

Managing Clinical Research in the UK

Summary of findings

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preface

This report reports the findings from a two-year project which commenced in October 2007 and was funded by the Engineering & Physical Sciences Research Council (EPSRC)¹ through a healthcare management research programme developed by the Warwick Innovative Manufacturing Research Centre (WIMRC). The study was conducted by a research team from the Innovation, Knowledge & Organisational Networks research centre (IKON), based at Warwick Business School at the University of Warwick, and the School of Management at Queen Mary University of London.

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This document provides a summary of the findings of the study. The full report can be obtained from the IKON Research Centre.

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Disclaimer:

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¹ "The Management & Organisation of Clinical Trials" (RIBK 9223) - The research was funded by the Engineering and Physical Sciences Research Council (EPSRC) via the Warwick Innovative Manufacturing Research Centre.

executive summary

Over the last decade UK scientists, clinicians and industrialists have expressed growing concern about the ‘translational gap’ between basic scientific discovery and innovation that will benefit patients. High quality clinical research is key to closing this gap and underpins innovation and improvement in health services. Clinical research is also central to the UK’s pharmaceutical, biotechnology and medical devices industries, which combined are an essential component of the UK’s economy. Yet the UK clinical research base is increasingly under threat from global competition and the time and cost of research and development continues to be a major challenge. The successful management and organisation of clinical research projects will be pivotal to overcoming these challenges in the future.

This report presents the findings from a 2-year EPSRC-funded study¹ which was undertaken to systematically explore the challenges of organising and managing different models of clinical research.

Aim: To identify the key social, organisational and managerial factors that influence clinical research projects with a view to improving the clinical research process and reducing the costs and risks of development.

The study employed a multi-method design incorporating:

Phase 1

- i. A systematic literature review of previous work in this area, containing 129 articles.
- ii. 57 interviews with key stakeholders which focused on the challenges of conducting different types of clinical research in the UK.

Phase 2

- iii. A large scale survey generating data on the management of 247 clinical research projects conducted in the UK.

Major findings

There has been an *overall improvement* in the proportion of projects that complete within time over the last decade. However, this improvement is largely related to improvements in time to recruit patients, whilst the project set-up stage continues to be a significant challenge. There is a slight drop in the proportion of projects that reach the anticipated recruitment target expected from UK sites within agreed time frames.

Projects led by pharmaceutical companies were more likely to complete on time and to patient recruitment targets, as compared to other projects led by commercial organisations and those led by non-commercial research groups. 45% of pharmaceutical-led projects completed on time, compared with 32% of non-commercial studies, and 24% of projects led by other commercial organisations. 68% of pharmaceutical-led projects completed on budget, compared to 64% of non-commercial studies and 48% of projects led by other commercial organisations.

From the analysis of the data derived from both phases of the study, the greatest challenges affecting the management of clinical research were found around four areas:

- **Regulation & Governance:** Successfully completing the governance approval process was identified as a particular challenge for project management. In particular, different types of research organisation naturally conduct different models of research, all of which experience dissimilar pressures in managing the regulatory and governance process.

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Researchers that do not adopt standard randomised controlled trial (RCT) models face particular challenges in the approvals process.

- **Knowledge & Expertise:** Retaining project team expertise was critical for successful project management. This underpinned many of the problems (e.g. recruiting and retaining patients) commonly associated with the conduct of all models of clinical research. However, skills shortages create particular difficulties for non-commercial and smaller commercial research organisations.
- **Networks & Strategy:** Project management is reliant on the development of successful working relationships between the research organisation and other key groups within the sector. Each research organisation must shape their strategy for research to fit in with the UK strategic context and to facilitate successful networking with other stakeholder groups.
- **Incentives & Drivers:** To develop and maintain a network of relationships, research organisations and policy makers must develop insight into what incentivises different organisations, communities and individuals to engage in clinical research. In practice this may require balancing dissimilar or even antagonistic actions. The heterogeneous groups that are critical to the UK's clinical research sector require different levels of support to incentivise involvement with research projects.

“Project management requires the development of practical, nuanced knowledge

2. This finding highlights the importance of *local knowledge and expertise* in managing clinical research in the UK. Project management requires the development of *practical nuanced knowledge* that develops through on-going relationships with stakeholders across numerous organisations and clinical sites. When project teams are disrupted, often much of this local knowledge is lost, adversely affecting project outcomes.
3. Changes to the governance system that were introduced following implementation of the EU Clinical Trials Directive and Research Governance Framework appear to have had little effect on set-up time. For projects conducted over the last decade, the average time to *prepare* and submit an application, and receive an outcome for approvals was found to be 114 days (R&D), 91 days (ethics) and 77 days (regulatory). For projects that obtained approval from 2007 onwards, the average time to prepare and submit an application, and receive an outcome for approvals was found to be 102 days (R&D), 90 days (ethics) and 83 days (regulatory). These figures are significantly longer than MHRA and NRES figures on approvals, suggesting that *preparation time continues to be a major challenge*.
4. All research groups, other than pharmaceutical firms, experience significant difficulty in *obtaining information*, completing paperwork and ensuring that the features of their models of research correspond with the requirements for regulatory and R&D approval.

The major findings were found to be:

1. The major predictor of success in terms of completing a project on time, with sufficient patients and on budget, was the *ability to retain a project team*.

5. The greatest impediments to conducting clinical research in the UK were considered by researchers and managers to be *time and cost*. In addition, R&D approval, contract negotiation and NHS research culture were also considered major impediments.

6. There was considerable variation in the time taken to obtain R&D approval across the UK. In conjunction with problems of contract negotiation, this suggests that there remains considerable variation across NHS Trusts with respect to these two aspects of conducting clinical research.
7. The regulatory and ethical approval processes are viewed as having improved in recent years. The introduction of the NIHR Integrated Research Application Scheme (IRAS) and the Coordinated System for gaining NHS Permission (CSP) were considered to be a significant improvement in terms of ease of conducting research in the UK.
8. The development of productive relationships between research organisations and other stakeholder groups is influenced by the different drivers that promote involvement with a project. Research organisations need insight into how different organisations, communities and individuals are incentivised, which may in practice require balancing dissimilar or even antagonistic actions.
9. Distinct features of NHS Trusts act as incentives for research organisations to select particular recruitment sites. The findings highlight that the *resources provided by a site*, and the *reputation of a Trust* for patient recruitment, together with the *reputation of the lead clinician*, were important aspects which influenced the selection of sites for the projects reported.
10. Clinical Researchers believed that their expertise of planning and designing the project, such as *inclusion criteria & recruitment strategy and presenting an interesting topic*, were more important factors for recruitment than explicit incentivisation through the provision of rewards, such as financial and non-financial remuneration.
11. Different types of research organisation have different priorities which influenced their motivation in developing a clinical research project. *Financial reward* was important for commercial groups. *Research group reputation and informing UK policy* were more important for non-commercial research.

The full report presents detailed findings as to the many different challenges that influence the ease of managing clinical research projects within the UK. It is proposed that it is constructive to consider the relationship between the macro-level system that may generate operational and management challenges for the research organisation, and the issues experienced with the day-to-day management of clinical research projects. We suggest that the current system tends to operate as a *'one size fits all model'*, where projects that do not confirm to the features of the Randomised Clinical Trial (RCT) model of research experience greater challenges with overall project management. However, policy response to these challenges needs to recognise and support *all* the research groups that constitute the clinical research sector within the UK.



summary of findings

Over the last decade UK scientists, clinicians and industrialists have expressed growing concern about the ‘translational gap’ between basic scientific discovery and innovation that will benefit patients. High quality clinical research is key to closing this gap and underpins innovation and improvement in health services. Clinical research is also central to the UK’s pharmaceutical, biotechnology and medical devices industries, which combined are an essential component of the UK’s economy. Yet the UK clinical research base is increasingly under threat from global competition and the time and cost of research and development continues to be a major challenge. The successful management and organisation of clinical research projects will be pivotal to overcoming these challenges in the future.

This summary report describes an overview of findings from a 2-year EPSRC-funded study¹ which was undertaken to systematically explore the challenges of organising and managing different models of clinical research in the UK context. The ease with which clinical research can be conducted is also strongly influenced by both the strategic/market environment and by national policy and regulation.

In particular, this research was conducted following considerable changes within the last decade to the management of the clinical research process within the UK. Extensive modifications to the UK regulatory and governance approval processes have been implemented. Significant attention from UK strategists and policy makers has also brought greater government investment into healthcare research, and catalysed the development of numerous initiatives which have influenced the UK context within which clinical research projects are organised. These macro institutional factors can

pose major coordination challenges for the successful management of clinical research projects at the micro level.

This multilevel research study identified and mapped the macro-level issues surrounding clinical research in the UK, and systematically explored how these influenced the organisation of research and project management at the micro-level. The purpose of this research was to identify the key social, organisational and managerial factors that influence the management of clinical research projects.

Specifically this research aimed to:

- Map alternative models of clinical research and identify the key challenges they generate, from the perspectives of the different research groups and key actors.
- Identify the macro institutional and policy drivers that frame the strategic environment within which research is conducted within the UK.
- Identify the barriers and enablers influencing the day-to-day management and organisation of clinical research projects within the UK.
- Explore the relationship between the macro-level context and the day-to-day challenges associated with managing different models of research.

The findings inform understanding of how and why clinical research projects succeed or fail and what kinds of management and organisation are required to support success. We report on the completion rates of UK clinical research projects included in our study. The challenges of managing and organising clinical research are addressed across 4 major themes, and associated recommendations on how policy makers and clinical research communities might tackle these challenges are presented.

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Research Design

The study employed a multi-method design incorporating:

- A systematic literature review of previous work in this area, generating 129 core articles found from a total of 5,191.
- 57 interviews with key stakeholders which focused on the challenges of conducting different types of clinical research in the UK.
- A large scale survey generating data on the management of 247 clinical research projects conducted in the UK. This report details researchers' own experiences of conducting one clinical research project, together with their perceptions about the current UK clinical research context.

The survey generated data about researchers' experiences of setting-up and conducting 247 clinical research projects and trials. The majority of the responses depict recent experiences of managing projects, with 63% of projects reported commencing during or after 2006. However, the design of the survey also enabled the collection of a representative sample of projects that took place earlier than this date. These data provide baseline data that help to show how changes in the UK context have influenced the management of projects over time.

The survey gathered behavioural data on the management and outcomes of clinical research projects as well as attitudinal data on barriers and enablers. The former are important in lending support (or otherwise) to the many personal theories and questions that abound around what predicts clinical research outcomes. The latter are important in assessing perceptions amongst different groups on how easy it is to conduct clinical research in the UK. These perceptions are important since they will influence the willingness of certain groups to participate in clinical research, even where they may not concur with facts and figures and perceived wisdom on governance arrangements.

Sample profile:

- 27% of the projects were led by pharmaceutical organisations, and 16% by other commercial groups, including medical devices, biotechnology & start-up companies and contract research organisations. 57% of the projects were led by non-commercial research organisations, including university (40%), NHS and charity research groups.
- 56% of the projects were focused on medicines research, 11% were for medical devices or surgical studies, 15% focused on complex interventions and 18% focused on service & healthcare evaluation.
- 83% of the projects led by commercial organisations were medicines trials. Projects led by non-commercial groups were more heterogeneous - 36% focused on medicines, 9% on medical devices or surgical studies, 26% on complex interventions and 29% on service & healthcare evaluation projects.
- 26% of projects were focused on cancer research, 26% focused on either respiratory, cardiovascular, stroke or diabetes diseases. The remaining 48% covered many other disease areas.
- 16% of projects obtained regulatory approval before May 2004, 31% between May 2004 and the end of 2006, and 53% obtained regulatory approval from 2007 onwards.

Project outcomes

There has been an *overall improvement* in the proportion of projects that complete within time over the last decade. *The project set-up stage however continues to be a significant challenge*, with the major improvement associated with improvements in time to recruit patients. That said, there is a slight drop in the proportion of projects from 2004 onwards that reach the anticipated recruitment target expected from UK sites within agreed time frames. The latter findings reflect an overall change in project management strategy; there is now greater pressure to conclude a project, even when it has not recruited to target, rather than to provide additional time to recruit further patients.

The findings reveal that projects led by pharmaceutical companies were more likely to complete on time and to patient recruitment targets as compared to other commercial organisations and to projects led by non-commercial research groups. 45% of pharmaceutical-led projects completed on time, compared with 32% of non-commercial studies, and 24% of projects led by other commercial organisations.

Commercial organisations, other than pharmaceutical companies, experience greater difficulties completing within budget, with only 48% of projects completing on budget and 17% running over-budget by more than 50%. This compares with 68% of pharmaceutical-led projects, and 64% of projects led by non-commercial organisations completing on budget. Extremely few projects run by these groups were considerably over budget with only around 10% running more than 20% over budget.

Different types of research organisation experience different kinds of financial and budgetary pressures. Respondents from projects led by commercial organisations found that budget pressures considerably influenced the ease of contract negotiation with NHS sites. Respondents from non-commercial organisations believed that financial issues adversely affected their ability to retain staff following completion of a project.

The results from non-linear multivariate regression analysis models identified that *retaining a project team* is a critical predictor of overall project completion, and influences the ability to recruit to target. *Ease of contract negotiation* also accounted for much of the variability in project completion, and also influenced the overall patient recruitment levels that were achieved.

From the analysis of the data derived from both phases of this study, the greatest challenges affecting the management of clinical research were found around four areas:

- Regulation & Governance
- Knowledge & Expertise
- Networks & Strategy
- Incentives & Drivers

Regulation & Governance

Understanding, and successfully obtaining, the necessary regulatory approvals and governance permissions was identified as a particular challenge for project management. Projects led by different types of research organisation experienced varied challenges in this regard. We suggest that the current system tends to operate as a '*one size fits all model*', where projects that do not conform to a model of research that entails Randomised Clinical Trials (RCTs) experience greater difficulty obtaining regulatory & governance approvals. As non commercial groups are more likely to engage in non-standard clinical research models, they also experience greater challenges overall in securing approvals.

Changes to the regulatory & governance approvals system that were introduced in 2004 following implementation of the EU Clinical Trials Directive and the creation of the Research Governance Framework in 2001 have had little effect on overall set-up time. Since 2004, the duration required for researchers to prepare the necessary documentation and gain regulatory approval has increased slightly. The time taken to complete ethical approval has not changed, whilst the time taken for obtaining R&D approval has noticeably dropped.

For projects conducted over the last decade, the average time to prepare and submit an application, and receive an outcome for approvals was found to be 114 days (R&D), 91 days (ethics) and 77 days (regulatory). For projects that obtained approval from 2007 onwards, the average time to prepare and submit an application, and receive an outcome for approvals was found to be 102 days (R&D), 90 days (ethics) and 83 days (regulatory). These figures are significantly longer than MHRA and NRES figures on approvals, suggesting that preparation time continues to be a major challenge.

Commercial research organisations experience a higher proportion of regulatory and ethical applications approved following first submissions (81% & 73%, respectively), compared with non-commercial organisations (76% & 65%). The overall time taken to prepare, submit and receive an outcome for ethical approval was also lower for commercial organisations (81 days) than for non-commercial research groups (100 days). Both groups reported similar regulatory approval durations (80 & 82 days). Commercial groups experienced a longer time to prepare, submit, and obtain NHS Trusts R&D permissions than non-commercial groups (118 days compared with 112 days).

All research groups, other than pharmaceutical firms, experience significant difficulty in obtaining information, completing paperwork and ensuring that the features of their models of research correspond with the approval requirements for regulatory and R&D approval. This is less to do with the amount of information available and more to do with a proliferation of varied and new sources of information, some of which is seen to contain apparently conflicting advice. Commercial organisations often have dedicated resources to handle the submission process and so complete it more efficiently than non-commercial research groups.

Whilst changes in the regulatory and approvals system have been welcomed, some research groups perceive the current system as overly cumbersome due to an increase in the information and documentation that was required to satisfy legal and governance framework requirements. Certain research groups, such as consultant-led non-commercial projects had previously received regulatory exemptions, but after 2004 were required to apply for Clinical Trials Authorisation. This will account for much of the increase revealed by the above findings.

The introduction of several initiatives, including the Integrated Research Application Scheme (IRAS), Coordinated Sign-off Procedure (CSP), Research Passport Scheme and the Bipartite/ Tripartite model clinical trial/ investigation agreements

(mCTA/ mCIA) for commercial NHS collaboration, which are all aimed at improving the management of the set-up of projects are considered to be a significant improvement. However, respondents stressed that only time would prove the actual effect of these initiatives, and whether this would in practice improve the process of engagement with NHS Trusts. Some argue that the approvals and monitoring systems need to focus more heavily on *risk-based* assessment of different models of research than on a highly standardised and prescribed approach.

The findings highlight that additional challenges are experienced when research does not conform to a standard RCT model, as it can be more difficult to fit research that exhibits non-typical features with the standard paperwork and requirements of the approval system. Particular types of research which are valuable for supporting UK healthcare, such as essential medicines, acute & rare diseases, preventions research, and healthcare & service evaluation are less likely to conform to the features of the RCT model. These projects typically have greater challenges around managing patient recruitment and often use non-typical (non RCT) approaches, such as non-standard identification and consent processes to address these issues.

In addition, late phase and post-marketing medicines research have longer ethical and R&D approval times compared with early phase research. Cancer research projects have longer R&D approval times, perhaps reflecting the particular liability concerns associated with this type of research.

Overall, many researchers reported that they felt discouraged from including innovative features that were non-typical in applications to review bodies (e.g. incorporating novel recruitment methods). They felt that this would potentially increase the overall time taken to obtain approvals, as they would need to engage in additional discussion to justify their approach, and it was more likely that the application would

require re-submission.

Recommendations

- i. The process for obtaining R&D approval from NHS Research Governance offices should be streamlined and made transparent.
- ii. Performance data on R&D approval times for different NHS Trusts should be publically available for comparison
- iii. Standard documentation and information should be used across all NHS Trusts, with a guaranteed turn-around for decisions.
- iv. Information on how to obtain approvals (including regulatory, ethics and R&D) should be provided in the form of a 'one-stop-shop', with clearly signposted pathways for different models of research. Applicants should demonstrate they have consulted this information.
- v. Examples of completed documentation (such as the 'mock forms' for a medicines and biotechnology product which are provided by the MHRA) should be provided by approval bodies for different models of research.
- vi. The regulatory & governance system needs to reflect the particular *risks* and endemic features of different models of research. Training for committee members should include greater detail about how to assess the risks of different models of research.
- vii. The system of 'flagged' ethics committees for medical devices should be further extended with dedicated ethics committees being set up for other different models of research.
- viii. The regulatory & governance system should actively encourage the inclusion of innovative forms of research. There should be different routes provided through forms, and greater flexibility to include novel approaches.
- ix. Members of approval bodies should receive training in how to assess novel approaches for research design to ensure that assessment of non-standard research features accurately assesses the risk.

Knowledge & Expertise

The survey data depict that *retaining a project*

team is one of the most important aspects that influenced whether a project successfully recruited the required sample size and finished on time. Individual team members' expertise is extremely important for successful project management, as often this is very practical, tacit knowledge that can only be obtained through experience and the development of working relationships with individuals from many organisations.

The importance of *local knowledge* and expertise is emphasised as critical for successful management of clinical projects in the UK. Whilst helpful, knowledge from written, highly codified sources - such as information provided by websites or documentary sources - is not in itself sufficient. Instead project management requires the development of practical, nuanced knowledge that develops through on-going relationships with stakeholders across numerous organisations and clinical sites. Often *clinical research nurses are essential conduits of local knowledge*. When project teams are disrupted, much of this local, tacit knowledge may be lost, which can adversely affect project outcomes. The disruption of project teams is more likely in non commercial research projects that rely on contract funding.

There are many different sources from which researchers can access support and information to help develop their own expertise and to assist with project management. However, again, challenges arise not because the information is not available, but because it is not in an appropriate form. An overabundance of sources actually makes it difficult for researchers to work out what is current 'state of the art' advice. Many sources of information also assume a certain level of expertise, and provide information which is too specialised.

Support and advice from patient groups and charities is viewed as highly useful in developing and managing clinical research. However, actual contact with these groups by researchers is relatively low. These organisations can provide



sources of information that are very specific to the day-to-day reality of a condition. Research groups that do incorporate this support, such as through patient representation on advisory boards, have access to a different perspective enabling them to design projects that are more likely to be practically achievable and to avoid unnecessary time spent revisiting approvals in order to change protocols.

Whilst many of the recent initiatives aimed at improving the process over the last 2 years are viewed positively, challenges for managing projects still emerge because changes in the last decade mean that researchers continually need to obtain new expertise and knowledge. Confusion can arise from identifying what changes have been made and from the need to develop an understanding of how they can actually benefit from new initiatives.

Different organisations face varied challenges in terms of sourcing relevant skills and expertise. Smaller organisations are more reliant on individuals who have specific expertise within smaller teams, meaning that there is less flexibility with the management of projects to transfer individuals across projects when there are particular pressure points during a project. In addition, these organisations are vulnerable to loss of expertise if team members leave, as it is hard to preserve an organisational memory of the local knowledge that has been acquired by individuals.

Similarly, public-funded projects, typically in non-commercial organisations, often employ research staff on fixed-term contracts. These types of research organisations are therefore particularly vulnerable to losses in expertise once a project draws to a close. Even if the team acquire further funding, which in principle would allow them to retain staff, there are often difficulties in agreeing contracts between funders and the research organisation in time to ensure continuity of staff contracts. This can lead to research staff with valuable local knowledge being forced to leave for alternate positions elsewhere.

The geographical location of a research organisation can also influence access to the necessary skills required. If a research organisation is not based in an area where there is a strong clinical research base, there is a much smaller pool of individuals in the locality from which to select. Similarly, not being located in an area where there is high level of clinical research is also perceived to influence the attractiveness of an organisation to receive financial backing to support development of innovative, but inherently risky products, that are typical of the portfolio of biotech start-up companies.

Churn in employment can also encourage knowledge sharing across organisations as individuals bring with them experience of other sites and projects. However, this can act as a disincentive for organisations to develop training schemes for novice researchers. It can also encourage a turnover of more experienced staff as there are often incentives to transfer to other organisations.

There are clearly many different roles and types of expertise required for clinical research. This complexity, coupled with a lack of an obvious career route in clinical research itself presents challenges. It was felt that clearer career trajectories in clinical research could help to narrow the skills gaps experienced in this sector. There were particular concerns regarding a skills shortage in experienced clinical research associates, clinical research nurses and project managers. Given the importance of local knowledge noted above, this adversely affects both commercial and non commercial research. In the UK public health system most projects, including commercial ones, rely to some degree on NHS staff. With regards research nurses, clinical research was not perceived as a 'typical' career path, major disincentives being that often the work was conducted on fixed-term contracts and that promotion opportunities were less. Hence it can be difficult to develop and retain experienced nurses. It was also felt that support for clinical research varies widely across NHS Trusts and Executives.

Recommendations

- i. A dedicated portal for UK Clinical Research should be set up to assist less experienced clinical researchers in acquiring relevant knowledge and expertise. The portal should ideally hold and up-date information about approval requirements, project management support, training provision, contract research services, professional and trade bodies, and charities and patient organisations.
- ii. The support provided by recently implemented NIHR Research Design Services should be extended to actively support innovative and atypical research models that do not conform to the RCT approach.
- iii. A review of current training and accredited provision should be undertaken.
- iv. A UK-wide strategy should be developed that identifies a career trajectory for clinical research. Career profiles of the range of roles engaged in clinical research should be developed.
- v. Greater resources should be granted to patient and charity groups to enable these groups to increase the level of active support they can provide to research organisations.
- vi. Research organisations should be incentivised to provide accredited training provision.
- vii. More flexible forms of employment (for example secondments, positions jointly funded by commercial and non-commercial organisations, or multi-host contracts) should be implemented to promote retention and ease skills shortages experienced by small organisations and groups reliant on fixed-term contracts.
- viii. Faster contracting should be a priority to help secure continuity across university and other publicly funded research projects. Bridge funding should be available for research staff experiencing temporary gaps in funding.

Networks & Strategy

Project management is reliant on the development of successful working relationships between the research organisation and other

key stakeholder groups. The findings highlight that challenges arise due to difficulties in creating and sustaining these networks. ***Research organisations need to build on expertise in the form of local, nuanced knowledge to facilitate the development of successful working relationships with other stakeholder groups.*** However, each research organisation will naturally be required to develop different strategies for forming these networks.

For most clinical research conducted within the UK, it is paramount that research organisations collaborate with NHS Trusts, as these are the gatekeepers to patients. There was ***considerable variation in the time taken to obtain R&D approval across the UK***, despite attempts to develop more coordinated sign off and approvals systems. In conjunction with problems of contract negotiation, this suggests that there remains considerable variation across NHS Trusts in terms of their working relationships with particular research teams.

The different perspectives that research organisations and Trusts hold regarding clinical research appear to have created some challenges. Researchers recognise that Trusts have a legal responsibility to protect their patients and resources. However, it was perceived that the ***disparate procedures in place to gain NHS permissions were a great impediment*** to successful project management. Some Trusts were 'known' to have bought-into streamlining and standardising this process, by for example, using standardised forms and reducing the amount of Trust-specific information requested. Thus researchers believed that it should not be legally problematic for other Trusts to also follow suit.

The findings highlight that many research organisations would ideally return to the same sites for subsequent research, demonstrating the value placed on previously established relationships and the challenges that can sometimes be faced when there is a need to develop new partnerships. Through maintaining

these relationships, researchers are able to develop the practical, nuanced knowledge that can only be obtained from actually working with individuals.

The findings show that commercial organisations experience greater difficulty with developing relationships at the Trust level. This is because their contract negotiation is inherently more complex due to financial aspects that need to be agreed. Challenges experienced when smaller commercial organisations attempt to develop relationships with NHS sites emerge because often Trusts do not distinguish between this model of research and the global pharmaceutical sector, and do not recognise that they have lower financial resources.

Additional challenges emerge from competition between different research groups for use of NHS resources. As each Trust follows its own procedures, it can be more difficult to obtain knowledge about a new Trust's procedures, meaning it can take more time to develop successful working relationships. Therefore, it can be difficult for Trusts (including both hospital and primary care) that do not have a reputation for previous research involvement, and have large numbers of patients not already involved in studies, to become part of the network of relationships that a research organisation works with.

Recent policy initiatives developed by the NIHR have the potential to support network relationships, providing more structured arrangement to bring together different stakeholder groups. Survey data indicated that *recent NIHR policy initiatives aimed at streamlining the set-up stage of projects have been positively embraced*. In particular the Integrated Research Application System (IRAS) and Co-ordinated System for gaining NHS Permissions (CSP) are perceived as having the potential to provide significant improvements to the process. However a number of interviewees, whilst welcoming the idea of a research passport, and the development of bipartite/ tripartite model

Clinical Trial/ Investigation Agreements (mCTA/ mCIA) between the NHS Trusts, Research Organisations (pharmaceutical/ medical devices companies) and Contract Research Organisations that would be valid across all Trusts, expressed some scepticism as to its practicability, and whether all Trusts would now follow similar practices.

The NIHR Clinical Research Network is an example of a prescribed network structure, which provides formalised links between different stakeholder groups. The National Cancer Research Network is considered to be very effective at supporting clinical research in this disease area. However, overall the survey data indicated that reaction to the effect of the creation of the NIHR Clinical Research Network on the management of clinical research projects was more temperate and restrained. Whilst the networks work well for the clinical discipline of cancer, the specific features of other diseases and historical underpinning of other clinical specialities present challenges for the adoption of this model across all clinical disciplines. Therefore, it is important to ascertain the features that make the cancer CRN successful, to inform the development of other networks.

Clinical research organisations must engage with a variety of intermediary bodies, including professional & trade groups, patient groups, regulators and governance organisations, to try to gain the knowledge required to successfully manage a project. These provide a useful source of nuanced, tacit information. Contact with professional and trade groups strengthens network relationships with groups specifically relevant for the context of different models of research, as this can provide access to other relevant stakeholder groups. The findings suggest that, at times, research groups find it difficult to form relationships with patient groups and charities. However, when collaboration is developed, these types of groups can act as a bridge for developing connections between the public and researchers.

The diversity of research organisations influences how they can develop collaborations with other stakeholder groups, as the interests of all groups need to be balanced to create and maintain networks. Naturally, respondents from different types of research organisation will sometimes have different perceptions about the effect of policy initiatives and what the future focus of policy attention should be. The policy direction taken by different intermediary groups affects whether a network of relationships is successfully established and maintained. In particular, tensions can arise between balancing the support for commercial research (given its important role in significantly contributing to the UK economy), with the support that needs to be provided to non-commercial organisations so that they can focus on particular UK-relevant health priorities.

Different types of research organisation are inherently grounded in particular models of research which confer a specific context for how a network of relationships with other stakeholder groups is formed and maintained. All groups must have an appreciation of the underlying objectives and values of each respective organisation for successful partnerships to be created. However, research organisations must develop a strategy of how to work successfully with key UK groups (such as regulators, governance bodies and assessment groups such as NICE), and how to balance the UK context with a global network.

Recommendations

- i. Further support is required to strengthen relationships between research organisations and the NHS.
- ii. NIHR initiatives to support the development of good relationships between the NHS and commercial research organisations are welcomed, and should be further reinforced and monitored as to their effects.
- iii. Transparent information on NHS Trusts' clinical research governance processes should be easily available.
- iv. Information on NHS Trusts' approval times and site-level recruitment and completion

figures should be publically available.

- v. There should be an evaluation of what makes effective clinical research networks, such as the Cancer CRN, to support the development of networks in other areas.
- vi. Involvement with patient and charity groups should be promoted. There should be provision to cost charitable donations into publically funded research.
- vii. All research organisations should be encouraged to work with NICE to ensure that research findings are tailored to the NHS context.
- viii. A 'community of practice' for UK clinical research managers and research nurses should be fostered, in order to support the sharing of knowledge and expertise and build a strong identity and job market around UK clinical research.

Incentives & Drivers

The development of productive relationships between research organisations and other stakeholder groups is influenced by the different drivers that promote involvement with a project. Research organisations need insight into how different organisations, communities and individuals are incentivised, which may in practice require balancing dissimilar or even antagonistic actions. The findings highlight that *different types of research organisation have different drivers for clinical research, and thus respond differently to the support provided by UK strategists and policy makers.*

Enrolling NHS sites necessitates skilful balancing of incentives at the organisational level when setting-up contracts and obtaining permissions from R&D offices. It also needs attention to individual incentives in order to enlist clinicians to become site investigators and to commit clinical departments to recruit patients. The time taken for these negotiations, and the cost, could be difficult to predict accurately in advance and there was significant variation in ease of contract negotiation and approvals, which affected overall project management.

Distinct features of NHS Trusts act as incentives for research organisations to select particular recruitment sites. The findings highlight that the resources provided by a site, and the reputation of a Trust for patient recruitment, together with the reputation of the lead clinician, were important aspects which influenced the selection of sites for the projects reported.

Certain aspects are perceived to affect the level of recruitment at sites. The findings indicate that respondents believed that their expertise of planning and designing the project, such as inclusion criteria & recruitment strategy and presenting an interesting topic, were more important factors for recruitment than explicit incentivisation through the provision of rewards, such as financial and non-financial remuneration.

Data showed that researchers perceived that changes to the Consultant Contract through the 2002 framework (Department of Health, 2002) and its subsequent amendments resulted in a change of emphasis on NHS Consultants' participation in clinical research. Whilst the changes to the rewards system ultimately increased overall pay, it was felt that this contract conferred lower prominence on rewarding clinicians to participate in research.

The drivers for individuals to get involved in any role within a clinical research project vary. To successfully recruit and retain team members and collaborate with other key stakeholder groups, (such as clinicians based at clinical sites), requires a local insight into what drives different people to participate. This understanding is developed through experience, such as when a skilled project manager develops an appreciation of the practical level of involvement clinicians from sites actually want to have.

The findings indicate that certain features are considered to be more important drivers for why the research project was developed. Unsurprisingly, patient benefit is of high importance for all groups. In addition, further

developing an existing area of expertise was rated highly, illustrating that organisations value the experience that team members have previously acquired, and that research organisations can subsequently leverage existing networks of relationships and expertise.

Different types of research organisation have different priorities which influenced their motivation in developing a clinical research project. Financial reward was obviously important for commercial groups. Enhancing a particular research group's reputation and informing UK policy were more important motivators for non-commercial research teams. This reflects the importance to these groups of building a reputation for producing good quality research findings, in order to increase the likelihood of further funding.

The different drivers for conducting research are related to a tendency for different types of research organisations to develop projects based on different models of research. As different types of research organisation respond to different types of policy support, the decisions made by government strategists and policy makers creates support for certain groups, and ultimately influences the type of enterprise that takes place within the UK.

Commercial organisations need to develop profit from their enterprise to be a viable business. Therefore they are skilled at efficient research that can be achieved through a streamlined RCT model based on a straightforward design. These organisations typically operate at a global level, at which the UK constitutes one of many possible locations for clinical research sites, and one of many target markets for the end-product. However, the UK is considered a good place to conduct clinical research projects that adopt the RCT model, as there are robust patient populations that will ultimately constitute a target market. The NHS as a potential market continues to be highly valued, such that often clinical research projects for late phase or marketed



innovations will be framed specifically with the UK context in mind. The UK also provides high levels of clinical expertise and access to highly qualified individuals.

Smaller biotech and start-up organisations however do experience difficulties. In general, this type of organisation is founded on developing a single or small number of clinical innovations which often carry a greater risk of failure. Whilst still aiming to generate profit, these smaller organisations do not have the same level of available resources and often experience skills shortages and lack expertise in project and business management.

Medical devices companies operate a different commercial model. They do not have the same type of patent cover as medicines so it is much easier to make amendments to the innovation. This can lead to different types of competition issues and time-pressures compared with medicines research, as there is less incentive to achieve a 'first-to-market' product. However, once marketing approval is received, these organisations are under increased pressure to continuously develop modifications and improvements to the product.

Many non-commercial research groups develop a research stream that is actively shaped by government funding priorities, such as the development of essential medicines which are not necessarily the focus of the commercial sector. These groups must develop expertise in managing projects that are typically more complicated and non-standard. For example, research into rare diseases and acute diseases presents inherent challenges for project management as there is generally a smaller patient population from which to recruit. However, the findings demonstrate that these types of projects achieve lower levels of recruitment. As this type of research does not necessarily conform to the RCT model, policy support and development would be welcomed to further promote this particularly valuable clinical research.

Recommendations:

- i. NHS Trusts need to be flexible in how they negotiate contracts and permissions with different types of research organisation which reflect the different incentives that need to be offered. In particular, Trusts should recognise the specific financial and resource constraints experienced by smaller commercial organisations.
- ii. Incentives to encourage greater NHS involvement in clinical research need to be targeted at different levels of the NHS: the organisational-level, site-level and individual-level.
 - o All Trusts should be strongly encouraged to 'buy into' initiatives to develop a streamlined consistent system of approval and access.
 - o Trusts should promote participation of clinical departments in clinical research, and ensure that benefits are directly received from this involvement.
 - o Greater attention should be given to encouraging the active involvement of clinicians as lead investigators in clinical research projects.
- iii. Research conducted by pharmaceutical organisations can be supported through policy initiatives that encourage approval bodies and NHS Trusts to participate in a generic and streamlined procedure for the set-up of projects, and for clinical sites to increase the efficiency with which they recruit patients.
- iv. Smaller commercial organisations can be supported through the development of a national network of support organisations that could provide expertise in areas such as project management, legal and regulatory issues and business management, which these organisations typically lack.
- v. Research conducted by the non-commercial sector needs to be incentivised through the availability of public funding that supports projects which support the UK's healthcare needs. These research groups require more flexible forms of employment to retain existing contract research staff.

conclusions

Challenges of managing clinical research in the UK

The full report presents detailed findings as to the many different challenges that influence the ease of managing clinical research projects within the UK. Time and cost continue to be seen as significant impediments to UK clinical research. However, our study showed further that retaining a project team, R&D approval, contract negotiation and NHS research culture were also seen as major impediments.

Respondents from different types of organisations had differing opinions about the current impediments that influence the management of clinical research in the UK. Respondents from pharmaceutical organisations perceive aspects such as patient safety, obtaining funding and obtaining ethical approval as not being an impediment to their research management. Whilst time and cost issues were viewed as important by researchers from all organisations, they were perceived as particularly important by respondents from pharmaceutical, and other commercial organisations. Whilst respondents from all organisations perceived obtaining R&D approval as a great impediment, this was particularly marked for pharmaceutical, other commercial and university/ academic research groups. The respondents from university and other non-commercial organisations rated funding as a particularly significant impediment, which reflects their reliance on external finance for projects.

Respondents from commercial organisations identified time and cost, and other aspects that reflect efficiency concerns such as R&D approval and contract negotiation as significant impediments. However, relative to other research organisations, pharmaceutical companies experience less difficulty with completing projects on time. Nevertheless this group are most directly influenced by global pressures. It should therefore be recognised that comparisons of their experiences of managing

projects should not necessarily be made with other UK research organisations, but rather with other global enterprises.

This study was conducted in the context of considerable changes to the UK system within which clinical research is organised and managed. Major alterations to the regulatory & governance approval process have occurred, and considerable attention from UK strategists and policy makers has resulted in the implementation of numerous initiatives that ultimately aim to improve the UK environment within which clinical research is conducted. However, these have also changed the context within which research is organised and managed within the UK.

Our findings suggest that it is constructive to consider the relationship between macro-level issues that possibly generate operational and management challenges for the research organisation, and the issues experienced with the day-to-day management of clinical research projects. A systematic literature review was used initially as a tool to identify the types of challenges that influence the management and organisation of clinical research. This synthesis of the literature supported the development of a two-tier model categorising macro-level and micro-level issues that affect the management of clinical research within the UK. This distinction can be an important aid for policy review in terms of how to respond to the different types of issues that exist, as the first group reflects issues that stem from beyond the research organisation and influence the overall research environment (e.g. policy initiatives and regulation & governance), whilst micro-level issues reflect challenges that are generated at the project-level and influence the management of research at a day-to-day level.

The detailed findings presented in the main report highlight numerous challenges that influence the successful management of clinical research projects within the UK. It has been emphasised that the

policy response to these challenges needs to recognise and support *all* the research groups that constitute the clinical research sector within the UK, in order to promote 'UK PLC'. Clinical research is a knowledge-intensive industry and its future is reliant on developing and nurturing the expertise that this sector is based upon. However, the findings underline the fact that many of the challenges of conducting clinical research are compounded because of the complex array of different stakeholder groups involved and the different models of research that are being conducted. This presents challenges for policy makers in balancing the support required for different types of research organisation, whilst more generally promoting the clinical research sector within the UK.

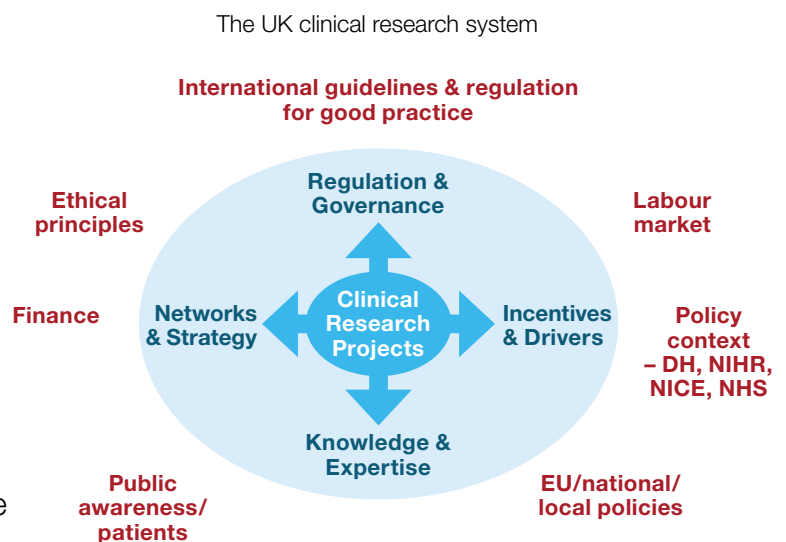
At best the system is a 'one size fits all model', where what is perceived as good research is framed by a standard RCT model. Other models of research experience considerable challenges. This has the potential to discourage research groups from developing innovative approaches to clinical research which are based on atypical features that might differ considerably from a standard RCT. That is not to say, however, that large commercial groups do not experience challenges as they experience the greatest pressures from the global context in which they operate, and often feel marginalised by other groups within the healthcare sector. Policy makers should recognise that different clinical groups require different levels and types of support, and should also be aware that strategic changes to the UK environment may inadvertently create additional challenges for the organisation and management of particular types of research.

The findings presented in this report provide particularly valuable insight into how certain groups view particular aspects of the process of managing clinical research projects. Other stakeholder groups, including policy makers and the regulatory & governance approval groups should recognise that these attitudes exist, even if they debate the legitimacy of these views from the context of their own remit and the actions that they have taken. This is important because attitudes shape whether people become involved in research. In short, if researchers

see the UK context as too challenging, then they may choose to conduct projects elsewhere, or cease to engage in clinical research. However, it also needs to be recognised that attitudes and perceptions of the effects of very recent initiatives, such as the introduction of the UKCRN, are not reflective of actual behaviours at a project level, and in-depth research should be undertaken to explore their actual impact on the successful management of clinical research projects. It is vital that research is undertaken to generate in-depth findings regarding the actual experiences of managing clinical research within the UK, which survey data, however detailed cannot adequately capture.

This report has explored the challenges experienced when managing clinical research projects under four themes. These themes are interlinked and the issues that have been highlighted over-lap these areas. For example, challenges related to a lack of expertise are also inherently linked to the incentives to recruit and retain project team members. Nevertheless, it is important to reiterate that it is the macro-level context, including global and market pressures, the UK strategic emphasis and policy initiatives, ethical principles and the regulatory & governance framework, that influence how the challenges associated with these four themes are experienced in the day-to-day management of projects.

Figure (i) Schematic model depicting the UK clinical research system





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