

ORIGINAL ARTICLE

Remote or on-site visits were feasible for the initial setup meetings with hospitals in a multicenter surgical trial: an embedded randomized trial

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Abstract

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

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

Results: Thirty-nine sites were randomized and 33 sites set up to recruit (19 on-site and 14 remote). For sites randomized to an on-site meeting compared with remote meeting respectively, the time from first contact to the first recruit was a median of 246 days (interquartile range [IQR] 196–346) vs. 212 days (IQR 154–266), mean recruitment was 10 participants (median 10, IQR 2–17) vs. 11 participants (median 6, IQR 5–23), 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 setup.

Conclusion: Remote or on-site visits are feasible for the initial setup meetings with hospitals in a multicenter surgical trial. This embedded trial should be replicated to improve generalizability and increase statistical power using meta-analysis. ISRCTN78899574. © 2018 Elsevier Inc. All rights reserved.

Keywords: Costs; Feasibility; Study within a trial; Randomized controlled trial; Recruitment; Response rate

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1. Introduction

Randomized controlled trials (RCTs) are the gold standard for evaluating the effectiveness and safety of health-care interventions [1]. They often require substantial amounts of public funds but around half fail to reach their recruitment target within their original timescale and budget [2]. 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 [3].

In our experience, setting up hospital sites to recruit into multicenter RCTs usually requires an initial contact meeting between the trial coordinator (TC) and hospital staff to discuss (i) the trial rationale and design; (ii) assessment of feasibility and capacity of the site to deliver the

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 multicenter 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 coordinators (TCs) on trial conduct.

What is the implication and what should change now?

- TCs 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 TC contact with sites and to evaluate strategies across a range of participant groups and settings.

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 multicenter 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 [4].

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 Scaphoid Waist Internal Fixation for Fractures Trial (SWIFFT) multicenter, orthopedic surgical trial [5] and was registered as number 27 (ISRCTN78899574)

with the Northern Ireland Hub for Trials Methodology Research program. The protocol is publicly available online 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 setup times, recruitment, data collection, and the costs of these two approaches.

2. Methods

2.1. Population, design, and interventions

A feasible 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 years or above with a clear bicortical fracture of the scaphoid waist seen 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 endpoint). Patients attended hospital outpatient 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 standardized 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 predefined 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 [6].

2.2. Randomization and sample size

Sites were randomized 1:1 to receive either an on-site or remote initial contact meeting using minimization (via MinimPy software, [7]) 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 an RCT; and (iii) whether the site had an RN in place. The randomization was conducted by a statistician at York Trials Unit, University of York (the trial coordinating center), at the point when new sites were identified to be approached.

Although 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 jeopardize 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 setup, 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) the final on-site SIV, and (iv) the first randomized participant, as well as the number of patients screened and the proportion of eligible patients who were randomized. 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, and 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, that is, 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, and 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 online using Qualtrics software (Utah, USA, 2017) [8] and focused on understanding preferences toward the need for a remote or on-site visit both for the

initial contact meeting and SIVs. Participation was voluntary, and responses were anonymized. 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 basis including all sites in the groups they were assigned to at randomization. Analyses were conducted in Stata, version 13 [9], using two-sided statistical tests at the 5% significance level.

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

To investigate the effect of noncompliance 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 summarized 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 (Fig. 1). The chief investigator’s site was not included. Therefore, 39 sites were randomized: 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 after randomization because agreement had not been reached to formally take part in SWIFFT. This resulted in 37 eligible, randomized 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 multicenter trial ($n = 25$, 68%), and two-thirds had RN support ($n = 25$, 68%; Table 1). Minimization ensured that the two groups were well balanced on these characteristics.

3.1. Site setup

Four (11%) of the 37 sites withdrew their interest in the trial before applying for R&D approval (3 remote and 1 on-

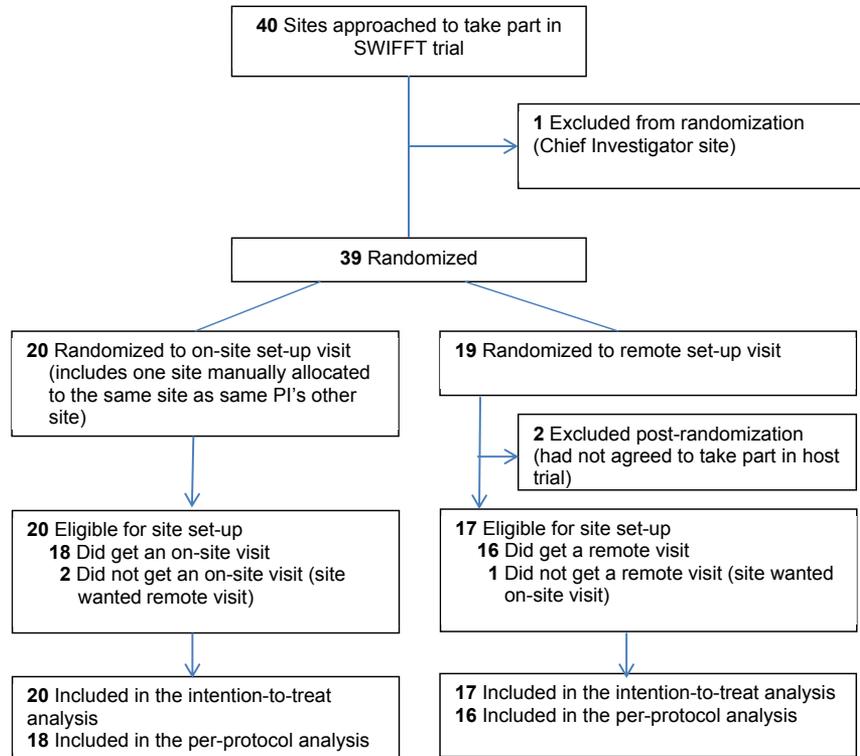


Fig. 1. Flow of sites in the embedded trial.

site). For the remaining 33 sites, it took a median of 119 days (interquartile range [IQR] 75–189 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 89–196 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 after 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 5–38) 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 six across all sites (range from 0 to 35, median of 10 [IQR 1.5–17] and 6 [IQR 5–23] 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 four participants were recruited per site in the on-site group (IQR 0–5.5; Table 3) and two per site (range 1–5) in the remote group (total 68 in the on-site group and 79 remote).

3.3. Follow-up

The percentage of participant questionnaires returned at weeks 6 and 52 appears similar between the on-site and

Table 1. Summary of the minimization factors for the sites, presented overall and by the randomized group

Minimization factor, n (%)	On-site ($n = 20$)	Remote ($n = 17$)	Total ($n = 37$)
Population			
Large ($\geq 500,000$)	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 setup of the site

Time in days between first contact and the following key milestones in the setup of the site	On-site (<i>n</i> = 20)	Remote (<i>n</i> = 17)	Total (<i>n</i> = 37)
R&D submission			
<i>N</i> , 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			
<i>N</i> , 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)			
<i>N</i> , 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			
<i>N</i> , 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)

remote groups; however, there is a slight difference at weeks 12 (80.2% vs. 84.5%) and 26 (68.4% vs. 74.6%) favoring 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 favors 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.

3.4. PP results

In total, there were three crossovers 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 while in the intention-to-treat analysis, the median time to R&D approval was less in the on-site group, and in the PP analysis, it was less in the remote group (139 days vs. 135). Among sites receiving an on-site or remote visit, mean recruitment was 10 participants (median 10, IQR 2–17) and 11 participants (median 5.5, IQR 4.5–23.5), respectively.

3.5. Time and costs

TCs 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, 1 site received 0 face-to-face visits, 2 received 1 visit, 16 received 2 visits, and 1 received 3 visits (37 in

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

Measures of recruitment	On-site (<i>n</i> = 20)	Remote (<i>n</i> = 17)	Total (<i>n</i> = 37)
Number of eligibility forms returned			
<i>N</i> , 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			
<i>N</i> , 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			
<i>N</i> , 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 the final site opened date			
<i>N</i> , 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)

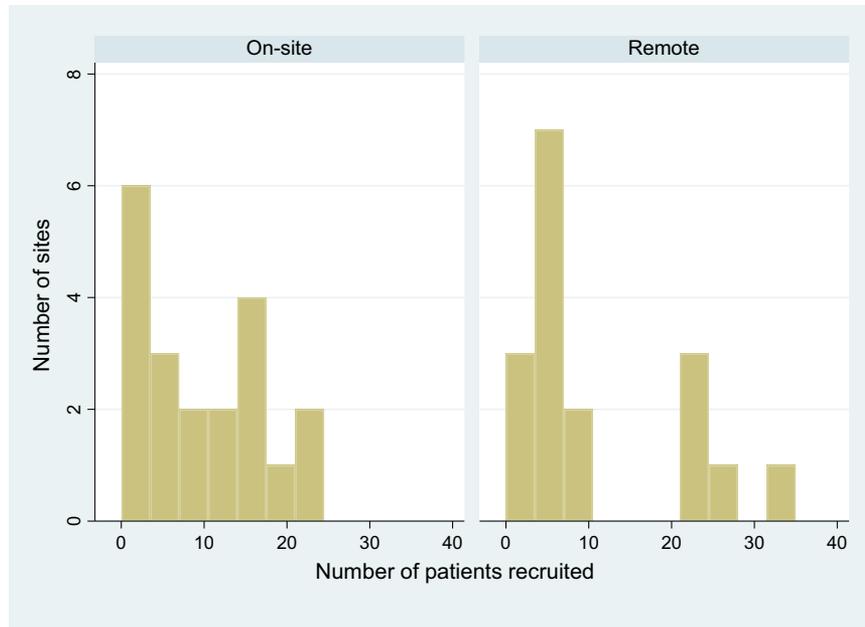


Fig. 2. Distribution of the number of participants recruited between on-site and remote groups.

total); and in the remote group, 2 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 £1,016.93 in the on-site group, a difference of £289.83.

3.6. 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, that is, 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-year experience (range 1.5–18) with RCTs. For the on-site group, respondents comprised seven PIs, five RNs, three RPs, and one surgeon with an average of 5-year experience (range 1–12) 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 while the on-site meetings help with communication (seven respondents), information could be adequately exchanged remotely at this stage of site setup (eight 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 setup 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 8 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, that is, a difference of eight 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

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

Follow-up questionnaires/form	On-site (<i>n</i> = 193)	Remote (<i>n</i> = 185)	Total (378)
Participant questionnaires			
Week 6			
Returned, <i>n</i> (%)	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, <i>n</i> (%)	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, <i>n</i> (%)	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, <i>n</i> (%)	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, <i>n</i> (%)	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, <i>n</i> (%)	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, <i>n</i> (%)	126 (65.3)	131 (70.8)	257 (68.0)
Time to return, days			
Median (IQR)	17 (6, 40)	12 (3, 33)	14 (5, 35)

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

0–10 participants and a few sites recruited around 20–35 participants. With the small number of hospitals involved, it is difficult to conclude whether this difference in the

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

	On-site (<i>n</i> = 20)	Remote (<i>n</i> = 17)	Total (<i>n</i> = 37)
Telephone			
<i>N</i> , 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			
<i>N</i> , 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			
<i>N</i> , 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			
<i>N</i> , 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 (<i>n</i> = 20)	Remote (<i>n</i> = 17)	Total (<i>n</i> = 37)
Telephone			
<i>N</i> , 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			
<i>N</i> , 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			
<i>N</i> , 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			
<i>N</i> , 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			
<i>N</i> , 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			
<i>N</i> , Mean (SD)	20, 1,016.9 (743.0)	17, 727.1 (408.4)	37, 883.8 (622.0)
Median (IQR)	870.8 (603.6, 1,054.1)	738.2 (486.2, 919.7)	781.2 (588.1, 919.7)

^a Not all sites were visited.

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, favoring 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 was spent 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 setup 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 setup 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 because information could be adequately exchanged remotely at this stage of site setup. 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 was 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-randomized trials 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 [3]. This compares with over one million records of trials on the Cochrane Central Register of Controlled Trials as of August 2017. Initiatives like START [10] and SWAT [11] 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 nonvisited group) [4]. A second international RCT about patients with diabetes and vascular disease with 167 centers found that the median number of recruits at sites that had additional communication from the coordinating center compared with usual communication was 37.5 vs. 37.0, respectively ($P = 0.68$) [12]. A further study found that at the site chosen to be visited by the lead researcher, recruitment target rates increased postintervention 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 [13]. 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 question 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 orthopedic, 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 setup times, screening and recruitment, or 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 meta-analyses to increase statistical power and to extend the generalizability of the evidence.

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