2. Methods

2.1. Study design and scope

This evaluation used a multi-method approach, drawing on evidence from diverse stakeholders: principal investigators (PIs) on i4i contracts, co-applicants, collaborators, representatives of the selection panel and external stakeholders. In addition to a focused review of background documentation from i4i, we used three key methodologies: key informant interviews, a survey of successful recipients of i4i contracts, and in-depth case studies of specific i4i contracts. Together, the data provide a rounded picture of the outcomes and impacts achieved through the i4i contracts, and of the process by which they have been achieved. The sections below discuss each method in more detail, and highlight associated caveats.

2.2. Methods

2.2.1. Key informant interviews

We first conducted ten key informant interviews (KIIs) with i4i award holders and representatives of the selection panel. i4i-award-holder interviewees were randomly selected. The interviews were semi-structured and lasted between 30 minutes and one hour. The purpose of the interviews was to scope out issues relevant to i4i project evolution and impacts and to help inform the design of the evaluation survey (see Appendix A for protocol). The KIIs also helped to identify areas for further exploration in the survey, such as the ways in which the i4i Secretariat has worked with grantees, and the challenges grantees have experienced throughout their projects. We also consulted two external stakeholders (one from the medical device investment community and one from a research charity organisation) on the wider medical device innovation context in the United Kingdom, and on the role i4i plays in that context.

2.2.2. Survey

The survey aimed to gather evidence on the outputs and impacts of the i4i programme (i4i funding and management, and operational support) on the guided progression of medical technologies, devices and diagnostics. A core aim of the survey was to understand if i4i has helped projects to 'move from A to B', and if so, to identify what A and B have been. For example, we were interested in understanding whether the i4i programme has helped projects to move from proof of concept to a prototype, or from a prototype to testing phases. The survey also aimed to identify the wider perceptions award recipients had of the i4i programme, their experiences with the i4i Secretariat, and the enablers and challenges experienced along

the way. To capture these different aspects of the awards, the survey covered the following topics (see Appendix B):

- *Introduction and background* – to capture the characteristics of the survey participants and their projects (e.g. size, scientific and technological focus area, funding duration, start and end points).
- *Funding* – to understand why applications were made to i4i and to understand the perceptions of i4i as a funder.
- *Application and selection* – to capture awardee experience with and perception of the application and selection process.
- *Commercialisation and Intellectual Property* – to capture possible changes made to the commercialisation and IP aspects of applications.
- *Role of the i4i Secretariat during projects* – to capture interactions with the i4i Secretariat and their utility.
- *Outputs* – to capture the outputs achieved through the i4i grant and the related challenges and enablers.
- *Future funding* – to capture perspectives on the next stage of funding and explore any additional funding leveraged.
- *The path to commercialisation and/or uptake* – to capture progress and expectations of the next steps along the path towards commercialisation and uptake.

The survey was developed and piloted by the RAND Europe evaluation team in consultation with the NIHR i4i Secretariat. It was administered by the NIHR i4i team using Survey Monkey. The results are discussed in Chapter 3.

2.2.3. Case studies

We conducted four case studies of i4i projects, representing diverse health innovation challenges, to examine how they experienced the early innovation journey, and to learn about associated enablers and barriers. The NIHR i4i Secretariat provided a long-list of 16 case studies, and the final selection was decided in consultation between i4i and RAND Europe. The case studies were selected to reflect the diversity of the i4i portfolio and to highlight the diverse types of outputs achieved through i4i-supported innovators, in different areas of medical need. The case studies enable more in-depth illustrations of the way in which i4i is contributing to product development and how this could benefit patients, and represent a narrative of the journey to impact. As such the case studies have been used to complement the findings from the survey and interviews.

There are two key sources of data for the case studies: (i) available documentation on a project provided by i4i, including the initial application and progress reports; and (ii) semi-structured interviews with the PIs and collaborators/co-applicants on i4i projects (see Appendix C for protocol). In total, three interviews were conducted for each of the four case studies (12 in total).

2.3. Caveats

There are a number of caveats associated with this evaluation:

1) First, the data collected on progress and outputs through the survey and case studies is self-reported and it is beyond the scope of the study to independently validate the reported progress. While there is no reason to assume that inaccurate information would be provided, this remains a caveat in the interpretation of the findings.

2) Second, although we have tried to assess the unique character of i4i and its added value as a funder of early-stage innovations, we do not have a counterfactual and did not examine comparators within the scope of this evaluation. To mitigate this, we asked evaluation participants about their perceptions of i4i and factors which might differentiate i4i from other funders in this space.

3) Third, caution should be taken in the generalisation of the findings. The survey response rates reported in Chapter 3 are in some cases quite low, which makes it difficult to generalise the findings beyond the sample. Nevertheless, the relatively large number of PIs completing the survey allowed us to capture a diversity of perspectives on i4i. We also aimed to mitigate relatively low survey response rates with insights obtained through other methods, including interviews and case studies.

4) Two other caveats apply to the survey. We aimed to target responses from completed projects, but the survey included responses from a mix of completed and ongoing contracts. In addition, a minority of survey respondents, who were identified by the i4i Secretariat as PIs on projects, went on to identify themselves as collaborators rather than PIs.

3. Results: insights from the survey and key informant interviews

3.1. Chapter summary

1. **i4i is widely seen as rare and unique funder of high-risk early innovation in the medical devices, diagnostics and technologies landscape in the United Kingdom.** According to our survey data, the two key reasons for applying for i4i funding were: (i) the fit of the funding stream with project aims, goals and objectives; and (ii) the uniqueness of i4i as a funding source. According to interviewees, a number of factors make i4i unique, including: (i) being a rare source of early-stage innovation funding in the medical technologies, devices and diagnostics space; (ii) being a less conservative funder than some others in this space, willing to support individuals outside of the 'usual suspects'; (iii) an openness to diverse themes and disease areas; and (iv) a flexible, transparent and less bureaucratic funding model than some other investors in this space. A quarter of surveyed PIs reported complementary funding from other sources. This suggests that the majority of projects were dependent solely on i4i or that the funding provided by i4i was sufficient for the immediate needs of innovators. Although survey respondents widely saw i4i as a unique source of early-stage innovation finance, they did not see it as funder from which it was easy to secure funding from.

2. **The application and selection process for i4i funding is widely perceived as useful for proposal improvements. There is scope for encouraging earlier consideration of adoption challenges and potential design issues, at application phases.** Survey respondents considered scientific advice to be the most common and most useful type of feedback that innovators received during the application phase. Approximately one third of PIs surveyed also received business-related and other feedback which they found useful. The application and selection process led to adaptations in proposals for funding, spanning areas such as testing and trialling processes, IP arrangements, aspects of research, staffing and other elements. Changes in original proposals were more common for recent contracts. Our interviewees provided additional nuance and context on the usefulness of the application and selection process: the key perceived strengths that they highlighted included an approachable i4i Secretariat, useful responses to queries and an efficient telephone support service, and a well-designed application form. Interviewees also noted an improved web-portal, and a well-rounded selection panel bringing together complementary science, business and patient and public involvement skills. Selection panel members found the guidance document provided by i4i and the existence of a 'pre-screen' process very useful. Interviewees reported that key weaknesses included the level of detail requested about technical issues, and the lack of mechanisms to encourage early consideration of adoption issues and design challenges at proposal phases. The appropriateness of technical knowledge of the selection panel specifically, for objective assessment of very diverse proposals, was raised as a potential challenge.

3. **Selection panel members noted that the quality of applications for i4i funding has improved over time, as the programme has evolved.** Although meriting further investigation, this is possibly due to a combination of the enhanced profile of i4i, clearer guidance, a better understanding of what the i4i programme is about, and increased importance of grant-like funding to the sector.

4. **The key role that i4i plays during projects is one of monitoring and oversight, but it also provides an advisory role on an as-needed basis.** PIs surveyed found the most useful interactions with the i4i Secretariat during project life to be progress reports (68 per cent), regular project meetings (52 per cent) and ad hoc phone calls (50 per cent). According to our interviewees, direct interactions with the i4i Secretariat were generally seen as helpful for enabling project teams to reflect on project evolution and progress, see things from a different perspective, and at times raise questions relevant for advancing projects. The i4i Secretariat supported progress though providing clarity on project structure and timelines. IP, scientific and business advice were also considered important by some of those surveyed.

5. **Some interviewees felt that the i4i Secretariat could provide additional support to projects through network brokerage, awareness raising and training roles.** This included raising awareness about i4i externally; sharing insights and learning from other i4i projects and possibly the wider NIHR and research councils (to the extent that this is appropriate in the context of commercial sensitivities); brokering contacts with industry, clinicians and knowledge transfer networks locally and nationally; and providing business skills training.

6. **Most i4i projects involve collaboration between at least two partners from academia, the NHS and industry, despite generally being academically led. Consultation with other external stakeholders occurs on an as-needed basis. Consultation with bodies responsible for NHS procurement decisions and charities appears to be rare, which could ultimately impact on prospects for adoption of innovations in clinical practice and on the appropriateness of product specifications for patients.** Approximately two thirds of projects in our survey were academically led, with the remainder led by either clinical organisations or industry. In addition to establishing formal collaborations, innovators consulted with clinicians, academics and patient representatives or patient groups during the application process. The i4i Secretariat could explore ways to encourage more consultation with NHS procurement and patient voice groups in future calls for applications.

7. **The i4i programme aims to help innovations and innovators progress through the innovation lifecycle with the ultimate goal of contributing to the development of products that will benefit patients. The survey findings show that the programme supports projects with diverse starting points through early innovation stages.** Some of the funded projects were pre-proof of concept (PoC) (21 projects, 50 per cent) at the initiation of the contract; others completed a PoC early on in the contract (6 projects, 14 per cent) and thereafter focused on more downstream product development; some began with a completed PoC and a focus on prototype development (12 projects, 29 per cent); and a minority (3 projects, 7 per cent) had a prototype completed before the start of the contract.[33]

8. **The progress made by grantees varied across the survey sample. However, the survey data suggest that the i4i programme is widely enabling the tackling of bottlenecks in early-stage innovation finance.** The projects analysed varied in size and duration, and therefore their progress is not readily comparable. In over half of the cases investigated (27 projects, 64 per cent), the i4i programme enabled

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[33] 42 out of 44 PIs completed the section on outputs. The percentages are based on the 42 responses.

the development and completion of a proof of concept. Many moved further along the development pathway – the majority of projects (39 cases, 93 per cent) worked on prototype development and in 37 cases (88 per cent) the prototype was completed within the project. In 23 cases (55 per cent), testing or a pivotal clinical trial were started during the project lifespan. The contracts also helped an additional 6 projects (14 per cent) to get to the stage where they were ready to start testing or start a pivotal clinical trial soon after project completion.[34]

9. **The i4i programme placed innovators in a position to pursue further downstream development post-project completion, including further testing and pivotal clinical trials, commercialisation (IP-related outputs, start-ups and licensing) and, in a minority of cases, uptake in the NHS and placing a product on the market.** Most commercialisation activity related to the finalisation of IP arrangements (23 PIs reported this, 52 per cent) and business plans (12 PIs reported this outcome, 27 per cent). Six PIs (14 per cent) also reported starting a company on the basis of i4i funded work, and an additional seven PIs (16 per cent) noted that another company continued downstream development. The majority of PIs (75 per cent) intend to apply for further development funding from bodies such as the Department of Health (DH)/Wellcome Trust (WT) Health Innovation Challenge Fund, the TSB Small Business Research Initiative, angel funding, venture capital and EU funding. The i4i programme may wish to follow up on success rates.

10. **Key reported enablers of project progress included the expertise and skills of the project team, the technical and scientific nature of the project, and access to clinicians as a useful source of insight on the usability of an innovation.** The adaptability of the grant (e.g. to changing project circumstances and needs) was also seen as an important enabler of progress by some interviewees. Expected future enablers of commercialisation and uptake include the involvement of clinicians in the innovation process, support from key opinion leaders and a high-profile publication in a journal (which can legitimise the value of an innovation). Over a quarter of PIs also considered the following factors as particularly important for facilitating uptake: local pilots to better understand adoption processes, a better understanding of procurement challenges, and professional body recommendations.

11. **Key challenges to uptake included technical and scientific issues in the project and challenges in product design and usability, as well as regulatory constraints.** Less frequently mentioned challenges included insufficient access to patients, funding constraints and demands from the i4i Secretariat. The majority of PIs (75 per cent) in our survey sample stated that they expect future challenges to uptake and 55 per cent of all PIs had thought about ways to address them. Inertia and resistance to change, procurement channels into the NHS and financial challenges to implementing pivotal clinical trials were thought to be key barriers.

12. **Health economics analyses have become an important part of product development for many innovations, and could influence future development and uptake of i4i-supported advances. Such analyses were only conducted in a minority of i4i projects.** Although some PIs plan to conduct health economics assessments in the future, the Secretariat may wish to consider ways of encouraging such analysis as parts of project design.

13. **Caveats to bear in mind:** (i) The response rate for PIs was 30 per cent, so we advise caution in the generalisation of findings – although the variety of projects represented still offers useful insights on the

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[34] 42 out of 44 PIs completed the section on outputs. The percentages are based on the 42 responses.

nature and impact of i4i funding; (ii) despite aiming to target responses on completed projects, the survey responses included a mix of completed and ongoing contracts. The second point has two key implications: first, the impacts from ongoing projects may require more time to accrue relative to those that have been completed; second, i4i may wish to update its information management systems to keep clearer records of completed and ongoing work. In addition, a minority of survey respondents who were identified by the i4i Secretariat as PIs on projects went on to identify themselves as collaborators rather than PIs. The Secretariat may want to revisit their records on projects as part of information management, to reflect any changes in participant roles that may happen during the life of a project. Finally, it is important to emphasise that the data presented are self-reported, and that an external audit is outside the scope of the current work.

3.2. Background of survey respondents

Through the key informant interviews, we generated a rounded understanding of the topics to be explored in the survey. In general, the aim of the survey was to collect feedback from i4i-funded PIs and their collaborators on the lifecycle of their contract. We collected information on the entire journey, from the application stage through to the outputs and the prospects for uptake.

3.2.1. Interviews: respondent profile

The ten scoping interviews solicited insights from recipients of i4i funding and representatives of the selection panel. The aim of the interviews was to scope a diverse range of issues that could inform the survey design. Not all interviewees could comment on each issue and we did not aim to quantify the strength of different responses in this scoping element of the evaluation. In the results section, we present interview findings in the context of enriching the survey results and to assess whether the interviewee views support or challenge survey findings.

Eight of the interviews were conducted with recipients of i4i contracts, who held contracts of different sizes and durations. Two were conducted with representatives of the selection panel. The identity of all respondents is confidential.

3.2.2. Survey response rates, respondent and grant profiles

The survey was completed by 44 participants identified by the i4i Secretariat as PIs out of a total of 146 PIs contacted, yielding a response rate of 30 per cent. Of the 44 participants identified by the i4i Secretariat as PIs, 41 identified themselves as PI and three identified themselves as collaborators on specific project contracts. These three were incorporated in the analysis of PIs. The section on outputs was completed by 42 respondents.[35] Given the response rate of 30 per cent, some caution is required in the generalisation of the findings.[36]

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[35] This section asks what outputs have been achieved through the project (e.g. prototype development).
[36] The completion rate is based on 44 responses.

In addition to PIs, the survey was completed by 11 participants identified by the i4i Secretariat as co-applicants, and by 12 identified by the i4i Secretariat as collaborators. The respective response rates were 10 per cent for the co-applicants and 18 per cent for the collaborators. Given the low response rates amongst these groups, the survey analysis focuses primarily on answers provided by the PIs. We refer to the co-applicants and the collaborators to complement core findings from the PIs, with the aim of highlighting any major differences or to emphasise answers which support overall PI findings. In the majority of this chapter we will focus on the data collected from PIs; in Section 3.4 we will return to the data collected from co-applicants and collaborators.

Of the 44 surveys completed by the PIs, 27 related to completed projects and 17 to ongoing projects. There is a broadly equal spread between the different sizes of the contracts, as shown in Figure 1. The majority of the PIs (66 per cent) identified the place where they work most of their time as an academic institution, with some project leadership working in the NHS or private clinical organisations (16 per cent) or in the private sector (18 per cent) (Figure 2). Of the PIs, 8 were female and 36 male. The majority of PIs (72 per cent) indicated that a 'medical device' best describes the focus of their innovation project, 14 percent of the projects focused on diagnostics and 14 percent on other types of innovations, such as web-based therapy and in-vivo diagnostics (Figure 3).[37] Finally, 22 contracts (50 per cent) started in 2009–2011; the other 22 contracts (50 per cent) started in 2012 or after (Figure 4).

Figure 1: Reported size of grant
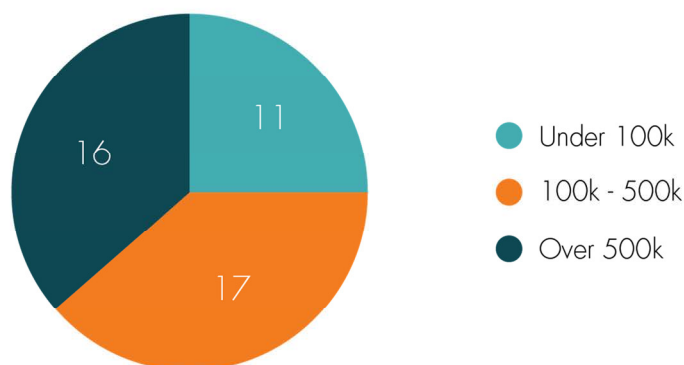
Figure 2: Reported workplace

- Academia
- Clinical Practice (NHS or private)
- Private sector (industry)
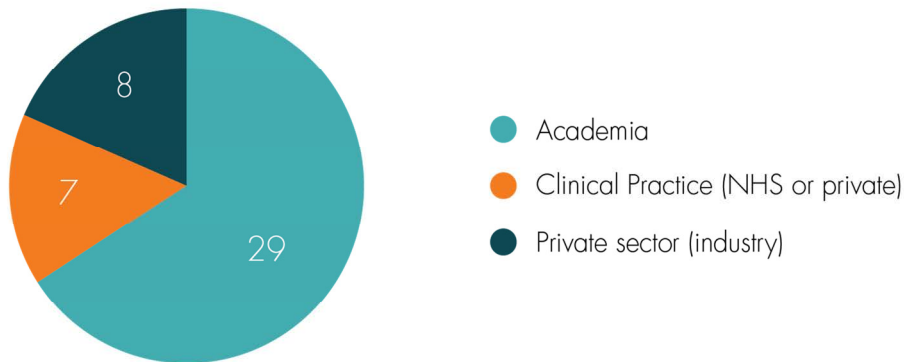
Figure 3: Reported type of innovation

- In vitro diagnostic (EU Directive 98/87/EC)
- Medical device (EU Directive 2007/47/EC)
- Other
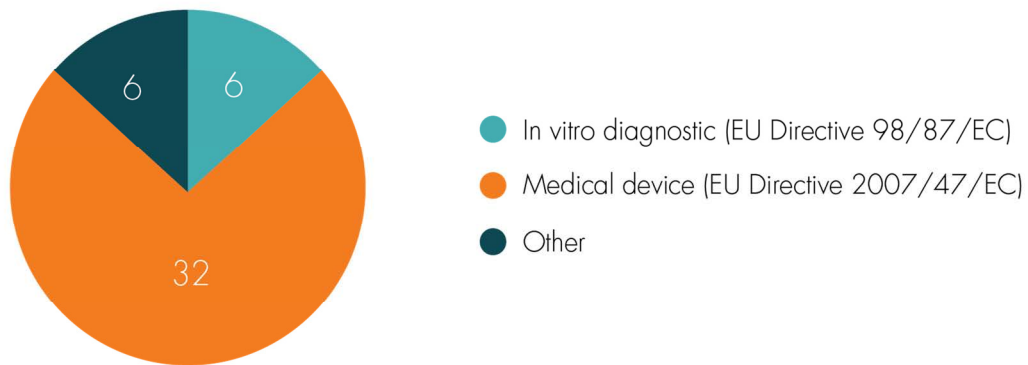
Figure 4: Reported start year

- 2009
- 2010
- 2011
- 2012
- 2013
- 2014
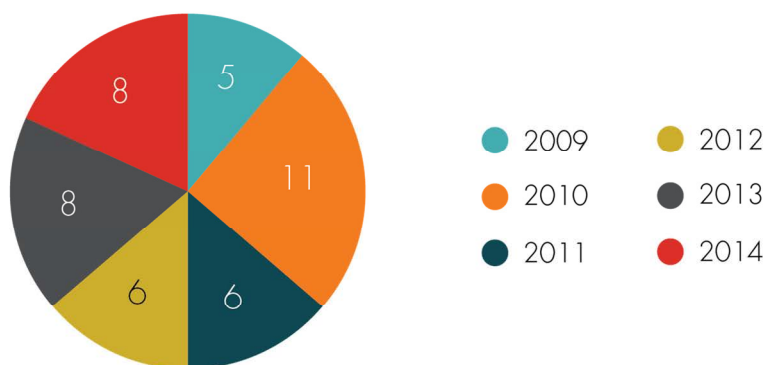
3.3. Insights on i4i outputs, impacts and processes

3.3.1. Reasons for applying to the i4i programme

The survey identified diverse reasons for applying to i4i for funding, but two key motivations were particularly notable (Table 1). First, as can be expected from applications to a fairly specialised research funder, 86 percent of PIs (38 in total) noted the programme's fit with their aims, goals and objectives. Second, 48 percent of PIs (21 in total) highlighted that i4i is one of the few funder sources for the type of work that the projects sought to undertake (early-stage innovation in the medical device, diagnostics and technologies space). This suggests that i4i is perceived as a niche funder, filling a gap in the early-stage innovation finance space. Approximately one third of those surveyed (13 PIs, 30 per cent) indicated that their project would have been abandoned had it not been for i4i funding, while over half (25 PIs, 57 per cent) indicated they would have applied for funding elsewhere. The remaining six PIs (14 per cent) noted they would have applied for i4i funding again.

Table 1: Reasons for applying to i4i

	Response	% of PIs
Good or best fit with project's aims, goals and objectives	38	86
Perceived likelihood of success	3	7
One of the few funding sources for the type of work the project addresses	21	48
Prestige/kudos associated with i4i	7	16

The alternative sources of finance which would have been targeted are diverse (Figure 5), including funders with broad portfolios across research and innovation pipelines (e.g. charities, the MRC, EU funding, or venture capital (VC)) as well as funding programmes focused on early-stage innovation (e.g. the TSB Small Business Research Initiative, Wellcome Trust Health Innovation Challenge Fund, or angel funding). However, it does not appear that there are many alternative funding sources of early-stage innovation in this space that have quite the same focus or profile as i4i. Of the 44 PIs, only 11 (25 per cent) indicated that they actually had any complementary cash funding for their project, suggesting that the majority of projects were dependent solely on i4i for funding or that the funding provided by i4i was sufficient for the immediate needs of innovators.

Figure 5: Alternative funding sources mentioned
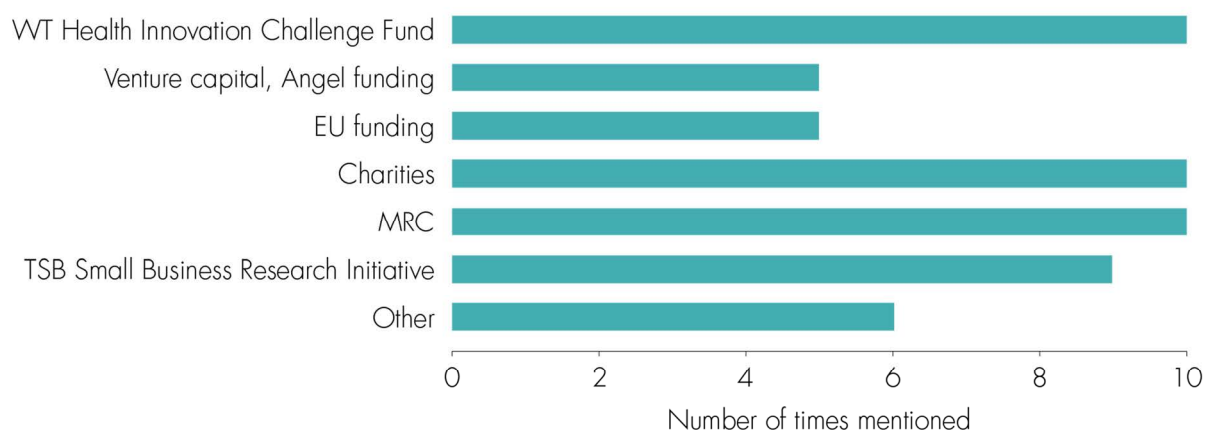
The individuals we interviewed provided additional insights on key features which distinguish i4i from other innovation funding programmes in the medical devices, diagnostics and technologies space:

- i4i is a relatively rare funding source for early-stage, high-risk innovation. One interviewee noted that without i4i, high-risk funding would be limited to high-net-worth individuals, as banks would not fund the organisations that i4i funds (including SMEs) and venture capital firms seek later-stage investments. i4i was also seen to be less conservative than some of the other national funding schemes, in terms of being open to funding individuals outside of the 'usual suspects' (i.e. already established and well-known researchers and innovators).

- i4i was seen to enable clinical/NHS involvement in innovation and to be driven by patient need. In contrast, the MRC was seen to be more focused on academic research, and the TSB/SBRI on the private sector. The i4i programme enables the NHS to not only be involved in R&D, but also to lead applications.

- i4i has a broad focus and supports a very diverse project portfolio. Charities tend to be more specialised in specific disease areas, and some research councils focus on laboratory research. Diverse projects spanning devices, diagnostics and new materials are funded through i4i. Proof of concept and prototype phases most commonly receive i4i support, with some examples of preclinical testing and early clinical testing.

- Interviewees saw i4i as a flexible and transparent funder, as well as less bureaucratic than some other funders (especially EU ones).

Interviewees also shared views on the impacts of a *perceived* funding ceiling within the i4i programme.[38] Although there has in reality been no funding ceiling associated with i4i since 2010, most interviewees felt that the funding criteria were strict and that they would have benefited from applying for a bit more funding had it not been for the *perceived* ceiling (e.g. to cover some early testing or trials or additional staff). Some interviewees suggested that a responsive review mechanism (or alternative way of supporting adaptation in the total funds awarded to a project) would be useful. In such an approach, the funding and protocol could be revised after an initial phase of work, and funding needs reassessed. According to one

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[38] A funding ceiling was removed in 2010.

interviewee, it would be important not to leave a long gap between the reassessment and continuation of work, as this could interfere with project momentum and sustainability (e.g. staffing).

3.3.2. Application and selection process

The survey findings show that, during the application and selection procedures, the business plan was changed for the projects of 18 PIs (41 per cent), while the other 26 (59 per cent) were left unchanged (Figure 6). Changes appear to be more common for recent contracts than for those with an earlier start date. Changes applied to a range of elements of the business plan and no single element seems to stand out as particularly notable (Figure 7). Areas of change included testing and trialling processes (mentioned by 18 per cent of PIs, 8 in total), IP arrangements (for 14 per cent of PIs, 6 in total), aspects of research (12 per cent of PIs, 5 in total), staffing (9 per cent of PIs, 4 in total) and other proposal elements (5 per cent of PIs, 2 in total).

Figure 6: Reported changes made to the business plan
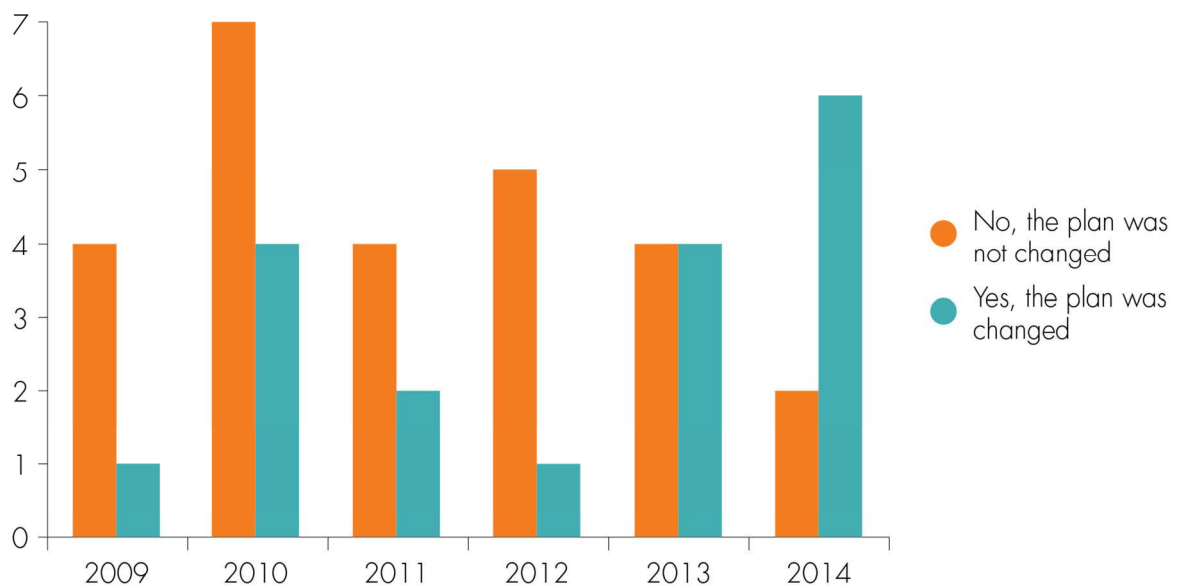
Figure 7: Elements changed at the application and selection stage

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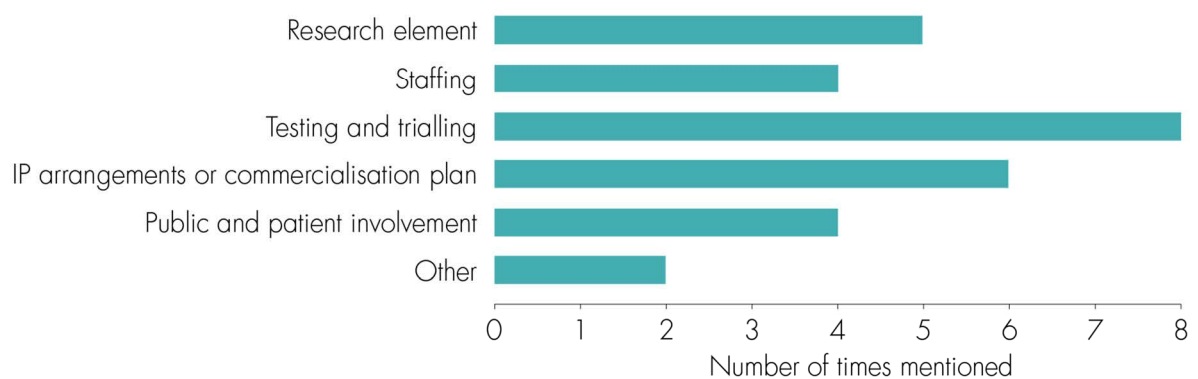
Apart from changes to the content of a proposal, 16 PIs (36 per cent) indicated that the amount of funding associated with their original application also changed (and in most cases the budget was increased). Figure 8 illustrates the different budget-related changes reported by the PIs. Experiences with the application and selection process were generally positive.

Figure 8: Reported changes to the budget and reasons for changes made
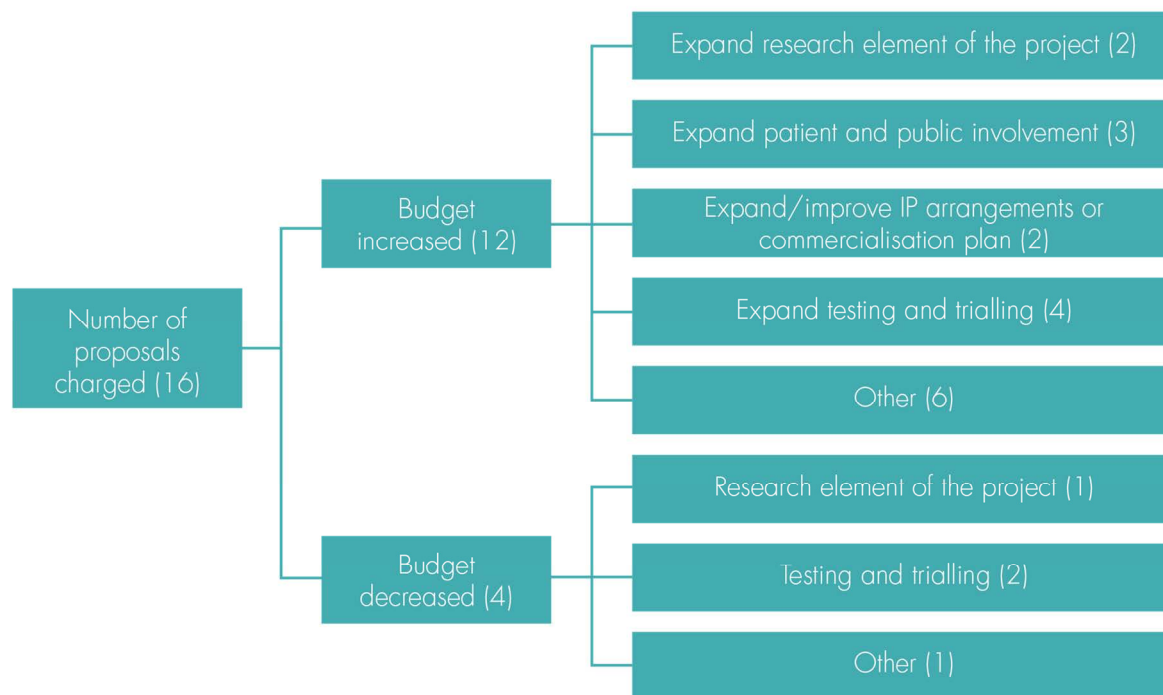
Note: more than one type of change can apply to an increase in budget, hence they are not cumulative.

Our interviewees provided additional nuance and context on the usefulness of the application and selection process. The key perceived strengths included: (i) the approachability of the i4i Secretariat and its useful guidance when contacted with queries; (ii) a well-structured and designed application form; and (iii) an efficient telephone support service. In more recent streams, interviewees observed: (iv) an improved web-portal; and (v) a selection panel with complementary skills (e.g. technical, business and patient and public involvement related). Some interviewees appreciated the guidance from the selection panel during the interview process and from the i4i Secretariat at kick-off meetings (e.g. on how to refine project plans and avoid mistakes others have made in the past).

The perceived weaknesses related to (i) a very detailed technical focus in the application form, and (ii) unharnessed potential through the application process to enable earlier consideration of adoption issues and challenges (e.g. to maximise chances of success in the longer term), and scope to consider design challenges more rigorously at application phases (where applicable). There were limited concerns over time demands associated with the application process.

Selection panel members found the guidance document very useful. They also felt that having a pre-screen process helps to identify promising projects efficiently, and can help highlight potential issues to resolve in the full proposal. They noted that the quality of applications has improved over time, possibly

due to a combination of the enhanced profile of i4i, clearer guidance, a better understanding of the goals of the i4i programme, and the increased importance of grant-like funding to the sector.

3.3.3. Presentation to the selection panel and feedback

Presentation to the selection panel has been compulsory since 2010.[39] Of the 44 PIs participating in the survey, 24 (55 per cent) indicated that they had presented to a selection panel as part of their application, with the majority of these presentations taking place recently. Of the 11 contracts started in 2010, 10 PIs indicated that they did not present to the panel, whereas all eight PIs of contracts starting in 2014 indicated they had presented to the panel (Figure 9). As Table 2 shows, most of the PIs received scientific feedback, which was deemed useful in all but one case.[40] Business and other advice was also well received, though less common.

As part of the application and selection process, i4i selection panel members score bids, as do external assessors and at least two members of the Secretariat. The panel includes diverse individuals with a mix of scientific and technological, business and patient and public involvement skills. The appropriateness of the technical knowledge of the selection panel for objective assessment of very diverse proposals was raised as a potential challenge during our key informant interviews. Interviewees also noted that very little feedback is provided to applicants once a funding decision has been made.

Figure 9: Reported presentations to the panel

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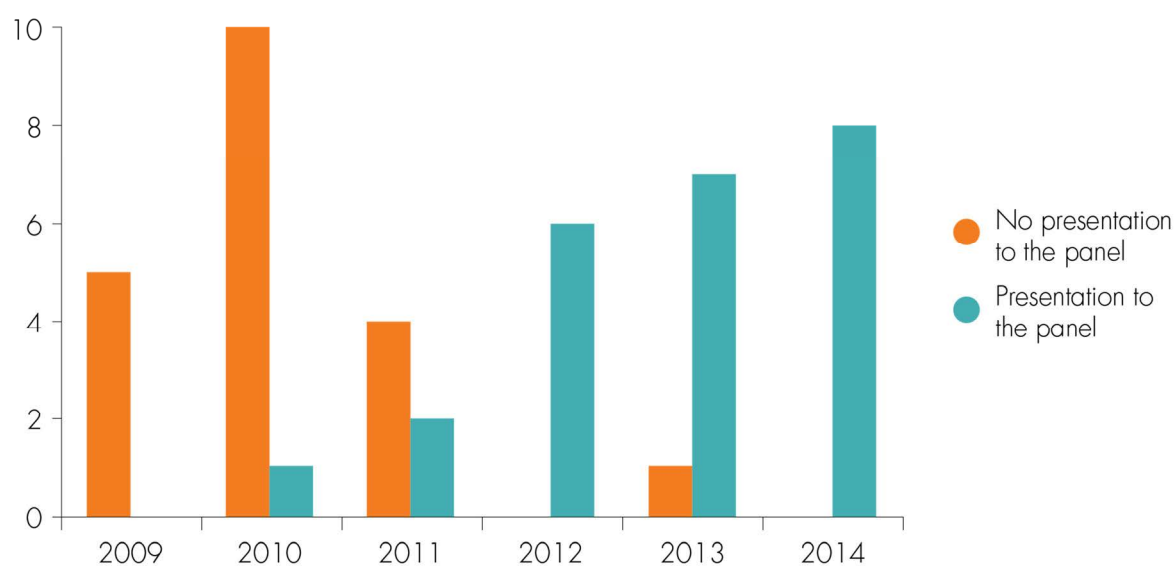
[39] Not all members of a proposal team will join the presentation to the panel. This may explain why even after 2010 some PIs note that they did not present to the panel. Still, in the survey it was not possible to further inquire into this.
[40] The classification 'useful' in Table 2 combines the answer categories 'very useful' and 'useful'.

Table 2: Reported feedback from the selection panel

Feedback received?			Feedback useful?			
	Yes (%)	No (%)		Yes (%)	No (%)	n/a (%)
Scientific	20 (83%)	4 (17%)	Scientific	19 (80%)	1 (4%)	4 (16%)
Business	8 (33%)	16 (67%)	Business	8 (33%)	0	16 (67%)
Other	9 (38%)	15 (62%)	Other	8 (33%)	2 (8%)	14 (59%)

3.3.4. Consultation and collaboration on the application

i4i projects involve both formal collaborations between diverse stakeholders and less formal networks for information exchange and consultation. Collaborators are parties actually named on the application, whereas groups consulted are considered informal collaborators.

The vast majority (all but one) of the i4i projects in our survey sample involved collaboration between partners from academia, the NHS and business. Before actual collaborations on the application started, a number of project investigators consulted with stakeholders informally to help frame their applications. Most frequently consulted, as Figure 10 illustrates, were direct stakeholders such as practicing clinicians, academics and patients or patient groups. Less frequently consulted were stakeholders responsible for NHS procurement decisions.

Formal partners on bids provided different types of inputs into the process of preparing applications for i4i funding (Figure 11). All partners seem to be consulted on the subject area. More specifically, clinical partners tended to provide a user perspective and insights on usability specifications, industry provided advice on IP and commercialisation, and academics provided scientific insights and grant-writing expertise.

Figure 10: Stakeholders consulted at application stage
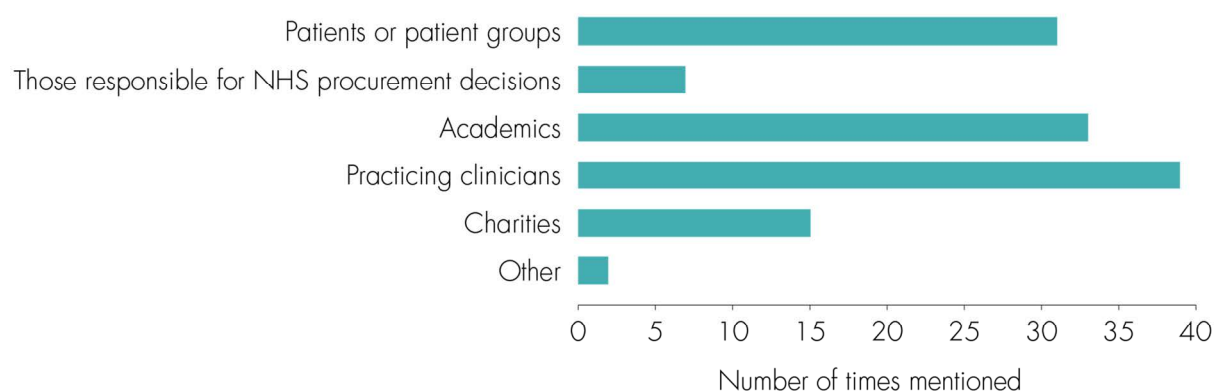
Figure 11: Input provided by collaborators
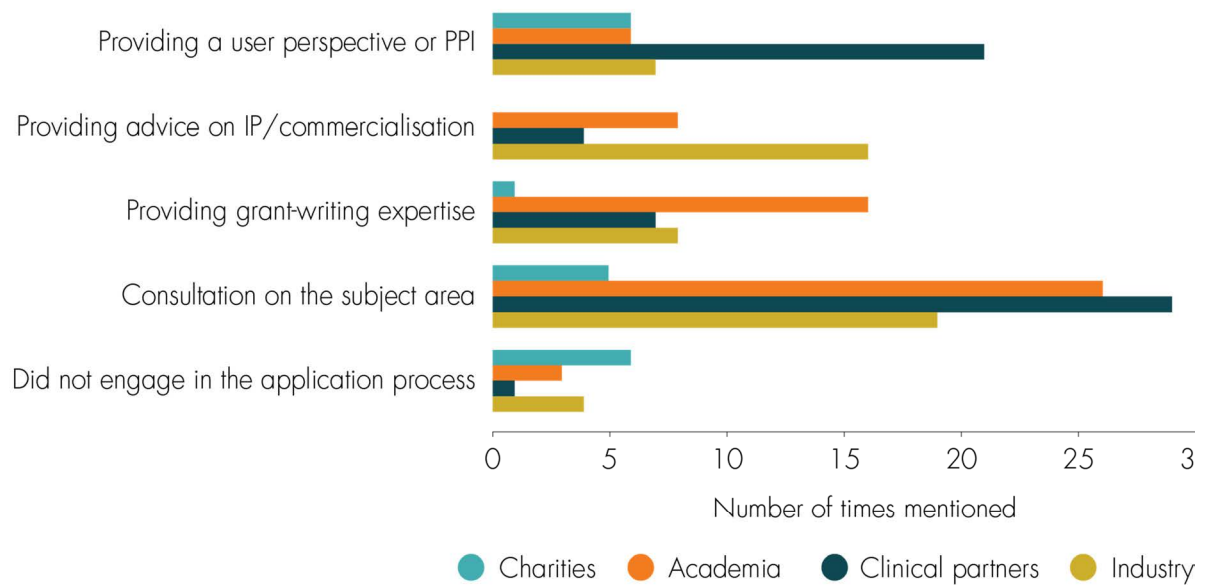
Our interviews highlighted that some of the collaborations grew from prior history of joint working (e.g. between university departments), while others were entirely new (e.g. a company finding a clinical and academic partner to advance a technology idea so that it is suitable for a clinical setting).

3.3.5. Interactions with i4i over the running of the project

Throughout the duration of the projects, the i4i Secretariat interacted with grantees in a number of ways, of which progress reports (68 per cent), regular project meetings (52 per cent) and ad hoc phone calls (50 per cent) were deemed to be the most useful by the PIs we surveyed. However, a substantial number of respondents indicated that ad hoc meetings (52 per cent) and regular phone calls (55 per cent) were not applicable, perhaps indicating that these means of interaction were not used across the i4i project portfolio (Figure 12).

Figure 12: Usefulness of interactions with i4i Secretariat
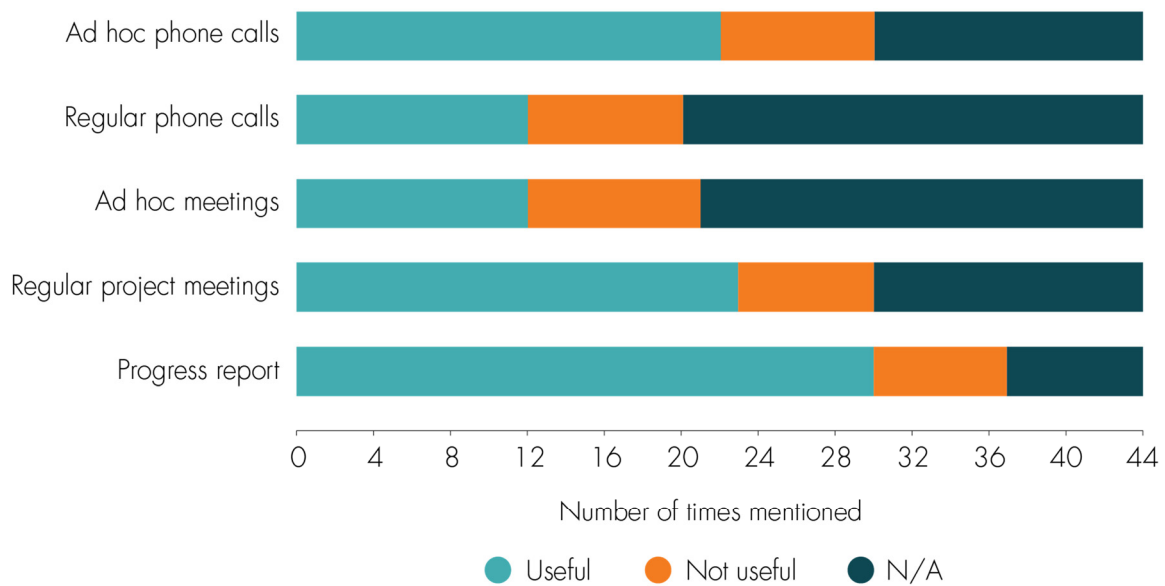
Our interviews highlighted that the key role i4i plays is one of monitoring and oversight, which generally works well, is not considered overly burdensome, and consists of a combination of formal reporting and attendance at meetings by an i4i representative. The direct interactions were seen as helpful for enabling project teams to take stock, see things from a different perspective, and at times raise questions relevant to advancing projects. In one instance an interviewee felt that that the face-to-face interaction might not be necessary unless specific problems need to be discussed. Aside from monitoring and oversight, interactions also revolve around requests for extensions and approval for publications.

Some interviewees felt that the following types of additional support would be helpful:

- *Coordinating, raising awareness and information sharing*: the i4i Secretariat has oversight of all i4i projects, and could play a role in sharing insights and learning from other i4i projects and possibly the wider NIHR and research councils (to the extent that this is appropriate in the context of commercial sensitivities). Keeping the profile of i4i high is important, and investing in dissemination and publicity could also be beneficial.
- *Brokerage and network facilitation*: i4i could play a greater role in 'linking up' and brokering potential partners for further project development. Universities tend to have good local links but there may be a need for more national contact and linkage; brokerage applies to both clinical engagement and industry (e.g. biotech, pharma, design, manufacturing).
- *Business skills training*: some concerns were voiced about the costs of the accelerator programme.

3.3.6. Outputs achieved through i4i contracts

At its core, the i4i programme aims to help innovations and innovators progress through the innovation lifecycle with an ultimate goal of contributing to the development of products that will benefit patients. We assessed the progress made by grantees over the course of their project. To understand the lifecycle

that a product goes through in its development – as it applies to the stages of innovation that i4i supports – three key stages were identified as focal points for this analysis:

- Proof of concept (PoC) development
- Prototype development
- Testing or Pivotal Clinical Trial (PCT).

The section on outputs was completed by 42 out of 44 PIs and the main milestones achieved are listed in Table 3. In this section all percentages will refer to the 42 PIs that actually completed the questions. The data show that over the course of the project, 27 out of 42 (64 per cent) developed and completed a proof of concept. Furthermore, 39 projects (93 per cent) worked on prototype development and in 37 cases (88 per cent) the prototype was completed within the project. The contracts helped six projects (14 per cent) to get to the stage where, at the end of the project, they were ready to start testing or start a PCT, while in 23 cases (55 per cent) such testing or a PCT was actually started during the project.

Table 3: Main milestones achieved through i4i contracts by start-year

Outputs achieved by 42 i4i projects	2009	2010	2011	2012	2013	2014	Total number of projects	Total%
Proof of concept developed and completed (Question 27)	3	9	5	4	3	3	27	64%
Prototypes in development (Question 28)	4	10	4	6	7	8	39	93%
Prototypes finished (Question 29)	2	9	5	6	7	8	37	88%
Output of the project was testing or PCT (Question 30)	0	2	0	2	1	1	6	14%
Testing or PCT at the start or during grant (Question 30)	1	6	4	2	5	5	23	55%

Note: The question numbers refer to the survey questions from which the data is derived. The survey is attached in the Appendix.

However, further disaggregation of the data is required to get a more detailed understanding of the 'paths travelled' by the different projects. All projects travel from A to B, yet what A is and what B is differs. In order to provide some insight into the paths travelled, we identified four different groups of contracts on the basis of the status of the proof of concept (PoC):

1. PoC was completed before i4i grant
2. PoC was completed at the start of the i4i grant
3. PoC was completed during the i4i grant
4. Finished PoC as a key output of i4i grant (and in some cases also achieved further development).

While it is important to remember that starting points 1, 2 and 3 already indicate outputs achieved through i4i contracts, the paths travelled towards different outputs ('B') can now be outlined as shown in Figure 13. The figure shows, for example, that seven projects which finished a PoC as a key output of the project also completed a prototype and started testing or a PCT during the project. Another example

shows that four projects that finished the PoC early on in the project also completed a prototype and started testing or a PCT during the project.

A different way of representing the same data is by assigning each project an arrow, the length of which indicates the path travelled, as shown in Figure 14. An important caveat for this visualisation is that each step along the way may not carry the same weight. It is not necessarily the case that developing a prototype is equally time- or resource-consuming as PoC development. The length of the arrows therefore cannot be taken as a direct indication of the amount of work that was undertaken. In short, while the arrows indicate the path travelled, they cannot easily be compared with each other.

Figure 13: Main milestones achieved by start position (1)

START	Proof of concept - completed (Question 27)	Prototype		Testing or PCT (Question 30)
		Development (Question 28)	Completion (Question 29)	

PoC was completed before i4i grant

	15	15	14	12

PoC was completed at the start of the i4i grant

	6	6	5	4

PoC was completed during the i4i grant

	10	9	8	6

Finished PoC as a key output of the i4i grant (and in cases also achieved further development)

	11	10	10	7

Note: The numbers are not cumulative as a single project can move across different stages of the pathway. The question numbers refer to the survey which is attached in the Appendix.

26

Figure 14: Main milestones achieved by start position (2)
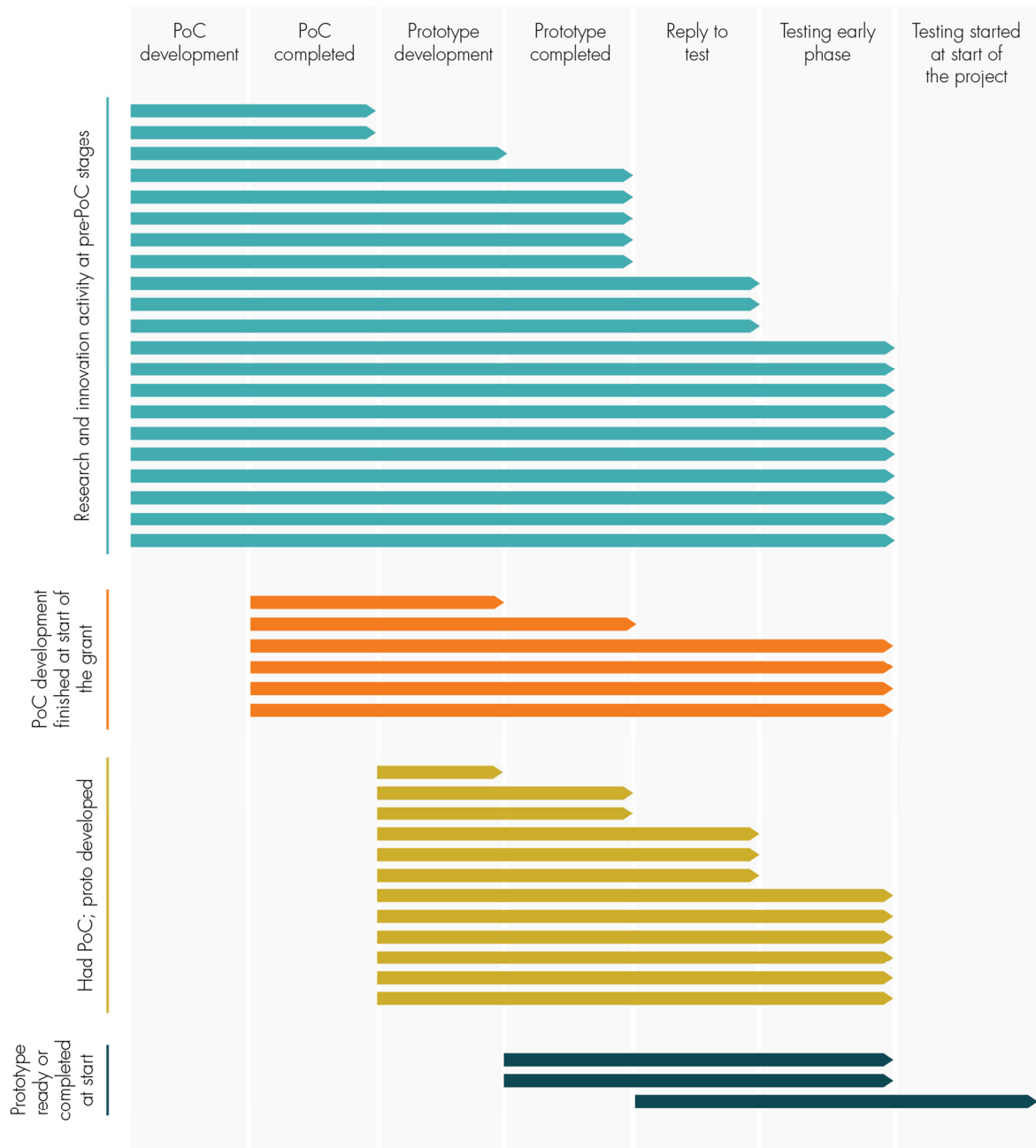
3.3.7. Outcomes enabled by i4i projects – development impacts further downstream

After completion of their i4i funded project, 31 PIs (70 per cent) indicated that it had enabled them to start testing or a PCT, 18 (41 per cent) to start commercialisation, four (9 per cent) to start a large scale clinical trial, and in four cases it enabled (9 per cent) uptake in the NHS. A separate question further separated the types of commercialisation achieved through i4i projects, as shown in Figure 15. Most commercialisation activity related to the finalisation of IP arrangements (23 PIs, 52 per cent) and business plans (12 PIs, 27 per cent). Six (14 per cent) PIs indicated that a company was started on the basis of i4i-funded work, and seven (16 per cent) stated that another company continued downstream development. According to an external stakeholder we interviewed: '*The i4i programme has really evolved [under the new leadership] to attempt to bring venture funders into the picture and to ensure where NIHR is devoting its funding will help move products along the innovation pathway. Recent activity to better link award winners with clinical research networks is really helpful in that regard.*'

Figure 15: Reported downstream commercialisation

3.3.8. Enablers and challenges to project progress

Figure 16 and Figure 17 show the reported enabling and challenging aspects of the projects. Significant enablers of progress were the expertise and skills of the project team and the technical/scientific content (mentioned by 38 PIs, 86 per cent), as well as access to clinicians (mentioned 36 times, 82 per cent).[41]

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[41] The classification 'important' in Figure 16 combines the answer categories 'very important' and 'important', and vice-versa for 'not important'.

Figure 16: Key enablers of outputs achieved
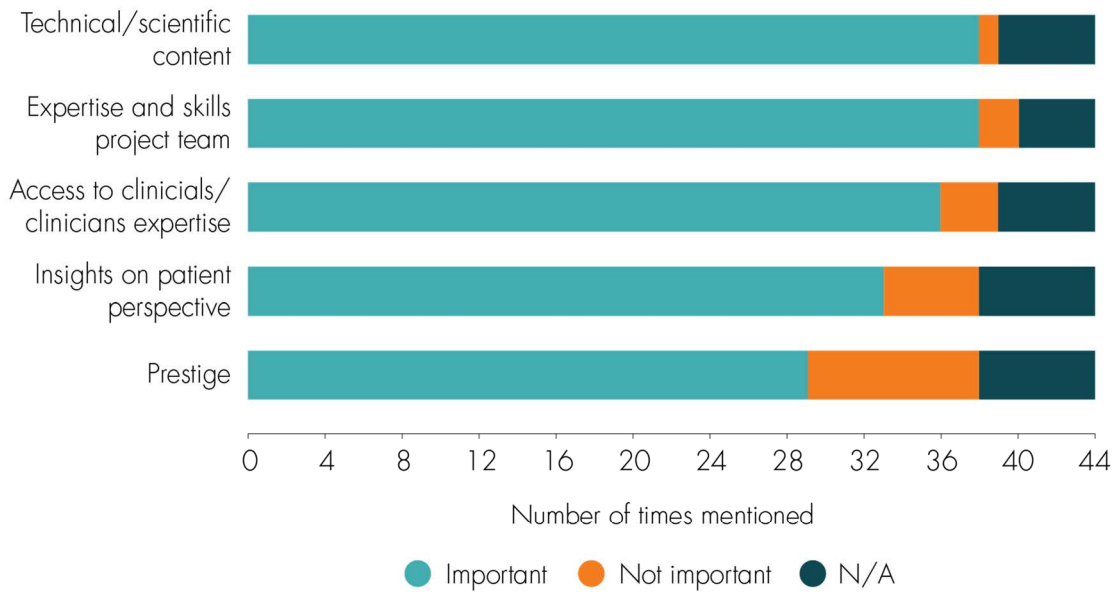
Significant challenges to achieving outputs were mainly technical and scientific issues (89 per cent of PIs mentioned this as a challenge, 39 PIs in total) and challenges in product design and usability (reported by 68 per cent, 30 PIs), but also regulatory constraints (66 per cent or 29 PIs mentioned this challenge). Though less significant, the demands of the i4i Secretariat (reported by 9 PIs or 20 per cent), lack of money (reported by 13 PIs or 30 per cent) and access to patients were also identified as challenges (reported by 13 PIs or 30 per cent).[42]

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[42] The classification 'significant' in Figure 17 combines the answer categories 'very significant' and 'significant', and vice-versa for 'not significant'.

Figure 17: Key challenges in achieving outputs

Number of times mentioned

● Significan   ● Not significant   ● N/A
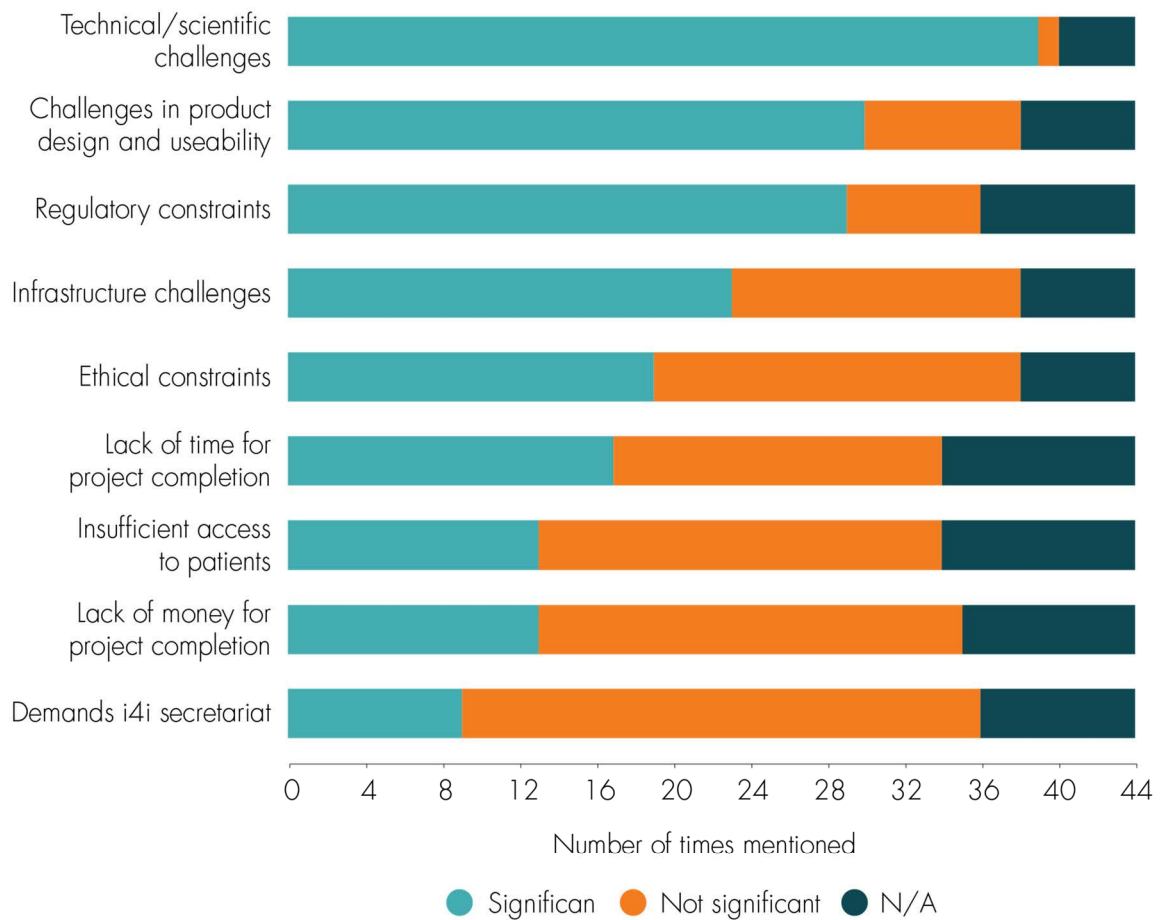
3.3.9. The role of the i4i Secretariat in supporting and enabling outputs

The specific role of the i4i Secretariat was also explored through the survey. Over half of the PIs (24, 55 per cent) found their role in providing structure for projects through clear timelines and milestones to be important. Providing IP advice was also valued (16 PIs or 36 per cent found this important). Deemed less important were scientific advice (12 PIs or 27 per cent found this important) and business advice (11 PIs, 25 per cent). There does not seem to be any clear relation between these answers and the start year of the contracts.

Figure 18: PI views on the most useful aspects of i4i Secretariat involvement in enabling outputs
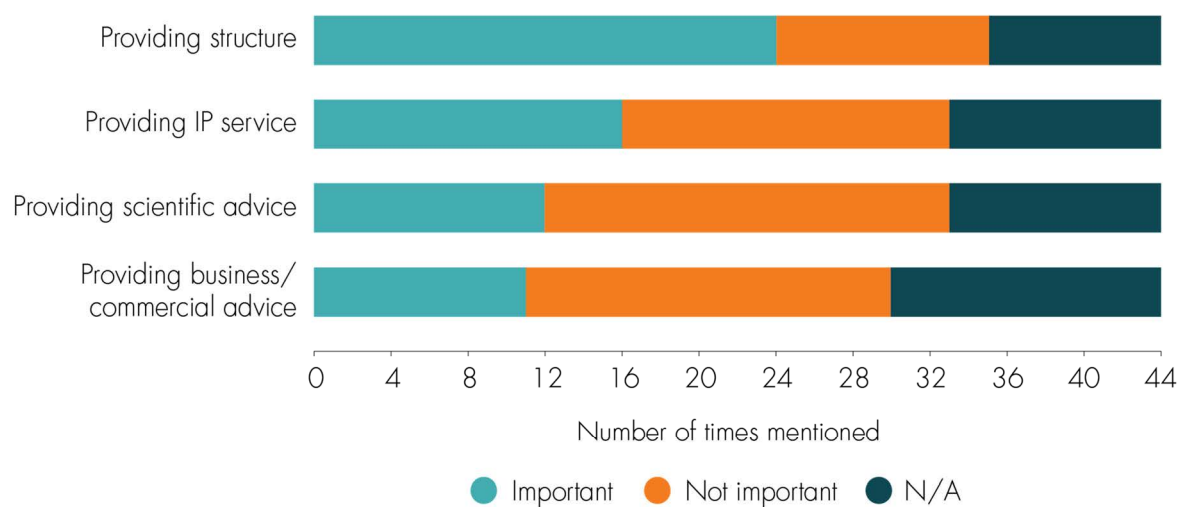
Finally, PIs identified access to key experts (36 PIs, 82 per cent), Knowledge Transfer Networks (KTNs) (31 PIs, 71 per cent) and access to industry (31 PIs, 71 per cent) as important areas in which the i4i Secretariat could help projects in the future.

Figure 19: Potential future roles for the i4i Secretariat
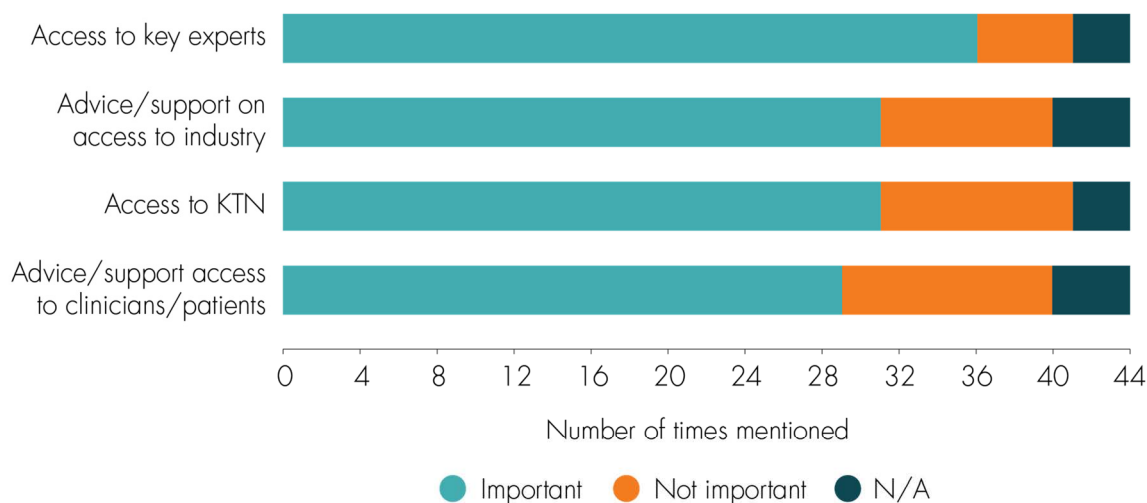
3.3.10.   Further development and uptake

Future funding prospects

The majority of PIs (33, 75 per cent) indicated that they intend to apply for future funding. The most frequently mentioned sources of potential future funding were the DH/WT Health Innovation Challenge Fund (14 PIs, 32 per cent) and the TSB Small Business Research Initiative (11 PIs, 25 per cent). Angel or venture capital funding was mentioned by 10 PIs (23 per cent), and EU funding by 9 PIs (20 per cent).

The i4i programme may wish to follow up on success rates with future funding ambitions across its project portfolio to get a sense of the future funding that it has enabled.

Health economic analyses

Health economics analyses have become an important part of product development for many innovations.[43] Of the 41 PIs that completed the question on this issue a minority of nine (22 per cent) indicated that a health economics study had been conducted or commissioned. A further nine noted plans for a health economics study to be conducted or commissioned (22 per cent), while 23 PIs indicated that no health economics study has been conducted or commissioned (56 per cent). There are no clear time trends for the commissioning of health economics studies.

Figure 20: Reported health economics studies
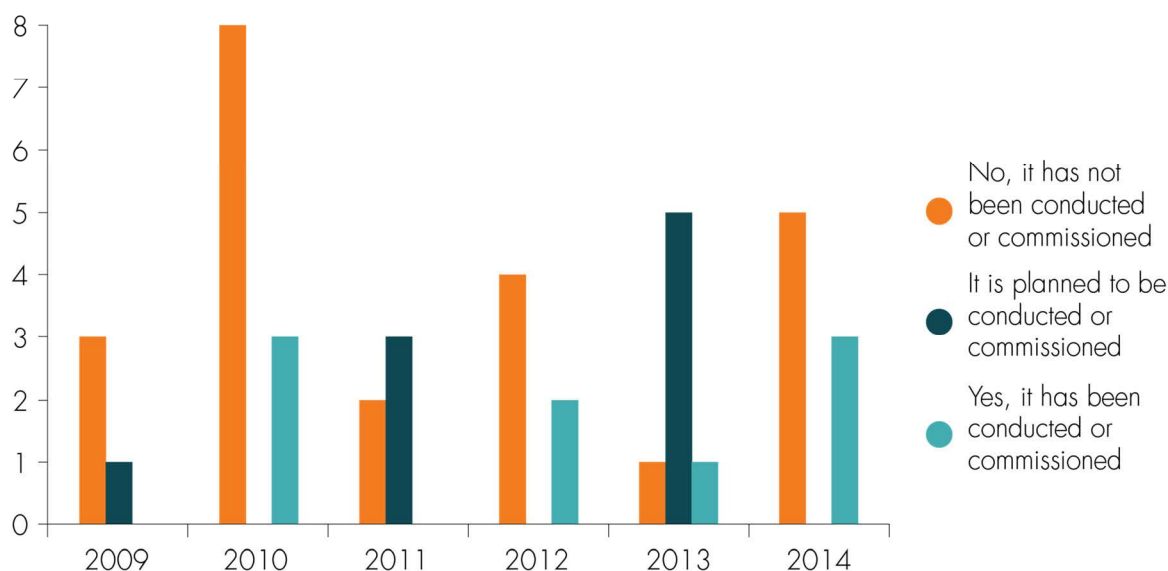
Finally, possible enablers and barriers to the uptake of innovations were explored. As Table 4 shows, the majority of PIs indicated that they expect challenges to uptake (33 PIs, 75 per cent); of these, 24 indicated that they have considered how to address such challenges (55 per cent).

Table 4: Consideration of barriers to uptake

No, and have not considered how to address this	2
No, but have considered how to address this	6
Yes, and have considered how to address this	24
Yes, but have not considered how to address this	9

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[43] Consultation with external stakeholder representative.

Among the most frequently mentioned barriers to uptake are inertia and resistance to change (27 PIs, 61 per cent), the procurement channels into the NHS (26 PIs, 59 per cent), and financial challenges to implementing pivotal clinical trials (31 PIs, 48 per cent). Training (7 PIs, 16 per cent) and clinician incentives (6 PIs, 14 per cent) were mentioned far less frequently as barriers to uptake.

Table 5: Expected barriers to uptake

Barriers to uptake	
Inertia/resistance to change – (e.g. difficult to convince NHS staff of the superior nature of a device or treatment)	27
Entry into the NHS – (e.g. the procurement channels into the NHS serve as a barrier to the uptake of a new device or treatment)	26
Conducting a pivotal clinical study – (e.g. due to lack of funds cannot conduct a pivotal clinical study that is a prerequisite for uptake)	21
Promotion – (e.g. it is difficult to reach the relevant stakeholders to inform them of the new device or treatment)	8
Training – (e.g. specialists will require additional training in order to work with the new device or treatment)	7
Clinician incentives – (e.g. clinicians have no interest or stake in the uptake of the new device or treatment)	6

The most frequently reported enablers of uptake were the involvement of clinicians in the innovation process (27 PIs, 61 per cent), support from key opinion leaders (16 PIs, 36 per cent) and a high-profile publication in a journal (16 PIs, 36 per cent).

Table 6: Expected enablers of uptake

Enablers to uptake	
Involvement of clinicians in the innovation process – (e.g. involving clinicians early on in the development phase proves conducive to uptake)	27
Support from key opinion leaders – (e.g. harnessing the support from a recognized expert in the field to support and promote the new device or treatment)	16
High-profile publication – (e.g. article in a leading journal)	16
Local pilots to understand adoption – (e.g. conducting local piloting studies to understand the process of adoption)	13
Understanding the entry into the NHS – (e.g. dedicating time and resources to understand the procurement channels relevant to the new device or treatment)	13
Professional body recommendation – (e.g. supportive statement by a professional or Royal society)	13
Awareness raising with Commissioners – (e.g. of the new device or treatment)	8

3.4. Co-applicants and collaborators

Generally the co-applicants and collaborators who completed the survey provided answers similar to those of PIs. Given the small numbers of participants (11 co-applicants and 12 collaborators), the results should

be interpreted with caution. However, a few key messages can be drawn from the results to complement the analysis of PI results.

- A larger share of collaborators are from the private sector (50 per cent) than PIs (18 per cent) or co-applicants (none). This may not be surprising as many projects are set up with a PI from academia and collaborators from other sectors.
- Among co-applicants and collaborators, i4i is also generally perceived as a unique, niche funder. Combined, around half of the co-applicants and collaborators indicate that i4i is one of the few funding sources for the type of work the projects address. Furthermore, around a third of collaborators and co-applicants indicated that without i4i funding their project would have been abandoned. Similar to the PIs however, only two out of 23 (9 per cent) co-applicants and collaborators report actually having complementary cash funding.
- A relatively larger share of collaborators and co-applicants mentioned 'uptake in the NHS' as an enabled output (30 per cent), yet actual numbers are the same as those reported by PIs. Overall, similar levels of outputs achieved were reported by the co-applicants and the collaborators.

Table 7: Reported milestones achieved by collaborators and co-applicants

Outputs achieved by 42 i4i projects	Total	Total %
Proof of concept developed and completed	15	65%
Prototypes in development	19	83%
Prototypes finished	19	83%
Output of the project was testing or PCT	7	30%
Testing or PCT at the start or during grant	14	61%

4. Case studies

This chapter presents case studies of four i4i-supported projects. The projects were selected through consultation between the i4i Secretariat and RAND Europe. The Secretariat provided an initial long-list of projects of interest. From that list, the Secretariat and the evaluation team selected four projects to reflect the diversity of innovations and stages in the innovation pathway that i4i supports. The four case studies included are:

- A saliva-based chronic obstructive pulmonary disease sensor (COPD)
- A low-cost, non-invasive visual aid for severely sight impaired individuals
- Next-generation mobile HIV diagnostics with wireless connectivity
- A cervical orthosis for people with motor neuron disease (MND).

Each case study draws on evidence from a combination of formal documents associated with the project (e.g. progress reports, proposals) and interviews with 3 project team members – the PI and two collaborators. The NIHR Secretariat informed project participants that documentation would be shared for the purposes of the research and that the case studies would be publically available.

As the case studies that follow show, all of the projects advanced their original ideas with the support of i4i funding and travelled unique trajectories. Some common enablers included the multidisciplinary skill mix of the team and the support received from the i4i Secretariat, as well as consultation and access to patients (users) in 3 of the 4 cases. According to interviewees, there were also some more unique enablers of particular projects such as particularly committed partners, timely and proactive efforts to understand the regulatory landscape or high levels of media attention (as an enabler of fundraising). The challenges experienced were unique to each case, with examples ranging from issues related to securing IP protection and engaging industry partners, to staffing challenges or identifying appropriate product distribution channels. Some of the interviewees also expected to experience challenges related to barriers to uptake in the NHS in the future. All of the projects pursued or plan to further develop their innovations after the completion of i4i-funded work.

Across the case studies, we obtained evidence on how i4i could further enhance the support it offers to projects. Key recommendations included: (i) considering a more active role in brokering networks and raising awareness about the programme and supported projects (within commercial constraints), and (ii) reflecting on funding scope and scale (including prospects for adaptation in funding levels for a project) through time. Health economics assessments to establish reimbursement potential in a timely manner were rare in the cases we examined (this is supported by survey data), and this may be another aspect of funding applications that i4i might be able to encourage through the design of future application rounds.

More detail is provided in the case studies that follow.

4.1. Saliva-based chronic obstructive pulmonary disease sensor

Key messages

- *Key outputs*:

  This project aimed to develop a prototype device to predict and manage chronic obstructive pulmonary disease (COPD) exacerbations at point of care, based on biomarkers in saliva. Key achievements were:
  - o Completion of a longitudinal study involving 60 patients to establish that three key saliva biomarkers could be used to predict COPD exacerbations.
  - o Advance of a saliva-based point-of-care COPD sensor from proof of concept initiation to prototype initiation.
  - o Development of an electronic patient wellbeing diary mobile application (app) which combines saliva biomarker results with patients' health scores. The app is available from the Apple store.
  - o Significant progress with securing IP protection needed for future commercialisation. The team were (1) granted a US patent on saliva biomarkers and filed for a similar patent in Europe and Canada; (2) filed for an UK patent on the saliva sampler design; (3) secured Europe (EU) and US copyrights on the electronic wellbeing diary mobile app; (4) filed for US and EU patents on the saliva-based COPD sensor.
- *Key enablers*:
  - o A well-defined clinical problem stemming from an earlier feasibility study fully funded by i4i.
  - o Access to a proven sensor magnetic immune-affinity assay (MIA) technology to build on, for developing the COPD sensor.
  - o A multidisciplinary and fully engaged team ensuring the right breadth of expertise: clinicians, biochemists, engineers, software developers, data analysts, regulatory experts and health economists.
  - o Access to patients to conduct a longitudinal study.
  - o Consultation and engagement with patient groups: focus groups to test the electronic wellbeing diary and obtain users' insights on the COPD sensor design features.
  - o Substantial consultation with regulatory experts and healthcare professionals to (1) understand the regulatory framework and (2) obtain perceptions on clinical device costs, implementation routes and potential barriers for adoption. These consultations helped to focus the development of the technology since the earlier stages.
  - o Perceived prestige of an i4i grant, which facilitated contacts with stakeholders.
  - o I4i Secretariat support and panel suggestions (e.g. advice to move from a paper-based to an electronic patient wellbeing diary).
- *Key challenges*:
  - o Difficulty in engaging an industry collaborator to identity commercialisation strategies going forward at this early product development stage.
  - o Though not explicitly mentioned as a challenge, IP protection and commercialisation ambitions can present challenges to dissemination and the awareness-raising efforts of a project.

- *Next steps*: Develop a close-to-market fully integrated prototype; define a more detailed commercialisation strategy and pathway.
- *Messages for i4i:* According to one interviewee, it would be useful for i4i to help funded projects by providing access to networking and showcase events bringing together grant recipients and broader stakeholders (e.g. the NHS, industry, patient groups and policymakers).
- *Other:* The team conducted an economic evaluation to establish an estimate of the reimbursement potential for the COPD sensor, as basis for dialogue with commissioners at a later stage.

4.1.1. Background and context

Health innovation challenge

With 44 million cases globally, COPD is the second most common cause of chronic disability and the fourth most common cause of death worldwide. [44] In Britain, over 30,000 people die from COPD each year, one of the highest COPD death rates in Europe.[45] Patients have frequent exacerbations, which severely impair their lung function, leading to inability to work, additional GP visits and emergency hospital admissions. COPD exacerbation episodes remain the second greatest cause of emergency hospital admissions in Britain. One in three of those patients discharged are re-admitted within three months, making it a very costly illness for the NHS.[46][47]

Early diagnosis and treatment of exacerbations can reduce their severity and limit lung damage, yet often treatment is delayed because early 'worsening of symptoms' goes unrecognised. Despite attempts to find suitable technologies to identify exacerbations, none seems to have proved practical for near-patient testing.[48] Therefore there is a need for a non-invasive sensitive monitor that allows patients to assess their condition at home, help spot exacerbations early and initiate prompt treatment.

The COPD biosensor monitor project we discuss in this case study aims to fill this gap. The project was fully funded by i4i. The project team received £552,129 over 33 months. The project ran from 1 April 2012 to 31 December 2014. The team consisted of a clinical and laboratory-based component, conducted at the University Hospital of North Staffordshire (UHNS), and a technological (assay and platform) component, developed at the Institute of Bio-Sensing Technology, University of the West of England (UWE).

Below we discuss the evolution of the project in more detail, drawing on evidence from two main sources. First, we conducted three semi-structured interviews with three members of the project team. Second, we consulted the project documentation made available to the case study team by the i4i, namely: the application form, highlight reports, milestones reports and project completion report.

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[44] British Thoracic Society (2006)

[45] Wouters (2003)

[46] Calverley (2003)

[47] Price (2003)

[48] Celli & MacNee (2004); Jones & Augusti (2006); Cazzola et al. (2008); Holz (2005); Kharitonov & Barnes (2006).

Project goal

The COPD biosensor project aimed to develop an early-stage prototype device to detect COPD exacerbations at point of care based on saliva samples. As a point-of-care device, once developed, the COPD biosensor should have two key distinctive features from patients' point of view: convenience and fast results. With the COPD biosensor, patients should be able to test for COPD exacerbations in their home environment, using a simple saliva sample. Moreover, patients should be able to read the test results in less than five minutes. The clinical usefulness of the COPD biosensor was also taken into account: once developed, the device should combine saliva biomarker results with patients' health scores recorded via a user-friendly electronic wellbeing diary mobile application (app). This technology should facilitate patient–clinician interaction and would enhance the quality of the data reported.

According to the three interviewees, with this i4i-funded project the project team was able to move the COPD biosensor from proof of concept to the early prototype stage.

4.1.2. Developing the innovation idea and prospect

Origin of idea behind the project

The COPD biosensor project built on earlier clinical findings showing two key things. First, like blood, saliva also has levels of three biomarkers[49] associated with COPD inflammation and infection. Second, patients considered saliva a more acceptable bio-sample for everyday home monitoring as compared to blood tests or sputum. These findings stemmed largely from a previous one-year feasibility study conducted by a research team led by the same PI. This first study ended in September 2010 and was also fully funded by i4i.

The project team felt that applying to i4i for follow-on funding was a natural choice as the i4i programme funds early-stage innovation and as such was a good fit with the focus of the follow-on project (i.e. for R&D moving from proof of concept to prototype). Additionally, the project team felt that the prestige associated with i4i funding would facilitate necessary interactions with clinicians, patients, patient groups and regulatory bodies, which were seen to be critical for the success of this project.

Developing the proposal

The proposal was a joint effort between a team of clinical researchers at the UHNS, whose leader was the PI in this project, and a team of biochemists and electronic engineers at the Institute of Bio-Sensing Technology, UWE, whose leader was co-applicant in this project. The team at UHNS had a long track record in researching biomarkers in saliva. The team at UWE had invented a technology to measure biomarkers known as the magnetic immune affinity (MIA) detection technique,[50] although not specifically intended for saliva.

The two teams realised that their complementary expertise would be ideal for moving the COPD biosensor from proof of concept to the prototype stage and worked together to apply for i4i funding. The

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[49] The three biomarkers are C-reactive protein, procalcitonin and neutrophil elastase.
[50] Department of Health (2011); National Institute of Clinical Excellence (2010).

PI's team at UHNS contributed in the form of the clinical problem, access to patients and access to data from prior trials. The team at UWE contributed in the form of the technology to develop the prototype device.

Initially the application included a budget of £481,021 with a time frame of 30 months. During the application review process the i4i Secretariat suggested the inclusion of an additional piece of research to demonstrate that the MIA technology had the required sensitivity to measure the three biomarkers of interest at levels present in saliva. Consequently, the budget was increased to £552,129 and the duration of the grant to 33 months.

As a result of the comments received from i4i panel members during the application review process, the team amended the original proposal to include initial assay sensitivity experiments as well as development and production of an electronic wellbeing diary app (as opposed to the paper format proposed initially).

4.1.3. Implementing the project

Key factors in project evolution

One of the first steps in this project was the development and validation of the MIA technique to measure the levels of the three biomarkers of interest in human saliva, as well as benchmarking it against conventional and modified ELISA assays. The assays were then used in a longitudinal clinical study involving 60 COPD patients. The longitudinal study demonstrated that saliva had measurable and reproducible levels of the three biomarkers of interest. It also showed that saliva biomarkers' levels varied depending on the severity of COPD inflammation and infection and, as such, saliva biomarker measurement could predict COPD exacerbations.

Next, the project team incorporated the validated saliva biomarker assays into a detection system tailored to saliva biomarker measurement. This technology built on that previously developed by the project team at UWE. The next stage was the development of an early-stage prototype magnetometer device incorporating the saliva biomarker measurement technology. The resulting product was an early-stage prototype of size 13x8x6 cm, fully compatible with a hand-held biomarker sensor for point of care and able to measure biomarkers in a small sample of saliva (200 microlitres) in less than five minutes. The development of the prototype benefited from valuable insights regarding the desired design and operability features of a saliva-based point-of-care device, which were gathered via focus groups with patient and healthcare professionals. These focus groups involved about 40 patients from several patient groups (e.g. the British Lung Foundation, Breathe Easy and Macmillan support groups), as well as representatives from the Research User Group and Arthritis Research UK Centre.

Another work stream in this project focused on the development of an electronic wellbeing diary mobile app to register saliva biomarker results and simple patient-derived health scores. Through focus groups, patients and healthcare professionals were also actively involved in testing successive versions of the wellbeing app and their feedback was crucial to refining it; the app is now available from the Apple store.

Alongside these developments, the project team also conducted a study mapping the regulatory approval pathway that the COPD biosensor will have to follow as it moves along the development pathway. This

exercise involved a consultation with regulatory bodies facilitated by regulatory experts collaborating with the project team.

The project team also conducted a preliminary economic evaluation of the COPD biosensor, which provided an initial estimate of the reimbursement potential for the product. The purpose of this model was to create a basis for discussions with commissioners and the National Institute for Health and Care Excellence (NICE) in a later stage of the development process. As such, the model was developed with the flexibility to accommodate different values for the key parameters, as evidence about the technology, health benefits and health costs accumulates. The development of the economic model involved consultation with healthcare professionals, National Health Service (NHS) managers and commissioners to obtain across-sector perceptions on clinical device costs, implementation routes and potential barriers for adoption. This consultation was facilitated by experts in health economics collaborating with the project team.

Key enablers and challenges to the project

Enablers

According to the project team,[51] the evolution of the COPD biosensor from proof of concept to prototype was enabled by the following key factors:

- The early feasibility study, which not only clearly identified the clinical problem but also established the levels of expertise that would be necessary to move from proof of concept to first prototype: '*The feasibility study was very useful because it was there that we determined the skills and expertise that we would need to bring together for this project…*'.[52]
- A multidisciplinary team with leading experts in their fields and with complementary skills. The team involved clinicians, biochemists, engineers, software developers, data analysts, regulatory experts and health economists: '*We were absolutely lucky with the first-class team we put together*'.[53]
- Regular communication among the members of the teams based in UHNS and UWE through both face-to-face meetings (at UHNS and UWE) and across-site interactions through teleconferences, technical and steering committee meetings. The three interviewees confirmed that there was also an excellent working relationship at the ground level between the UWE laboratories and the UHNS clinical and laboratory facilities.
- Availability of a nearly ready-to-use technology (the MIA technology) to build upon to develop a point-of-care device able to measure biomarkers in saliva within a few minutes.
- Access to patients' saliva samples to test the technology. These saliva samples were obtained from the group of 60 COPD patients involved in the longitudinal study:[54] '*We developed a novel technology that had been proved in other areas and applied it into saliva. What was very useful [to*

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[51] This was confirmed by the three interviewees.

[52] Interview 2

[53] Interview 2

[54] According to the project's official documentation, the patients involved in the longitudinal study gave their consent for their saliva samples to be used to test the technology.

validate the technology] was the fact that we could compare the [saliva biomarker] measurements done with the technology with the measurements done in hospital for the same patients...'.[55]

- Access to patients to engage with, mainly through focus groups. This engagement was key to test the electronic wellbeing diary mobile app, as well as to gain insights on the features the COPD would have to have to be a truly hand-held point-of-care device.

- The work developed by the team to understand the regulatory framework upfront, which helped to focus the development of the technology since the beginning of the project.

- Perceived prestige associated with the i4i grant, which facilitated contacts with clinicians, patient groups and other stockholders consulted during the project.

- i4i Secretariat support and suggestions at all stages of the project (see below).

Challenges

According to the interviewees, there was difficulty in engaging an industry collaborator to identity commercialisation strategies going forward at this early product development stage. However, the i4i Secretariat advised on possible commercial strategies going forward, which were appropriate for that stage of the project. There were no other significant challenges reported to the case study team which the project team had not been able to address.

The role of i4i in the project

According to the three interviewees, the support received from the i4i Secretariat, starting with the application review (as discussed above) and throughout the process was crucial for project progress. The i4i Secretariat team had a diversified background, was always supportive, and provided constructive and valuable feedback on both technology development and commercialisation strategies going forward. As illustrated by one interviewee: '*I was very impressed by the support i4i gave us; we had questions about what i4i wanted around the commercialisation plan and they got back to us on that. ...They came to all board meetings and were very positive and gave good suggestions were it was required....*'[56]

4.1.4. Outputs and impact from the i4i-funded work

Product development

As a result of the i4i funding, the project team moved the COPD sensor from proof of concept to the prototype stage by achieving the following three main outputs:

- Completed a longitudinal community-based study involving 60 patients to clearly establish that the three saliva biomarkers of interest could be used as earlier predictors of COPD exacerbations.

- Developed a functional prototype of a point-of-care biomarker sensor able to detect COPD exacerbations based on a small sample of saliva and within five minutes.

[55] Interview 1
[56] Interview 1

- Developed a mobile application (app) to generate an electronic wellbeing diary, which combines saliva biomarker results with patients' health scores. This app was tested and refined via focus groups involving 40 COPD patients and healthcare professionals. In the future, the amalgamation of health scores and biomarkers at the patient level will be used to develop better predictive algorithms for COPD exacerbations.

Commercialisation

Most of the commercialisation progress made to date had to do with securing IP protection for key project outputs. This is not surprising given the relatively early stage of development of the biosensor. Specifically, UHNS was granted a US patent on the saliva biomarkers during the project, and filed for a similar patent in Europe and Canada. UHNS also filed for a patent for the saliva sampler design in the UK. Also, UHNS secured copyrights on the electronic wellbeing diary mobile app in both Europe and the US. UWE filed for patents on the saliva-based COPD sensor in Europe and in the US.

According to the three interviewees, progress with securing IP is a crucial step for establishing a future commercial strategy.

Dissemination

The teams at both UHNS and UWE were cautious in disseminating their outputs to avoid releasing their IP and jeopardising future commercial initiatives. As such, the dissemination activities around the COPD biosensor project were limited and targeted two main audiences: academics and patients. Healthcare professionals were also targeted.

Dissemination to academic audiences was limited to presentations of overall findings at academic conferences, as well as publication of key findings in academic journals (e.g. publication of [1] the patients' experience with the mobile wellbeing app and [2] the utility of salivary biomarkers and correlation to wellbeing scores in COPD management in open-access journals).

Dissemination among patients (and healthcare professionals) happened primarily via focus group engagement and as part of the project.

Interaction with policymakers

According to the interviewees, interaction with policymakers was largely confined to engagement with regulatory bodies facilitated by regulatory experts. The purpose of this consultation was to map out the regulatory requirements that such a device would have to comply with, should it enter the next stages of the development pathway.

In addition, the project team also consulted with healthcare professionals, National Health Service (NHS) managers and commissioners to obtain across-sector perceptions on clinical device costs, implementation routes and potential barriers for adoption. This consultation was facilitated by experts on health economics. The outcome of this consultation was a top-level economic evaluation of the COPD biosensor, which provided an initial estimate of its reimbursement potential. The purpose of the economic model was to provide a basis for discussions with commissioners and the National Institute for Health and Care Excellence (NICE) in a later stage of the development process. As such, the model was

developed with the flexibility to accommodate different values for the key parameters, as evidence about the technology, health benefits and health costs accumulates.

4.1.5. Further developments, next steps and future prospects

- The project team is now seeking follow-on funding to refine the prototype and proceed towards the commercialisation stage. They submitted a follow-on application to i4i in June 2014 but had not received notification of the final outcome at the time of interview.[57] If successful,[58] the further funding will be used over a period of 30 months to:
- Develop a close-to-market fully integrated prototype. This will be a hand-held COPD sensor suitable for home use and inclusive of: (1) disposables (e.g. saliva collector and assay cartridge to measure the three biomarkers) and (2) the electronic wellbeing diary mobile app.
- Run a pilot study with patients to inform further refinements and validate the close-to-market prototype.
- Define an appropriated commercialisation strategy and route to market.
- Prepare a dossier for regulatory approval.

4.1.6. On reflection

The COPD biosensor project is an interesting example of how i4i funding supports innovations in earlier prototype stages, particularly those combining early clinical studies and instrument development. The project team realised the aims and objectives they set at the beginning of the project, and it hopes to take the biosensor to market with further financial support and with appropriate commercialisation partners. The technical and business advice and flexibility of the i4i Secretariat throughout the project were widely valued by the team and helped maintain focus on overall goals and objectives.[59] With the benefit of hindsight, one interviewee[60] mentioned that the project team would have welcomed i4i-initiated networking and showcase events, which could bring together other grant recipients and broader stakeholders (e.g. the NHS, industry, patient groups and policymakers). According to this interviewee, such events could present an excellent opportunity for i4i funding recipients to learn from each other and share experiences, within commercial confidentiality constraints. They could also present a forum for project teams to establish downstream commercialisation and uptake partners and to proactively get feedback on their early-stage innovations.

Finally, it is worth bearing in mind that the findings reflected in this case study are not without methodological limitations. In particular, the insights we obtained stem largely from interested parties and an independent audit of the data is outside the scope of this evaluation. Nevertheless, we believe that we

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[59] This was confirmed by the three interviewees. One example of this is the suggestion made by the i4i panel members in the application stage about replacing the paper-based wellbeing diary by an electronic wellbeing diary to be filled in via a mobile application.

[60] Interview 2

established a candid rapport with interviewees. We also aimed to triangulate evidence by combining data from the interviews with formal project-related documents.[61] Finally, we looked into peer-reviewed papers supporting some of the findings of this case study, when available and applicable.[62]

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[61] These included: application form, highlight reports, milestones reports and project completion report.

[62] These are cited throughout the case study.

4.2. A low-cost non-invasive visual aid for severely sight-impaired individuals

Key messages

- *Key outputs and achievements:*
  - The i4i contract allowed the project team to develop a visual aid that could significantly improve the quality of life for sight-impaired people. The project moved from a very early prototype to a prototype that is nearly ready for market.
  - After the i4i contract, the team won a Google Impact Challenge of £500,000 to collect further data from a take-home trial to support the final phase towards commercialisation.
- *Key enablers:*
  - Early consultation with patients helped the project team better understand patient needs and how they relate to product design and function aspects, across different areas of application and patient segments.
  - Flexibility within the i4i contract allowed the team to make modifications to the original research plan that contributed to the rapid development of the device.
  - According to the PI, substantial media attention helped enable fundraising efforts.
  - Co-location of the key team members facilitated establishment of the team as well as interactions throughout the project.
- *Key challenges:*
  - Staff resources; more specifically a lack of capacity at the start of the project hindered initial progress at the desired pace. With additional resources from i4i, this was resolved by hiring an additional team member to manage patient trials.
  - Clinical time was not costed, which limited clinical collaborator ability to contribute to the extent they may have desired.
  - Ensuring realistic patient expectations – though not reported as a formal challenge – was identified as a potential risk area needing careful management, so as not to create false expectations about product availability and health potential.
- *Next steps:*
  - On the basis of the data collected through the take-home trial, and with the support of investors, the team will aim to launch a spin-out company.
- *Other points to note:*
  - The project focused as much on the technological aspects of the overall product that was being developed as on the design and user-experience aspects. The team saw both to be important for overall product uptake. As a result, the process of innovation involved substantial consultation with potential users.
  - Estimates of staffing and costing of clinical staff can be hard to provide upfront, and may be an area to which i4i can pay more explicit attention at the proposal stage.
  - The NHS is not seen as the primary channel of distribution as the NHS at present has limited access to assistive technologies and new healthcare developments with resource implications would need assessment by NICE.. i4i may wish to consider how it can support innovative health projects targeting different types of procurement and distribution channels.

4.2.1. Background and context

Health innovation challenge

The UK currently is home to 1.8 million people with impaired vision of whom 360,000 are severely sight impaired.[63] Despite research efforts, cures for the conditions causing sight impairment, such as age-related macular degeneration, diabetic retinopathy and glaucoma, are not expected in the short term. This means that sight impairment will continue to impact on daily life by restricting travel, mobility and by limiting work opportunities. As a result, individuals with sight impairment can suffer from depression and isolation, causing substantial personal and economic costs.[64] It was noted in the application form that a cane or a guide dog are the only real assistive technologies or aids available today for such individuals.

Project goal

A team of researchers and clinicians based at the Department of Clinical Neuroscience at Oxford University and the Oxford Eye Hospital set out to develop a low-cost, non-invasive visual aid to address the gap in innovative solutions, which could improve the quality of life for severely sight-impaired individuals. The device aims to help such individuals regain a degree of independence, vision and mobility. The project focused on user-friendly design with the product resembling a pair of spectacles. The spectacles are fitted with various sensors to aid mobility and navigation, and with a display that can be 'read' by sight impaired individuals to observe objects.

The project started in October 2012 and after a two-month extension it was completed in November 2014. It built on an earlier NIHR-funded feasibility study in which a first prototype was developed. The team at Oxford used the i4i contract (that is the subject of this case study) to further develop the visual aid prototype into a model that is nearly ready for market. The first prototype of the device, developed in the NIHR-funded feasibility study, was based on the knowledge that '90% of registered blind people have some light perception'.[65] By engaging the remaining light perception of sight-impaired individuals, the study focused on the development of a prototype that would enhance their perception of objects. The success in the design of a working prototype in the feasibility study was the starting point of the current grant in which the prototype was further developed. Further development was necessary because, as stated by the PI, the original prototype was a 'clunky proof of principle'.[66] For the device to be ready to be worn by individuals on a day-to-day basis, additional work was required, currently being conducted in the take-home trials. Product development became the central focus of the project, but in a broader sense than just technical development. Based on work conducted in the feasibility study, the project also focused on the 'emotional component' of the device, that is, the experience of the device by the wearer. The PI noted that the challenge for this kind of innovation is to develop a device that provides all the required functionalities but also engages the wearer. According to the PI, the problem with innovations is often that the technology already exists, and then an application is sought for it. This frequently results in

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[63] National Institute for Health Research (2015b).
[64] National Institute for Health Research (2015b).
[65] National Institute for Health Research (2015b).
[66] Interview 1.

devices that are not user friendly. The aim of the project was to focus on the needs of the individual with sight impairment, and how the device should feel and what would be useful to them, and from there to work towards a device that would function on a day to day basis.[67]

While the team has received several awards over the duration of the grant, one of which was from the Royal Society, around 90 per cent of funding came from i4i.

This case study draws on the project's application form to i4i and the progress reports completed over its course. In addition, in total three semi-structured interviews were conducted, with the PI and two collaborators.

4.2.2. Developing the innovation idea and prospect

Origin of idea behind the project

The idea behind the device was developed by the PI and began with his PhD research in neuroscience, in which he studied spatial awareness and spatial memory in guinea pigs. More specifically, the PI became interested in applications in neuroscience, and especially how you can interface a human and a machine. After his PhD, the PI arrived at Oxford where he continued his research on applications. The best version of an interface that he could find was retinal implants, and he worked on improving the effectiveness of such implants. However, by the end of this project, and following various conversations with clinicians, the PI and his colleagues realised that wearable displays are potentially a much better way to improve the vision of many more people. This led him to the field of 'enhanced vision' - that is the study of how to improve the vision and perception of sight-impaired individuals, and gave rise to the idea behind the i4i project.[68]

Developing the proposal

The PI became aware of i4i as a potential funding source following a conversation with a colleague at a conference.[69] According to the PI, i4i's programme focus on medical applications made it a very suitable funder to apply to, as it allowed for rapid product development. Apart from i4i, an application was simultaneously made to the Wellcome Trust Translation Fund. By the time the Wellcome Trust application had got through the first round, the PI already received notice of success with the application to i4i, and did not further pursue the Wellcome Trust application.[70]

The project team was built through existing connections and was labelled by one of the members as a 'happy coincidence'. The PI and the first co-applicant are housed in the same building as the Oxford Eye Hospital, in which the second co-applicant works. The close proximity facilitated the links. The project team has also worked closely with the Royal National Institute of Blind People (RNIB), with which links were established when the RNIB approached the PI following media attention regarding the prototype.

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[67] Interview 1.
[68] Interview 1.
[69] Previously, he had not heard of i4i, but the entire field was new to him.
[70] Interview 1.

The application was largely prepared by the PI, with support from the co-applicants on patient ethics and patient groups and on technical and engineering aspects. At the proposal stage no other possible collaborators, such as charities or industry, provided input and no further consultations were made with the NHS or NHS procurement bodies. A co-applicant noted, however, that it would have been too early to have met with NHS procurement bodies. Through her years of experience in the Eye Hospital she already knows what is available in the NHS today and from being involved in the care of individuals with sight impairment what might be helpful. To conclude the application stage, the PI presented to the i4i panel. However, the PI observes that no feedback was received from the panel, nor were any modifications made to either the project plan or the methodology.[71]

4.2.3. Implementing the project

Key factors in project evolution

The project had three types of milestones, all of which were reached over the course of the project:

1. Technological: relating to the technological development of the device such as the display and the portable computer.
2. Software-associated: milestones relating to the development of software that can be incorporated into the device to provide assistance with 'wayfinding' and using public transport.[72]
3. Patient/participant milestones relating to the testing and trialling of the technological and software aspects of the device, including tests such as 'controlled real-world navigation' and 'public transport assistance'.

Key enablers and challenges to the project

No research project proceeds without hurdles and the evolution of this project was affected by a number challenges. Equally, many features of the project's design enabled the innovation journey.

Enablers

First, the three interviewees stated that the project was able to move forward rapidly by making changes to the original plan, which were possible due to the flexibility of the i4i grant.[73] As the device integrates various new and emerging technologies, the PI emphasised that the flexibility that the i4i programme allowed was useful in enabling the team to experiment with and follow new ideas, as they arose. Some of the changes to original plans that the team made included outsourcing of particular elements of the device and the move of the 'real-world navigation' trial from facilities in London to a facility built by the team in Oxford. This was useful as it allowed the team to tailor the testing facility to the needs of product development.[74]

Second, access to a large number of patients created the opportunity to collect feedback on product design and testing throughout the project. Spending substantial amounts of time with patients helped to discover

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[71] Interview 1.
[72] Wayfinding is the technical term used by the PI (Interview 1).
[73] Interviews 1, 2 and 3.
[74] Interview 1.

what the main issues that they found important were, and helped the project team explore a range of prototypes. Through early tests, for example, the team was able to develop a focusable display (i.e. it can zoom in and out) that participants liked.[75] Still, in hindsight, the team members noted that it would have been good to have worked with even more patients at the start of the project to get a more objective understanding of the type of device that would work for *different types* of patients. Only through engaging with a lot of patients did the team realise that the device might actually work for a much larger group of visually impaired individuals than initially anticipated. This could have been realised sooner through earlier interaction with more patients.[76]

In addition, substantial media exposure during the life of the project helped attract attention and the engagement of patients and patient groups, such as the RNIB. According to the PI, both the media attention itself and the engagement of recognised patient groups could be seen as proxies for wider 'impact', as they helped secure follow-on funding from other sources. Finally, a collaborator mentioned that a key enabler for any project to be a success is an intelligent and committed PI, who pulls the project forward.

Challenges

Apart from expected technological hurdles around, for example, the development of the display, and the administrative duty to complete progress reports, no other major challenges were reported by the project team.[77] Despite not receiving explicit mention, analysis of project evolution suggests that staff capacity may have presented a challenge at some points, and that the capacity needs may not have been fully foreseen during the application phase.[78] According to one interviewee, it may be helpful for experts on the i4i panel to assess applications for realistic staffing estimates.[79]

A co-applicant also made the suggestion that future applications should consider explicitly costing clinical staff time. Clinical staff time was not recognised as a cost on the project, which can make it more difficult for them to provide desired levels of input.[80]

Finally, a co-applicant commented on the management of patient expectations that is required with the development of a new device. He observed that it was important for the researchers to explain to patients that the device would not be a 'magic thing' and that full development could still take a few years. Furthermore, to make patients feel comfortable with the tests, the team explicitly assured them that the trials would not test them or their sight, but rather were a test of the device.[81]

The role of i4i in the project

The team reported that interactions with the i4i Secretariat were largely confined to the reports on progress. No feedback was provided after the presentation of the application to the panel and no changes

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[75] Interview 1.
[76] Interviews 1, 2 and 3.
[77] Interviews 1, 2 and 3.
[78] Interview 1.
[79] Interview 1.
[80] Interview 2.
[81] Interview 3.

were made to either the budget or proposal. A breakfast for grantees organised by i4i in 2013 was seen as useful by the PI as it enabled meetings with venture capitalists and angel investors. Although it did not directly result in funding, it did create an understanding and awareness of how to pitch a product and how to make the device into a sellable proposition. It therefore proved a good learning experience on the road to commercialisation.

4.2.4. Outputs and impact from the i4i funded work

Product development

In line with expectations, the i4i grant was a significant help in moving the device forward, and along the way all milestones were reached. The PI observed that at the end of the project the device was '12 months short of a product that we could sell', which was their expected end point.[82] The device developed from a 'clunky proof of principle' to an advanced prototype that has been tested in multiple settings with various purposes. Furthermore, as the i4i grant enabled the development of the prototype it also put the team into a position to generate further funding for the final steps towards commercialisation. The team was able to secure a prestigious Google Impact Challenge award for £500,000, as well as funding from a private investor to get the device ready for market.

During the project, the team also commissioned a study to estimate the market size for the visual aid. As this was very light touch study that did not yield a large amount of information, the PI said the team would not do it again.[83] Within the Google Impact Challenge however, a large-scale health economics study is being undertaken to gather data that will support the business case.

Commercialisation

Commercialisation has been a central focus of the project. The team had considered establishing a spin-out company but this was delayed to focus on product development in house for somewhat longer than originally anticipated. Using the additional user experience data gathered through the Google Impact Challenge and with the backing of an investor, the current plan is to launch the spin-out company at the end of 2015.

The next step would be to distribute the device through a number of channels, primarily online, for example through the RNIB website, and through high street retailers. The NHS is not seen as the primary channel of distribution as the NHS does not usually provide assistive technologies. This does not mean, however, that the NHS cannot still play a role in the uptake of the device. A co-applicant suggested that references to the device by NHS clinicians, for example, could increase the uptake, but in order for clinicians to be convinced of the benefit, they would require evidence of how the device works for different types of patients. The data collected under the Google Impact Challenge aims to provide just that kind of data.

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[82] Interview 1.
[83] Interview 1.

Dissemination

Apart from the usual channels of dissemination for research, such as journal publications and conference presentations, the project has received quite substantial attention in the media. Mainstream media such as the BBC and the *Guardian* have covered the development and progress of the device and have given it substantial positive coverage. More recently, the Google Impact Challenge helped to generate media attention. Finally, the RNIB has given substantial support and attention to the project and has thereby created access to the primary target group. There have been interactions with charities and interested specialists over the course of the project, but there has not been any systematic consultation with policymakers.

4.2.5. Further developments, next steps and future prospects

The next step will be to use the Google Impact Challenge to conduct a large-scale trial of the device with users in the UK. Through take-home trials the team will explore how the device works in the real world, and how it could be useful for patients with different types of sight impairment. The data gathered through this trial will provide the final input to get the device market ready. In addition, a thorough market forecast study will be conducted to assess the market and estimate the number of potential users. This will form the core of the business case that will be used to raise funds to put the device into production.

The PI observed that i4i could provide further support by providing access to contacts (e.g. investors) and by giving advice (e.g. about NHS procurement channels). However, it was also observed by a co-applicant that the project team had been relatively well connected and was able to make use of local support systems to deal with any problems (e.g. IP arrangements). As such there was no direct need for further support from i4i, but it was recognised by the co-applicant that not all grantees would be in a similar situation and that for some i4i contracts additional support could be valuable.

While the NHS will not be the primary channel through which it is planned to distribute the device, a co-applicant stated that there are several conditions that will need to be fulfilled in order for the device to be considered for NHS procurement. First, proof is needed that the device is helpful and useful. Patients will need to be able to wear it and it will need to be cost effective. Second, a study should show that patients actually benefit from it. These conditions need to be fulfilled before it can be launched on a commercial scale.

4.2.6. On reflection

Through i4i funding, the project made substantial progress in the development of a prototype visual aid which has the potential to improve the quality of life and independence of severely sight-impaired individuals. Progress to date was enabled both by i4i funding itself, and by the funding stream's flexibility. Rapid product development was made possible by the flexibility within the funding that allowed for changes to the original plan. Perhaps unusually for the i4i programme, the main distribution channel envisioned for the device is not the NHS. As the device will be an assistive technology, the team expects online sales and high street opticians to be the primary sales channels. This constitutes a route to market that is quite different from most medical devices. It is likely that some unique challenges will be

encountered on this route to market (e.g. contacting high street opticians), which has implications for the types of commercialisation and wider business support the innovators may need.

The next steps of the project are getting the prototype ready for commercial production. According to the PI, data gathered through the take-home trial funded by the Google Impact Challenge will provide the final information required. Over the next year, the team expects to launch a spin-out company that can commercially produce the visual aids.

4.3. Next-generation mobile HIV diagnostics with wireless connectivity

Key messages

- *Key achievements and outputs*: The project aimed to address the need for more widely available, accurate and fast HIV testing outside a hospital setting and focused on developing a prototype for a wirelessly connected HIV diagnostic device. Its key achievements were:
  - o Development of an initial proof of concept (during the proposal phase).
  - o Development of a pre-market prototype of a portable device.
  - o Associated microchips and the coatings for the detection of HIV antibodies.
  - o The project tested the device in a small-scale clinical pilot.
  - o The team also developed an exploitation plan and a roadmap for the next stages of the work.
- The team achieved the milestones and overall objectives of the i4i-funded project, which helped to attract further support from the EPSRC (an £11 million grant) to further investigate the engineering and physical science research challenges and wireless connectivity aspects of diagnostic devices. It is important to note that this funding does not support product development.
- *Key enablers*:
  - o Team members brought complementary skills and expertise from a wide range of backgrounds (e.g. clinical research, chemistry, technology management).
  - o Strong and committed leadership made successful cooperation possible between a large and diverse group.
  - o The industry partner's openness to sharing detailed information on the technology development process facilitated effective academic-industry cooperation by providing an extended evidence base to the development of chemical compounds used in the device.
  - o A series of site visits with stakeholders enabled the team to understand the needs of the prospective users of the diagnostic device and to integrate these into product development.
- *Key challenges*:
  - o Developing the technology and the chemical compounds in parallel: design changes to either of these resulted in setbacks to the clinical validation phase.
  - o Potential future challenge to uptake: current regulation requires extensive counselling for patients diagnosed with HIV, which can limit the uptake of a HIV device of this nature.
- *Other points to note*:
  - o The project has conducted no formal health economics analysis to date, and did not incorporate regulatory, procurement or pricing considerations into the design. Affordability of the device is one of the explicit priorities of the project, so this may be an area for future attention.
  - o The partners were ready to proceed with the project in the absence of i4i funding, but the scope of the work would have been compromised. It may be interesting to reflect on the role of matched public-private financing arrangements in which i4i could participate in the future, where there is willingness from industry to invest in the same areas supported by i4i.
- *Next steps*: Finalising the development of the prototype and starting the regulatory approval process.
- *Messages for i4i*: i4i could consider ways to support funded projects in identifying suitable follow-on funders for their innovations in development.

4.3.1. Background and context

The health and innovation challenge

It is estimated that in 2015 110,000 people in the UK are living with HIV, but that more than a quarter are unaware of their infection.[84] This has serious consequences for the individual because needed treatment can be delayed. It also raises the risks of spreading the infection, particularly during the early acute stage of infection.[85] While hospitals have very well-functioning tests, this is often not true for point-of-care services.[86] Pilot studies have shown that widening access to testing is key to reaching sections of the population who would not normally encounter HIV testing through traditional services.[87] Moreover, studies have shown that – in typical populations around the world – up to a third of tested individuals do not wait or do not return for their test results.[88] Along with a growing global interest in rapid HIV testing, developing an easy-access point-of-care test is in line with recent policy developments in the UK, such as the recommendation from the Department of Health to overturn the ban on self-testing for HIV in 2014 and the recommendation of the House of Lords Select Committee on widening access to HIV testing.[89]

Project goal

The project aimed to develop an innovative HIV diagnostic tool. More specifically, the team aimed to develop a prototype mobile phone connected device to rapidly diagnose HIV, based on multiplexed antibody-antigen detection, with inbuilt wireless connectivity, which works similarly to a pregnancy test (testing a drop of blood with a chip).[90] i4i was the sole funder of the project and supported the team with £820,937 over two years. The lead partner was University College London (UCL) where the PI was affiliated with the UCL London Centre for Nanotechnology, with OJ-Bio as co-applicant. OJ-Bio is a biotechnology SME that was formed as a joint venture between a Newcastle University spin-out company, Orla Protein Technologies Ltd., and Japan Radio Company. The partners were located in London and Newcastle respectively. The work was supported by staff exchanges and regular site visits as well as conference calls.

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[84] National AIDS Trust (2012).

[85] Application form; Interview 3.

[86] Interview 3.

[87] Project final report p.8.

[88] Project exploitation plan (confidential). See, e.g., Holt (2009).

[89] Project final report p.8, Holt (2009).

[90] In the proposed technology, the silicon microchip is coated with proteins that capture HIV markers in a finger prick of blood. These markers are constituted by antigens (the viral particles that elicit a response from the patient's immune system) and antibodies (proteins that aim at the elimination of a specific antigen). The testing is "multiplex", as it is able to test for multiple agents (antibodies and antigens) simultaneously. The project had seven sub-objectives: (i) to develop a prototype low cost portable device; (ii) to develop a system for multiplexed antibody-antigen detection; (iii) a diagnostic that could provide rapid results within 30 minutes; (iv) sensitive detection (pg/ml); (v) specific detection with extremely low risk of false positives/negatives; (vi) a simple user interface; and (vii) ability to transmit results to a server. Source: project application.

During the 24 months of the work funded by i4i, the project developed the diagnostic tool from a preliminary proof of concept to a pre-market prototype. This included a small-scale pilot testing phase in a clinical setting.[91]

Below we discuss the evolution of the project in more detail, drawing on evidence from two main sources. First, we conducted three semi-structured interviews with (1) the principal investigator (PI), (2) the co-applicant from the industry partner and (2) a co-applicant with a background in surface chemistry. Second, we consulted the project documentation made available to the case study team by the i4i, namely: the application form, highlight reports, milestones reports and project final report.

4.3.2. Developing the innovation idea and prospect

Origins of the idea behind the project

Prior to forming the consortium, the partners had already completed work on the technology and chemical compounds that were later incorporated in the diagnostic device. UCL had done previous work in identifying lead capture antibody coatings to detect multiple HIV markers, as part of a preceding £2 million EPSRC Grand Challenge grant. OJ-Bio had patented technology for the development and large-scale manufacture of surface acoustic wave (SAW) devices and had published on the topic. The company planned to grow their business and saw opportunity in the application of the technology in HIV diagnostics and devices.[92]

The co-applicant from OJ-Bio was introduced to the work of the PI and her research group at UCL at a Nano KTN knowledge exchange event in 2011. The two leads had identified synergies between the expertise, goals and objectives of their respective organisations. Based on these synergies, they were actively searching for an opportunity to collaborate. According to one interviewee, '*We decided to try and find a way to work together, our technology and [The PI's] work in the HIV area… the i4i call was a perfect occasion to try and establish cooperation*'.[93] The partners were enthusiastic about the potential for collaboration and were ready to pursue the work even in the absence of i4i funding. However, according to an interviewee, this would have meant a reduction in the scale of cooperation. A co-applicant noted that i4i funding was particularly attractive due to the growth opportunity it offered by '*the particular focus on the healthcare needs of the NHS. We felt that we had the opportunity to drive our platform and technology forward in that particular application area*'.[94]

Developing the proposal

The bid was academically led by the UCL research team, with the co-applicant (OJ-Bio) leading work packages related to the technical development of sensors. The team had already developed a preliminary proof of concept during the proposal stage. This included the completion of a feasibility study to

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[91] The project took place between 1 January 2013 and 31 December 2014.
[92] Application p.28.
[93] Interview 1.
[94] Interview 1.

demonstrate the detection of model HIV antibody-antigens in buffer.[95] Furthermore, the partners set up a joint studentship to support work on the diagnostic tool in April 2012. In the words of the PI: '*This was one of the nicest collaborations that we've had. …Despite this being the first time that we've worked together, quite early on we were able to do some early concept work in the process of developing the proposal. We were pretty sure that we were going to work together and we got a joint studentship, co-funded by OJ-Bio and the UCL impact award*'.[96]

The team involved patient representative groups in the proposal development process, which helped to include an end user perspective in the design considerations. However, there was no consultation with NHS procurement bodies to inform potential market strategy.[97] The project team did not perform a formal health economics assessment at the proposal stage either, but received informal consultations and drew on pre-existent health economics assessments. As recalled by one interviewee, '*…A lot of work in the area has been done by NICE and the Health Protection Agency (now Public Health England) showing a very clear health economic benefit for widening access to HIV testing. We were able to use this data in the proposal and exploitation plan. We have had informal discussions with health economists and in the next stage of development will invest in a more detailed health economic evaluation of our technology in collaboration with the Imperial NIHR DEC which specialises in point-of-care tests*'.[98]

Once the bid was shortlisted, the team presented it to a panel. According to the PI, feedback from the panel focused on some minor aspects of the work plan (such as the sample matrices applied) and on project management. The feedback panel also suggested taking the phrase 'wireless connectivity' out of the title of the project as it was seen not to be a core aim of the project (the core aim being the development of the diagnostic tool itself and not the mechanisms through which it connects to the health system). However, the project team challenged this as they saw the device's ability to transmit information to healthcare systems as crucial added value as opposed to a non-connected diagnostic device.[99]

4.3.3. Implementing the project

Key factors in project evolution

The project focused on three streams of development work: developing the device; the microchips; and the chemical elements (coatings used to detect specific HIV antibodies in blood samples). An initial proof of concept was developed during the proposal stage. This was refined in successive work packages to develop a prototype with adequate connectivity and diagnostic capabilities. The microchips and capture coatings were tested for their detection abilities. The outcomes of these tests were benchmarked to competing technologies and original project targets. Subsequently, the team performed a small-scale pilot study of 35 patient samples in partnership with the University College London Hospital diagnostic laboratory, to examine the incidence of false positives and false negatives in the diagnostics performed by

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[95] Application p.28.
[96] Interview 3.
[97] Interview 1.
[98] Interview 3.
[99] Interview 2.

the prototype device. Finally, the team developed an exploitation plan and a roadmap for the next stages of the work.

The interviewees felt that the approach and methodologies applied to their project worked well overall. The collaboration also led to a series of unforeseen positive consequences, which are discussed below. For example, UCL networks with leading clinicians, researchers and policymakers in the HIV prevention space facilitated outreach activities. These were important to raise the profile of the project and offered opportunities for the further development and clinical testing of the device. With one member of the original research team being appointed as a Director the Wellcome Trust Africa Centre for Health and Population Studies in South Africa, the PI recognised that this link could open up future opportunities to evaluate the technology in the heart of the HIV pandemic.[100] The industry partner recognised that access to this network was of great value to the company and would have likely not happened without the project.[101]

During the lifetime of the project, in 2014 the Department of Health announced proposals to overturn the ban on self-testing for HIV in the UK. This is a major change in the policy and market context for the project, as no diagnostic tests are currently approved for home use in the UK. Such changes raise the need for devices with wireless connectivity, as these can ensure that diagnostic data is shared with the public health system. Therefore, the diagnostic device can support patients in accessing care while providing the public health system with relevant information.[102] This policy development could make the market proposition for the device in development more attractive, as it could stimulate demand for accurate and low-cost connected diagnostic devices. The team plans to focus on regulatory approval and the wider procurement and pricing environment in a subsequent stage of product development.[103]

Key enablers and challenges to the project

Enablers

According to the project team, key enablers of project progress included:

- Academic and policy networks: more specifically, the extended network of the PI, which helped the project gain visibility. The network also facilitated access to clinicians and end-user representatives, along with patient advocates, which was important in providing insights for product development.
- Regulatory changes in self-testing policy (discussed above) implied further gains in visibility for the project. Furthermore, regulatory support for home and point-of-care testing would expand market opportunities for the device in development.
- The multidisciplinary skill set of the team, which included clinicians, along with researchers specialised in chemistry and virology, and partners with expertise in technology development. Interviewees considered the expertise of all the researchers and partners involved in the project

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[100] Project final report p.24, Interview 3.
[101] Interview 1.
[102] Project final report p.24.
[103] Interview 1.

crucial to its success. In addition to the PhD studentship, the project team also engaged three funded post-doctoral research associates.[104] OJ-Bio increased the number of their full-time employees in the UK from 4 to 7 during the lifetime of the project.

- One co-applicant also highlighted the strong and professional leadership of the team, which made it possible for a large group from varying backgrounds to work efficiently together and maintain the focus of the project.[105]

- The PI highlighted the contribution of the stakeholders that worked with them as fundamental enablers, despite the early stage of the project. They included epidemiologists and clinicians along with patient organisations and advocacy groups. Through a series of site visits with these stakeholders, the research team were offered the possibility of understanding the needs of the prospective users of the diagnostic device in different settings, such as patients and clinical professionals.[106]

- A transparent and open approach to technology development from the industry partners also contributed to the success of the project. Some details are often withheld in industry-clinical collaborations, creating difficulties in the design of components, for example. As the industry partner made all information on the progress of the technology available to the clinical team, the two teams were able to co-ordinate and streamline their work processes.[107]

Challenges

Although the project documentation refers to some difficulties in staff recruitment, which were overcome in the first quarter of the project, these were not reported as key challenges by interviewees.[108] The interviews highlighted the following challenges:

- Some technical complexity resulted from the necessity of balancing rapidity of the diagnosis with accuracy, but according to interviewees, this was mitigated during the project without causing delays in delivery of planned objectives.[109]

- Interviewees also described challenges resulting from the early stage of the innovation: as the work was simultaneously ongoing on the chip development and the chemistry, design changes to either of these resulted in setbacks to the clinical validation phase. However, the interviewees felt that these challenges also represented a learning opportunity for the planning and management of future projects. [110]

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[104] Project final report p.7.
[105] Interview 2.
[106] Interview PI, Project final report p.6.
[107] Interview 2.
[108] Project first quarter report.
[109] Interview 2.
[110] Interview 1.

The role of i4i in the project

The interviewees considered interactions with the i4i Secretariat during the project to be helpful and constructive, 'without being overbearing'.[111] At the same time, one of them felt that reporting duties took considerable effort, especially at the beginning of the project.[112] The main areas of support received from the Secretariat had to do with IP arrangements, as well as advice related to strengthening patient engagement and health economic analysis.[113] Team members were appreciative of site visits from i4i as well as being invited to dissemination events with policymakers and were '*very pleased with how the i4i project helped raise [our] visibility and the overall impact of our work*'.[114] In reflecting on further support needed, a co-applicant drew out the importance of facilitating connections between projects and appropriate follow-on funding instruments. '*There is a whole bunch of organisations supporting this work, but it isn't always easy to work out which funding instrument is right for you to continue the work, given the current point of arrival of your project – you can be too early or too late stage. It would be really important if [i4i] could give advice on what funding tools would be appropriate for follow-up work.*'[115]

According to one interviewee, the i4i program has evolved and matured significantly over time, especially in the way it facilitates the participation of companies in projects.[116] However, it was felt that the main role for i4i in reaching the goals of the project remains that of a funding instrument that takes the interest of UK society and British industry into account and offers related infrastructure, such as device evaluation communities.[117]

4.3.4. Outputs and impact from the i4i funded work

Product development

During the period funded by i4i, the project began, tested and finalised the developed of a pre-market prototype for a mobile HIV diagnostic device. Furthermore, the team conducted a preliminary clinical validation with clinical samples of HIV-infected sera of 31 anonymised HIV-positive individuals and four healthy volunteer donors.[118]

In order to continue work on the device, the project team developed and submitted a bid for follow-up funding with i4i, which would cover the further development of the device and the activities needed for regulatory approval of the device. At the time of writing of the present case study in April 2015, the outcome of this bid was not known.

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[111] Quote: Interview 1.
[112] Interviews 2, 3.
[113] Interview 3.
[114] Interviews 1, 3.
[115] Interview 2.
[116] Interview 1.
[117] Interview 1.
[118] Project final report, p.21.

Commercialisation

Commercialisation activities reflected the early stage of the project itself. The partners concluded an IP agreement among themselves regarding ownership of IP resulting from work on the project, and developed an exploitation plan.[119] The team also considered filing patent applications for certain components of the diagnostic device in the early stages of the project, but subsequently decided not to do so, given the high costs and significant amount of time involved in the application.[120] IP issues will also be considered as part of a future commercialisation strategy. The team also continually reviews the IP landscape, downstream regulatory and market access opportunities. As part of this review exercise, the team identified potential partners and stakeholders for the next stages of commercial development.[121] OJ-Bio, together with UCL and UCLH, have continued collaboration: they expressed an interest in taking the product forward to the next stages of commercial development. The industry partner plans to lead this stage of the work.[122]

Productive working relationships between the core partners also helped give rise to new ideas which in turn drove applications for additional and related funding. According to one interviewee, '*There were ideas that triggered other thoughts and we managed to take some ideas forward beyond the [i4i] project*'.[123] A consortium (also including partners not involved in the project object of this case study) led by the project lead won one of the largest EPSRC contracts ever awarded: an £11 million EPSRC Interdisciplinary Research Collaboration (IRC) in Early Warning Sensing Systems for Infectious Diseases. This major funding programme is a direct follow on from the NIHR i4i award and funds basic engineering and physical sciences research to complement translation work funded by NIHR.[124]

Dissemination

A team member noted that the i4i Secretariat was instrumental in '*raising the visibility and the overall impact of the work*'.[125] The work was widely disseminated in academic settings as well as trade shows and received substantive coverage in mainstream media, including the *BMJ* and *Huffington Post*.[126] However, although the interviewees thought that media visibility contributed to the career progression of the members of the study team, we do not have evidence of the specific effect of the media exposure.[127] The project partners also interacted with patient representatives and patient groups, such as the Bloomsbury user group and a HIV treatment activist group (i-Base).[128] Furthermore, three scientific publications were in progress in connection with the project at the time of writing of this case study.

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[119] Project exploitation plan (confidential).
[120] Interviews 1, 2.
[121] Project final report, p.24.
[122] Interview 1.
[123] Interview 3.
[124] Project final report p.24, Interview 3; It is important to note that this award does not support product development and OJ-Bio, although affiliated, is not receiving funds under it.
[125] Interview 3.
[126] Project final report p.32.
[127] Interview 1.
[128] Project exploitation plan.

Interaction with policymakers

Interviewees highlighted the early opportunities that were facilitated by i4i for briefing the project to policymakers at i4i events, including the Chief Medical Officer, the House of Commons and senior NHS leadership.[129] The work also benefitted from previously built networks of the PI with patient engagement groups and the clinical community. Furthermore, one of the members of the original project team moved to a more policy-oriented position during the lifetime of the project (to the Wellcome Trust Africa Centre for Health and Population Studies in South Africa), further expanding the linkages of the project team with the policy community.

4.3.5. Further developments, next steps and future prospects

Following the completion of the project at the end of 2014, the team has submitted a product development award proposal to i4i for the continuation of the work. This stage would be industry-led (as opposed to the first project, led by UCL) and would focus on developing the pre-commercial prototype into a product that would be fit for being approved through regulatory approval processes. The team envisioned the involvement of additional partners to facilitate regulatory approval, such as the NIHR Diagnostic Evaluation Co-operatives. This work would also include the further testing of the prototypes in clinical samples. Depending on the timeline of this award, the work on further development would start approximately in September to October 2015 and aim to develop a product ready for regulatory approval (but likely not be available in the market) within two years.[130]

4.3.6. On reflection

The project team delivered on core planned milestones. Although the work had encountered some initial technical challenges during the parallel development of the technological and chemical components, these were resolved during the planned timeframe. Overall, the team is very confident about the market and development potential for the device.

Despite the early stage of product development, the project has already received attention from policymakers and the media. The work was also topical in light of HIV policy developments in the UK, which may have contributed to media interest and facilitated dissemination. The connected HIV diagnostic device has the potential to support the objectives of UK HIV healthcare policy and to help address an important public health challenge.

The team interviewed for this case study appeared to be very driven and committed to their project. However, beyond the availability of the device, the team saw a cultural shift towards the 'normalisation' of HIV testing as one of the needed steps to mainstream uptake of the diagnostic device in the NHS. This would mean circumventing the requirement for extensive counselling around testing and making it routine, similarly to antenatal testing.[131] At present, this represents a substantial potential barrier to widespread uptake.

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[129] Interviews 1, 3.
[130] Interview 1.
[131] Project final report p.30.

PI and co-applicants emphasised the value added through the support of the i4i Secretariat throughout the project. This was particularly notable in terms of i4i enabling and incentivising connections between industry and clinical researchers. The industry partner drew out the fact that that the project funded by i4i aligned well with their strategic intentions to move into the HIV diagnostics market. They were also ready to proceed with the project in the absence of i4i funding, although they admitted that the scope of the work would have been compromised. Therefore, it may be interesting to reflect on the potential role of matched public private financing arrangements in which i4i could participate in the future in areas where there is a clear interest for industry and an ability to co-fund development.

Health economics evaluations (relative to the actual device, beyond the overall value of early HIV diagnostics), regulatory and procurement considerations did not appear to be a priority at the design phase of the device. These may be aspects that become more prominent as the product development progresses further.

Finally, it is worth bearing in mind that the findings reflected in this case study are not without methodological limitations. In particular, the insights we obtained stem largely from interested parties and an independent audit of the data is outside the scope of this evaluation. Nevertheless, we believe that we established a candid rapport with interviewees. We also aimed to triangulate evidence by combining data from the interviews with formal project-related documents.[132]

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[132] Application form, project milestone reports, project exploitation plan and project final report.

4.4. Head Up: a cervical orthosis for people with motor neuron disease

Key messages

- *Key outputs and achievements*: The project aimed to develop a supportive neck collar for patients with motor neuron disease (MND). With i4i support, the project team established a prototype and performed an early clinical evaluation of a small set of devices, manufactured in-house
- *Key enablers*:
  - The involvement of patient groups enabled recruitment of patients for testing, input into product design, feedback and adaptations in design. Related to this, a patient association was included as a co-applicant on the project.
  - i4i was seen a flexible and approachable funder. Personal relationships and approachability made it possible for the project team to deal with unforeseen developments during the lifetime of the project. These included delays in finding a manufacturing partner and the consequent need to apply for CE marking in house (as opposed to relying on a partner for this).
- *Key challenges:*
  - An initial, conservative costing of the project – tailored partially around innovators' perceptions of 'funding ceilings' in the i4i programme – created challenges for project delivery. This resulted in the team contributing significant resources to the work beyond the funding.
  - The project team originally underestimated the amount of evidence from prototype testing that would be necessary to construct a business case that would be attractive to potential licensed manufacturing partners, which complicated efforts to find such a partner.
- *Next steps:*
  - The project has received an extension from i4i to support further testing and to assist with finding a manufacturing partner.
- *Other points to note:*
  - The need for a novel cervical orthosis was identified by end users – this was a demand-driven innovation project.
  - The project team conducted a health economics assessment and developed initial design concepts during the application phase. This helped address reviewer concerns from an initially rejected bid.
  - The team that worked on the Head Up project has continued to collaborate on other initiatives, such as preparing another NIHR grant application in a different area of work.
  - A project team member suggested that i4i should consider seed funding for preparatory work at proposal stages.
  - According to the interviewees, the most effective outreach method towards the MND community was a YouTube video produced by the team, in which a patient with MND described her experience with the collar. This received 1057 hits.

4.4.1. Background and context

Health innovation challenge

Motor neuron disease (MND) is the third most common neurodegenerative disease, with an annual incidence of 2 in 100,000 and prevalence of 5–7 per 100,000.[133] Approximately 5,000 people in the UK and 400,000 globally have MND.[134] Patients with MND experience increasing weakness affecting the limb muscles, neck muscles, muscles of speech and swallowing, and muscles of breathing.[135] Current practice and guidelines recommend the use of cervical orthoses to compensate for the weakness and provide surrogate head control.[136] The collar models currently in use all have shortcomings: either they provide little support, lack lateral support, or overly restrict functional movement. Furthermore, they can cause pain, discomfort, skin breakdown, social embarrassment and can present a communication barrier as patients are unable to look at the people they are talking to.[137] Consequently patients are left with a choice, either to use no orthosis or to accept the restriction and side effects of a sub-optimal orthosis.[138]

Project goal

The overall goal of the project was to develop a fit-for-purpose cervical orthosis for people with MND. More specifically, the project aimed to progress an innovative device from a preliminary design concept to a tested and evaluated prototype that can be manufactured by a licensed commercial partner.[139] The project hoped to complete the design and production of a prototype, as well as small-scale testing with patients during the lifetime of the i4i contract. The majority of the work took place over a 28-month period with £402,202 in funding from i4i.[140,141] The project team also received a one-year extension and an additional 10 per cent supplement in funding supported by i4i, to enable further testing of the prototype device.[142] The team was led by the University of Sheffield with the PI based in the Department of Neuroscience. The co-applicants were based at Devices for Dignity (D4D) at Sheffield Teaching Hospitals NHS Trust and the Art and Design Research Centre at Sheffield Hallam University. The team also included a member of the MND Association. The work took place at the University of Sheffield, Sheffield Teaching Hospitals NHS Trust and Sheffield Hallam University.

Below we discuss the evolution of the project in more detail, drawing on evidence from two main sources. First, we conducted three semi-structured interviews with (1) the principal investigator (PI), (2) a co-applicant with a background in assistive technology, and (3) the co-applicant who headed the design team. Second, we consulted the project documentation made available to the case study team by the i4i, namely the application form, highlight reports, milestones reports and project final report.

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[133] Mcdermott & Shaw (2008).

[134] NHS (2012).

[135] EFNS Task Force on Diagnosis and Management of Amyotrophic Lateral Sclerosis (2005); Miller et al. (2009).

[136] Motor Neurone Disease Association (2014); Thumbikat et al. (2006).

[137] Project application; Interview 3

[138] II-ES-0511-21003 Primary Form Application (henceforth: 'Original application'), Background section.

[139] Interviews 1, 2, 3.

[140] Final report. Final project costs are confidential and have been redacted from the documentation provided to RAND.

[141] Final report field 2, from 1 April 2012 to 31 July 2014.

[142] Interviews 1, 2, 3.

4.4.2. Developing the innovation idea and prospect

Origins of the idea behind the project

The need for a novel cervical orthosis was identified directly by users and carers.[143] The development of a new neck collar was initially proposed by the Dementias and Neurodegenerative Diseases Research Network (DeNDRoN) Clinical Studies Group for MND, with support from carers and patients, who approached co-applicant D4D with the view that current cervical orthoses are inadequate in terms of function, comfort and aesthetics.[144] The idea of a novel collar was further explored in a two-day innovation workshop with patients and device designers, where multiple innovative ideas were considered. Following this workshop, D4D became convinced that the idea was worth developing further.[145] D4D also acted as the catalyst which put the members of the team (all based in Sheffield but at different institutions) in contact.

Developing the proposal

The proposal team was led by the PI (a clinician) at the University of Sheffield Institute for Translational Neuroscience. Each member of the consortium was responsible for the parts of the proposal which were relevant to their expertise: Sheffield Hallam University (SHU) for the design portions and the commercial/regulatory experts working with D4D for the intellectual property and commercialisation aspects. The Sheffield Teaching Hospitals NHS Trust team also designed the part of the proposal describing the testing phase of the product, based on their expertise with clinical trials.[146] Patient groups were central to the development of the proposal and the project itself. A Research Advisory patient group commented on the proposal and continued to meet once a month during the life of the project offering input.

The team felt that i4i funding would be a good fit for their focus on early stages of product development. The team was aware of the i4i funding programme due to prior experience of it the University of Sheffield.[147] They had also applied to the Medical Research Council (MRC) and Technology Strategy Board (TSB) development schemes, but these applications were rejected as the plans for the device were considered to be at a too early stage of development for funding by these bodies.[148] The team's initial proposal to i4i was also rejected on the grounds of being at too early a stage and reviewers felt that the project team had not made a sufficient product design case. Following this feedback, the team invested six additional months into gathering the necessary evidence on the relevance and feasibility of the device to address reviewer concerns. The team was also extended to include the design team from SHU (in the

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[143] Application field 6.
[144] Application field 6.
[145] Interviews 1, 2.
[146] Interviews 1, 3.
[147] People in the project team and in the wider institution.
[148] Interview 3.

rejected proposal, design would have been outsourced to an independent agency). Preliminary design concepts and health economics assessment were completed during the application phase.[149]

The proposal team costed the project using a bottom-up approach based on the activities foreseen by the project team and i4i expectations. However, all interviewees agreed that the costing was not completely realistic, as the team was trying to avoid prejudice to the application by quoting too high a price. According to the PI and the co-applicants: '*We had an expectation that the usual i4i project would be 2–3 years and we did the costing and time based on that. Time constraints were more significant than money. However, we also underestimated patent costs therefore we ran out of [funding for that work].*'[150] '*We originally applied for about 400k contribution, but we all ended up putting in an in-kind contribution over and above that amount.*'[151]

The i4i Secretariat notified the applicants that they were shortlisted soon after submission of the bid and provided reviewer comments on the application. The project team then attended an interview and presentation to a panel. According to interviewees, this was challenging but also reflected a thorough engagement of the i4i Secretariat with their applications. According to all interviewees, the presentation was 5–10 minutes and '*…was intimidating. There were twenty-odd people around a table staring at the three of us. It was intimidating but it also felt that they were examining the proposal quite thoroughly.*'[152] The team addressed feedback on further developing some of the commercialisation and business case aspects of the proposal prior to the approval of the grant.

4.4.3. Implementing the project

Key factors in project evolution

During the implementation phase, the team developed the design concepts for the neck collar into a prototype.[153] They had originally also planned to find a manufacturing partner to whom the production and distribution of the collars could be licensed. The design phase of the project (during the proposal phase) contributed to enriching the knowledge base on devices for patients with MND. This involved testing the existing neck collars with 30 volunteers.[154] The concept development stage during the project implementation furthered work on the initial design concept and resulted in the construction of high-fidelity prototypes, able to replicate details and functionality of the final product (a further step in the design process than low-fidelity prototypes aiming to capture the central design concept but not offering details). These prototypes were developed through five successive design iterations incorporating feedback from experts and user group volunteers in five workshops with each (10 workshops total), and were

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[149] The assessment looked at the likely cost effectiveness of the collar in the context of the improvements of the quality of life of MND patients. Based on NICE cost effectiveness thresholds, the analysis suggested that the impact on quality of life would be so apparent with an effective cervical orthosis, that this new product may be considered cost effective even at an annual incremental cost of £1000 per patient. This analysis was performed by a health economist within the School of Health and Related Research (ScHARR), and was funded through a prior arrangement with D4D. See also: Latimer et al. (2011).

[150] Interview 3.

[151] Interview 1.

[152] Interview 2.

[153] Original application, Abstract.

[154] Project final report p.9.

manufactured in-house.[155] In the clinical evaluation work package, 20 patients tested the new prototype and provided feedback through standardised forms. The team has received an extension of funding for further testing from i4i and D4D. The ongoing extension, approximately 10 per cent of the value of the current project, will see the testing of the product with 100 additional patients.[156]

Overall, interviewees found the design and methods used to be appropriate for purposes of the project. They emphasised the importance of patient interaction in achieving fit-for-purpose product design. SHU worked with a member of the MND Association and the Research Advisory Board to engage the MND patient community in all iterations of product design. Working closely with patients also linked the research team with the wider MND community comprising carers and clinicians. .

The interviewees all highlighted that high levels of interest and involvement from patients and their families all over the world led to confidence in the commercial case for the product they were developing, by recognising demand that could go beyond that from health systems. As a result, the team intended to investigate commercialisation of the collar both through national health systems and as an over-the-counter product. This high level of interest also meant that the team could rely on the community for recruiting patients to test the prototypes and gather input and feedback during the design process.[157] In the words of a co-applicant: '*We had great access to patients through the MND society – opposed to a scenario where we would have had to look for participants, we actually had to say no to patients*'.[158] The research also included an economic analysis, which took into account the cost-efficiency of the collar for NHS resources and underpinned the design of the device.[159]

Two team members also saw the multidisciplinary approach to the project (where medical and design colleagues routinely worked together) as important for ensuring an appropriate final design.[160] However, one interviewee also emphasised that team members needed to learn how to communicate better across disciplines, which sometimes had differences in their vocabularies and cultures.[161]

Key enablers and challenges to the project

Enablers

According to interviewees, key enablers of progress with the innovation included:

- Patient interactions and engagement with product design (as highlighted above).
- The skill set and expertise of the research team: this included the involvement of design team colleagues all along the project, but also the expertise of D4D and SHU in the regulatory aspects of medical device development.[162]

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[155] Project final report p.9.
[156] Interview 2.
[157] Interviews 1, 3.
[158] Interview 1.
[159] Project final report p.11.
[160] Interview 3.
[161] Interview 2.
[162] Interview 1.

- A committed and focused team with a 'can do' attitude: The team working on the Head Up project has continued to collaborate in further ventures, such as preparing an NIHR grant application.[163] As the PI commented: '*The right skill set amongst team members [was an enabler], but also the attitude and the approach to things which we all had despite never having worked together, which was motivated by helping patients with MND – we worked really well as a team*'.[164]

Challenges

Interviews with the project team as well as project documentation highlighted the following challenges:

- Some of the challenges encountered by the project were due to the timeframes included in the original planning. The team attempted to be as cost-efficient as possible at the costing phase, to improve their chances of a successful bid. However, this meant that certain stages of the design process were not covered in the original planning. As a result, the team had to put in time from their own resources, e.g. to allow for the incorporation of feedback from the design workshops with patients.[165]
- Challenges emerged at the final stages of the project as well, most notably regarding the identification of a commercial and manufacturing partner. As one interviewee commented, '*We were trying to be as lean as possible to maximise our chances of winning the proposal. However, in doing so, we probably compromised the quality of the evidence [on] effectiveness and commercial viability that we were able to gain during the bulk of the project.*'[166] Due to the limited evidence underpinning the business case (gained from the testing of the prototypes with 20 patients), the team did not succeed in finding a commercial/manufacturing partner during the course of the project. An extension phase was necessary.
- The project encountered difficulties in the patent application in terms of the establishment of non-existence of prior art. The team is currently planning on re-submitting an application with a different legal counsel.[167]
- Filing for conformity marking for the European Economic Area (CE marking certification) was a notable challenge. The original project plan had foreseen the certification to be conducted by the commercial partner, but the difficulties in finding an adequate partner meant that the team had to rely on the expertise of the in-house medical engineering team of the Sheffield Teaching Hospitals NHS Trust, who have the qualifications to file for CE marking.[168] Although this arrangement allowed the work to proceed in the absence of a commercial partner, the time and costs involved turned out to be greater than anticipated, and were an in-kind contribution of the team.[169]

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[163] Interview 3.
[164] Interview 3.
[165] Interview 2.
[166] Interview 2.
[167] Interview 2.
[168] It was felt that going to any single potential commercial manufacturer for regulatory processes might jeopardise the project team's position with other potential partners. See Project final report p.10.
[169] Interviews 1, 2, 3.

- One interviewee highlighted the challenges represented by a perceived lack of transparency in the NHS procurement environment. More specifically, this referred to a lack of clarity about the best practices for certain kinds of devices to follow in order to better respond to NHS procurement priorities.[170]

The role of i4i in the project

Generally, all interviewees were appreciative of the support received from the i4i Secretariat, in particular feedback on the commercialisation strategy and the need to develop additional evidence.[171] They expressed a particularly positive view of the informal responsiveness of the i4i Secretariat to e-mails and the close interest that the Secretariat took in the progress of the project. According to one interviewee, i4i took a '*pragmatically light touch on the oversight of the project: they were there when needed but didn't pressure us for reporting*'.[172] A co-applicant noted that site visits by i4i enabled informal discussions and updates on how the project was progressing. The leadership of i4i of the program had an important role in facilitating these relationships.[173] According to the interviewees, personal relationships and approachability made it possible to deal flexibly with unforeseen developments during the lifetime of the project, e.g. with regards to CE marking and an extension received to support manufacturing.[174] One of them suggested that participating in networking events involving i4i projects funded in the same round would have been a further useful resource in mutual learning about the challenges of project implementation.[175]

4.4.4. Outputs and impact from the i4i-funded work

Product development

The main outputs from the activities of the project linked to product development consisted of a fully developed prototype and a completed clinical evaluation of a small number of prototype devices, which were manufactured in-house. These represented most of the functionalities and details planned for the final design intended for industrial production. Furthermore, the project contributed to an enriched evidence base on currently available devices and the needs of the patient community.

Commercialisation

The project team developed an exploitation strategy 12 months before the end of the project.[176] This involved the certification of the collar as a CE-marked device for the clinical evaluation phase, as well as applying for international and UK patent protection. The IP applications originally applied for were rejected on the grounds of prior art and the team is planning re-submission at the time of writing.[177]

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[170] Interview 2.
[171] Interview 1.
[172] Interview 2.
[173] Interviews 1, 3.
[174] Interviews 2, 3.
[175] Interview 2.
[176] Project final report p.9.
[177] Interview 2.

The original project plan included the identification of a commercial and manufacturing partner within the lifetime of the project. Therefore, the team contacted a number of companies with UK manufacturing bases and a significant international orthotic business. Following the completion of the clinical evaluation phase, a brochure was compiled detailing the main aspects of the project of relevance to companies in negotiating a licensing deal.[178] However, to date, the team has not negotiated a licensing deal with any of the manufacturers that had been approached. These steps have been shifted to the extension phase of the project.

Dissemination

Members of the team have disseminated information about the project through presentations at UK and pan-European MND symposia, an MND conference in Australia and an academic publication in an engineering journal. However, according to the interviewees, the most effective outreach method towards the MND community was a YouTube video produced by the team, in which a patient with MND describes her experience with the collar.[179] The video has received 1,057 hits at the time of writing and has contributed to extending the reach of the project to the global MND patient community.[180] The team has not had interactions with policymakers.

4.4.5. Further developments, next steps and future prospects

The team has secured an extension to the project funded by i4i and D4D. With this extension, they will produce 100 collars for further clinical testing at four sites across the UK. It is hoped that this will create scope for gathering further evidence and insight from patients on the clinical effectiveness of the collar. The supporting evidence is planned to further build the business case for a licensing agreement with the manufacturing partner producing the sample batch.[181] The project team is also working on further developing the business case for patients with conditions other than MND, but involving muscle weakness.

In terms of uptake in the NHS and other health systems, the interviews drew attention to the particularly dynamic and close-knit nature of the MND patient community and the healthcare professionals working with them as a potential enabler. However, the practical implications of this attitude for the marketing of the device are yet to be seen. Although tentative, the PI and co-applicant were confident that the patient demand and feedback from professionals would likely create a sufficient pull factor to influence health systems towards adopting the collar.[182]

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[178] Final report, p.17.
[179] Interview 1.
[180] Interview 1.
[181] Indicatively, the timelines estimate the production of the 100 additional collars to be concluded within May or June 2015. Results from the trial will be collected by the end of 2015 and in ideal conditions, production to market could start as early as 2016. Interview 2.
[182] Interviews 2, 3.

4.4.6. On reflection

The Head Up team set out to tackle an important health need for patients with MND, which has the potential to improve the quality of life for these patients and their carers. Despite some financial hurdles and challenges with IP and the identification of manufacturing partners, the Head Up project achieved several key outcomes during the timeframe of this ambitious project, and currently has a prototype ready for manufacturing.

Support and a flexible approach from the i4i Secretariat were considered key enablers of the work.

The interviews conducted for the case study also shed light on some of the potentially unintended consequences of the application process and perceived funding limits. As the applicants were keen to obtain funding for their project and were somewhat conservative in their costings, they ended up committing significant resources of their own. One co-applicant suggested that some milestone-based, responsive funding could enhance the commercial sustainability of projects and help to support the commercial viability of the products in development. Similarly, seed funding at proposal phases could help with scoping the landscape and identifying levels of financial support more accurately.[183]

The team remains committed to the initiative and confident about the market potential of the finalised device, and continues to work on addressing the challenges of finding a viable route to market for the collar.

Finally, it is worth bearing in mind that the findings reflected in this case study are not without methodological limitations. In particular, the insights we obtained stem largely from interested parties and an independent audit of the data is outside the scope of this evaluation. Nevertheless, we believe that we established a candid rapport with interviewees. We also aimed to triangulate evidence by combining data from the interviews with formal project-related documents.[184]

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[183] Interview 2.
[184] Application form, project milestone reports, project exploitation plan and project final report.

5. Discussion and recommendations

5.1. On reflection: key findings

As outlined earlier in this report, the i4i product development programme aims to support the development of innovative healthcare technologies and the translation of promising innovations into practice, with patient benefit as the ultimate goal. It seeks to achieve this through the guided progression of early-stage innovations (e.g. proof of concept and prototypes) and the provision of business advice. i4i is seen as a unique funder of early-stage innovation in the medical devices, implantable devices, in-vitro diagnostics and medical technologies space.

Evaluation evidence suggests that the programme is enabling bottlenecks in early-stage innovation finance to be tackled and is supporting projects with diverse starting points – ranging from pre-proof of concept to (less frequently) a completed prototype. The paths travelled by individual projects also vary, with some, for example, moving from pre-proof of concept to a completed prototype, others starting at proof of concept phase and reaching readiness for clinical testing, and some projects entering the programme to develop prototypes and progressing to conduct early phase clinical testing as part of the funded project. Direct comparisons between projects are not possible due to differences in size, duration and scientific and technological focus areas.

Findings from the survey and interviews point to i4i support being particularly valuable in bridging the 'valley of death' and helping medical technology innovators reach a position where they can attract funding for further downstream development and commercialisation. The i4i Secretariat was also seen to be delivering on its oversight roles and providing helpful advice to projects through regular meetings and on an as-needed basis.

There are a number of areas for policy consideration that emerge from the evaluation evidence. These relate to programme design, the role of the Secretariat in facilitating impact and knowledge management. We first present the recommendations and areas for action that have emerged from our analyses, and then supplement this with additional points for consideration that were specifically suggested by either survey respondents or interviewees.

5.2. Recommendations for the future of the programme

The recommendations below focus on actions which could help maximise i4i programme impacts, drawing on insights provided across our evaluation:

Programme design

1. **Consider introducing a responsive review mechanism for projects, as a way of managing financial risk but maximising continuity in support for promising innovations. It would be important to manage time-lags between the reassessment and continuation of work, to ensure that project momentum and sustainability (e.g. staffing) is not compromised.** In such an approach, the amount of funding awarded and the work protocol could be revised after an initial phase of work, and the funding needs reassessed to enable further product development (for example early clinical testing if a prototype is developed successfully). This could also help minimise the risks of applicants tailoring bids around a *perceived* funding ceiling (despite it not existing in reality since 2010), rather than around product development needs.

2. **Encourage applicants to consider adoption and product design issues at application and selection stages, possibly through the design of funding application forms.** The i4i programme ultimately aims to support the translation of innovations into practice, for patient benefit. Some of the challenges to adoption, including those related to product design, might be foreseeable and mitigated if they are identified in a timely manner, and if potential ways of addressing them are considered. Issues related to product design and usability and financial obstacles to conducting pivotal clinical trials, which are a pre-requisite for uptake, were frequently reported challenges for i4i projects. Barriers related to NHS procurement channels were also widely perceived as an anticipated challenge for longer-term uptake, but there was very little consultation with commissioners by i4i contract recipients – neither during application nor project implementation phases.

3. **Encourage health economics analysis as part of the innovation process for i4i projects.** Health economics analyses are increasingly important for product development and uptake but currently seem to be conducted only in a minority of i4i projects.

4. **Reflect on the mix of academically, industry and clinically led projects in the portfolio and the roles and levels of engagement by different project partners, throughout the duration of projects.** At present, the majority of i4i projects involve cross-sector collaboration, and two thirds (66 per cent) are academically led, followed by industry (18 per cent) and clinically led projects (16 per cent). This may be an appropriate mix, but academically led projects in particular may benefit from active external support in identifying commercialisation and NHS uptake partners.

The role of the Secretariat

5. **Reflect on the scope and scale of business-related guidance and advisory support that the i4i Secretariat can provide.** There are three key areas of additional support which the programme participants we surveyed and interviewed thought would be useful for advancing their project and maximising prospects for impact:

a. **Additional engagement in facilitating networks with industry, clinicians and other stakeholders in the innovation pathway:** i4i may wish to consider scope for funding some early scoping studies into the adoption-related aspects of a project, as these can input into and influence the design of the technical work. Brokering networks was seen as particularly important for product development and uptake, with identifying industry partners reported to be particularly challenging.

b. **Awareness raising and information sharing about the i4i programme:** Raising awareness of i4i and investing in dissemination and publicity was seen as important for enabling investor confidence in the products under development, and the Secretariat may wish to consider roadshows or showcase events. One suggestion was an 'innovator of the year award' to maintain relations with successful applicants and promote i4i.

c. **Providing training in business and entrepreneurship skills:** Some of this training takes place as part of the i4i 'accelerator' programme, but the cost of the programme may be a barrier for potential beneficiaries.

d. **Consider providing more feedback to applicants, including unsuccessful ones, to help improve future bids:** It could also potentially be useful to aggregate information on where common issues are emerging for unsuccessful applicants, which the panel may want to act on to inform guidance and the process of selection for future bids.[185]

Knowledge management and evaluation

6. **Consider how best to track long-term impacts from i4i projects, after the completion of i4i funding.** The i4i programme has placed many of the innovators it has supported in a position to pursue further downstream development. The i4i Secretariat may wish to follow-up on success rates with downstream fundraising, commercialisation and uptake of innovations stemming from the projects it has supported. Some mechanisms to consider might include alumni events, surveys and internal tracking of PI-related information. It may also wish to consider how to evaluate and learn from the experiences of i4i contract recipients on an ongoing basis, to inform adaptations in the programme through time.

7. **Revisit internal management information systems.** The process of conducting this evaluation identified scope for improvement in information management databases and record-keeping within i4i (e.g. updating registers of completed versus ongoing projects, and updating information on the roles of key individuals within projects to ensure accuracy and reflect any changes over time).

5.3. Additional points for consideration – participant suggestions

In addition to the recommendations stemming from the evaluation, individuals we interviewed provided some suggestions related to the future of the programme for consideration by the Secretariat:

8. **Given the absence of a thematic focus in the programme, i4i may wish to reflect on the constitution of the i4i selection panel in the context of the appropriateness of technical**

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[185] Communication with selection panel member.

knowledge for diverse types of applications. There may be ways to engage technical or topic-specific experts on an as-needed basis. A potential risk raised by an interviewee was that there may be areas which are not being funded due to lack of technical skills in these areas amongst the selection panel. One interviewee saw potential value in panel members having a more sustained role during the life of projects. Panel members do not stay involved with projects once they have been funded but could potentially give guidance that would be useful to the project team.

9. **The Secretariat may wish to consider engaging with host institutions around IP issues, to coordinate IP management.** This is because i4i contract recipients are also subject to host institution IP policies. Building relationships and a mutual understanding of the governance cultures of different organisations may address some of the challenges related to IP management

10. **Clarify the relative weighting of different technical, social and commercial criteria in the application and selection guidance,** so that applicants have a clearer picture of expectations for successful bids.

11. **Consider how the i4i programme can most effectively engage with the wider NIHR research infrastructure** (e.g. Biomedical Research Centres, Health Technology Cooperatives).

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Appendix A: Key informant interviews protocol

Introduction

Thank you for participating in this interview.

Introduce the specific project in question, confirming funding size and start/end dates. Make explicit that if at any point they are talking about associated work before or after the i4i project in question, that we kindly ask them to please make that clear in their responses.

Name of project:

Start/end date and duration:

Size of funding:

Questions

Context

1) Can you very briefly tell us what your i4i project was developing/developed and how you came about the idea? (Internal note: keep this very brief, around two minutes)
2) What were the specific aims and objectives of your project? (i.e. What did you hope to achieve through and during the i4i-supported contract?)
3) Did you have any partners/collaborators and were these formal contractual collaborations or less formal arrangements?
4) Why did you apply to i4i specifically for funding (as opposed to some other stream) and how did you hear about the opportunity for i4i funding?

Inputs

5) Did you develop the actual application for funding independently or with a partner(s) and did you consult any stakeholders in your local/regional/national environment during the application process? (Internal note: e.g. did they speak to people in the NHS (e.g. CCGs, Trusts, clinicians), local TTOs, and University Enterprise Offices, industry, patient groups, etc., to inform the proposal/make the case for funding stronger?) If yes, who, why and how was it useful? In not, why not?
6) Did you find the application and selection process useful? If yes, in what ways? If not, why not? Do you think there are any ways it could be improved?
7) Did you get the full amount of funding you applied for? Why did you apply for that specific amount? In reflection, was the amount of funding and duration you applied for appropriate?

Processes

8) What were your interactions with the i4i Secretariat/NIHR like over the life of the project?
9) Would you have benefited from additional types of (non-financial) support or engagement from:
    a. NIHR/i4i
    b. Other/external stakeholders
    If so, what types of advice or additional engagement would you have found useful and why?

10) What type of ownership (ROI) arrangement do you have with NIHR? (Internal note: e.g. equity, royalties, other such as discounted price for NHS procurement of product, share in revenues from licensing or consulting services.) How was that agreed on? Do you think this was an appropriate arrangement?

Outputs, outcomes and impacts

11) What have been some of the key outputs, impacts and/or milestones from your project? For example:
    a. Stage of development of innovation
    b. Attraction of new collaborators [any proof of concept studies ongoing with commercial partners?]
    c. Attraction of downstream developers
    d. New funding for downstream development [If so, how much equity was given away?; if not, explore reasons why something struggled to get funding]
    e. Adoption in clinical setting (explore number and nature of locations and total number of patients treated)
    f. Any insights on patient benefit [e.g. reduced mortality or morbidity, patient experience, etc.] or cost-savings for the NHS or other interventions being avoided
    g. Commercial returns [or licence agreements/revenue share within collaboration]
    h. Reduction of invention-to-market period
    i. Unintended consequences [e.g. spin-off projects, market approvals, NICE guideline changes, IP generated, patents granted]
12) What has enabled them?
13) What have been barriers/challenges to realising your project goals, and why? How did you try to manage these challenges?
14) What do you think would have happened with your project and idea, had it not been for i4i funding/support?
15) What do you expect to happen over the next 1 year, 3 years, and beyond?

Other / in reflection

16) Related to the above and based on your experience:
    a) Is the i4i programme fundamentally different from other funding opportunities for healthcare innovation projects (especially in the devices, diagnostics and surgical implantation space), and how is it or not different? (e.g. WT Health Innovation Challenge Fund/translation awards, UK catapult centres, Small Business Research Initiative (TSB))
    b) Is there any relevant potential learning for how i4i works from other funding initiatives – public especially, but also private sector ones?
17) With the benefit of hindsight, if there was anything you would suggest to the i4i /NIHR Steering Committee for improving any aspect of the programme, what would that be?
18) What were the key lessons for you personally from the entire experience?

Appendix B: Survey

Introduction

RAND Europe, an independent, not-for-profit, public policy research institute has been commissioned by NIHR to undertake an evaluation of the Invention 4 Innovation (i4i) programme. The evaluation aims to examine the outputs and the impacts of the programme in light of its goals, and to learn about associated enablers and challenges. This will help inform the future implementation of the programme. As part of this process, we are conducting a survey of principal investigators and co-applicants on i4i projects. The survey will ask about your experiences of the programme and the outputs and impacts from your i4i-supported project(s). It is an opportunity for you to contribute positively to future programme development, through reflection on expectations and outcomes. There are no 'right' or 'wrong' answers; please respond as you see the programme from your perspective and experience.

Confidentiality and anonymity will be respected throughout this process: all answers will be aggregated into a database for further analysis. It will not be possible to identify individuals in the findings of the study.

More specifically, this survey will ask questions related to: the i4i funding model, application and selection process, outputs and impacts from i4i projects, enablers and barriers to impact and adoption of outputs, and reflections on ways in which the programme could be strengthened looking forward.

This questionnaire should take up to 30 minutes to complete. If you have any questions about the contents of this survey or the wider evaluation, please do not hesitate to contact the RAND team on i4i@rand.org. For technical issues, please contact the NIHR Central Commissioning Facility team on ccf-is@nihr-ccf.org.uk or 020 8843 8038.

Questions

Introduction and background

1. How many i4i contracts have you received to date? [drop down list: 1–5]
2. What is/was the size of your i4i contract? [drop down list: under 100k, 100–500k, over 500k]
3. What is/was the total duration (in months) of your i4i contract? [drop down list: 6, 12, 18, 24]
4. What was the start date of your i4i contract? [Month and year]
5. What role did you play in your i4i contract?
    a. PI

     b.   Collaborator

     c.   Subcontractor

6.   Where do you work most of the time? [single answer]

     a.   Academia

     b.   Clinical practice

     c.   Private sector

7.   Could you indicate whether you are:

     a.   Female

     b.   Male

8.   Which of the following best describes your i4i project? [Single answer]

     a.   Medical device (EU Directive 2007/47/EC)

     b.   Active implantable device (EU Directive 90/385/EEC)

     c.   In vitro diagnostic (EU Directive 98/97/EC)

     d.   Other, please specify [open text box]

Funding

9.   Why did you apply for i4i funding? [Please select your top 2 reasons]

     a.   Good or best fit with my project's aims, goals and objectives

     b.   Perceived likelihood of success

     c.   One of the few funding sources for the type of work the project addresses

     d.   Prestige/kudos associated with i4i

     e.   Other, please specify [open text box]

10.   What do you think would have happened to your project if you had not applied for i4i funding? [Single answer]

     a.   Would have applied for funding from elsewhere

     b.   Would have applied for i4i funding again

     c.   The project would have been abandoned

     d.   Other, please specify [open text box]

11.   [Routing: If selected option 'a' for Question 10 Where would you have applied for further funding? [Please select all that apply]

     a.   WT Health Innovation Challenge Fund

     b.   TSB Small Business Research Initiative

     c.   MRC

     d.   Other charities, please specify [open text box]

     e.   EU funding

     f.   Venture capital, Angel funding

     g.   Other, please specify [open text box]

12.   Did you have any other complementary (as opposed to follow-on) cash funding for your project in addition to the i4i contract?

     a.   Yes

     b.   No

13.   If you answered yes to question 12, who did you receive complementary funding from? [Open text box]

14.   Approximately what percentage of your project did i4i funding support? [Drop-down box with: less than 25%; 25–50%; 50–75%; more than 75%]

Application and selection

15.   During the application stage, did you have to adapt the business plan/application submitted at the beginning of the project or your plans for the use of funds?
        a.   Yes. What elements were changed:
                a.   Research element
                b.   Public and patient involvement
                c.   IP arrangements or commercialization plan
                d.   Testing and trialling
                e.   Other, please specify [open text box]
        b.   No

16.   Did the amount of money that you requested change during the application process?
        a.   Yes, the budget was increased. What was the purpose of the additional funding:
                a.   Expand research element of the project
                b.   Expand patient and public involvement
                c.   Expand/improve IP arrangements or commercialization plan
                d.   Expand testing and trialling
                e.   Other, please specify [open text box]
        b.   Yes, the budget was decreased. What part of the application was limited in the revised budget:
                a.   Research element of the project
                b.   Public and patient involvement
                c.   Provisions to establish IP arrangements or commercialization plan
                d.   Testing and trialling
                e.   Other, please specify [open text box]
        c.   No

The questions in this section exclusively refer to the selection panel presentation and Q&A session.

17.   Did you present your application to a selection panel as part of the application and selection process?
        a.   Yes
        b.   No

[Internal routing note: If answered 'no' skip to Question 20]

18.   Did you receive any of the following feedback from the selection panel?
        a.   Scientific feedback [yes/no] – If yes: was it useful? [yes/no]
        b.   Business feedback [yes/no] – If yes: was it useful? [yes/no]
        c.   Other feedback [yes/no] – If yes: was it useful? [yes/no]
19.   How do you think the feedback be made more useful? [open text box]

Collaborations

20.   Did you consult with any of the following external stakeholders during the application process (Please select all that apply):
        a.   Patients or patient groups
        b.   Charities
        c.   Practicing clinicians
        d.   Academics

     e.   Those responsible for NHS procurement decisions

     f.   Other, please specify [open text box]

21.   Did your project involve collaborations with any of the following? (Please select all that apply)

     a.   Industry

     b.   Clinical partners (including practicing clinicians, health boards, NHS Trusts)

     c.   Academia (including internal and external university collaborations)

     d.   Charities

22.   [For each option ticked in Question 21, ask the question:] Did the collaborators engage in the application process?

     a.   Did not engage in the application process

     b.   Consultation on the subject area

     c.   Providing grant-writing expertise

     d.   Providing advice on IP/commercialization

     e.   Providing a user perspective or PPI

     f.   Other, please specify [open text box]

Commercialisation and intellectual property

23.   Was the IP position presented at the start of the application adjusted in the course of the application and selection process?

     a.   Yes, it has been adjusted during the application process

     b.   No, it has not been adjusted during the application process

24.   [If yes to Question 23] How did interactions with the i4i Secretariat change the IP position? [tick all that apply]

     a.   Introduced/adjusted IP arrangements

     b.   Introduced/adjusted commercialization plan/arrangements

     c.   Changed ownership arrangements

     d.   Other, please specify [open text box]

Running of the project

Role of i4i Secretariat during project

25.   How useful did you find your interactions with the i4i Secretariat to be to further the progress of your project? [Rate 1–4 where 4 is very useful and 1 is not useful at all]

     a.   Progress reports

     b.   Regular project meetings (either face-to-face or via telephone)

     c.   Ad-hoc meetings

     d.   Regular telephone calls

     e.   Ad-hoc telephone calls

26.   How have your interactions with i4i helped to guide the development of your project? [open text box]

Outputs

This section will cover the outputs that have arisen from your project. Please indicate for each of the following outputs if they have arisen, and if so, in what form.

27. Proof of concept (i.e. in early conceptual phases of project only, usually lab-based). Please indicate at which stage of the project this was achieved:
   a. Before i4i funding was received
   b. Start of the project
   c. During the project
   d. The output of the project was a proof of concept
28. Prototype development. Did you further develop a prototype over the duration of the project?
   a. Yes
   b. No
29. Prototype completion (i.e. model or process outline or gadget developed in lab). Please indicate at which stage of the project this was achieved:
   a. Not achieved – prototype not completed during the project
   b. Completed at start of the project
   c. Completed during the project
   d. The output of the project was a prototype
30. Testing or Pivotal Clinical Trial (i.e. preliminary evaluation and testing of the product on small number of patients or clinical settings). Please indicate at which stage of the project this was achieved:
   a. No testing or pivotal clinical trial took place
   b. Start of the project
   c. During the project
   d. The output of the project was the commencement of Testing or a Pivotal Clinical Trial
31. [If yes to 30] Please indicate if you know:
   a. The number of patients/participants involved (e.g. for implantable or medical device) [open text box]
   b. The number of samples tested (e.g. for in vitro testing) [open text box]
   c. How many centres, hospitals, etc. were involved [open text box]
   d. Time period for all data collection for the trial (please do not include analysis nor reporting nor set-up phase) [open text box]

Future product development

32. For the outputs not yet achieved, did your i4i project enable you to develop your product to get it ready to directly conduct any of the following:
   a. Testing or Pivotal Clinical Trial
   b. Large scale Clinical Trial
   c. Commercialization
   d. Uptake in the NHS

Commercialization and/or uptake

33. Please indicate which of the following elements of commercialization and/or you have achieved through your project? [tick all that apply]
   a. Finalised commercial/business plan
   b. Finalised IP position/IP arrangements/ownership arrangements
   c. Started a company based on the outputs from i4i-funded work
   d. Licensing out/ensured the downstream development of the product by another company
   e. Placed product on the market/made product available for use
   f. Product was adopted in practice
   g. Other, please specify [open text box]

Please consider the outputs mentioned above in the next questions

34.   How important were the following in enabling you to achieve the outputs in your i4i project? (Please rate each option from 1–4, 4 being very important and 1 being not at all important)
    a.   Prestige associated with i4i funding (e.g. in attracting new collaborators or leveraging further funding)
    b.   Expertise and skills of the project team
    c.   Technical/scientific content
    d.   Access to clinicians/clinical expertise
    e.   Insights on patient perspectives
    f.   Other, please specify [open text box]

35.   How significant were the following challenges to achieve the outputs in your i4i project? (Please rate each option from 1–4, 4 being very significant and 1 being not at all significant)
    a.   Technical/scientific challenges
    b.   Infrastructural challenges
    c.   Challenges in product design and product usability
    d.   Insufficient access to patients
    e.   Lack of time for satisfactory project completion
    f.   Lack of money for satisfactory project completion
    g.   Demands from the i4i Secretariat (e.g. reporting, etc.)
    h.   Regulatory constraints
    i.   Ethical constraints
    j.   Other, please specify [open text box]

36.   In what ways has the i4i Secretariat enabled you to achieve your outputs? (Please rate each option from 1–4, 4 being very important and 1 being not at all important)
    a.   Providing scientific advice
    b.   Providing business/commercialization advice
    c.   Providing IP advice
    d.   Providing structure to the project through clear timelines
    e.   Other, please specify [open text box]

37.   In what ways do you think the i4i Secretariat could help you in the future to achieve your outputs? (Please rate each option from 1–4, 4 being very important and 1 being not at all important)
    a.   Providing advice or support on access to patients/clinicians/NHS
    b.   Providing advice or support on access to industry
    c.   Providing access to key experts
    d.   Providing access to Knowledge Transfer Networks
    e.   Other, please specify [open text box]

The future of your i4i project

Future funding

38.   Do you intend to apply for further funding to take your project to the next stage?
    a.   Yes
    b.   No
    c.   N/A

39.   If you answered 'yes' to the previous question, where will you apply for further funding?
    a.   DH/WT Health Innovation Challenge Fund

b. TSB Small Business Research Initiative
c. EU funding
d. Angel or Venture capital funding
e. Other public sector funding, please specify [open text box]
f. Other charities, please specify [open text box]
g. Other, please specify [open text box]

The path to commercialisation and/or uptake

40. Have you conducted or commissioned, or do you plan to conduct or commission, a health economics study to quantify or monetize the savings and benefits of your project?
  a. Yes, it has been conducted or commissioned
     If yes, could you briefly describe the results [open text box]
  b. It is planned to be conducted or commissioned
  c. No, it has not been conducted or commissioned

41. Do you expect any challenges in getting stakeholders (e.g. the NHS) to adopt/acquire/purchase/implement the final product/technology of your i4i project (once any follow-on work, including any work that is not funded by i4i, is completed)?
  a. Yes, and have considered how to address this
  b. Yes, but have not considered how to address this
  c. No, but have considered how to address this
  d. No, and have not considered how to address this

42. What do you expect the likely barriers to commercialisation and uptake of the product/technology your i4i project is working towards will be? Please tick the three most likely barriers:
  a. Inertia/resistance to change – (e.g. difficult to convince NHS staff of the superior nature of a device or treatment)
  b. Clinician incentives – (e.g. clinicians have no interest or stake in the uptake of the new device or treatment)
  c. Training – (e.g. specialists will require additional training in order to work with the new device or treatment)
  d. Promotion – (e.g. it is difficult to reach the relevant stakeholders to inform them of the new device or treatment)
  e. Entry into the NHS – (e.g. the procurement channels into the NHS serve as a barrier to the uptake of a new device or treatment)
  f. Conducting a pivotal clinical study – (e.g. due to lack of funds cannot conduct a pivotal clinical study that is a prerequisite for uptake)
  g. Other, please specify [open text box]

43. What do you expect the likely enablers to commercialisation and uptake of the product/technology your i4i project is working towards will be? Please tick the three most likely enablers:
  a. Involvement of clinicians in the innovation process – (e.g. involving clinicians early on in the development phase proves conducive to uptake)
  b. Awareness raising with Commissioners – (e.g. raising awareness among NHS Commissioners of the new device or treatment)

c.   Local pilots to understand adoption – (e.g. conducting local piloting studies to understand the process of adoption)
d.   Support from key opinions leaders – (e.g. harnessing the support from a recognized expert in the field to support and promote the new device or treatment)
e.   Understanding the entry into the NHS – (e.g. dedicating time and resources to understand the procurement channels relevant to the new device or treatment)
f.   High profile publication – (e.g. a journal article in a leading journal)
g.   Professional body recommendation – (e.g. a supportive statement by a professional or Royal society)
h.   Other, please specify [open text box]

Appendix C: Case studies interview protocol

Questions

Background and context

1) What were the goals and objectives of your project? What health and innovation needs was it addressing? What specifically were you trying to achieve within the duration of the i4i funding project?
2) What phase/stage of innovation did the work focus on (e.g. proof of concept, prototype, testing, pivotal trials, etc.)?
3) Where was most of the work done?
4) Was your project solely funded by i4i? Or was i4i a co-funder?

Developing the innovation idea and prospect

5) How was the idea behind the project born?
6) Why did you apply for i4i funding specifically? How did you find out about the i4i funding stream?
7) Can you talk us through the story of developing your proposal?
    a. How were collaborations formed?
    b. What were the respective roles and contributions of different collaborators in developing the proposal?
    c. Which other groups were consulted on and on what (even if not formal collaborators)?
8) How did the review process of your application work? Did you present to a panel? Did you make amendments to the initial proposal? (Which, why?) How did you decide how much money to apply for?
9) Did you consult with NHS procurement bodies at the proposal state? If yes, was it helpful? If not, would that have been helpful?
10) Did you consult charities, as the 'voice of patients'? If yes, was it helpful? If not, would that have been helpful?
11) Did you do any health economics-based assessments or cost benefit analysis of the value of your innovation for the health system, at either the proposal or project development phases?

Implementation to date

12) If you reflect on the project, and with the benefit of hindsight, do you think the design of your project and methods used were appropriate?
13) [Ask only if applicable] Was the current design of pivotal clinical trials a barrier?

14) What helped you progress the i4i project – i.e. what did you see as key enablers (both in terms of internal factors and wider external environment conditions)?

15) What about key challenges? Can you elaborate?

16) What were your interactions with the i4i Secretariat like during the project? Did/how did i4i help/hinder progress in achieving your outputs?

17) How does/did regulation influence the space within which your project was developing?

18) What about the procurement and pricing environment?

Outputs and impact to date

19) Product development stages:
    a. Which aspects of product/technology development did you achieve during the i4i project? Given where you started, how far did you progress? Were your expectations in terms of progress met?
    b. Were there further developments post the i4i project funding?

20) Commercialisation. How far did you go down the commercialisation pathway:
    a. During the i4i project?
    b. Have there been further developments re commercialisation since?
    c. What type of IP/ownership arrangement do you have with i4i?

21) Dissemination: Did you/how did you disseminate emerging insights from the work? To whom?

22) Influence on policy? Did you interact with policymakers and/or as a result of this work influence policy at local, regional or national levels?

23) Influence on the NHS and patients: Was there any uptake of your innovation during the life of the i4i project (pilot or wider scale)? What about post project completion?

Next steps and future prospects

24) What do you think the next steps are for this project (if there are any)?
    a. Development work.
    b. Further commercialisation that may be needed.
    c. How do you see that happening (who will fund, who will do, timelines etc.)?

25) What is needed for uptake in the NHS? What would be the top three things that need to happen and be present for this to move into the NHS? International health systems?

26) In what ways do you think the i4i Secretariat could help you in the future to achieve your outputs? (e.g. Providing advice or support on access to patients/clinicians/NHS; Providing advice or support on access to industry; Providing access to key experts; Providing access to Knowledge Transfer Networks; Other, please specify)

27) On reflection, is there anything you would do differently with the benefit of hindsight?

Time permitting

28) Can you think of any examples of good practice in medical device/diagnostics/innovation in your space, nationally or internationally, that we/i4i could learn from? (These can be either in terms of supporting the innovation process and/or facilitating uptake.)