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Original Article

# Radiotherapy Trial Set-up in the UK: Identifying Inefficiencies and Potential Solutions

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## Abstract

*Aims:* Radiotherapy clinical trials are integral to the development of new treatments to improve the outcomes of patients with cancer. A collaborative study by the National Cancer Research Institute Clinical and Translational Radiotherapy Research Working Group and the National Institute for Health Research was carried out to understand better if and why inefficiencies occur in the set-up of radiotherapy trials in the UK.
*Materials and methods:* Two online surveys collected information on the time taken for UK radiotherapy trials to reach key milestones during set-up and the research support currently being provided to radiotherapy centres to enable efficient clinical trial set-up. Semi-structured interviews with project managers and chief investigators identified better ways of working to improve trial set-up in the future.
*Results:* The timelines for the set-up of 39 UK radiotherapy trials were captured in an online survey showing that the median time from grant approval to trial opening was 600 days (range 169–1172). There were 38 responses from radiotherapy centres to a survey asking about the current support provided for radiotherapy research. Most of these centres have more than one type of staff member dedicated to supporting radiotherapy research. The most frequent barrier to radiotherapy trial set-up identified was lack of physicists' time and lack of time for clinical oncologists to carry out research activities. Four main themes around trial set-up were identified from semi-structured interviews: the importance of communication and building relationships, the previous experience of the chief investigator and clinical trials units, a lack of resources and having the time and personnel required to produce trial documentation and to process trial approval requests.
*Conclusions:* This unique, collaborative project has provided up to date information about the current landscape of trial set-up and research support in the UK and identified several avenues on which to focus future efforts in order to support the excellent radiotherapy trial work carried out across the UK.


*Key words:* Cancer; radiotherapy; trials

## Introduction

Radiotherapy clinical trials are integral to the development of new techniques and the testing of new treatments to improve the outcomes of patients with cancer. There have been many excellent examples of radiotherapy trials that have made an impact on clinical practice [1]. However, it has previously been recognised that there is scope for

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shortening the time it takes to set up non-commercial trials in the UK [2]. In order for UK radiotherapy trials to deliver timely answers to relevant clinical questions and, ultimately, to have the desired impact on clinical practice and patient care, trial set-up must be efficient and streamlined. There is growing focus on increasing the impact from research to ensure the maximum return for funder investment and for participating patients' efforts and time [3,4].

We present the results of a project carried out to understand better if and why inefficiencies occur in the set-up of UK radiotherapy trials in order to improve this process in the future. This was a collaborative project undertaken by two national organisations in the UK: the National Cancer Research Institute, through its Clinical and Translational Radiotherapy Research Working Group (CTRad), and the National Institute for Health Research (NIHR), which supports the national Radiotherapy Trials Quality Assurance Group (RTTQA) and also has responsibility to support the timely set-up and delivery of clinical research studies in England.

The specific objectives of this project were:

(i) to understand better the barriers to the timely set-up of radiotherapy trials in the UK;
(ii) to understand better the research support currently provided to radiotherapy centres to enable clinical trial set-up and delivery;
(iii) to identify better ways of working to improve set-up times.

For the purposes of this project, the 'central site' refers to the co-ordinating clinical trials unit (CTU), the 'recruiting site' refers to the sites recruiting patients into a trial and the 'radiotherapy centre' refers to a centre that is providing a radiotherapy service.

Improving clinical trial set-up times is not a UK-only challenge. Therefore, the lessons learned from the study will be of interest to both UK and international clinical trialists.

## Materials and Methods

Two online surveys collected information about radiotherapy trial set-up times and the current research support available at radiotherapy centres in the UK.

Survey 1 was developed by a multidisciplinary team from work stream 3 (WS3) of CTRad and piloted for content and face validity by one clinical trial co-ordinator. A list of all UK radiotherapy trials that had required RTTQA approval between January 2013 and November 2016 was generated from a RTTQA database and the survey was sent to both the CTU project managers and chief investigators for each of these trials. Although not mandatory, since 2010 it is strongly encouraged and an expectation of CTRad and funders that all radiotherapy trials in the UK have RTTQA assessment. Survey 1 collected information on the type of trial, its radiotherapy complexity and funding source and asked respondents to report key milestone dates from grant submission through to site opening and recruitment. Radiotherapy complexity assessment was based on the quality assurance activity as described in key radiotherapy quality assurance memoranda [5,6]. One open-ended question asked respondents trial set-up could be improved in the future. The survey was developed and distributed using Survey Monkey and analyses were carried out using Microsoft Excel.

Survey 2 was developed by the NIHR and piloted internally. There were two main sources of potential survey participants. First, the survey was sent to all radiotherapy leads and research delivery managers in the 15 local clinical research networks (LCRNs) in England. Those recipients were asked to distribute the survey to clinical oncology consultants in their local radiotherapy centres. Second, the RTTQA group sent the survey to all heads of radiotherapy physics and the associated radiotherapy service managers in radiotherapy centres in the UK, with the aim of capturing both the physics and radiographer perspectives. The main objective of this survey was to gain an understanding of the radiotherapy research support that exists at radiotherapy centres in the UK. This survey was developed using Google forms and analyses were carried out using Microsoft Excel.

Both surveys were online only and were distributed via embedding an online link into email correspondence. Descriptive statistics were used to report the results.

To address the third objective for this project, the chief investigators, and/or their assigned clinical research fellow or CTU project manager, of eight UK radiotherapy trials were invited to take part in a semi-structured interview to discuss the set-up process for their particular trial. The trials were purposively selected by CTRad WS3 to cover a range of disease sites, radiotherapy complexity and a mixture of pharmaceutical and investigator-led trials. Three chief investigators, one senior research fellow and two project managers were interviewed. Three interviews were face to face and two were via telephone (one being a joint interview with a chief investigator and a project manager). Interviews were carried out using a topic guide, but the interviews were informal and participants were able to lead the conversation to explore issues outside those on the topic guide if relevant. Thematic analysis [7] using a framework approach [8] was undertaken by two researchers.

Figure 1 provides a detailed overview of the methods used in this study.

## Results

### *Survey 1 to Radiotherapy Trial Project Managers to Elucidate Current Timelines*

Responses from the chief investigator or trial co-ordinator of 35/55 (71%) trials were received. Table 1 shows the trial characteristics and the time taken to reach key set-up milestones. Figure 2 shows the time to achieve these milestones based on the complexity of radiotherapy treatment.

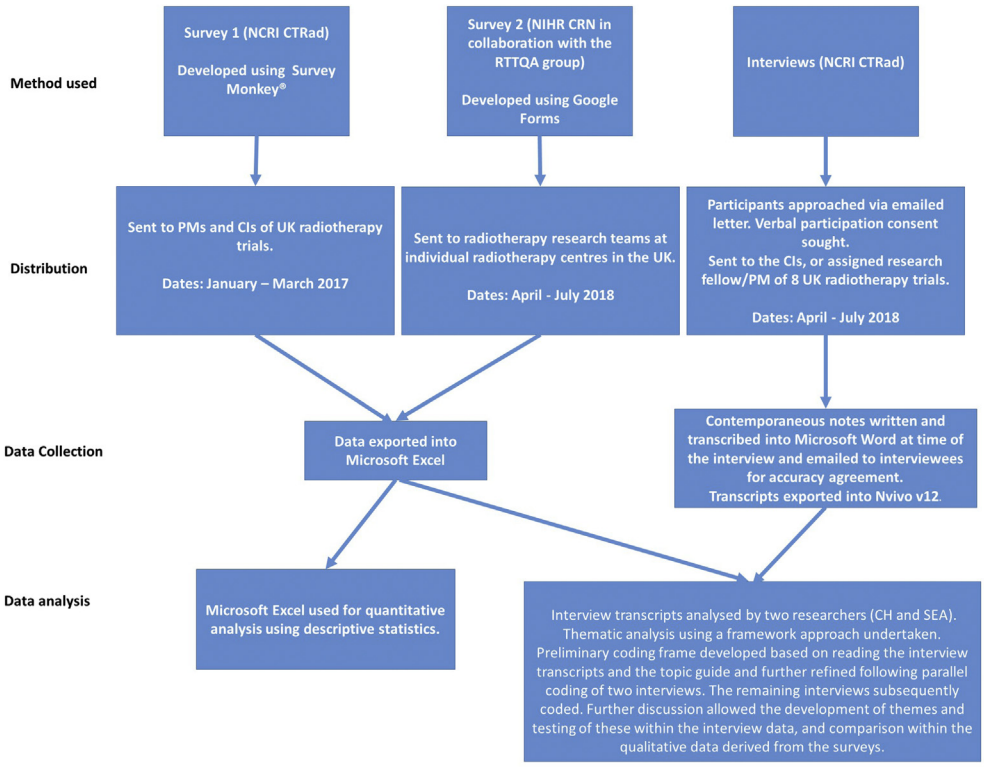


**Fig 1.** Methods used for study data collection and analysis.

*Survey 2 to Radiotherapy Research Staff to Understand Current Research Support*

Thirty-eight responses to Survey 2 were received overall, 37 from 13 LCRNs and one from Scotland. Four centres submitted more than one response. Therefore, in total, 34 individual centres of a possible 62 centres responded. The professional roles for individual respondents were not captured.

Thirty (76%) respondents indicated that they were working at radiotherapy centres that recruited to clinical trials. Thirty-five (92%) indicated they had dedicated research staff within their radiotherapy departments and most of these (33/35) had more than one type of staff member (Table 2). Most staff, regardless of type, were funded by the NIHR Clinical Research Network or by other means, such as commercial trial income. The number of whole time equivalent (wte) staff for each type of post is shown in Figure 3. Most centres have between 0 and 1 wte of each staff type in post.

Table 2 outlines the time for key milestones in the process of radiotherapy quality assurance. Most respondents rated the quality and responsiveness of RTTQA as 3–5 out of 5 (28/29 responses; 97%). Of 30 responses, 20 respondents indicated that they had experienced a delay in trial set-up due to processes related to their local research and development department, but most (25/29 responses; 86%) still rated the quality and responsiveness of their department between 3 and 5.

Finally, respondents chose factors that they identified as the biggest barriers to efficient trial set-up in their centre. Overall, 72 responses were generated (Table 2). There was also a free text box to allow respondents to describe other barriers they encountered that were not prespecified in the survey. These free text responses were analysed thematically alongside the responses to the open questions.

*Semi-structured Interviews with Trial Chief Investigators, Clinical Co-ordinators and Project Managers*

Four main themes relevant to trial set-up were derived from the interviews. The themes are summarised in Figure 4 and direct quotations from the interview transcripts that are relevant to each theme can be found in Supplementary Table S1. During the analysis, barriers were identified that occurred at the central site and the recruiting sites, but the themes that emerged are cross-cutting, with relevance at both. This finding indicates that common strategies can be used to tackle these barriers.

*Theme 1: Establishing and Maintaining Relationships and Pathways of Communication with Key Individuals and Organisations*

This theme encompasses the value of constructive relationships between individuals and the importance of efficient communication. At the CTU level, establishing and maintaining strong pathways of communication with individuals and teams, such as medical physicists,

**Table 1**
Results of survey 1

| | Number $n = 39$ trials (%) |
|---|---|
| Radiotherapy trial details | |
| Included an investigational medicinal product | 16 (41) |
| Randomised | 33 (85) |
| Complexity of radiotherapy treatment used in the trial | |
| Minimal | 4 (10) |
| Basic | 4 (10) |
| Moderate | 9 (23) |
| Complex | 22 (56) |
| Treatment Intent | |
| Neoadjuvant | 5 (13) |
| Radical | 21 (54) |
| Adjuvant | 8 (21) |
| Palliative | 4 (10) |
| Mixed | 1 (3) |
| Trial funder | |
| Industry only | 1 (3) |
| Government, including research council | 5 (13) |
| Charity | 31 (79) |
| Charity and industry | 2 (5) |
| Trial milestones ($n$ = number of completed responses to each question) | Median time in days (range) |
| Grant approval to ethics approval ($n = 32$) | 375 (16–1169) |
| Grant approval to radiotherapy planning document finalisation ($n = 18$) | 365 (128–1238) |
| Grant approval to first recruiting site opening ($n = 30$) | 600 (169–1172) |
| Ethics submission to ethics approval ($n = 37$) | 72 (16–133) |
| Ethics approval to first recruiting site opening ($n = 34$) | 203 (75–431) |
| MHRA submission to MHRA approval ($n = 13$) | 51 (24–374) |
| Time between planned start date and actual start date ($n = 28$) | 175 (7–353) |
| First site opened to patient recruited at that site ($n = 29$) | 36 (0–202) |

MHRA, Medicines and Healthcare products Regulatory Agency.

laboratory personnel and pharmaceutical companies, was important.

> *I did not have any links in the medical physics department to help push this part of the work forward.*

> *There are inevitable delays when dealing with a large corporation …. forming good relationships will make this easier for future projects.*

At recruiting sites, communication between the CTU, recruiting sites, local research and development teams and the RTTQA group was an issue. Communication problems were occasionally attributed to 'one off' issues, such as an organisational change or changing staff members, but more frequently, there were broader issues of knowing who to contact, having effective pathways of communication and agreeing designated roles and responsibilities in advance of set-up.

> *… very difficult to get information from the (RTTQA) website and you really need a contact there to get any information.*

> *No-one had spoken to radiology to ask if they would have the capacity to report all of the central research scans to RECIST criteria.*

Making use of the skills and resources associated with organisations such as CTRad and RTTQA and identifying key individuals, involving them in key meetings such as those of the trial management group and keeping pathways of communication open through active efforts were important solutions.

> *There was a physicist and a radiographer on the trial management group who interacted with the RTTQA team.*

Once established, the advice was to foster relationships formed to build a 'network'. One example of an extremely efficient trial set-up was attributed to the work carried out by the CTU, chief investigator and RTTQA for a previous, similar trial, in building relationships with sites and providing support in the set-up and radiotherapy quality assurance of a novel radiotherapy technique.

Finally, incorporating set timelines into radiotherapy quality assurance reviews was proposed to improve the current challenge of effective and timely feedback on radiotherapy test cases.

*Theme 2: Role and Previous Experience of the Chief Investigator, Clinical Trials Unit and Recruiting Sites*

The second theme identified was the role and previous experience of the chief investigator, the CTU and the recruiting sites. There was a perceived correlation between inexperience and a lack of insight into the work required. The issue of the chief investigator having time within their normal job plan allocated specifically to trial-related activities was raised.

> *It would be difficult to imagine how this workload would feasibly fit with a chief investigator who does not have dedicated research time – it would be impossible.*

It was suggested that it helps to choose a chief investigator, CTU or recruiting site with experience in the particular type of trial being run, but when this is not possible, encouraging experienced individuals and sites to mentor others can build an environment in which more junior researchers, and sites with less trials experience, can flourish. In particular, using resources and contacts provided by CTRad, the use of a deputy chief investigator and a buddy system between principal investigators at recruiting sites were mentioned.

> *CTRad has created a network of people who I could approach for advice.*

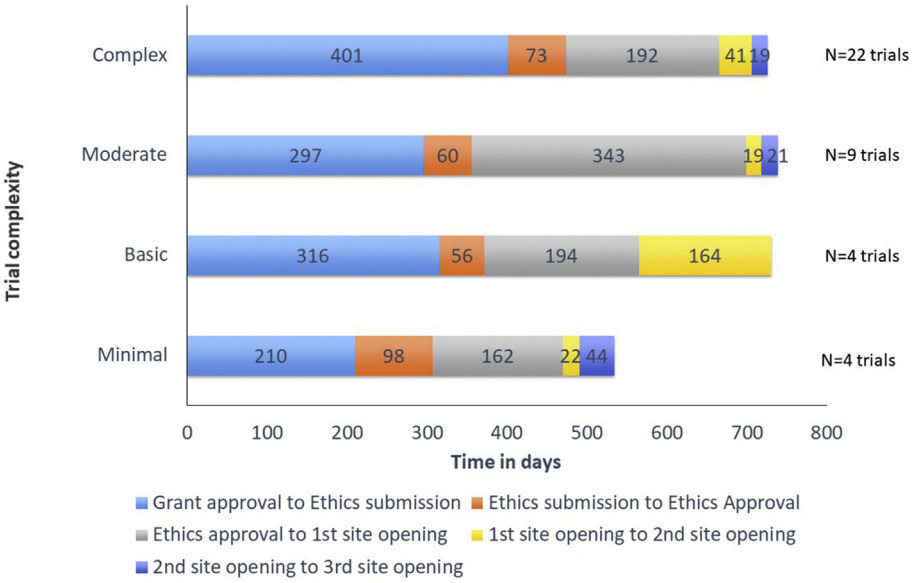


**Fig 2.** Time to reach key milestones based on the complexity of radiotherapy treatment used within the trial.

*Chief Clinical Coordinator Role (Associate Chief Investigator). This helped communication between the sites/trial team and RTTQA.*

The personal attributes of the chief investigator or their delegate, such as the ability to be flexible, committed and willing to dedicate time to the set-up, were recognised as important and, for the CTU, having robust administrative abilities is important.

Finally, finding avenues of support for recruiting sites that are not always reliant on the chief investigator or the CTU was offered as a possible solution to improve trial set-up.

*Use the RTTQA … This gives another avenue rather than always having to ask the chief investigator.*

*Theme 3: Resources: Funding, Staffing and Infrastructure*

The third theme addressed the resources required for efficient trial set-up. This recognised the challenge of identifying all funding needs at the outset and securing funding to cover all aspects of the trial no matter how small. Infrastructure at a national level affected the ability of central (CTU) sites to proceed with core trial set-up activities. Once the trial had opened at its first recruiting site, additional sites that were affected by poor national infrastructure, such as a lack of specialist radiotherapy equipment, were slower to open. Lack of staffing at recruiting sites, in particular research nurses, clinical oncologists and medical physicists, was a common frustration that led to 'bottlenecks' in the set-up process.

*There was a lack of radiotherapy resources at sites - not enough linacs at some sites to absorb this trial.*

*Some consultants were working alone … and did not have time to do the voluming.*

Some interviewees felt that there was 'no slack in the system' and there were 'no solutions' to address national infrastructure and staff capacity. Others identified using national commissioning programmes (Commissioning through Evaluation) in England or employing additional staff to do specific tasks in the CTU as possible solutions.

*Theme 4: Time and Personnel Needed to Produce Trial Documentation and to Process Trial Approval Requests*

The last theme identified was the work required by all parties during trial set-up. This included the development of trial documentation, specifically the trial protocol and radiotherapy aspects of the protocol or radiotherapy planning guideline document, as well as pharmacy and radiotherapy quality assurance documents. If there were external parties such as pharmaceutical companies involved, any iteration of documents, such as the trial protocol, required approval from all key players.

*Each time the protocol for the trial was altered the pharmaceutical company, as well as all the other parties involved in the trial, had to review each iteration, which took time.*

The advice given was to start development early, to use help from national organisations and to avoid using irrelevant document templates.

*RTTQA acted as a 'safety net' as physicists were reviewing the RT protocol.*

*I would now be wary of trial protocol templates … make sure that it is appropriate for the trial that you are developing.*

*Surveys 1 and 2 Free Text Comments: Qualitative Analysis*

Free text responses to open questions in the two online surveys were coded independently of the interview data, followed by a comparison between the two different

**Table 2**
Results of survey 2

| Radiotherapy research strategy | Number of responses (38 replies to this question) |
|---|---|
| Radiotherapy centres with a research strategy | 20 (53%) |
| Patient and public involvement | Number of responses (20 replies to this question) |
| Patient and public involvement in the research strategy | 12 (60%) |
| Number of trials open at each radiotherapy centre | Number of responses (30 replies to this question) |
| None | 1 (3%) |
| 1–5 trials | 11 (37%) |
| 6–10 trials | 6 (20%) |
| 11–20 trials | 9 (30%) |
| >20 trials | 3 (10%) |
| Types of radiotherapy research staff* | Number of responses (100 responses from 38 respondents) |
| Radiographer | 31 (31%) |
| Physicist | 23 (23%) |
| Research nurse | 16 (16%) |
| Data manager | 17 (17%) |
| Other (e.g. clinical oncologists, PhD students, clinical fellows, statisticians and clinical scientists) | 13 (13%) |
| Biggest barriers to efficient radiotherapy trial set-up* | Number of responses (72 responses from 38 respondents) |
| Lack of clinical oncologists' time | 16 (22%) |
| Lack of physicists' time | 19 (26%) |
| Lack of radiographer or research nurse support | 13 (18%) |
| Lack of local research and development support | 8 (11%) |
| Other | 16 (22%) |
| Important milestones in the radiotherapy quality assurance process | Number of responses |
| Time for clinical oncologist to volume test case (30 responses) | |
| 2 weeks | 5 (16%) |
| 1 month | 12 (40%) |
| 2 months | 9 (30%) |
| >3 months | 4 (13%) |
| Time from physics department receiving to physicist completing benchmark case (29 responses) | |
| 1 week | 2 (7%) |
| 2 weeks | 3 (10%) |
| 1 month | 16 (55%) |
| 2 months | 6 (21%) |
| >3 months | 2 (7%) |
| Time for feedback from central RTTQA after benchmark case submission (29 responses) | |
| 1 week | 3 (10%) |
| 2 weeks | 12 (49%) |
| 1 month | 10 (34%) |
| 2 months | 4 (14%) |

RTTQA, Radiotherapy Trials Quality Assurance Group.
* Respondents could choose more than one answer for this question.

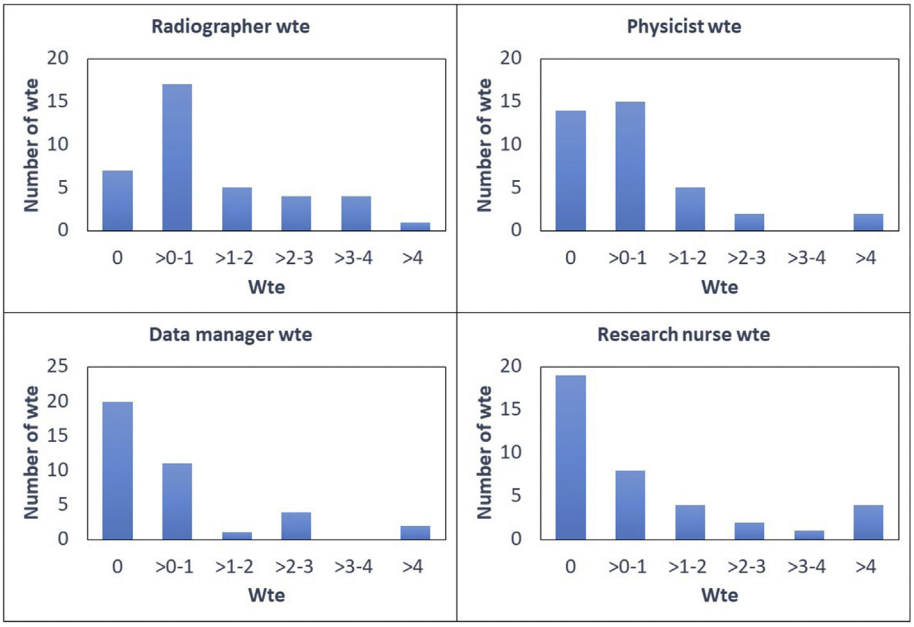


**Fig 3.** Whole time equivalent (wte) radiotherapy research staff in UK radiotherapy research centres.

sources. The themes arising from the surveys were consistent with those developed from the interview data.

In Survey 1, a specific solution proposed to improve communication between CTUs and RTTQA was to include all interested parties (CTU, RTTQA and recruiting sites) into correspondence to improve transparency around timelines and review activities. A barrier not mentioned in the interviews was the challenge of dealing with an international trial group, particularly when organising trial documents. Adapting radiotherapy guideline documents to be used by sites across the UK with different planning systems and differences of opinion in correct cost attribution of research-related activity between CTUs and some recruiting sites were also barriers not picked up in the interviews.

In Survey 2, the 'other' barriers to set-up identified by radiotherapy research staff were analysed. There was a strong focus on the theme of resources, in particular funding for all staff and difficulties with staff capacity of data managers, trial co-ordinators, nurses, clinical oncologists and medical physicists.

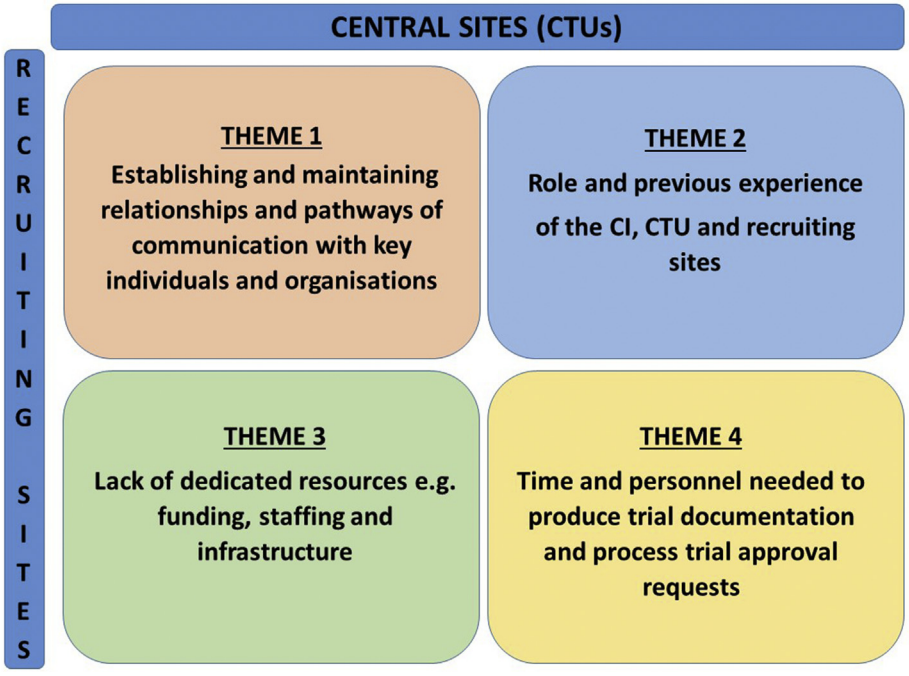


**Fig 4.** Themes identified from interview data (CI = Chief Investigator, CTU = Clinical Trial Unit).

**Table 3**
Strategies to improve UK radiotherapy trial set-up

| | Strategy for change | Already in action or possible future solutions |
|---|---|---|
| Establishing and maintaining relationships and pathways of communication with key individuals and organisations | | |
| RTTQA group responsiveness | Implement turnaround time for RT QA submissions. | Turnaround times for pre-trial and on-trial case reviews defined.<br>All trials allocated a trial-specific generic email address for multiple user access to ensure back up for RT QA review. |
| RTTQA group accessibility | Improve website organisation and functionality. | Website facility being reviewed as part of the larger RTTQA group IT infrastructure development. |
| Role and previous experience of the CI, CTU and recruiting sites | | |
| Supporting the CI and CTU | Develop RT trial protocol and planning guideline templates. | RT protocol checklist available through CTRad to support the writing of the RT aspects of a protocol.<br>RTTQA can provide RT planning guideline templates.<br>Previous trial documentation available on request through the appropriate channels to support the writing of new trial protocol and guidelines. |
| | Develop a practical guide to setting up a RT trial to assist less experienced CIs and CTUs identify work required. This should include expected timelines with the aim of reducing the lengthy time between grant approval and ethical approval. | CTRad WS3 and RTTQA working group convened to promote closer relationships and standardise working practices between RTTQA and all UK CTUs.<br>There are plans by RTTQA to routinely record and audit trial set-up times for every trial at each centre from April 2020. This will provide transparency, indicate if expected timelines are realistic and being met, and highlight areas for ongoing improvement. |
| | Supporting and educating CTU specialist staff. | CTRad and NCRI Cancer CTU Group RT workshop to explain RT treatment, delivery and side-effects to CTU staff working on RT trials. |
| | Improved correspondence and sharing of information between RTTQA and CTUs. | Include all parties in correspondence where appropriate but particularly in relation to site approvals. |
| | Invite key members of the multidisciplinary team onto the TMG. | Incorporate this suggestion into any guidelines regarding protocol development group. |
| | Support recruiting centres that have less experience in setting up and running RT trials. | Set up buddying of high recruiting centres with new centres that share the same RT technology to offer support with planning aspects in the early stages. |
| | Encourage more junior researchers to get experience in trial set-up early in their career. | Create ‘chief clinical co-ordinator’ or ‘associate CI’ role for junior investigators to work under the mentorship of the trial CI.<br>Create similar roles for trainees at recruiting sites: ‘associate PI’ roles. This is already in progress for UK surgical trainees. |
| Lack of dedicated resources (e.g. funding, staffing and infrastructure) | | |
| Efficiency of IT infrastructure | Better data uploading facilities. | RTTQA group addressing data upload and storage for clinical trials. New platform in pilot testing phase. Full implementation by 2020. |
| CRNs/funding | Highlight correct cost attributions for RT QA activity. | In 2010, the Department of Health agreed that clinical trial RT QA is over and above routine QA, and therefore should be defined as a NHS service support cost and funded through local CRN funding.<br>Study teams should ensure RT QA activities are clearly defined in the Schedule of Events and Cost Attribution Tool (SOECAT) as service support costs. |

(*continued on next page*)

**Table 3** (*continued*)

| | Strategy for change | Already in action or possible future solutions |
|---|---|---|
| Time and personnel needed to produce trial documentation and process trial approval requests | | |
| Reduce RT QA workload | Streamline RT QA submissions with previous QA completed and define timelines for submissions and review. | Streamlining implemented on an anatomical site basis.<br>Funding available for RT QA workshops to support implementation of new RT techniques in clinical trials. |

CI, chief investigator; CRNs, clinical research network; CTRad, Clinical and Translational Radiotherapy Research Working Group; CTU, clinical trials unit; IT, information technology; NCRI, National Cancer Research Institute; NHS, National Health Service; PI, principal investigator; QA, quality assurance; RT, radiotherapy; RTTQA, Radiotherapy Trials Quality Assurance Group; SOECAT, Schedule of Events and Cost Attribution Tool; TMG, trial management group; WS3, Work Stream 3 (phase III trials and methodology).

*Trials should have a funding component for centre (local) physics support that could be given to centres to support staffing.*

One respondent suggested a national approach of enhancing funding and there was some cautionary advice from previous experience.

*Savings made by centres taking part in trials (e.g. leading to less radiotherapy, hypofractionated trials leading to less costs) should be reinvested to centres/RTTQA to ensure excellent radiotherapy nationally.*

*When intensity-modulated radiotherapy was rolled out, many centres including our own had no help or teaching in what we were doing. The same will be true of stereotactic ablative radiotherapy and any other techniques.*

Survey 2 also asked respondents to suggest how the radiotherapy quality assurance and research and development processes could improve. There was a resource-specific suggestion for radiotherapy quality assurance concerning better data uploading facilities for benchmark cases, but most suggestions centred on communication. Some responded that the research and development teams did not understand the processes involved in the set-up for trials involving radiotherapy, in particular the radiotherapy quality assurance component and the excess treatment costs required at sites. With regards to research and development staffing, there were frustrations around holiday cover, dealing with the work required in a timely manner and giving trial staff proper training to complete the required paperwork. Finally, delays in drafting and organising documents, such as Ionising Radiation Medical Exposure Regulations (IRMER) and finance approvals, were highlighted.

## Discussion

The median set-up time for the sample of radiotherapy trials included in our study was lengthy at 600 days. Although this is not felt to be unusual for academic cancer trials, the set-up of high-quality radiotherapy trials requires some additional steps that can extend the set-up period. We used a mixed methods approach to identify the challenges facing radiotherapy trial set-up and the solutions that have been used by UK trial teams to make this process more efficient. The participation in this project from project managers, radiographers, physicists, clinicians and chief investigators shows a willingness to engage in research to find ways of improving the set-up process.

Respondents highlighted their perceptions of the benefits of good-quality and efficiently run radiotherapy trials.

*Radiotherapy research should be an essential and mandatory aspect of daily work. It is not. It is the best way to ensure national quality assurance and for teaching new techniques. All centres should be made to take part, if they have the right support.*

*Patients can then be treated close to home, knowing they are offered the latest trials and treatments.*

Encouragingly, there were some examples of trials opening in less than 1 year from grant approval (an often applied expectation) and most opened within 6 months of their planned start date. Approvals from large organisations, such as the Health Research Authority (HRA) and the Medicines and Healthcare products Regulatory Agency (MHRA), were efficient and respondents explained that this was because the timelines for the processes involving these organisations were often agreed in advance and were transparent.

It is clear that there is a significant amount of work during trial development that is resource intense and not feasible to complete before funding approval. It should therefore be expected that there will be considerable time between funding being awarded and submission for regulatory approvals to allow the detailed development of trial documentation, including protocol development and the definition of radiotherapy-specific guidelines.

Many respondents reflected that if they had understood better the main tasks involved in trial set-up, especially in relation to the radiotherapy component, they could have pre-empted the workload. There was often a lack of understanding at the site level, local research and development and at the LCRN level about how complex radiotherapy trials differ in expected local set-up time compared with clinical trials with investigational medicinal products alone. Local and national recognition of timelines, radiotherapy processes and documentation requirements would streamline progression once funding has been agreed.

There were several examples of insufficient funding or staff at central and recruiting sites to complete radiotherapy-specific tasks. This lack of funding, and realistic estimates of the time required to do the tasks, were often not recognised in research applications, funding awards or trial development timelines.

The limitations of the project include that there is no known denominator for Survey 2 to indicate how many individuals received the survey. For both surveys, there is no information on the non-responders, which means that the study is open to response bias. There is a possibility that those who replied to the surveys had more issues with trial set-up than the non-responders. A small number of interviews were undertaken, however these interviews covered trials with a range of radiotherapy complexity and involved different members of the set-up team. Also, despite these small numbers, there was concordance between the survey free text comments and the interviews.

In identifying and addressing these key challenges, it is hoped that the set-up of UK radiotherapy trials can further improve. This will help to drive forward trials that answer key clinical questions for patients and permit the UK clinical oncology community to build on its strong reputation for supporting excellent radiotherapy research. Some solutions to the challenges identified are not easily surmountable and will require time, better funding and improvements in national infrastructure and resources. However, to begin the process, we have proposed a number of pragmatic solutions that may be relatively straightforward in their implementation. Table 3 outlines strategies to address the challenges cited by survey respondents and interviewees, indicating those already in action plus possible future solutions to improve radiotherapy trial set-up in the UK.

## Conclusions

Clinical trial set-up times can be lengthy. One of the biggest barriers to efficient trial set-up at radiotherapy centres is a lack of dedicated medical physics time at sites and protected clinical time to carry out trial-specific activities. We identified key themes regarding the challenges faced by CTUs and recruiting sites during trial set-up and have reported examples of solutions adopted to overcome these barriers. All stakeholders must work together to support continued delivery of practice-changing radiotherapy trials in a timely manner. We highlight areas for development and have provided immediate pragmatic solutions to support timely opening of radiotherapy trials.

## Conflict of Interest

The authors report no conflicts of interest.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clon.2019.10.004.

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