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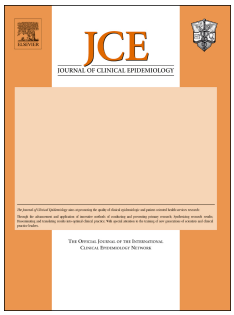

Remote or on-site visits were feasible for the initial set-up meetings with hospitals in a multi-centre surgical trial: an embedded randomised trial

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Title: Remote or on-site visits were feasible for the initial set-up meetings with hospitals in a multi-centre surgical trial: an embedded randomised trial

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Declarations

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Conflict of Interest

The authors declare that they have no competing interests except for AR whose department has received educational grants from DePuy Limited outside the scope of this work. These grants have not in any way influenced his contribution to this study.

Contributorship

All authors were involved in the conception and design of the study. LJ, SB, LC, MN and GT contributed to the acquisition of data and CF and IC undertook the analyses. All authors contributed to the interpretation of data, commented on drafts of the article and approved the manuscript to be submitted.

Abstract

Objectives

To investigate the effects, costs and feasibility of providing on-site compared with remote meetings to set-up hospital sites in a multi-centre, surgical randomised controlled trial.

Study Design and Setting

Hospitals were randomised to receive the initial trial set-up meetings on-site (i.e. face-to-face) or remotely (i.e. via teleconference). Data were collected on site set-up, recruitment, follow-up and costs for the two methods. The hospital staff experience of trial set-up was also surveyed.

Results

Thirty-nine sites were randomised and 33 sites set-up to recruit (19 on-site and 14 remote). For sites randomised to an on-site meeting compared with remote meeting respectively, the time from first contact to first recruit was a median of 246 days [interquartile range (IQR) 196 to 346] vs 212 days [IQR 154 to 266], mean recruitment was 10 participants [median 10, IQR 2 to 17] vs 11 participants [median 6, IQR 5 to 23] and participant follow-up at 12 months was 81% vs 82%. Sites allocated to an initial on-site visit cost on average £289.83 more to set-up.

Conclusion

Remote or on-site visits are feasible for the initial set-up meetings with hospitals in a multi-centre surgical trial. This embedded trial should be replicated to improve generalisability and increase statistical power using meta-analysis. ISRCTN78899574.

Keywords: Study Within a Trial; Randomised Controlled Trial; Recruitment; Response rate; Costs; Feasibility

A running title: Remote and on-site visits were feasible for the initial set-up meetings with hospitals in a multi-centre surgical trial

Word count: 3886

"What is new?"

Key findings:

- It was feasible to use remote or on-site visits for the initial contact with sites when setting up hospitals in a multi-centre surgical trial.

What this adds to what was known?

- The evidence from this study and the wider literature questions the need for on-site visits and the effectiveness of additional contact by Trial Co-ordinators on trial conduct.

What is the implication, what should change now?

- Trial Co-ordinators should consider being more selective as to when on-site visits are necessary and what type of additional contact with a site is required depending on the challenges that are specific to that site and the study.
- Further research is necessary to improve our understanding of what constitutes optimal Trial Co-ordinator contact with sites and to evaluate strategies across a range of participant groups and settings.

1. Introduction

Randomised controlled trials (RCTs) are the gold standard for evaluating the effectiveness and safety of healthcare interventions (Kunz et al, 2007). They often require substantial amounts of public funds, but around half fail to reach their recruitment target within their original timescale and budget (Walters et al. 2017). Poor recruitment can lead to underpowered studies that can increase the risk of not implementing an effective intervention. This raises ethical concerns about the involvement of participants in RCTs and can lead to a trial being extended which increases costs (Treweek et al. 2013).

In our experience, setting up hospital sites to recruit into multi-centre RCTs usually requires an initial contact meeting between the Trial Co-ordinator (TC) and hospital staff to discuss: i) the trial rationale and design; ii) assessment of feasibility and capacity of the site to deliver the trial; and iii) the submission for local governance approval to undertake the trial. This is followed by a site initiation visit (SIV), which is often conducted on-site (face-to-face), during which hospital staff are trained in trial procedures and checks are made to ensure that the necessary practical and governance arrangements are in place to start the trial.

We have often conducted the initial contact meeting on-site; although it could be undertaken remotely (via telephone/videoconference). The potential benefit of both the initial contact and SIV being on-site is to help foster a positive relationship between the trial team and site staff, expedite the timeliness with which sites are set-up and improve recruitment and data collection. However, in multi-centre RCTs it can be very time-consuming and costly for TCs to conduct both visits face-to-face for each site. Evidence from a single embedded RCT suggested that conducting on-site monitoring visits compared with no visit did not statistically significantly improve participant recruitment or data collection (Lienard et al. 2006).

Given the limited evidence available and the increasing demand from commissioners of research for more efficient RCTs, we decided to explore the feasibility of undertaking remote, rather than on-site, initial contact meetings when setting up hospitals. This study within a trial (SWAT) was embedded in the SWIFFT multi-centre, orthopaedic surgical trial (Dias et al. 2016) and was registered as number 27 (ISRCTN 78899574) with the Northern Ireland Hub for Trials Methodology Research programme. The protocol is publically available on-line at their SWAT Repository Store. The objectives were to investigate whether a remote meeting compared with an on-site visit was feasible for the initial contact with hospitals and to describe the effect on set-up times, recruitment, data collection and the costs of these two approaches.

2. Methods

2.1 Population, design and interventions

A feasibility RCT of on-site (face-to-face) versus remote (teleconference) initial contact meetings with hospital sites was embedded within the SWIFFT trial. SWIFFT is evaluating the clinical and cost-effectiveness of cast treatment versus surgical fixation in patients aged 16 or above with a clear bicortical fracture of the scaphoid waist on plain radiographs from hospital sites predominantly across England. Patients were recruited at fracture clinics and were asked to complete a questionnaire by post or in clinic at 6, 12, 26 (post only) and 52 weeks (primary end-point). Patients attended hospital out-patient clinics at 6, 12 and 52 weeks when data on treatment, grip strength, range of movement, complications and imaging were collected.

The initial contact meeting between the TC and hospital site was standardised across the two groups by: i) inviting the same staff at each site (the site-specific Principal Investigator (PI), Research Nurse (RN) and, where possible, Radiology contact) to discuss preparing the site for submission to local Research and Development (R&D) departments for study approval, using a pre-defined email depending on site allocation; ii) using the same presentation for each mode of meeting; and iii) devising a checklist to ensure all the same topics were discussed. All subsequent SIVs were held on-site for both groups.

The study complies with guidelines for reporting embedded recruitment trials (Madurasinghe et al. 2016).

2.2 Randomisation and Sample Size

Sites were randomised 1:1 to receive either an on-site or remote initial contact meeting using minimisation (via MinimPy software, Saghaei and Saghaei, 2011) based on: i) the size of the hospital catchment area (small [population <500,000]/large [population ≥500,000]); ii) whether the PI had previous experience of working on a RCT; and iii) whether the site had a RN in place. The randomisation was conducted by a statistician at York Trials Unit, University of York (the trial co-ordinating centre) at the point when new sites were identified to be approached.

While group allocation could not be blinded, participating sites were not aware of their involvement in this embedded trial. The hospital site of the Chief Investigator and Sponsor

was excluded because of their substantial involvement in setting up the embedded and host trials. Two sites in the same geographical area shared the same PI; therefore, to maintain blinding, both sites were allocated to the same group. In order not to jeopardise the setting up of trial sites for SWIFFT, the trial team did not insist that the initial contact meeting should be on-site or held remotely if the PI had a preference for how to meet.

As is common in embedded trials, no formal power calculation was conducted as the sample size was restricted by the number of hospitals taking part in SWIFFT.

2.3 Outcomes

There was no single primary outcome. A range of outcomes were explored relating to set-up, recruitment, and follow-up.

Site-level outcomes comprised: time from first contact with a site to (i) submission of local R&D application, (ii) receipt of R&D approval, (iii) final on-site SIV and (iv) first randomised participant, as well as the number of patients screened and the proportion of eligible patients who were randomised. Patient-level outcomes were the return, and time to return, of the *grip and range* hospital form (as completion of this form required the patient to attend hospital) and participant questionnaires by follow-up time point (for the latter either collected at the hospital or via post which could include a 2 and 4 week reminder letter and 6 week telephone call).

2.4 Time and costs

The time that TCs spent communicating with each site (via email, telephone, attending an on-site visit [door-to-door]) was entered into a spreadsheet. This started from when the site was formally invited to begin the process of being set-up until the 'greenlight' was given to recruit i.e. it included both the initial meeting (whether on-site or remote) and the follow-up on-site SIV. The cost of each of these methods of communication was calculated by multiplying the time in hours spent by a basic hourly rate for a TC at an appropriate pay grade that included employer contribution to National Insurance and pension (£27.85/hour). The total cost of travel (i.e. transport, hotel, subsistence) was calculated and communication and travel costs were summed to produce a total cost of setting up each site. *2.5 Site preferences*

When recruitment of trial participants into SWIFFT was completed in July 2016 we emailed a survey to collaborators (PIs, RNs, Research Physiotherapists (RPs), Surgeons, etc) at the participating sites to explore their experience of setting up the SWIFFT trial. This brief 10 item questionnaire was created on-line using Qualtrics software (Utah, USA, 2017) and focussed on understanding preferences towards the need for a remote or on-site visit both for the initial contact meeting and SIVs. Participation was voluntary and responses were anonymised. As a small incentive to take part, respondents could enter a free prize draw to receive a box of chocolates.

2.6 Statistical Analysis

The main analyses were conducted on an intention-to-treat (ITT) basis including all sites in the groups they were assigned to at randomisation. Analyses were conducted in Stata version 13 (StataCorp, 2013) using two-sided statistical tests at the 5% significance level.

Since this was an embedded, feasibility trial, outcomes were not formally compared and were summarised descriptively overall and by trial arm.

To investigate the effect of non-compliance with random group allocation, descriptive analyses were repeated on a per-protocol (PP) basis removing sites that crossed over to the alternative mode of delivering the meeting.

Communication time and costs for communication and travel were reported descriptively by trial arm and in total. Survey responses were summarised for individual items by trial arm and relevant free text comments were highlighted.

2.7 Ethical considerations

Sites did not know they were taking part in this embedded trial. All sites received as much training in trial procedures and governance issues as required ensuring there were no ethical concerns about the recruitment and follow-up of trial participants.

3. Results

Forty sites were approached to take part in SWIFFT between May 2013 and March 2015 (Figure 1). The CI's site was not included. Therefore, 39 sites were randomised: 20 to on-site initial contact meetings (including one site that was manually allocated to the same site as its sister site sharing the same PI) and 19 to remote initial contact meetings. Two sites (both allocated to remote) were excluded post-randomisation because agreement had not been reached to formally take part in SWIFFT. This resulted in 37 eligible, randomised sites (20 on-site; 17 remote) that could be included in the main analyses. Half the sites served 'large' populations (n=18, 49%), two-thirds had a PI with previous experience of working on a multi-centre trial (n=25, 68%), and two-thirds had RN support (n=25, 68%; Table 1). Minimisation ensured that the two groups were well balanced on these characteristics.

3.1 Site set-up

Four (11%) of the 37 sites withdrew their interest in the trial before applying for R&D approval (3 remote and 1 on-site). For the remaining 33 sites, it took a median of 119 days (interquartile range (IQR) 75 to 189 days) after first contact to submit to R&D (median 113 days on-site and 134 days remote; Table 2). R&D approval was granted a median of 139 days and 155 days after first contact with on-site and remote sites, respectively. SIVs took place a median of 126 days (IQR 89 to 196 days) after first contact (median 119 days on-site and 142 days remote).

In total, 33 of the 37 (89%) sites opened to recruitment (on-site: n=19, 95%; remote: n=14, 82%); however, three (all allocated to on-site visits) withdrew their interest in recruiting for

SWIFFT following the SIV (two of whom had commenced screening but had not recruited a patient). For the 30 sites who recruited at least one SWIFFT participant, the first recruit occurred after a median of 229 days (IQR 188 to 319 days) from first contact with the sites (median 246 days on-site and 212 days remote; Table 2).

3.2 Recruitment

A median of 22 eligibility forms per site (IQR 5 to 38) were returned (Table 3) and a total of 378 patients were recruited. The median consent rate of patients was 0.63 for the on-site group and 0.53 for the remote group. The mean number of participants recruited was 10 for the on-site group and 11 for the remote group. Figure 2 shows that recruitment data were positively skewed with a median of 6 across all sites (range from 0 to 35, median of 10 [IQR 1.5 to 17] and 6 [IQR 5 to 23] participants for on-site and remote groups, respectively; Table 3). There were 406 days (13 months) when all sites were open for recruitment. During this time, a median of 4 participants were recruited per site in the on-site group (IQR 0 to 5.5; Table 3), and 2 per site (range 1 to 5) in the remote group (total 68 in the on-site group and 79 remote).

3.4 Follow-up

The percentage of participant questionnaires returned at weeks 6 and 52 appear similar between the on-site and remote groups; however, there is a slight difference at weeks 12 (80.2 vs 84.5%) and 26 (68.4 vs 74.6%) favouring the remote group (Table 4). For the hospital grip and range form, the percentage returned is similar between the two groups at week 6, but favours the remote group at weeks 12 and 52 (73.6 vs 80.5%, and 65.3 vs 70.8%, respectively). For returned forms and questionnaires, the median number of days between the due date and the date of return does not differ between the two groups by more than 5 days at any time point.

3.5 Per-protocol (PP) results

In total, there were three cross-overs because of site preferences: two on-site to remote; and one remote to an on-site visit. Therefore, in the PP analyses, there were 18 sites in the on-site group and 16 in the remote group. Reasonable balance between the two groups was retained for size of the hospital catchment area (large population: on-site 44%; remote 50%); previous PI trial experience (Yes: on-site 67%; remote 69%); and presence of RN support (Yes: on-site 67%; remote 69%). Results of the PP analyses found that whilst in the ITT analysis the median time to R&D approval was less in the on-site group, in the PP analysis it was less in the remote group (139 days vs 135). Among sites receiving an on-site or remote visit respectively, mean recruitment was 10 participants [median 10, IQR 2 to 17] and 11 participants [median 5.5, IQR 4.5 to 23.5].

3.6 Time and costs

Trial Co-ordinators spent more time, on average, on the telephone corresponding with sites in the remote group (1.6 hours) compared with the on-site group (0.9 hours; Table 5). Conversely, more time was spent, on average, attending face-to-face visits in the on-site group (20.9 hours) compared with the remote group (12.9 hours). In the on-site group, one

site received 0 face-to-face visits, 2 received 1 visit, 16 received 2 visits, and 1 received 3 visits (37 in total); and in the remote group, two sites received 0 face-to-face visits, 14 received 1 visit, and 1 received 2 visits (16 in total). The average amount of time spent emailing sites was the same for the two groups (5.3 hours). Overall more time, on average, was spent setting up sites in the on-site group (27.2 hours) than the remote group (19.9 hours).

The cost of staff time to communicate with sites in the on-site group was more, on average, than the remote group (£757.10 vs £553.90; Table 6). The total cost overall, excluding travel, of the initial contact visits was £24,560 (£15,143 on-site and £9,417 remote). The total cost overall, including travel, was £32,700 (£20,339 on-site and £12,361 remote). Including additional travel costs, the average cost of setting up a site in the remote group was £727.10 compared with £1016.93 in the on-site group, a difference of £289.83.

3.7 Site preferences

We invited 96 collaborators to complete the survey. There were 12 respondents (from 9 of 17 sites) in the remote group and 16 respondents from (12 of the 20 sites) in the on-site group i.e. there were respondents from 21 of 37 (57%) sites. For the remote group respondents comprised five PIs, three RNs, one RP and two Surgeons with an average of 7 years (range 1.5 to 18) experience with RCTs. For the on-site group respondents comprised seven PIs, five RNs, three RPs and one Surgeon with an average of 5 years (range 1 to 12) experience with RCTs.

Only 2 of 12 respondents from the remote group indicated they would have preferred the initial contact meeting to be held on-site and half felt a remote meeting was sufficient. Most of the respondents in the on-site group (10 of 16) felt the initial contact meeting could have been held remotely; only 2 thought it needed to be on-site. Free text comments from both groups illustrated that whilst the on-site meetings help with communication (7 respondents) information could be adequately exchanged remotely at this stage of site set-up (8 respondents). For the final SIV meeting, the preference overall was for an on-site visit (17 of 28 respondents); although this was preferred more in the remote group (9 of 12 respondents) compared with the on-site group (8 of 16 respondents).

4. Discussion

We undertook a SWAT comparing on-site with remote meetings for the initial contact with a potential recruiting hospital in the SWIFFT trial. We considered set-up times, recruitment, data collection, the costs of the two approaches and the views of the hospital staff.

Hospitals allocated to receive an on-site visit met key milestones earlier, except for the time to first recruit. The on-site group took around a month later to recruit their first participant; overall it took around eight months to set-up a hospital site. Measures of recruitment were similar between the two groups. The on-site group (20 sites) and remote group (17 sites) recruited in total 193 and 185 participants, respectively i.e. a difference of 8 patients in total compared with the average of 12 participants recruited a month into the trial. The mean number of participants recruited per site was comparable, but the median recruited was around twice as high in the on-site group. This is because the number of participants

recruited per site was more uniform in the on-site group; whereas for the remote group most sites recruited around 0 to 10 participants and a few sites recruited around 20 to 35 participants. With the small number of hospitals involved it is difficult to conclude whether this difference in the distribution of recruitment is caused by the site having a remote meeting or by chance. There were no notable differences between the two groups in the timeliness of the return of hospital forms or participant questionnaires; some differences were observed in the proportion of participant questionnaires returned at weeks 12 and 26, and hospital forms at weeks 12 and 52, favouring the remote group.

Nearly twice the amount of time was spent by TCs on the telephone in the remote group, and nearly twice the amount of time attending face-to-face visits in the on-site group. In total, around one extra working day was spent by a TC setting up a hospital in the on-site group, equating to a months' work over 20 sites. The travel costs were also higher in the on-site group. This on average resulted in sites in the on-site group costing £289.83 more to set-up than sites allocated to a remote meeting. With the on-site group recruiting on average 1.2 fewer patients, this was a cost saving of approximately £242 per extra participant recruited for the remote group. However, data for number of participants recruited were skewed and so using the median, rather than the mean, the on-site group set-up costs an extra £72 per extra recruit. The response to the survey of collaborators found that the majority felt the initial meeting did not need to be face-to-face as information could be adequately exchanged remotely at this stage of site set-up. Not having an initial on-site visit meant the majority in the remote group did prefer the SIV to be on-site; the on-site group were split about this having already met. Overall, these findings provide evidence that it is feasible to undertake an initial contact meeting remotely and to undertake an embedded trial to inform trial conduct.

A systematic review of quasi-randomised and RCTs of interventions designed to improve recruitment into RCTs in both real and hypothetical settings identified 45 embedded trials with around 43,000 participants (Treweek et al, 2013). This compares with over one million records of trials on the Cochrane Central Register of Controlled Trials as of August 2017. Initiatives like START (Rick et al, 2014) and SWAT (Anonymous, 2012) are important to further encourage the conduct of embedded trials. Of the 45 embedded trials, two studies (302 trial sites) looked at the effect of greater contact from TCs. Both studies were assessed as low risk of bias. One RCT in France about breast cancer found that in 68 of the 135 participating hospital sites that received on-site visits there was no statistically significant difference in the number of trial participants recruited (302 in the Visited group versus 271 in the Non-visited group) (Lienard et al. 2006). A second international RCT about patients with diabetes and vascular disease with 167 centres found that the median number of recruits at sites that had additional communication from the co-ordinating centre compared with usual communication was 37.5 vs 37.0, respectively (p=0.68) (Monaghan et al, 2007). A further study found that at the site chosen to be visited by the lead researcher recruitment target rates increased post-intervention by 17% (p=0.01) and 14% (p=0.002) at 1 and 3 months respectively. No statistically significant difference occurred at either of the two other sites that had no visit (Smith et al, 2014). The study, however, was limited by a retrospective controlled before and after design, only involved three sites with a short follow-up assessment and the intervention site was selected because of reduced recruitment in the past months and therefore improvement could be attributed to regression to the mean. Taken together, the findings from this embedded trial and other studies questions how

effective and efficient is it for TCs to continue to invest limited time and resources with on-site visits and additional contact with a site? It might be that TCs should be more selective about when on-site visits are necessary and a different type of additional contact and strategy is required depending on the challenges that are specific to that site and study. Further research is necessary to improve our understanding of what constitutes optimal TC contact with sites and to evaluate strategies across a range of participant groups and settings.

Finally, we undertook an embedded trial to attempt as much as was feasible to rigorously answer this question and collected data on a variety of important outcomes and costs. The study was limited, however, by the number of sites involved and restricted to an orthopaedic, surgical trial setting. Furthermore we continued recording all the communication and travel with a site only until it was set-up to recruit. The perspective of the cost analyses is that of the trials unit without considering how the two different approaches may have affected the time and cost of setting up a site to the hospital. It is unlikely that it would change the results as the time spent communicating should be similar and the cost of travel was to the trials unit. This embedded trial was undertaken around when the Clinical Research Network in England introduced metrics about time taken for a study to start at a site and recruit the first participant. Hospital sites were also set-up before the new Health Research Authority process for undertaking research in England had been implemented.

5. Conclusions

We have demonstrated that it was feasible to conduct an embedded trial to explore efficient trial conduct in a host trial. Holding the initial contact meeting remotely did not appear to adversely affect set-up times, screening and recruitment, nor data collection. Any extra cost or saving of the two approaches was modest, although a remote initial visit may save TCs' time to set up a site. Our collaborators at hospital sites were amenable to the initial contact meeting being held remotely. Evidence from the wider literature also questions the effectiveness of on-site visits and additional contact by TCs on trial conduct. Further embedded trials about the type and extent of TC contact with sites in different patient populations and settings would permit a meta-analyses to increase statistical power and to extend the generalisability of the evidence.

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Tables and Figures

Table 1. Summary of the minimisation factors for the sites, presented overall and by randomised group

Minimisation factor, n (%)	**On-site (n=20)**	**Remote (n=17)**	**Total (n=37)**
Population			
Large (≥500,000)	9 (45.0)	9 (52.9)	18 (48.7)
Small (<500, 000)	11 (55.0)	8 (47.1)	19 (51.4)
PI had trial experience			
Yes	14 (70.0)	11 (64.7)	25 (67.6)
No	6 (30.0)	6 (35.3)	12 (32.4)
Research nurse support			
Yes	13 (65.0)	12 (70.6)	25 (67.6)
No	7 (35.0)	5 (29.4)	12 (32.4)

Table 2. Time between first contact with the site and key milestones in the set-up of the site

Time in days between first contact and…	**On-site (n=20)**	**Remote (n=17)**	**Total (n=37)**
R&D submission			
N, Mean (SD)	19, 152.1 (103.2)	14, 159.2 (128.1)	33, 155.1 (112.6)
Median (IQR)	113 (75, 200)	134 (97, 155)	119 (75, 189)
R&D approval			
N, Mean (SD)	19, 176.2 (99.7)	14, 179.3 (122.5)	33, 177.5 (108.1)
Median (IQR)	139 (99, 233)	155 (107, 190)	139 (107, 197)
Site Initiation Visit (SIV)			
N, Mean (SD)	19, 156.7 (95.6)	14, 172.2 (123.3)	33, 163.3 (106.7)
Median (IQR)	119 (85, 223)	142 (97, 183)	126 (89, 196)
First recruit			
N, Mean (SD)	16, 269.9 (105.8)	14, 251.4 (152.0)	30, 261.2 (127.4)
Median (IQR)	246 (196, 346)	212 (154, 266)	229 (188, 319)

Table 3. Measures of recruitment per site, overall and by randomised group

Measures of recruitment	**On-site (n=20)**	**Remote (n=17)**	**Total (n=37)**
Number of eligibility forms returned			
N, Mean (SD)	20, 23.5 (21.8)	17, 26.9 (31.2)	37, 25.1 (26.2)
Median (IQR)	22 (3, 35)	22 (8, 38)	22 (5, 38)
Proportion consenting / eligible			
N, Mean (SD)	18, 0.54 (0.29)	14, 0.58 (0.20)	32, 0.56 (0.25)
Median (IQR)	0.63 (0.38, 0.71)	0.53 (0.45, 0.71)	0.59 (0.41, 0.71)
Number of participants recruited			
N, Mean (SD)	20, 9.7 (8.1)	17, 10.9 (11.0)	37, 10.2 (9.4)

Median (IQR)	10 (2, 17)	6 (5, 23)	6 (4, 17)
Number of participants recruited from date final site opened			
N, Mean (SD)	20, 3.4 (3.3)	17, 4.6 (5.5)	37, 4.0 (4.4)
Median (IQR)	4 (0, 6)	2 (1, 5)	4 (1, 5)

Table 4. Return, and time to return, of participant and hospital forms by randomised group and time point, for all randomised participants

Participant questionnaires		**On-site (n=193)**	**Remote (n=185)**	**Total (378)**
Week 6	**Returned, n (%)**	160 (82.9)	151 (81.6)	311 (82.3)
	Time to return, days *Median (IQR)*	14 (7, 28)	10 (5, 19)	12 (6, 24)
Week 12	**Returned, n (%)**	150 (80.2)	153 (84.5)	303 (82.3)
	Time to return, days *Median (IQR)*	15 (7, 32)	13 (7, 30)	13 (7, 30)
Week 26	**Returned, n (%)**	132 (68.4)	138 (74.6)	270 (71.4)
	Time to return, days *Median (IQR)*	21 (12, 38)	17 (9, 31)	19 (10, 36)
Week 52	**Returned, n (%)**	157 (81.4)	152 (82.2)	309 (81.8)
	Time to return, days *Median (IQR)*	15 (8, 32)	12 (6, 32)	14 (7, 32)
Hospital grip and range form				
Week 6	**Returned, n (%)**	169 (87.6)	161 (87.0)	330 (87.3)
	Time to return, days *Median (IQR)*	10 (5, 19)	7 (3, 16)	9 (4, 17)
Week 12	**Returned, n (%)**	142 (73.6)	149 (80.5)	291 (77.0)
	Time to return, days *Median (IQR)*	10 (4, 20)	11 (5, 21)	11 (5, 21)
Week 52	**Returned, n (%)**	126 (65.3)	131 (70.8)	257 (68.0)
	Time to return, days *Median (IQR)*	17 (6, 40)	12 (3, 33)	14 (5, 35)

Table 5. Time spent in hours for each method of communication

	On-site (n=20)	**Remote (n=17)**	**Total (n=37)**
Telephone			
N, Mean (SD)	20, 0.9 (0.9)	17, 1.6 (1.5)	37, 1.2 (1.2)
Median (IQR)	0.8 (0.2, 1.3)	1.6 (0.5, 1.9)	1.1 (0.3, 1.7)
Email			
N, Mean (SD)	20, 5.3 (3.9)	17, 5.3 (3.7)	37, 5.3 (3.7)
Median (IQR)	4.7 (2.1, 8.0)	4.9 (2.2, 8.4)	4.8 (2.2, 8.4)
Face-to-face visit			
N, Mean (SD)	20, 20.9 (18.2)	17, 12.9 (10.2)	37, 17.2 (15.4)
Median (IQR)	16.5 (11.8, 21.5)	11.5 (8.3, 17.3)	13.0 (10.5, 21.0)
Total			

N, Mean (SD)	20, 27.2 (21.1)	17, 19.9 (12.4)	37, 23.8 (17.8)
Median (IQR)	21.9 (16.9, 27.78)	19.6 (13.3, 24.8)	21.5 (15.1, 24.8)

Table 6. Cost of basic pay in £s for each method of contact including additional travel costs

	On-site (n=20)	**Remote (n=17)**	**Total (n=37)**
Telephone			
N, Mean (SD)	20, 25.6 (24.5)	17, 45.6 (42.0)	37, 34.8 (34.7)
Median (IQR)	22.0 (4.6, 34.8)	44.1 (13.9, 53.4)	30.2 (9.3, 46.4)
Email			
N, Mean (SD)	20, 148.7 (107.4)	17, 148.5 (104.0)	37, 148.6 (104.4)
Median (IQR)	130.0 (57.8, 221.6)	135.5 (60.3, 234.4)	132.3 (60.3, 234.4)
Face-to-face visit			
N, Mean (SD)	20, 582.8 (508.2)	17, 359.9 (284.1)	37, 480.3 (429.9)
Median (IQR)	459.5 (327.2, 598.8)	320.3 (232.1, 482.7)	362.1 (292.4, 584.9)
Total communication			
N, Mean (SD)	20, 757.1 (588.1)	17, 553.9 (346.2)	37, 663.8 (496.3)
Median (IQR)	610.1 (471.1, 771.7)	545.4 (371.3, 689.3)	598.8 (421.0, 689.3)
Travel[a]			
N, Mean (SD)	20, 259.8 (183.6)	17, 173.2 (92.5)	37, 220.0 (153.3)
Median (IQR)	211.3 (131.3 338.8)	192.4 (119.3, 205.6)	192.8 (119.3, 285.1)
Total communication and travel			
N, Mean (SD)	20, 1016.9 (743.0)	17, 727.1 (408.4)	37, 883.8 (622.0)
Median (IQR)	870.8 (603.6, 1054.1)	738.2 (486.2, 919.7)	781.2 (588.1, 919.7)

[a] not all sites were visited

Figure 1. Flow of sites in the embedded trial

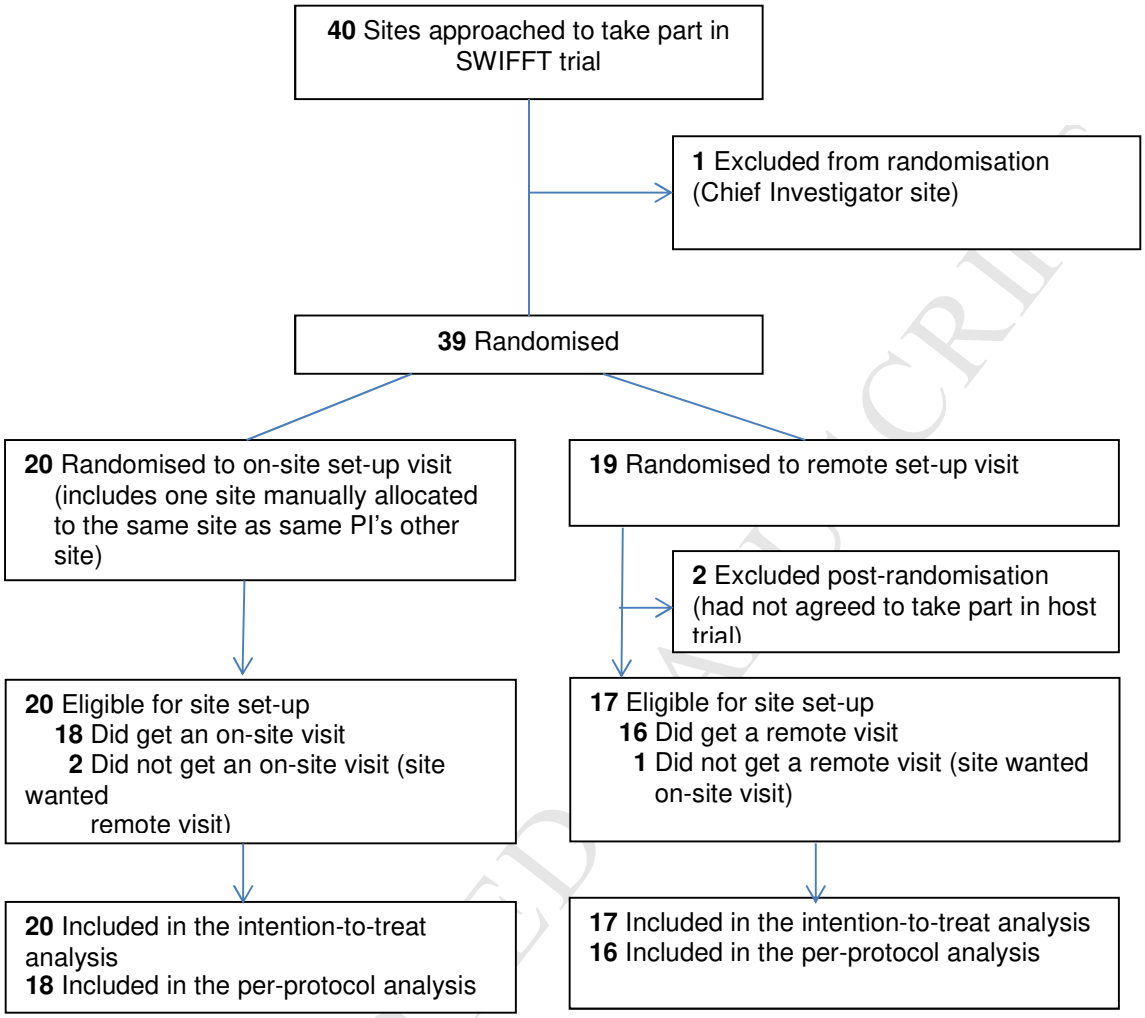
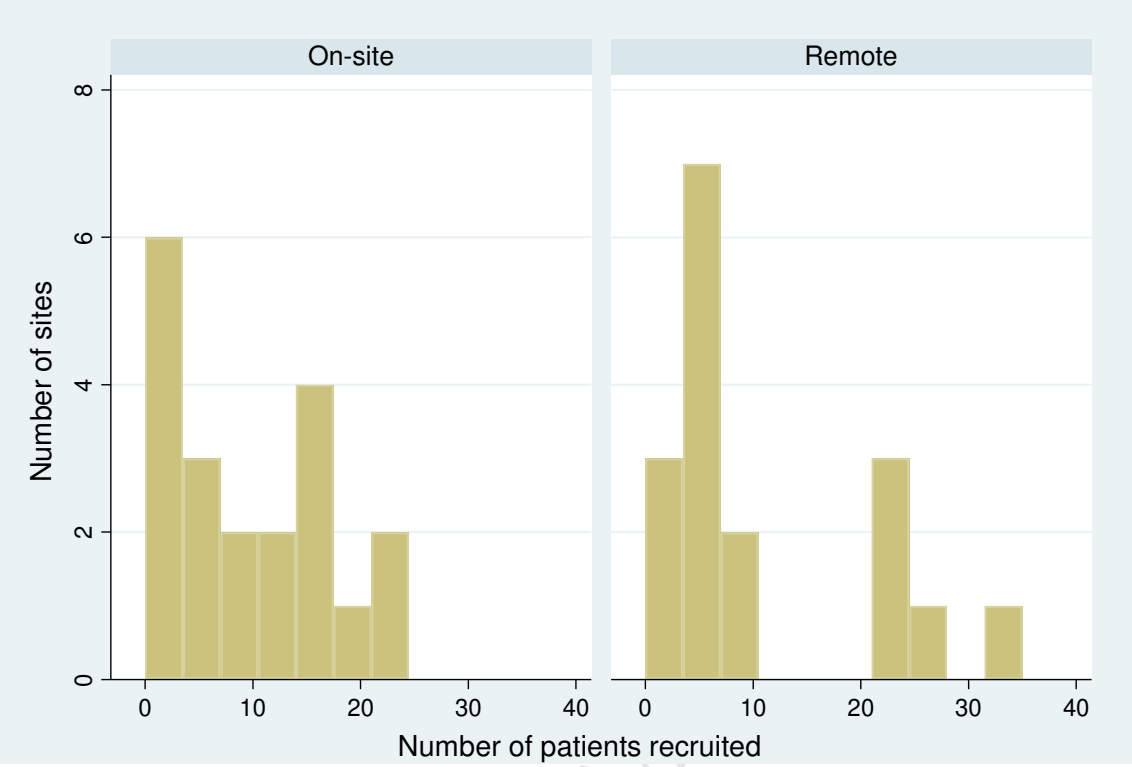


Figure 2. Distribution of the number of participants recruited between on-site and remote groups



"What is new?"

Key findings:

- It was feasible to use remote or on-site visits for the initial contact with sites when setting up hospitals in a multi-centre surgical trial.

What this adds to what was known?

- The evidence from this study and the wider literature questions the need for on-site visits and the effectiveness of additional contact by Trial Co-ordinators on trial conduct.

What is the implication, what should change now?

- Trial Co-ordinators should consider being more selective as to when on-site visits are necessary and what type of additional contact with a site is required depending on the challenges that are specific to that site and the study.
- Further research is necessary to improve our understanding of what constitutes optimal Trial Co-ordinator contact with sites and to evaluate strategies across a range of participant groups and settings.

Conflict of Interest

The authors declare that they have no competing interests except for AR whose department has received educational grants from DePuy Limited outside the scope of this work. These grants have not in any way influenced his contribution to this study.