
Article:
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Abstract

Objectives: To assess whether timing of SMS reminders improved postal questionnaire return rates from participants in a randomized controlled trial (RCT). Study Design and Setting: A Study Within A Trial (SWAT) embedded in a multi-centre RCT evaluating three treatments for frozen shoulder. Participants who provided a mobile telephone number were randomized to either pre-notification SMS on the day of the questionnaire mail-out or post-notification SMS four days following questionnaire mail out for the three-month follow-up. The primary outcome was the proportion of participants who returned a valid questionnaire. A systematic review was undertaken to identify other embedded trials to perform a meta-analysis. Results: Of the 269 participants, 122/135 (90.4%) returned a valid questionnaire in the pre-notification arm and 119/134 (88.8%) in the post-notification arm (difference of -1.6%; 95% CI of difference: -8.9%, 5.7%). There was no difference in time to response (HR=1.04; 95% CI: 0.80 to 1.34) or need for additional reminders (OR=0.71; 95% CI: 0.43 to 1.17). Meta-analysis of two RCTs showed no difference in response rates between pre and post-notification reminders (OR=0.78 95% CI: 0.42 to 1.45). Conclusion: Timing of SMS reminders did not improve response rates, time to response or affect the need for additional reminders.

Keywords	Randomized controlled trial; SMS; text message; retention; study within a trial; meta-analysis
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Research Data Related to this Submission

There are no linked research data sets for this submission. The following reason is given:
Data will be made available on request

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16th October 2019

Dear Editors

Timing of Short Messaging Service (SMS) reminders did not improve trial participant questionnaire return: an embedded randomized trial and meta-analysis

We are submitting to your journal an original article of an embedded trial about the timing of SMS reminders in a host trial investigating the treatments of frozen shoulder. A systematic review and meta-analysis were performed to investigate the timing of SMS and the role of SMS or electronic reminders in improving reponse rate to postal questionnaires. The study within a trial (SWAT) was registered as number 44 (ISRCTN1664238) with the Northern Ireland Hub for Trials Methodology Research programme and the protocol is publically available on-line at their SWAT Repository Store. The systematic review and meta-analysis was registered with PROSPERO (CRD42019134318).

SMS reminders are commonly used by Randomised Controlled Trials (RCTs) to improve patient response to questionnaires; however, there is a paucity of evidence of their effectiveness. In addition, the effect of the timing of SMS reminders on participant response rates has only been explored in one previous study (Keding et al, 2016). Our SWAT and a meta-analysis of two studies showed that timing of SMS reminders did not improve response rates; in addition a wider meta-analysis showed that electronic reminders (SMS or e-mail) did not improve response rates compared to no reminders. We thought you would be interested in our article that is aiming to improve the methodology of clinical research through the application of an embedded trial.

All authors have approved the manuscript for submission.

The content of the manuscript has not been published or been submitted for publication elsewhere.

We look forward to hearing from you.

Yours sincerely

Dr Prasanna Partha Sarathy (Joint First Author)

What is new?

Key findings

- Timing of SMS reminders did not affect response rates to postal questionnaires.
- There was no evidence that electronic reminders improved response rates

What this adds to what was known?

- Previous evidence suggested that post-notification SMS reminders were more effective than pre-notification.
- This embedded trial and a meta-analysis of 2 trials did not support these findings.

What is the implication and what should change now?

- Further research should focus on different participant groups and both postal and electronic completion of questionnaires.

Timing of Short Messaging Service (SMS) reminders did not improve trial participant questionnaire return: an embedded randomized trial and meta-analysis

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Abstract

Objectives: To assess whether timing of SMS reminders improved postal questionnaire return rates from participants in a randomized controlled trial (RCT).

Study Design and Setting: A Study Within A Trial (SWAT) embedded in a multi-centre RCT evaluating three treatments for frozen shoulder. Participants who provided a mobile telephone number were randomized to either pre-notification SMS on the day of the questionnaire mail-out or post-notification SMS four days following questionnaire mail out for the 3-month follow-up. The primary outcome was the proportion of participants who returned a valid questionnaire. A systematic review was undertaken to identify other embedded trials to perform a meta-analysis.

Results: Of the 269 participants, 122/135 (90.4%) returned a valid questionnaire in the pre-notification arm and 119/134 (88.8%) in the post-notification arm (difference of -1.6%; 95% CI of difference: -8.9%, 5.7%). There was no difference in time to response (HR=1.04; 95% CI: 0.80 to 1.34) or need for additional reminders (OR=0.71; 95% CI: 0.43 to 1.17). Meta-analysis of two RCTs showed no difference in response rates between pre and post-notification reminders (OR=0.78 95% CI: 0.42 to 1.45).

Conclusion: Timing of SMS reminders did not improve response rates, time to response or affect the need for additional reminders.

Keywords: Randomized controlled trial, SMS, text message, retention, study within a trial, meta-analysis

What is new?

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- Timing of SMS reminders did not affect response rates to postal questionnaires.
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What is the implication and what should change now?

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1. Introduction

Randomized controlled trials (RCTs) are the gold standard for investigating the efficacy, effectiveness and safety of health-care interventions (1). Recently, the primary focus of RCTs have shifted from physician-reported clinimetric outcomes to patient-reported outcomes measures (PROMs); these provide an invaluable insight into the impact of disease and treatment on patients' lives (2). A convenient method to collect this data is through self-administered postal or electronic questionnaires. A major challenge with self-administered questionnaires is non-response. This can introduce bias and reduce the statistical power to detect differences between groups (3).

Short Messaging Service (SMS) reminders have been useful in retaining participants in a range of contexts, such as improving patient adherence to clinical follow-up and to medication (4, 5). They have also helped increase response rates to survey research (6, 7). SMS reminders are simple, inexpensive and can easily be implemented in a variety of settings. A large numbers of participants can be reached quickly and reliably in the United Kingdom where 93% of adults use mobile phones (8).

RCTs often use SMS reminders to improve patient response to questionnaires; however, there is a paucity of evidence of their effectiveness and the results are equivocal (9-12). The timing of the SMS reminders could have an important impact on response rate: SMS can be sent as a pre-notification (before receipt of the postal questionnaire) or as a post-notification (after the receipt of the postal questionnaire). Only one trial has investigated the effect of the SMS timing on response rate (9); this three two-arm RCT suggested that post-notification was more effective than pre-notification.

Given the limited evidence available, we undertook a Study Within a Trial (SWAT) as a robust method to evaluate the effectiveness of timing of SMS messages embedded in a large multi-centre orthopaedic surgical trial (13). This SWAT was registered with the Northern Ireland Hub for Trials Methodology Research Program (SWAT 44, ISRCTN1664238) with the protocol available online at their SWAT repository store. The SWAT is also registered with PROMETHEUS (PROMoting THE USE of SWATs; https://bit.ly/2CP76lA) which is a national programme of research funded by the Medical Research Council to facilitate the routine embedding of SWATs into RCTs. The objectives were to evaluate the effectiveness of the timing of SMS text messages as pre- or post-notification reminders on questionnaire response rates, time to response and need for additional reminders. A systematic review and meta-analysis of other SWATs was undertaken to evaluate the effect of electronic reminders on improving participant questionnaire responses in RCTs.

2. Methods

2.1. Host trial and participants

This parallel two-arm RCT is embedded in the United Kingdom Frozen Shoulder Trial (UK FROST). In the host trial, 503 patients aged ≥18 years with primary frozen shoulder were recruited in hospitals between the 1st of January 2015 and the 31st of December 2017. Participants were randomized to either early structured physiotherapy including a steroid injection (ESP), manipulation under anaesthesia (MUA) or arthroscopic capsular release with manipulation under anaesthesia (ACR). Participants were followed-up at 3, 6 and 12 months with postal questionnaires. At recruitment into the host trial, participants with mobile phones who consented to be contacted by SMS were included in the SWAT. No additional inclusion criteria were used. The SWAT was initiated part-way through the host trial after the successful completion of the internal pilot.

2.2. Intervention

At 3-months post-randomization into the host trial, participants in the SWAT were posted a self-administered follow-up questionnaire to be completed and returned using a pre-paid envelope. The questionnaire was 12 pages in length and contained quality of life measures and questions about healthcare resource use.

Participants were randomized to either receive text messages as: pre-notification on the day of the questionnaire mail-out; or post-notification four days following questionnaire mail-out. The content for each reminder is shown in Table 1.

All participants were also sent a letter two weeks before the questionnaire was to be sent, two- and four-week letter reminders and an option to complete an abridged telephone questionnaire after six weeks. At 12 months, the primary end-point, all participants received an unconditional incentive of £5. During the trial, newsletters were also circulated to participants.

Study groups	SMS reminder content
Pre-Notification group	*UK FROST Trial: You will receive a questionnaire in the post in a few days. Your answers are important; so please help by returning it as soon as you can. Thanks.*
Post-Notification group	*UK FROST Trial: You should have received a questionnaire in the post by now. Your answers are important; so please help by returning it as soon as you can. Thanks*

Table 1 SMS reminders sent to participants

Questionnaires were sent from and returned to York Trials Unit (YTU). Mobile phone numbers were stored securely at YTU and the SMS were sent using a secure UK-based text message gateway service (IntelliSoftware).

2.3. Randomization and blinding

Participants were randomized to pre- or post-notification after the 3-month follow-up questionnaires were sent. Randomization was achieved using computer generated random permuted blocks with a 1:1 ratio, stratified by UK FROST treatment allocation. A statistician at YTU generated the allocation sequence and the assignment of participants to either SMS group. Participants did not know they were taking part in the SWAT and were therefore blinded.

2.4. Outcome measures

The primary outcome was the proportion of participants who returned a valid questionnaire at the 3 month follow-up. A valid questionnaire had to contain a completed response for the Oxford Shoulder Score (primary outcome of UK FROST).

Secondary outcomes were time to questionnaire return (number of days between the questionnaire being mailed out and it being recorded as returned) and the proportion of participants requiring at least one return reminder notice (in the form of a reminder at 2 and 4 weeks or a telephone call at 6 weeks).

2.5. Statistical analysis and sample size calculation

Statistical analyses were conducted in Stata 15 (StataCorp, College Station, TX) using two-sided statistical significance at the 5% level. The analysis was undertaken on an intention-to-treat basis by a statistician blind to group allocation.

Baseline characteristics of the participants of the SWAT and the host trial were compared descriptively.

For the primary outcome the proportion of participants who returned a valid questionnaire in each group was calculated with a 95% confidence interval (CI) and the chi-squared test was used to assess statistical significance. A logistic regression adjusting for age, gender and UK FROST treatment allocation was undertaken, and the odds ratio and associated 95% CI was reported.

The secondary outcome of time to questionnaire return was assessed using a Kaplan Meier curve and the text message interventions were compared using the log rank-test. We carried out Cox regression adjusting for age, gender and UK FROST treatment allocation. Questionnaire return times were censored at three months (91 days) for the time to event analyses. The requirement for any additional reminders was analysed as for the primary outcome.

Return rates were compared descriptively between participants who were recruited in the SWAT and participants who were recruited into the host trial before the SWAT was initiated. We estimated that a sample size of approximately 300 participants for the SWAT (150 per group) would give us 80% power at the 5% significance level to detect differences in return rates of approximately 12% or more. However, as with all SWATs we were limited by the sample size of the host trial (14).

2.6. Systematic review and meta-analysis

We undertook a systematic review and registered it with PROSPERO (available at https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=134318) . We performed an online search of nine databases from inception to the end of April 2019. The reference lists of included studies and relevant systematic reviews were hand-searched (15, 16). A list of databases searched and the search strategy for MEDLINE is included in appendix A. When possible, RCTs were pooled with a random effects model (DerSimonian-Laird method) and statistical was examined heterogeneity using the I^2 statistic. Subgroup analyses were also undertaken to test for an association between the use of an electronic reminder or not and: questionnaire length (short i.e. <10 pages compared to long i.e. >10); the type of electronic reminder (SMS and or email vs SMS only); and timing of reminder (pre- vs post-notification). Risk of bias was assessed using the ROB2 tool and the quality of the evidence was assessed using the GRADE tool (17, 18).

3. Results

In total, 269 participants were randomized to the SWAT, 135 (50.2%) to the pre-notification and 134 (49.8%) to the post-notification group. The baseline characteristics for each group in the SWAT and the host trial are presented in Table 2.

	Pre-notification (n=135)	Post-notification (n=134)	UK-FROST (n=503)
Gender, n (%)			
Male	47 (34.8)	47 (35.1)	184 (36.6)
Female	88 (65.2)	87 (64.9)	319 (63.4)
Age in years, mean (SD)	54.0 (7.7)	53.1 (7.6)	54.3 (7.7)
Host trial allocation, n (%)			
ESP	28 (20.7)	27 (20.1)	99 (19.7)
ACR	55 (40.7)	55 (40.7)	203 (40.3)
MUA	52 (38.5)	52 (38.8)	201 (40.0)

Table 2. Baseline characteristics of participants in the SWAT and host trial

A total of 241 (89.6%) participants in the SWAT returned a valid questionnaire at 3 months follow-up: 122 (90.4%) participants in the pre-notification group and 119 (88.8%) in the post-notification group (difference of -1.6% with a 95% CI: -8.9% to 5.7%). The chi-squared test showed no evidence of a difference between groups in the proportion of participants returning a valid questionnaire (p=0.67). In the adjusted regression, the two groups did not differ in the likelihood of returning a valid questionnaire (OR = 0.93; 95% CI: 0.41 to 2.08; p=0.85).

The median time for questionnaire return was 14 days for pre-notification (interquartile range [IQR]: 9 to 25) and 13 days for post-notification (IQR: 8 to 22 days). There was no statistically significant difference in the time to return the questionnaire between the two arms (HR = 1.04; 95% CI: 0.80 to 1.34). The results of the log-rank test showed no evidence of a difference in time to response between groups (p=0.93). Cox regression did not identify the timing of SMS reminder to be a significant predictor of time to return (p=0.79).

In total, 119 (44.2%) of the 269 participants required at least one return reminder: 64 (47.4%) in the pre-notification group and 55 (41.0%) in the post-notification group (difference of -6.4%; 95% CI: -18.2% to 5.5%). The chi-squared test showed no difference between groups in the proportion of participants requiring at least one reminder notice (p=0.29). In the adjusted regression, the two groups did not differ in the likelihood of requiring at least one reminder notice (OR = 0.71; 95% CI: 0.43 to 1.17; p=0.18).

When comparing participants who received no SMS reminders in the UK FROST trial to participants who were recruited to the SWAT, the return rates for the questionnaire were 87.2% (205/235) and 89.6% (241/269) respectively - a difference of 1.4%.

3.1. Systematic review and meta-analysis

Our search yielded 4850 records; after deduplication 3728 abstracts were screened and 94 full texts were assessed for eligibility. Seven studies met the inclusion criteria including the study embedded in UK FROST; six were included in the meta-analysis including the current study (9-11, 19-21). One study could not be pooled in the meta-analysis as it used a different intervention and comparator (21). Figure 1 illustrates the study selection process.

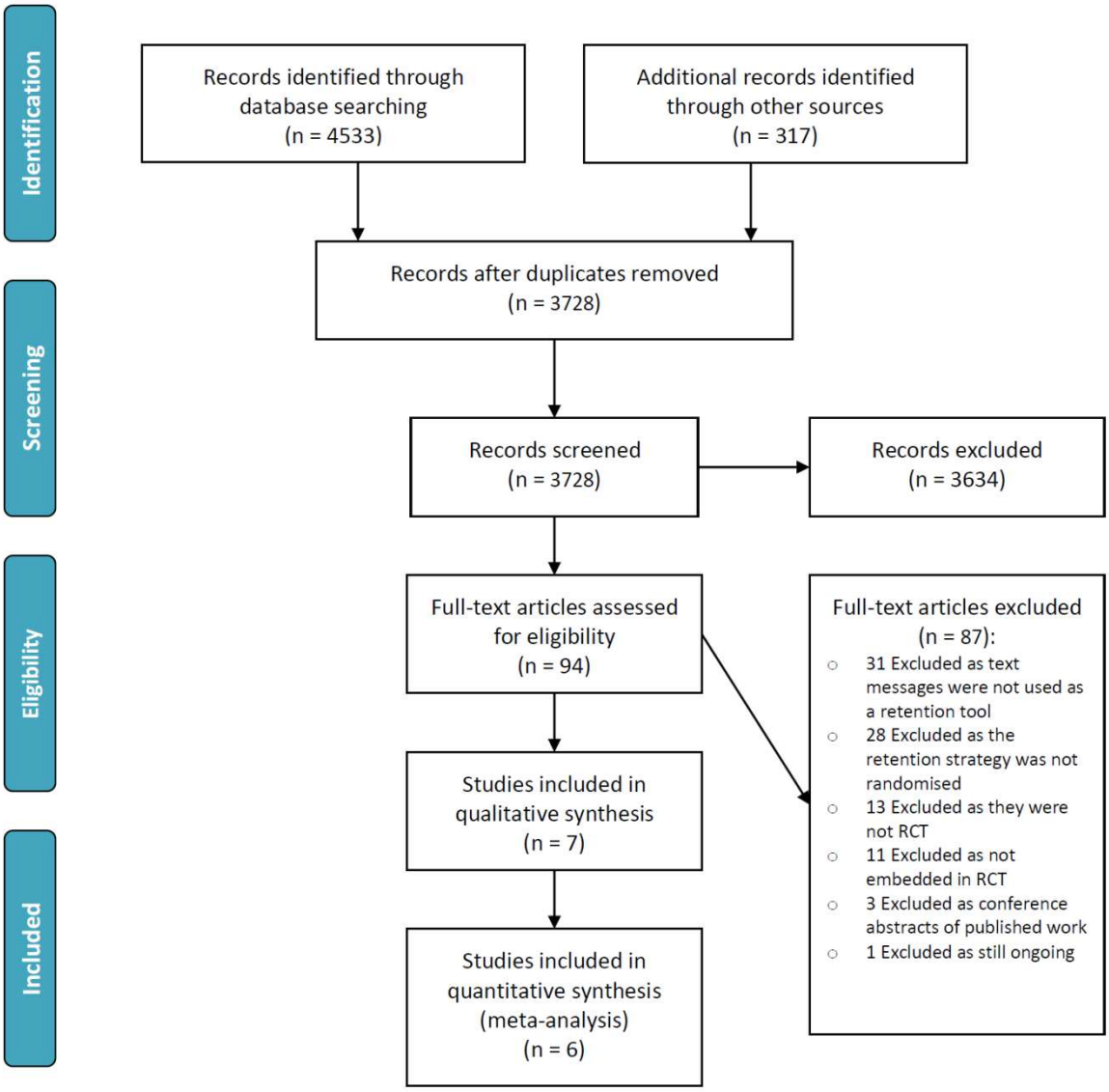

Figure 1 PRISMA flow-chart detailing the study selection process (22)

The characteristics of the embedded studies and their host trials, the risk of bias assessment for the individual trials and the GRADE assessment for the main meta-analyses are available as appendices B and C (17, 18).

Two RCTs (792 participants) were included in a meta-analysis of the effect on postal questionnaire response rates of pre- compared with post-notification SMS reminders (Figure 2) (9). The results favour post-notification; however, this was not statistically significant (OR = 0.78 95% CI: 0.42 to 1.45; p=0.44). Statistical heterogeneity was high (I^2 = 52%) due to the limited number of RCTs and the wide variation of effects reported in our orthopaedic and depressed patient populations (9). Based on GRADE, the quality of evidence was very low.

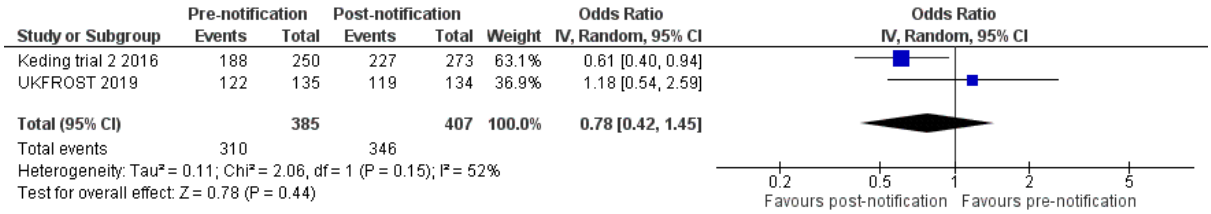

Figure 2 Forest plot for pre- compared with post-notification meta-analysis

We also included six RCTs to estimate the effect on postal questionnaire response rates of electronic reminders (SMS, e-mail or both) irrespective of timing compared to no reminders (Figure 3) (9-11, 19, 20). Pooling these RCTs provides evidence in favour of electronic reminders for increasing response rates; however, the difference was not statistically significant (OR = 1.15 95% CI: 0.95 to 1.41; p=0.16). Statistical heterogeneity was low (I^2 = 0%). Based on GRADE, the final quality of evidence was judged to be moderate.

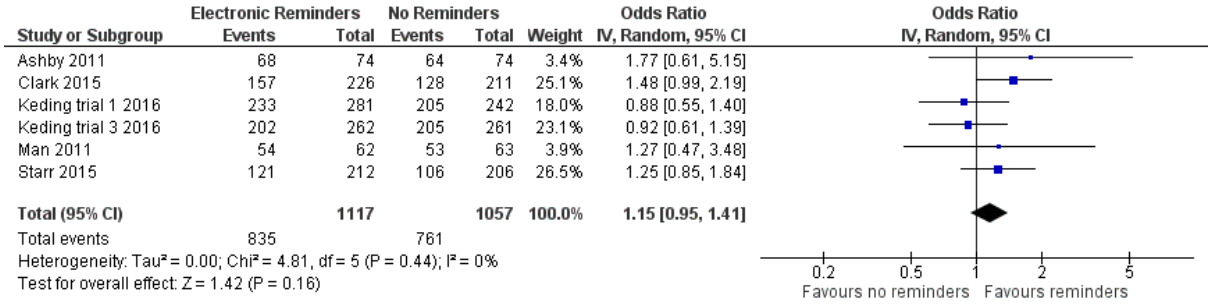

Figure 3 Forest plot for the SMS reminder against no reminder meta-analysis

The test for subgroup differences in these 6 RCTs indicates no statistically significant subgroup effect for both questionnaire length (short compared to long) and reminder modality (SMS and/or e-mail compared to SMS only) with p=0.09 for both tests. There was no statistical heterogeneity in either subgroup analysis (I^2 = 0% for all subgroups). However, electronic reminders were more effective than no reminders in shorter questionnaires (OR of 1.51, 95% CI: 1.04 to 2.19, p=0.03). A combination of electronic reminders (SMS and/or e-mail) was also more effective than no reminders (OR = 1.48, 95% CI: 1.04 to 2.09, p=0.03). The test for subgroup differences comparing the use of a pre- or post-notification combination of electronic reminders compared with no reminders showed no statistically significant subgroup effect (p= 0.65), and there was moderate heterogeneity in the post-notification subgroup (I^2 = 37%). The forest plots for the subgroup analyses are presented in appendix D.

4. Discussion

4.1. Summary of main findings

This is one of the first SWATs undertaken as part of the PROMETHEUS initiative investigating the effect of SMS reminder timings on retention in RCTs (23). We found no evidence to suggest that either pre- or post-notification SMS reminders improved postal questionnaire response rates, time to return of questionnaires or affected the need for additional reminders. When pooling our SWAT with another embedded trial, there was a suggestion that post-notification was more effective, but

it was not statistically significant. Nor was there statistically significant evidence that electronic reminders compared with no reminder improved postal questionnaire return.

4.2. Comparisons with existing literature

Only one other RCTs has compared the effect on trial participant questionnaire return of pre-notification with post-notification SMS reminders. In Keding et. al., post-notification significantly increased response rate and decreased time to response compared to pre-notification at 6-months follow-up (9). Our SWAT did not favour either pre- or post-notification and tested the effect of timing of questionnaires at the 3-month follow-up. Our SWAT had higher return rates compared to Keding et. al. which could limit the potential effectiveness of the timing of the SMS message. Both RCTs evaluated treatments in different settings and patient populations. Keding's study is further complicated by the study design: a three two-arm RCT in the same population which meant participants were being re-randomized to different SMS reminder strategies every 3-months which raises the issue of carry-over effect.

Only one previous systematic review has studied the role of additional reminders in improving retention, however that review included RCTs evaluating SMS reminders, telephone reminders and the provision of calendars with questionnaire due dates (24). Only three RCTs were included which investigated the effect of SMS reminders, the largest of which compared SMS reminders with an emphasis on the social benefit of participation in RCTs to simple SMS reminders (21). Brueton et. al. found a small but non-significant increase in response rates when using additional reminders (24). Little evidence exists assessing the effectiveness of SMS or electronic reminders over other forms of reminders.

4.3. Strengths and weaknesses of the SWAT and meta-analyses

As with every SWAT, our findings are limited to the participants recruited in the host trial. In UK FROST the participants were predominantly female and middle-aged. This study like many SWATs was underpowered, as the sample size was limited by the number of participants in the host trial and the intervention was not introduced from the outset. The host trial employed multiple other retention strategies which may have contributed to the already high questionnaire response rates (above 85%). The intervention was at the 3-month follow-up when trial participants may still be highly motivated to complete questionnaires.

We undertook a robust systematic review and meta-analyses assessing the effect of electronic reminders on the return of postal questionnaires. The meta-analysis comparing electronic reminders to no reminders included six high quality studies embedded in host trials in a variety of specialities (medicine, surgery and psychiatry) and settings (community, primary and secondary care). All the RCTs were, however, based in the United Kingdom and investigated middle-aged participants. Only two RCTs included participants aged above 65 and none included children or teenagers who have increasing access to mobile technology (25). It also only applied to the return of postal questionnaires rather the electronic completion. There is, therefore, still limited generalisability. We omitted grey literature and unpublished trials which could introduce publication bias. Results from the sub-group analyses should be interpreted with caution because of the potential for confounding between studies in the comparisons made. The meta-analysis comparing pre- against post-notification included only two studies, reporting different effects which resulted in a wide confidence interval. These factors lead to the very low GRADE certainty, which highlights the need for further research investigating the different timings of SMS reminders in improving retention in RCTs.

4.4. Implications of findings for research and retention of trial participants

The role of SMS, or electronic reminders more generally, remains unclear in improving the return of postal questionnaires in RCTs; we are aware of only two other SWATs in progress investigating SMS as a retention tool in RCTs (26, 27). The findings of our meta-analyses have a very low to moderate GRADE certainty and need to be interpreted with caution. Even a small increase in questionnaire response rate, however, could be useful given the ease of use of SMS reminders and their low cost.

Both the addition or not of SMS reminders and the timing of SMS reminders meets all the criteria of Trial Forge Guidance 2 for further investigation (28). Future research should focus on:

- Generating further evidence to improve the GRADE certainty, especially investigating the timing of SMS reminders.
- Exploring the role of SMS reminders in other contexts. Further research is needed in younger and older populations. Targeting participant groups known to have poor engagement with trials, such as IV drug user, would be useful. Other areas worth exploring include the role of SMS reminders in long-term follow-up, their synergistic effect with other retention strategies and their effectiveness with electronic questionnaires which can be completed immediately on mobile-phones or other devices.
- SMS reminders have little direct benefit for participants. However, whilst some might appreciate a reminder, it is possible that participants find these irritating. An understanding of the acceptability of SMS reminders in improving retention would be beneficial.
- Whilst in principle an SMS reminder is inexpensive, its cost-effectiveness has not yet been explored.

5. Conclusions

SMS reminders are simple to implement, inexpensive and increasingly being used in RCTs. Our SWAT in UK FROST, however, provided no evidence to suggest that pre- compared with post-notification SMS reminders improved postal questionnaire response rates, time to return of questionnaires or affected the need for reminders. The findings from the meta-analyses cautiously suggest that SMS reminders could be effective when combined with other retention strategies such as shorter questionnaires or other electronic reminders; however, further SWATs are required to provide robust evidence. Trialists should consider including embedded retention trials in their host RCTs to further evaluate the role of SMS and other electronic reminders, and their timing, in improving participant retention.

Ethics approval and funding declaration

The ethics approval for this trial was obtained as a substantial amendment to UK FROST from the North East (Newcastle & North Tyneside 2) Ethics Committee, 18/11/2014, REC Ref: 14/NE/1176. Substantial Amendment 1 – REC Favourable Opinion 02/02/2015.

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Availability of data and materials

The anonymised data used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

AR & LK declare that their department has received educational and research grants from DePuy J&J Ltd outside the submitted work.

Authors' contributions

All authors were involved in the conception and design of the study. PS, AP, SB and MN contributed to the acquisition of data and EC and AM undertook the analyses. All authors contributed to the interpretation of data, commented on drafts of the article and approved the manuscript to be submitted.

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Conflict of interests

AR & LK declare that their department has received educational and research grants from DePuy J&J Ltd outside the submitted work. The other authors declare no competing interests.

Appendix A

Database search

We conducted an electronic search of the following databases from inception to April 2019:

- the Cochrane Central Register of Controlled Trials (CENTRAL)
- MEDLINE, EMBASE, PsycINFO and AMED, searched using an Ovid platform
- Database of Abstracts of Reviews of Effects (DARE) via the CRD database
- CINAHL (Cumulative Index to Nursing and Allied Health), Education Resource Information Centre (ERIC) using the EBSCOHost platform
- Web of Science

The search strategy will identify terms corresponding to 'randomised controlled trials', 'SMS text messaging' and 'retention' (and their variants). Electronic bibliographic database searches will use a combination of medical subject headings (MeSH) and free text. The search strategy for MEDLINE is shown below and is based on the Cochrane review by Brueton et. al.:(1)

1. randomized controlled trial.pt.
2. controlled clinical trial.pt.
3. randomized.ab.
4. placebo.ab.
5. randomly.ab.
6. clinical trials as topic.sh.
7. exp humans/ not animals.sh.
8. trial.ti.
9. 1 or 2 or 3 or 4 or 5 or 6 or 8
10. 9 and 7
11. (minimi$ adj2 attrition).ab, ti.
12. (prevent$ adj2 attrition).ab, ti.
13. (lessen$ adj2 attrition).ab, ti.
14. (decreas$ adj2 attrition).ab, ti.
15. (reduc$ adj2 attrition).ab, ti.
16. (minimi$ adj2 drop-out).ab, ti.
17. (prevent$ adj2 drop-out).ab, ti.
18. (lessen$ adj2 drop-out).ab, ti.
19. (decreas$ adj2 drop-out).ab, ti.
20. (reduc$ adj2 drop-out).ab, ti.
21. (minimi$ adj2 drop-out$).ab, ti.
22. (prevent$ adj2 drop-out$).ab, ti.
23. (lessen$ adj2 drop-out$).ab, ti.
24. (decreas$ adj2 drop-out$).ab, ti.
25. (reduc$ adj2 drop-out$).ab, ti.
26. (minimi$ adj2 drop$-out).ab, ti.
27. (prevent$ adj2 drop$-out).ab, ti.
28. (lessen$ adj2 drop$-out).ab, ti.
29. (decreas$ adj2 drop$-out).ab, ti.
30. (reduc$ adj2 drop$-out).ab, ti.
31. (minimi$ adj2 dropout$).ab, ti.
32. (prevent$ adj2 dropout$).ab, ti.

33. (lessen$ adj2 dropout$).ab, ti.
34. (decreas$ adj2 dropout$).ab, ti.
35. (reduc$ adj2 dropout$).ab, ti.
36. (strateg$ adj2 drop$-out).ab, ti.
37. (strateg$ adj2 dropout$).ab, ti.
38. (loss adj2 follow-up).ab, ti.
39. (lost adj2 follow-up).ab, ti.
40. (loss adj2 followup).ab, ti.
41. (lost adj2 followup).ab, ti.
42. (minimi$ adj2 withdrawal).ab, ti.
43. (prevent$ adj2 withdrawal).ab, ti.
44. (lessen$ adj2 withdrawal).ab, ti.
45. (decreas$ adj2 withdrawal).ab, ti.
46. (reduc$ adj2 withdrawal).ab, ti.
47. (minimi$ adj2 withdrawal$).ab, ti.
48. (prevent$ adj2 withdrawal$).ab, ti.
49. (lessen$ adj2 withdrawal$).ab, ti.
50. (decreas$ adj2 withdrawal$).ab, ti.
51. (reduc$ adj2 withdrawal$).ab, ti.
52. (strateg$ adj2 attrition).ab, ti.
53. (strateg$ adj2 drop-out).ab, ti.
54. (strateg$ adj2 dropout).ab, ti.
55. (strateg$ adj2 follow-up).ab, ti.
56. (strateg$ adj2 followup).ab, ti.
57. (increas$ adj2 retention).ab, ti.
58. (encourag$ adj2 retention).ab, ti.
59. (maximi$ adj2 retention).ab, ti.
60. (promot$ adj2 retention).ab, ti.
61. (improv$ adj2 retention).ab, ti.
62. (strateg$ adj2 response$).ab, ti.
63. (strateg$ adj2 (questionnaire$ adj3 response$)).ab, ti.
64. (increas$ adj2 (questionnaire$ adj3 response$)).ab, ti.
65. (encourag$ adj2 (questionnaire$ adj3 response$)).ab, ti.
66. (maximi$ adj2 (questionnaire$ adj3 response$)).ab, ti.
67. (promot$ adj2 (questionnaire$ adj3 response$)).ab, ti.
68. (improv$ adj2 (questionnaire$ adj3 response$)).ab, ti.
69. (increas$ adj2 response$).ab, ti.
70. (encourag$ adj2 response$).ab, ti.
71. (maximi$ adj2 response$).ab, ti.
72. (promot$ adj2 response$).ab, ti.
73. (improv$ adj2 response$).ab, ti.
74. (retention adj2 strateg$).ab, ti.
75. retention rate$.ab, ti.
76. (retention adj2 method$).ab, ti.
77. (retention adj2 technique$).ab, ti.
78. attrition rate$.ab, ti.
79. (questionnaire$ adj3 (response$ adj2 method$)).ab, ti.
80. (questionnaire$ adj3 (response adj2 technique$)).ab, ti.

81. (questionnaire adj response rate$).ab, ti.
82. (difficult$ adj2 (retain$ or retention)).ab, ti.
83. 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82
84. SMS$.ab, ti.
85. Short message$ service$.ab, ti.
86. Instant messag$ service$.ab, ti.
87. (Short adj2 messag$).ab, ti.
88. (Instant adj2 messag$).ab, ti.
89. Text$.ab, ti.
90. (Text$ adj2 messag$).ab, ti.
91. Txt$.ab, ti.
92. (Txt$ adj2 message$).ab, ti.
93. MMS$.ab, ti.
94. (multimedia adj2 messag$).ab, ti.
95. (multi$media adj2 messag$).ab, ti.
96. 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95
97. (Phone$ or telephone$).ab, ti.
98. (Cell$ adj2 (phone$ or telephon$)).ab, ti.
99. (mobile adj2 (phone$ or telephon$)).ab, ti.
100. (wireless adj2 (phone$ or telephon$)).ab, ti.
101. ((mobile or handheld or hand-held) adj2 (device$ or technolog$ or app$ or health$)).ab, ti.
102. (smart phon$ or smartphone$ or blackberry$ or iphon$ or personal digital assistant$ or pda$ or electr$ or E).ab, ti.
103. ((android or google) adj2 phone$).ab, ti.
104. 97 or 98 or 99 or 100 or 101 or 102 or 103
105. (Communication$ or Messag$ or Reminder$ or notif$ or prompt$ or text$ or imag$ or mms$).ab, ti.
106. 104 and 105
107. 96 or 106

This search yielded 290 records in the end of April 2019.

Appendix B

Table 1 Characteristics of studies included in the systematic review

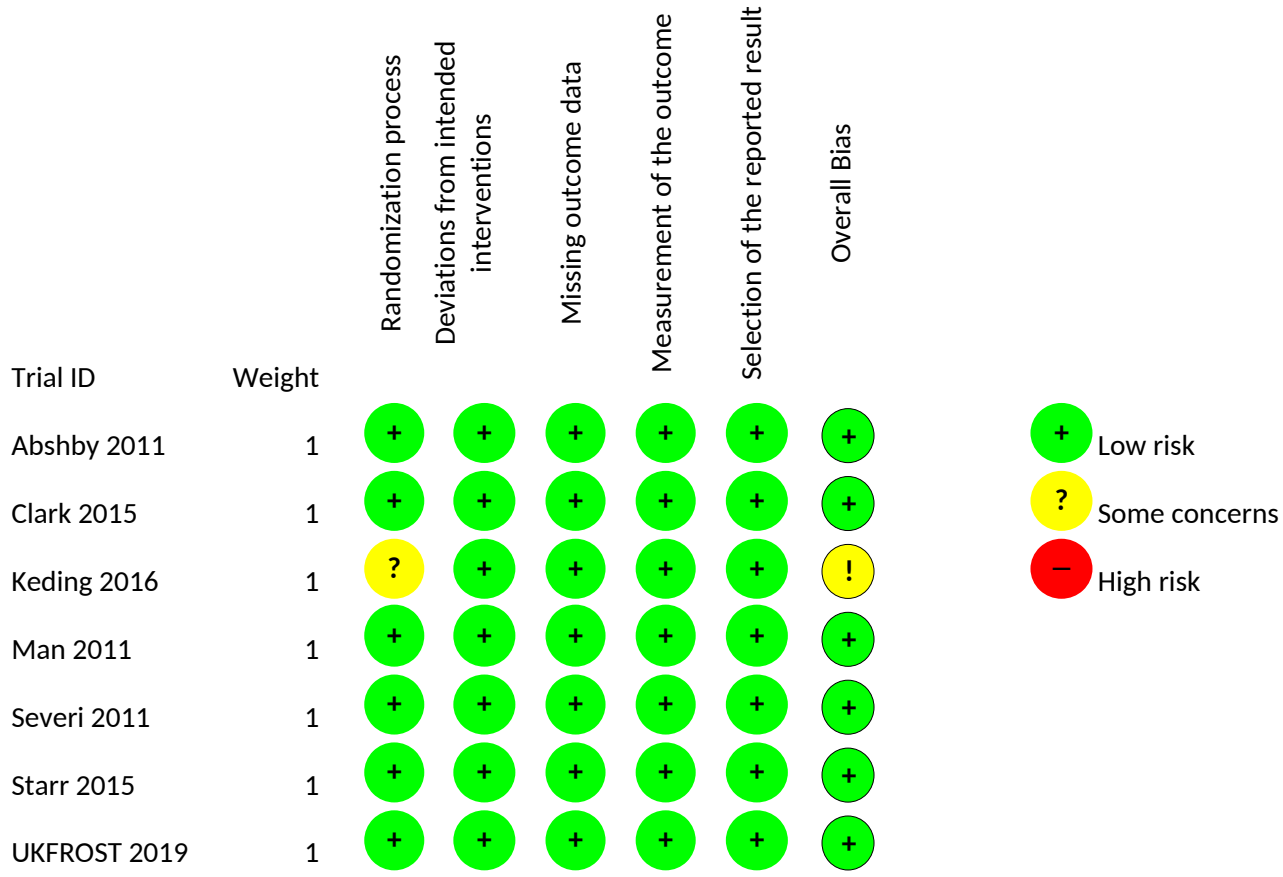
Embedded Trial	Disease/condition	Host trial	Design of embedded trial	Participants	Setting
Ashby 2011(2)	Treatment of migraine	Randomised controlled trial of food elimination diet based on IgG antibodies for the prevention of migraine like headaches (Published)(3)	2-arm RCT	Adults with self-reported migraines and proven food allergy on IgG testing	UK, community-based
Clark 2015(4)	Detection of COPD	DOC study (Published)(5)	2-arm RCT	Adults who are current smokers	UK, Yorkshire, Primary care-based
Keding 2016 trial 1(6)	Treatment of depression	ACUdep (Published) (7)	3 2-arm RCT on the same population	Adults with depression	UK, Yorkshire and North-East of England, Primary care-based
Keding 2016 trial 2(6)	Treatment of depression	ACUdep (Published) (7)	3 2-arm RCT on the same population	Adults with depression	UK, Yorkshire and North-East of England, Primary care-based
Keding 2016 trial 3(6)	Treatment of depression	ACUdep (Published) (7)	3 2-arm RCT on the same population	Adults with depression	UK, Yorkshire and North-East of England, Primary care-based
Man 2011(8)	Treatment of lower back pain	Yoga for Chronic Low Back Pain: A Randomized Trial (Published)(9)	2-arm RCT	Adults with lower back pain	UK, multi-centre, Primary care-based
Severi 2011(10)	Encouraging smoking cessation	TXT2STOP (Published)(11)	2-arm RCT	Adults who are current smokers who are willing to stop	UK, community-based
Starr 2015(12)	Treatment of ureteric stones	SUSPEND (Published)(13)	2X2 factorial RCT	Adults with unilateral ureteric stones	UK, multi-centre, Secondary care-based
Kottam (unpublished)	Treatment of frozen shoulder	UK-FROST(unpublished)	2-arm RCT	Adults with primary frozen shoulder	UK, multi-centre, Secondary care-based

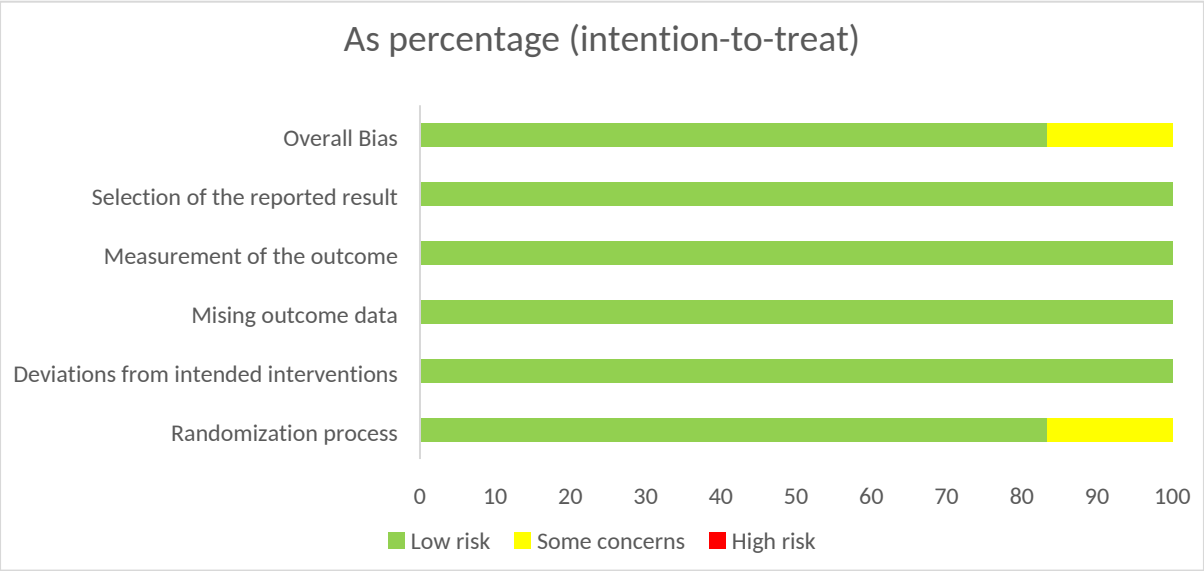
Table 2 Characteristics of studies included in the systematic review (continued)

Embedded Trial	Number randomised	Intervention(s)	Control	Outcome for retention trial	Time point used in analysis
Ashby 2011	148 (74 in both groups)	Electronic reminder (SMS, E-mail or both)	No electronic reminder	Primary outcome: Response rate for questionnaires, Secondary outcome: Time to return for the questionnaires	39 days
Clark 2015	437 (intervention: 226 and control: 211)	Electronic reminder (SMS, E-mail or both)	No electronic reminder	Primary outcome: Response rate for questionnaires, Secondary outcome: Time to return for the questionnaires	56 days
Keding 2016 trial 1	523 (intervention: 281 and control: 242)	SMS pre-notification for 3-month questionnaire	No SMS notification	Primary outcome: Response rate for questionnaires, Secondary outcome: Time to return for the questionnaires	91 days
Keding 2016 trial 2	523 (intervention: 273 and control: 250)	SMS post-notification for 6-month questionnaire	SMS pre-notification	Primary outcome: Response rate for questionnaires, Secondary outcome: Time to return for the questionnaires	91 days
Keding 2016 trial 3	523 (intervention: 262 and control: 261)	SMS post-notification for 9-month questionnaire	No SMS notification	Primary outcome: Response rate for questionnaires, Secondary outcome: Time to return for the questionnaires	91 days
Man 2011	125 (intervention:62 and control:63)	Electronic reminder (SMS, E-mail or both)	No electronic reminder	Primary outcome: Response rate for questionnaires, Secondary outcome: Time to return for the questionnaires	42 days
Severi 2011	1950 (intervention: 974 and control: 976)	SMS notification emphasizing the benefits to society when participating to research and a fridge magnet sent by post before the SMS reminder	SMS notification with no mention of the benefits to society	Primary outcome: Response rate for questionnaires at 30 weeks, Secondary outcome: Response rate for questionnaire at 26 weeks	30 weeks
Starr 2015	418 (intervention: 212 and control: 206))	Pre-notification SMS	No SMS reminder	Primary outcome: Response rate for questionnaires	NA
Kottam (unpublished)	269 (intervention:134 and control:135)	SMS post-notification	SMS pre-notification	Primary outcome: Response rate for questionnaires, Secondary outcome: Time to return for the questionnaires	91 days

Appendix C

Risk of bias in included studies





GRADE assessment

Question: Pre-notification compared to post-notification SMS reminders in increasing postal questionnaire return rate in RCTs

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consideration	Pre-notification	post-notification reminders	Relative (95% CI)	Absolute (95% CI)		
Questionnaire returned												
2	randomised trials	serious [a]	serious [b]	not serious	serious [c]	none	310/385 (80.5%)	346/407 (85.0%)	**OR** 0.78 (0.42 to 1.45)	**29 more per 1,000** (from 54 fewer to 81 more)	⨁◯◯◯ VERY LOW	NOT IMPORTANT

CI: Confidence interval; **OR:** Odds ratio

Explanations

a. Keding trial 2 contributed >50% in terms of weight, this study has a serious risk of bias due to the crossover study design

b. large differences in effect based on studies, considering only 2 studies were considered, this poses questions on the effects of the intervention

c. Wide confidence interval ranging from .69 to 2.37

Question: Electronic reminders compared to no electronic reminders in increasing postal questionnaire return rates in RCTs

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consideration	Electronic reminders	no electronic reminders	Relative (95% CI)	Absolute (95% CI)		
New Outcome												
6	randomised trials	serious [a]	not serious	not serious	not serious [b]	none	835/1117 (74.8%)	761/1057 (72.0%)	**OR 1.15** (0.95 to 1.41)	**27 more per 1,000** (from 10 fewer to 64 more)	⨁⨁⨁◯ MODERATE	IMPORTANT

CI: Confidence interval; **OR:** Odds ratio

Explanations

a. 23.1% of the weight is from Keding trial 2, for this trial there is a high risk of bias from carryover effect due to the crossover element of the study design

b. appropriate sample size and events, however the confidence interval was too wide to make any useful conclusions

Appendix D

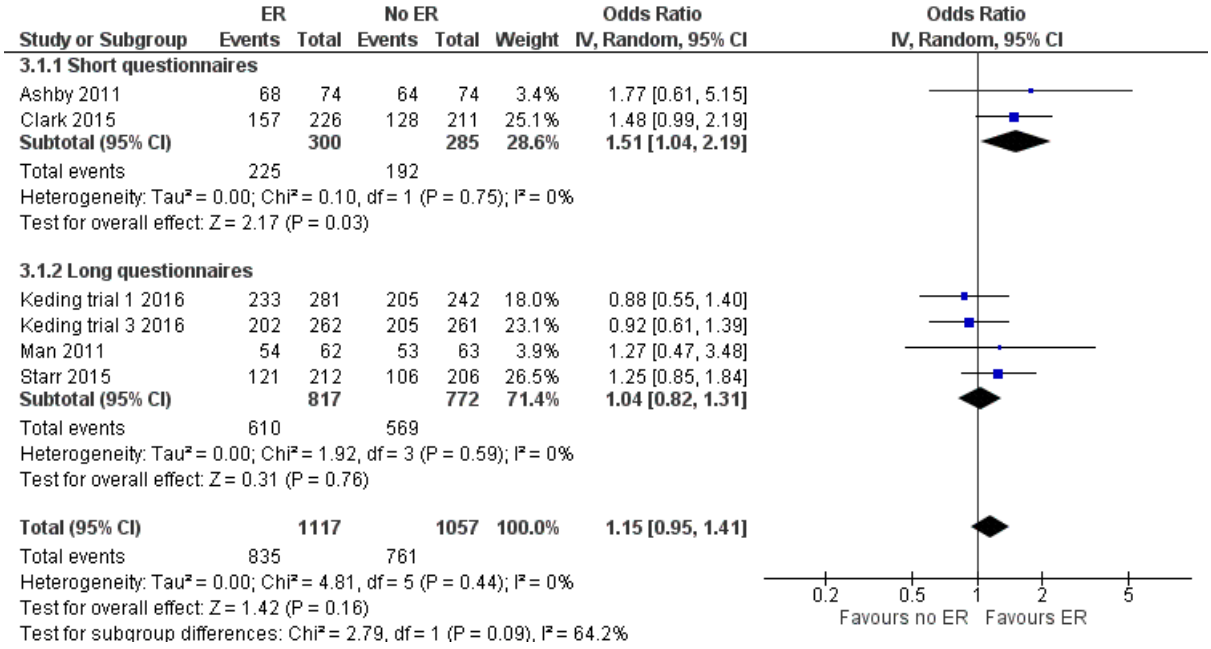


Figure 1 Subgroup Analysis by questionnaire length

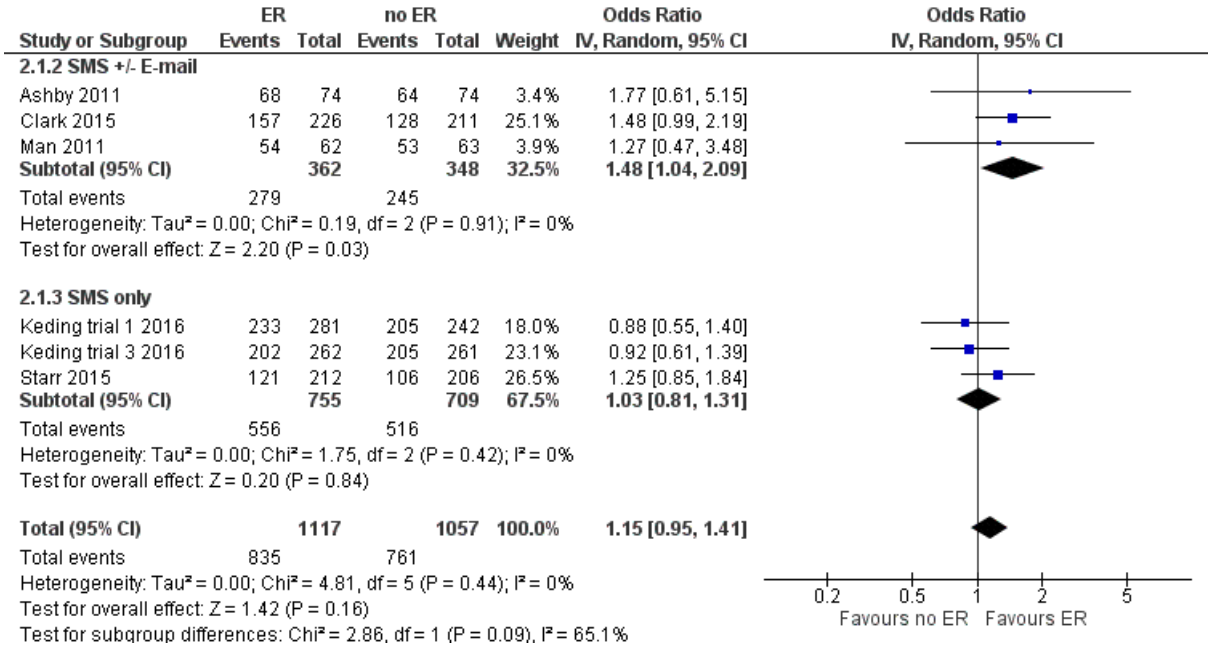


Figure 2 Subgroup analysis by reminder modality

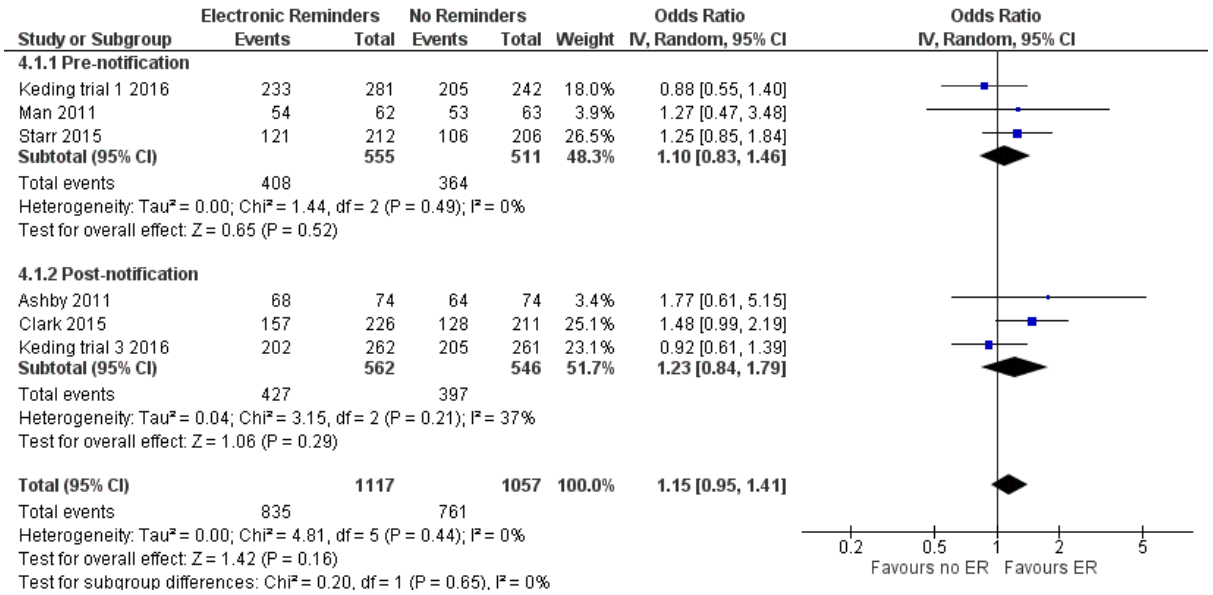


Figure 3 Subgroup analysis by reminder timing

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