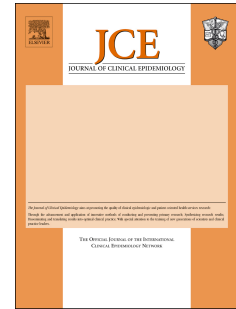


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Best practice guidance for the use of strategies improved retention in randomised trials developed from two consensus workshops

V. Brueton, S.P. Stenning, F. Stevenson, J. Tierney, G. Rait



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V. Brueton
Faculty of Nursing and Midwifery,
King's College, London,
57 Waterloo Road
London
SE1 8WA
email: valerie.brueton@kcl.ac.uk
Telephone: 00 (44) 2078483826

S.P. Stenning
MRC Clinical Trials Unit at UCL,
Aviation House,
125 Kingsway,
London,
WC2B 6NH

F. Stevenson
UCL Research Department of Primary care and Population Health
Royal Free and University College Medical School
Rowland Hill Street
London
NW3 2PF

J. Tierney
MRC Clinical Trials Unit at UCL,
Aviation House,
125 Kingsway,
London,
WC2B 6NH

G. Rait
PRIMENT Clinical Trials Unit,
Research Department of Primary Care and Population Health,
Royal Free and University College Medical School,
Rowland Hill Street, London,
NW3 2PF

Key words: retention; randomized clinical trials; consensus development; best practice guidance.

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Objective: To develop best practice guidance for the use of retention strategies in randomised clinical trials (RCTs).

Design: Consensus development workshops.

Setting: Two UK Clinical Trials Units.

Participants: 66 statisticians, clinicians, RCT coordinators, research scientists, research assistants, and data managers associated with RCTs.

Methods: The consensus development workshops were based on the consensus development conference method used to develop best practice for treatment of medical conditions. Workshops commenced with a presentation of the evidence for: incentives, communication, questionnaire format, behavioural, case management and methodological retention strategies identified by a Cochrane review and associated qualitative study. Three simultaneous group discussions followed, focused on: a) how convinced the workshop participants were by the evidence for retention strategies, b) barriers to the use of effective retention strategies, c) types of RCT follow-up that retention strategies could be used for, and d) strategies for future research. Summaries of each group discussion were fed back to the workshop. Coded content for both workshops were compared for agreement and disagreement. Agreed consensus on best practice guidance for retention was identified.

Results: Workshop participants agreed best practice guidance for the use of small financial incentives to improve response to postal questionnaires in RCTs. Use of 2nd class post was thought to be adequate for postal communication with RCT participants. The most relevant validated questionnaire was considered best practice for collecting RCT data. Barriers identified for the use of effective retention strategies were: the small improvements seen in questionnaire response for the addition of monetary incentives, and perceptions among trialists that some communication strategies are outdated. Furthermore, there was resistance to change existing retention practices thought to be effective. Face to face and electronic follow-up technologies were identified as retention strategies for further research.

Conclusions: We developed best practice guidance for the use of retention strategies in RCTs and identified potential barriers to the use of effective strategies. The extent of agreement on best practice is limited by the variability in the currently available evidence. This guidance will need updating as new retention strategies are developed and evaluated.

What is new?

- This is the first set of best practice guidance for the use of retention strategies in RCTs
- The extent of agreement on best practice is limited by the variability in the currently available evidence
- More evaluations of face to face and electronic follow-up technologies to improve retention in RCTs are needed
- There is some resistance to change existing retention practices thought to be effective
- This guidance will need updating as new retention strategies are developed and evaluated

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1. Introduction

Loss to follow-up in randomised clinical trials (RCTs) can lead to biased results. Until recently the evidence for strategies to improve participant follow-up in research was limited to broad systematic reviews of methods to improve response to questionnaires in research (1, 2) or methods to improve retention in prospective population based cohort studies(3). Narrative reviews describe retention strategies to maximize in person follow-up in research (4, 5). None of these reviews were focused on evaluations of strategies to improve retention in RCTs.

In a Cochrane systematic review of strategies to improve retention specifically in RCTs, six types of strategies were evaluated, namely: incentives, new questionnaire formats, and communication, behavioural, methodology and participant case management strategies (6). The strategies that improved retention were: offering or adding monetary incentives and, based on the results of single RCTs, recorded delivery of questionnaires and a package of strategies designed for sending postal questionnaires known as the Total Design Method (TDM) (7, 8). A related qualitative study found incentives, communication and new questionnaire format strategies are routinely used by trialists to try to improve retention in UK primary care RCTs, based on research experience rather than any knowledge of their effect (9).

Although, these two studies examine the use and effect of strategies to improve retention in RCTs, to our knowledge guidance on the use of retention strategies in practice does not exist. To address this we wanted to develop consensus based guidance for the use of retention strategies in RCTs based on the evidence available. Three commonly used methods for developing consensus for best practice are: a) the Delphi method, b) the Nominal Group Technique (NGT) and c) Consensus Development Conferences (10, 11). These methods differ in how: a) data is collected e.g. through questionnaires or face to face contact, b) opinion is aggregated, and c) decisions are fed back to participants for reconsideration (11). The Delphi method uses rounds of postal questionnaires to record experts' views on a topic (10, 11). NGT uses structured group discussions with experts associated with a topic, and Consensus Development Conferences bring individuals related to a topic together to hear the best evidence available to help make decisions about best practice (11). This method was used by the National Institutes of Health to develop best practice for the monitoring and treatment of medical conditions (11-13).

We used the Consensus Development Model to bring together trial personnel in order to: a) explore the evidence available for the use and effect of strategies to improve retention in RCTs,

b) develop best practice guidance for the use of retention strategies in RCTs, c) identify barriers to the use of retention strategies, and d) to identify retention strategies for future research.

2. Methods

2.1. Selection of consensus workshop participants

Research personnel associated with two UK CTUs with expertise in the design and management of RCTs conducted across diverse disease areas, clinical, and geographical settings were recruited to participate in the consensus development workshops. All research personnel listed on the seminar list for each CTU were invited via email to contribute to a workshop to develop best practice guidance for the use of retention strategies in RCTs. The invitation included an abstract summarising the results of the Cochrane review and the qualitative study. The invitation was sent one week before each workshop with a reminder sent on the morning of the workshop.

2.2. Format of consensus workshops

Our consensus workshops were held in November and December 2013 during a regular time tabled seminar slot at each CTU. Workshops commenced with an introduction and overview of the purpose and format of the workshop, followed by a twenty minute presentation of evidence for the effect and use of strategies to improve retention in RCTs from the Cochrane systematic review and the qualitative study (6, 9) (Table 1). Three concurrent facilitated group discussions followed to discuss the evidence for: a) incentives (Group 1), b) communication strategies (Group 2), and c) questionnaire format strategies (Group 3). The evidence for three seldom used retention strategies: i.e. methodology, behavioural and case management was discussed after the questionnaire format discussions at workshop 1, and after the communication strategy discussions at workshop 2.

Questions for each discussion group were agreed *a priori* by the authors (VB, FS, SS, GR). Discussion groups were asked: a) whether they were convinced by the evidence; b) to identify clinical areas and types of follow-up the strategy could be used for; and c) to identify barriers to the use of the retention strategy. For strategies with no evidence of an effect on retention (i.e. non-monetary incentives, priority/first class post, enhanced letters, modified questionnaires, case management, and behavioural strategies) the workshop participants were asked to: a) consider whether those strategies were in current use, and b) to identify barriers that prevent changing the use of such retention strategies (Appendix 1).

Questions for each discussion group, and tabulated summaries of the Cochrane review and qualitative study results for each discussion were distributed to the discussion group facilitators (FS, JT, SS, FS) before each workshop (Appendix 1, Table 1). The workshop participants were assigned to a discussion group by numbers 1- 3. The occupation/role, research area, contact details, and discussion group allocation were recorded for each workshop participant. Discussion groups were asked to consider the evidence presented and, where possible, to agree best practice for the use of retention strategies in RCTs. Facilitators encouraged participants to draw on their knowledge and expertise of retention in RCTs and to focus their discussions on the retention strategy allocated. Summaries of the group discussion, and best practice guidance agreed were presented to each entire workshop for agreement.

>> insert Table 1 Summary of evidence from the Cochrane systematic review of strategies to improve retention in RCTs, and qualitative study on the use of retention strategies in RCTs<<

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2.3. Ethics approval

The consensus workshops focused on discussions of published evidence and were held in the full knowledge of senior management at each CTU. Research personnel at each CTU were informed, prior to the consensus workshop, that the aim was to develop best practice guidance for retention in RCTs. Consent to participate in the workshops was considered given when research personnel attended. The Cochrane review, qualitative study and consensus workshops contributed to a PhD thesis. Ethics approval for the qualitative study was sought from University College London Ethics Committee UCL 2342/002.

2.4. Data management and analysis

The workshop discussions were recorded by either: hand written contemporaneous notes (workshop 1), or digitally by voice recorder (Olympus WS-300M, or Sony model ICD-UX522) (workshop 2). The discussion notes were subsequently typed (by VB), and the digital recordings transcribed (by VB) and anonymised by removing RCT identifiers and acronyms. Each discussion group transcript was emailed to the discussion group facilitator to check for accuracy, and any additions and corrections were clarified by email. Broad codes were used to code textual data for: how convinced participants were by the results; the types of RCTs using the retention strategy; the types of follow-up retention strategies were used for e.g. questionnaire follow-up; barriers to use of effective retention strategies; further research; and guidance for best practice. Discussion group notes and transcripts were read and re read. The discussion group questions were used as a framework for content analysis. Coded text was identified, summarised and interpreted grounded in the discussion group transcripts/notes. The results were compared across both workshops.

3. Results

Sixty six self-selected RCT personnel associated with both CTUs participated in the workshops. They represented the spectrum of research personnel working on RCTs including: chief and principal investigators, statisticians, RCT managers, data managers, research assistants, research associates, and PhD students. Three group discussions were held during each workshop. The characteristics and number of participants attending each discussion group are illustrated in Table 2. Discussion groups were heterogeneous in terms of the participants' occupation/research role and research area.

>> insert Table 2 Consensus workshop characteristics and participants<<

3.1. Incentive strategies

Table 1 summarises the results of the Cochrane review and the qualitative study. The consensus workshop participants agreed with the results of the Cochrane review and the qualitative study that financial incentives could be used to improve questionnaire response in RCTs(6, 9). They were not convinced that incentives would improve retention in all RCTs. They felt that the addition of a monetary incentive depended upon the age, socioeconomic group, educational level and medical condition associated with RCTs participants. The small benefit gained from adding a monetary incentive to improve questionnaire response and the additional administration needed to add the incentive were thought to be potential barriers to the use of monetary incentives (Table 1).

In agreement with the results of the qualitative study(9), the workshop participants felt that monetary incentives could be perceived as coercive and that the value of monetary incentives should not be so high that RCT participants become suspicious about the use of research resources. The workshop participants also felt that the value of monetary incentives used to improve retention in RCTs should not be so low that RCT participants feel undervalued. A value of £5-20 was agreed for financial incentives.

The workshop participants agreed with the results of the Cochrane review(6) and the qualitative study(9) that non-monetary incentives, e.g. mugs and pens with RCT information e.g. logos, may not improve retention. They felt that branded study gifts (i.e. letters, pens, and mugs) could impact negatively on retention in RCTs, particularly if the gift implied that the participant was associated with a medical condition that they felt uncomfortable about. Although there was no evidence of effect for non-monetary incentives in the Cochrane review(6), the workshop and qualitative study participants acknowledged that non-monetary incentives were used to thank RCT participants for their participation and they were keen to continue to do this.

3.2. Communication strategies

The workshop participants were unconvinced by the results for communication strategies in the Cochrane review(6). The review showed that enhanced letters, first class post, sending questionnaires early and additional reminders (i.e. telephone, email, text messages, calendars with reminders, telephone surveys, and monthly reminders to sites of upcoming assessments) had no impact on questionnaire response in RCTs. Yet the qualitative study found that additional telephone, letter and email reminders are routinely used with the aim of improving follow-up in primary care RCTs(9). The workshop participants felt that the evidence of effect

and no effect for communication strategies was limited as the results were based on few retention RCTs. They also felt that the use of a communication strategy to improve retention in RCTs was dependent upon other factors e.g. the medical condition, age, socio economic status of the RCT participants, and the method of data collection e.g. postal questionnaire, or face to face contact. Additional reminders were thought to be particularly important for improving low response to questionnaires in RCTs of behavioural interventions e.g. smoking cessation, or in RCTs with healthy volunteers. The workshop participants were reluctant to change this practice because of the improvements they believed they had seen to participant follow-up in RCTs.

Based on the results of single RCTs in the Cochrane review, recorded delivery (8), and a package of postal communication strategies for questionnaire follow-up known as the Total Design Method (TDM) (7) improved questionnaire response. The TDM encompasses a hand signed letter, white envelope with a hospital logo and commemorative stamp, and a self-addressed and stamped envelope (Table 1). The workshop participants thought that recorded delivery may inconvenience RCT participants if they were out when their post was delivered. The TDM was thought to be outdated, but some elements were thought to potentially improve questionnaire follow-up e.g. sending personalised letters with questionnaires. Electronic communication with RCT participants was thought to be used more than paper methods in current practice and the workshop participants felt that adapting the TDM for use with electronic questionnaires could help improve questionnaire response in RCTs. The workshop participants thought that a personalised approach to retention for RCT participants including an additional visit after recruitment to determine their preferred mode/s of contact, e.g. by email, or SMS text message, could improve retention. More evaluations of communication strategies were thought to be needed.

The only result for communication strategies that the workshop participants were convinced by was the evidence of no effect for first class post. There was agreement that 1st class post was costly and 2nd class post could be now be used for sending routine post to RCT participants.

3.3. New questionnaire formats

The workshop participants were convinced by the evidence from the Cochrane review for new questionnaire formats(6). The results of the review suggest that there was no clear evidence that long and clear questionnaires are more effective than short condensed questionnaires or that placing disease/condition questions before generic questions improves response. The findings also suggest that more relevant questionnaires (in the context of alcohol use) may improve response. The qualitative study showed that shorter questionnaires are used to try to improve response in primary care RCTs(9) (Table 1). Human nature, the RCT participant's

medical condition, and other factors e.g. RCT participant's time and priorities were thought to influence questionnaire response. Based on their experience, the workshop participants perceived that questionnaires measuring outcomes for treatments of terminal conditions, e.g. cancers, have a higher response than questionnaires collecting behavioural outcomes e.g. smoking cessation. They felt that RCT participants may abandon completing an electronic questionnaire without an option to save and return to later, or where the questionnaire was perceived to be too long. There was general agreement that offering alternative ways to complete outcome data e.g. by post, text, or email could improve response. There was scepticism about using less relevant questionnaires to collect outcome data (20) (Table 1). There was agreement that the most relevant and validated questionnaire should be used to measure RCT outcomes and that plain English should be used in questionnaires.

3.4. Other strategies

The workshop participants also discussed other retention strategies identified by the Cochrane review that were seldom evaluated or used to improve retention in RCTs(6). These strategies were: methodology (an open versus closed RCT design(38)), case management (where case managers were assigned to RCT participants(37)) and behavioural strategies (provision of a motivational strategy delivering information about goal setting and time management to RCT participants(36, 39)).

3.4.1. Methodology (open versus closed RCTs designs)

The workshop participants were not convinced by the evidence from the Cochrane review that an open RCT design improves retention (Table 1). They agreed with the findings of the qualitative study that using an open RCT design to improve retention could bias RCT results as participants would be aware of their treatment allocation. They felt that the decision to mask the allocation was informed if not dictated by: a) the type of intervention i.e. drug treatment, behavioural intervention, and b) the need to avoid biases associated with disclosing the intervention e.g. performance bias.

3.4.2. Case management

Some workshop participants said they would consider using case management (37) (Table 1) to improve retention for RCTs with elderly or disabled participants if they had more information about the time and resources needed. There was no evidence from the Cochrane review that this strategy improved retention in RCTs, however the qualitative study found that elements of

case management had been used with the aim of improving retention in RCTs conducted through primary care.

3.4.3. Behavioural strategies

There was also no clear evidence that behavioural retention strategies improve retention in RCTs. Even though the results from the qualitative study were very negative about the use of this strategy, the workshop participants reported having no experience using such strategies to improve retention in RCT and one participant felt behavioural/motivational strategies (35, 36) (Table 1) could increase retention in RCTs of interventions for the prevention and treatment of e.g. infectious diseases.

3.5. Retention strategies identified for further research

The workshop participants thought that more evaluations of: a) communication strategies to encourage RCT participants to return to sites for follow-up, and b) electronic follow-up technologies are needed. Some participants felt that some of the retention strategies evaluated to date were too similar to usual RCT follow-up practice to make a difference to retention e.g. sending a letter with an additional sentence estimating the length of time it should take to complete a questionnaire (26) (Table 1). The workshop participants generally agreed that retention strategies for future evaluation should be substantially different from usual follow-up procedures.

3.6. Best practice guidance for the use of retention strategies in RCTs

Best practice guidance agreed for the use of retention strategies in RCTs from the group discussions is summarised in table 3.

>> insert Table 3 Best practice guidance for the use of retention strategies in RCTs <<

4. Discussion

The consensus development workshop format provided an opportunity for RCT personnel to meet and discuss the evidence for strategies to improve retention in RCTs. Both workshops were well attended. Agreement was reached for the use of incentives, 2nd class post, and some general principles around questionnaire design to help improve retention in RCTs. Potential barriers to using effective retention strategies were identified i.e. the limited evidence available for each retention strategy identified by the Cochrane review, the heterogeneity of settings and the small gains in response from the addition of monetary incentives. Barriers to changing the use of strategies with no effect were the workshop participants' resistance to change the use of

existing practices perceived to be effective. Strategies potentially worthy of future evaluation were also identified.

4.1. Strengths and limitations of the consensus workshops

The consensus workshops provided the opportunity for a multidisciplinary group with RCT expertise to consider the quantitative and qualitative evidence available, agree best practice for the use of retention strategies in RCTs, and discuss potential barriers to the use of effective strategies in RCTs. The guidance provides a baseline upon which to add other best practice guidance as evidence on the effects of new retention strategies emerge.

The consensus workshop participants were self-selected and experienced in the leadership, design, management and analyses of RCTs conducted across diverse disease areas and settings, and were interested in improving retention in RCTs. They may have had prior knowledge of the results of the Cochrane review and qualitative study through the information provided in the workshop invitation and by attending conferences/meetings where preliminary results were presented. These characteristics and factors contributed to lively, well informed group discussions about best practice for the use of retention strategies in RCTs and potential barriers to use.

The workshops were held at each CTU during a regular seminar slot, and were very well attended. Convening workshops on CTU sites made it more convenient for participants to attend. Although the workshops were shorter than consensus development workshops held by the National Institutes of Health (11, 13) we found that there was adequate time to discuss the focused questions about the specific retention strategy assigned to each discussion group.

The best practice guidance agreed by the workshop participants for the use of retention strategies in RCTs has been informed by evidence from a Cochrane review(6), qualitative study(9) and expert opinion. A limitation of the guidance is that the views of RCT participants themselves are not represented. Future guidance on the use of retention strategies in RCTs would benefit from their involvement to help trialists better understand the priorities, barriers, and facilitators to retention from a participant's perspective. Moreover, it may also help identify new and preferred strategies needing future evaluation.

The extent of agreement on best practice for the use of retention strategies in RCTs is limited by the variability in the evidence from the systematic review and information from the qualitative study. Furthermore, no formal quantitative agreement through voting was used to agree feedback from the discussion groups. Nevertheless, there was qualitative agreement among the

workshop participants and opposing views were recorded. Even though the consensus workshops were limited to two CTUs this best practice guidance is broadly applicable to other UK CTUs.

4.2. Meaning and implications

Trialists can now consider adding small monetary incentives valued £5-20 to improve questionnaire response in RCTs, knowing that the recommendation is based on the best available evidence and endorsed by those involved in their conduct. How monetary incentives are delivered, i.e. given up front, or offered, will depend on the context of each RCT. Certainly, offers of incentives could be more cost effective for RCTs with lower response rates, as non-responders would receive no incentive.

Although the Cochrane review showed no effect for non-monetary incentives (i.e. gifts), it is clear from the qualitative study and the workshops that gifts are used in RCTs (6, 9), albeit with scepticism about the impact these have on retention. We are not aware of any research that identifies the most appropriate rewards for RCT participant's time. Therefore, involving RCT participants in the development of future best practice guidance on the use of retention strategies in RCTs may help to identify more acceptable non-monetary incentives for this group. More research is needed to identify and evaluate appropriate ways to demonstrate appreciation to RCT participants for their contributions to RCTs.

In considering the lack of evidence that priority/first class post improves questionnaire response in RCTs(6), workshop participants agreed that using 2nd class post should be used to cut the costs of postal communication with RCT participants, with the savings re directed to other RCT costs e.g. staff training. This guidance can be used to persuade trial personnel to use 2nd class post for future postal communication with RCT participants.

Even without clear evidence that modifying the format of a questionnaire improved response in RCTs(6), questionnaire length, readability, content and acceptability of the topic to RCT participants were still considered important factors for improving questionnaire response in the qualitative study (9) and in the consensus workshops. While the consensus was that questionnaires should be clear, relevant and validated in order to help to minimise bias, and maximise precision in effect estimates, testing the validity and reliability of new questionnaires is time consuming and costly (40). Therefore, trialists may wish to consider carefully the potential impact of questionnaire development on budgets and time lines for future RCT research proposals.

Lau's (2015) recent systematic review of systematic reviews of strategies for improving implementation of complex interventions in primary care practice found that educational outreach visits, educational meetings, audit, and feedback were the most effective ways to improve implementation of interventions(41). An evaluation of the use of this best practice guidance for the use of retention strategies in RCTs would inform how well the guidance has been implemented in RCTs at the CTUs where we conducted our consensus workshops, and the impact of the guidance on retention in those RCTs.

Our consensus development workshops identified some barriers to implementing the evidence for strategies to improve retention in RCTs. These barriers may change over time as new retention strategies are developed, and will need to be considered when the next set of guidance is developed.

To our knowledge this is the first set of guidance for the use of retention strategies in RCTs. We are aware of the results of other embedded RCTs published since the review that have evaluated the effectiveness of: SMS text messages(42), email reminders(43), a paper reminder to improve postal questionnaire response in RCTs(44) and offers of incentives(45). This best practice guidance will need updating when the Cochrane review of strategies to improve retention in RCTs is updated to incorporate this new evidence.

5. Conclusion

The consensus workshop discussions helped develop best practice guidance for the use of retention strategies in RCTs and identify potential barriers to the use of effective strategies. The extent of agreement is limited by the variability in the currently available evidence. More evaluations of newer retention strategies, particularly technological strategies are needed. This guidance will require updating as evidence on the effects of new strategies becomes available.

References

1. Edwards PJ, Roberts IG, Clarke MJ, DiGiuseppi C, Wentz R, Kwan I, et al. Methods to increase response rates to postal and electronic questionnaires. *Cochrane Database of Systematic Reviews* 2009, Issue 3 Art No : MR000008. 2009(3).
2. Nakash R, Hutton J, Jorstad-Stein E, Gates S, Lamb S. Maximising response to postal questionnaires - A systematic review of randomised trials in health research. *BMC Medical Research Methodology*. 2006;6(1):5.
3. Booker C, Harding S, Benzeval M. A systematic review of the effect of retention methods in population-based cohort studies. *BMC Public Health*. 2011;11(1):249.
4. Robinson KA, Dinglas VD, Sukrithan V, Yalamanchilli R, Mendez-Tellez PA, Dennison-Himmelfarb C, et al. Updated systematic review identifies substantial number of retention strategies: using more strategies retains more study participants. *Journal of Clinical Epidemiology*. 2015;68(12):1481-7.
5. Davis L, M B, R C. Maximizing Retention in Community-based Clinical Trials. *Journal of Nursing Scholarship*. 2002;34(1):47-53.
6. Brueton V, Tierney J, Stenning S, Nazareth I, Meredith S, Harding S, et al. Strategies to improve retention in randomised trials. *Cochrane Database of Systematic Reviews* 2013, Issue 12 Art No : MR000032 DOI: 10.1002/14651858.MR000032.pub2. 2013(12).
7. Sutherland HJ, Beaton M, Mazer R, Kriukov V, Boyd NF. A randomized trial of the total design method for the postal follow-up of women in a cancer prevention trial. *European Journal of Cancer Prevention*. 1996;5(3):165-8.
8. Tai S, Nazareth I, Haines A, Jowett C. A randomized trial of the impact of telephone and recorded delivery reminders on the response rate to research questionnaires. *Journal of Public Health*. 1997;19(2):219-21.
9. Brueton VC, Stevenson F, Vale CL, Stenning SP, Tierney JF, Harding S, et al. Use of strategies to improve retention in primary care randomised trials: a qualitative study with in-depth interviews. *BMJ Open*. 2014;4(1).
10. Fink A, Kosecoff J, Chassin M, Brook RH. Consensus methods: characteristics and guidelines for use. *American Journal of Public Health*. 1984;74(9):979-83.
11. Murphy M, Black N, Lamping D, McKee C, Sanderson C, Askham J, et al. Consensus development methods, and their use in clinical guideline development. 1998. Report No.: 2 (3).
12. Ganz PA, Barry JM, Burke W, Col NF, Corso PS, Dodson E, et al. National Institutes of Health State-of-the-Science Conference: Role of Active Surveillance in the Management of Men With Localized Prostate Cancer. *Annals of Internal Medicine*. 2012;156(8):591-5.
13. NIH. Consensus Statement on Total Knee Replacement. *NIH Consensus State Sci Statements*. 2003;20(1): 1–32.
14. Bauer JE, Rezaishiraz H, Head K, Cowell J, Bepler G, Aiken M, et al. Obtaining DNA from a geographically dispersed cohort of current and former smokers: Use of mail-based mouthwash collection and monetary incentives. *Nicotine & Tobacco Research*. 2004;6(3):439-46.
15. Gates S, Williams M, Withers E, Williamson E, Mt-Isa S, Lamb S. Does a monetary incentive improve the response to a postal questionnaire in a randomised controlled trial? The MINT incentive study. *Trials*. 2009;10(1):44.
16. Kenyon S, Pike K, Jones D, Taylor D, Salt A, Marlow N, et al. The effect of a monetary incentive on return of a postal health and development questionnaire: a randomised trial [ISRCTN53994660]. *BMC Health Services Research*. 2005;5(1):55.
17. Khadjesari Z, Murray E, Kalaitzaki E, White I, Mc Cambridge J, Thompson S, et al. Impact and costs of incentives to reduce attrition in online trials: Two randomised controlled trials. *Journal of Medical Internet Research*. 2011;13(1):e26.
18. COMMIT. Community Intervention Trial for Smoking Cessation (COMMIT): I. cohort results from a four-year community intervention. *American Journal of Public Health*. 1995;85(2):183-92.

19. Dorman P, Slattery J, Farrell B, Dennis M, Sandercock P. A randomised comparison of the EuroQol and Short Form-36 after stroke. United Kingdom collaborators in the International Stroke Trial. *BMJ*. 1997;315(7106):461-.
20. McCambridge J, Kalaitzaki E, White RI, Khadjesari Z, Murray E, Linke S, et al. Impact of Length or Relevance of Questionnaires on Attrition in Online Trials: Randomized Controlled Trial. *J Med Internet Res*. 2011;13(4):e96.
21. Bowen D, Thornquist M, Goodman G, Omenn GS, Anderson K, Barnett M, et al. Effects of Incentive Items on Participation in a Randomized Chemoprevention Trial. *Journal of Health Psychology*. 2000;5(1):109-15.
22. Renfroe EG, Heywood G, Foreman L, Schron E, Powell J, Baessler C, et al. The end-of-study patient survey: methods influencing response rate in the AVID Trial. *Controlled Clinical Trials*. 2002;23(5):521-33.
23. Sharp L, Cochran C, Cotton SC, Gray NM, Gallagher ME. Enclosing a pen with a postal questionnaire can significantly increase the response rate. *Journal of Clinical Epidemiology*. 2006;59(7):747-54.
24. Cockayne S, Torgerson D. A randomised controlled trial to assess the effectiveness of offering study results as an incentive to increase response rates to postal questionnaires [ISRCTN26118436]. *BMC Medical Research Methodology*. 2005;5(1):34.
25. Hughes J. Free reprints to increase the return of follow-up questionnaires. *Controlled Clinical Trials*. 1989.
26. Marson AG, Al Kharusi AM, Alwaidh M, Appleton R, Baker GA, Chadwick DW, et al. The SANAD study of effectiveness of carbamazepine, gabapentin, lamotrigine, oxcarbazepine, or topiramate for treatment of partial epilepsy: an unblinded randomised controlled trial. *The Lancet*. 2007;369(9566):1000-15.
27. Kenton L, Dennis C, Weston J, Kiss A. Abstracts from the 28th Meeting of the Society of Clinical Trials, Montreal, May 20–23, 2007: The effect of incentives and high priority mailing on postal questionnaire response rates: A Mini-RCT. *Clinical Trials*. 2007;4(4):371-455.
28. Man MS, Tilbrook HE, Jayakody S, Hewitt CE, Cox H, Cross B, et al. Electronic reminders did not improve postal questionnaire response rates or response times: a randomized controlled trial. *Journal of Clinical Epidemiology*. 2011;64(9):1001-4.
29. Ashby R, Turner G, Cross B, Mitchell N, Torgerson D. A randomized trial of electronic reminders showed a reduction in the time to respond to postal questionnaires. *Journal of Clinical Epidemiology*. 2011;64(2):208-12.
30. Severi E, Free C, Knight R, Robertson S, Edwards P, Hoile E. Two controlled trials to increase participant retention in a randomized controlled trial of mobile phone-based smoking cessation support in the United Kingdom. *Clinical Trials*. 2011;8(5):654-60.
31. MacLennan G, McDonald A, McPherson G, Treweek S, Avenell A. Advance telephone calls ahead of reminder questionnaires increase response rate in non-responders compared to questionnaire reminders only: The RECORD phone trial. *Trials*. 2014;15(1):1-5.
32. Couper PM, Peytchev A, Strecher JV, Rothert K, Anderson J. Following Up Nonrespondents to an Online Weight Management Intervention: Randomized Trial Comparing Mail versus Telephone. *J Med Internet Res*. 2007;9(2):e16.
33. McColl EM, Eccles MPM, Rousseau NSB, Steen INP, Parkin DWD, Grimshaw JMP. From the Generic to the Condition-specific?: Instrument Order Effects in Quality of Life Assessment. [Article]. *Medical Care*. 2003;41(7):777-90.
34. Subar AF, Ziegler RG, Thompson FE, Johnson CC, Weissfeld JL, Reding D, et al. Is Shorter Always Better? Relative Importance of Questionnaire Length and Cognitive Ease on Response Rates and Data Quality for Two Dietary Questionnaires. *American Journal of Epidemiology*. 2001;153(4):404-9.

35. Cox KL, Burke V, Gorely TJ, Beilin LJ, Puddey IB. Controlled comparison of retention and adherence in home- vs center-initiated exercise interventions in women ages 40-65 years: The S.W.E.A.T. Study (Sedentary Women Exercise Adherence Trial). *Prev Med.* 2003;36(1):17-29.
36. Chaffin M, Valle LA, Funderburk B, Gurwitch R, Silovsky J, Bard D, et al. A Motivational Intervention Can Improve Retention in PCIT for Low-Motivation Child Welfare Clients. *Child Maltreatment.* 2009;14(4):356-68.
37. Ford ME, Havstad S, Vernon SW, Davis SD, Kroll D, Lamerato L, et al. Enhancing Adherence Among Older African American Men Enrolled in a Longitudinal Cancer Screening Trial. *The Gerontologist.* 2006;46(4):545-50.
38. Avenell A, Grant AM, McGee M, McPherson G, Campbell MK, McGee MA, et al. The effects of an open design on trial participant recruitment, compliance and retention - a randomized controlled trial comparison with a blinded, placebo-controlled design. *Clinical Trials.* 2004;1(6):490-8.
39. Cox KL, Burke V, Beilin LJ, Derbyshire AJ, Grove JR, Blanksby BA, et al. Short and long-term adherence to swimming and walking programs in older women -- The Sedentary Women Exercise Adherence Trial (SWEAT 2). *Preventive Medicine.* 2008;46(6):511-7.
40. Edwards P. Questionnaires in clinical trials: guidelines for optimal design and administration. *Trials.* 2010;11(1):2.
41. Lau R, Stevenson F, Ong BN, Dziedzic K, Treweek S, Eldridge S, et al. Achieving change in primary care—effectiveness of strategies for improving implementation of complex interventions: systematic review of reviews. *BMJ Open.* 2015;5(12).
42. Clark L, Ronaldson S, Dyson L, Hewitt C, Torgerson D, Adamson J. Electronic prompts significantly increase response rates to postal questionnaires: a randomized trial within a randomized trial and meta-analysis. *Journal of Clinical Epidemiology.* 2015;68(12):1446-50.
43. Starr K, McPherson G, Forrest M, Cotton SC. SMS text pre-notification and delivery of reminder e-mails to increase response rates to postal questionnaires in the SUSPEND trial: a factorial design, randomised controlled trial. *Trials.* 2015;16(1):1-8.
44. Tilbrook HE, Becque T, Buckley H, MacPherson H, Bailey M, Torgerson DJ. Randomized trial within a trial of yellow 'post-it notes' did not improve questionnaire response rates among participants in a trial of treatments for neck pain. *Journal of Evaluation in Clinical Practice.* 2015;21(2):202-4.
45. Hardy P, Bell JL, Brocklehurst P. Evaluation of the effects of an offer of a monetary incentive on the rate of questionnaire return during follow-up of a clinical trial: a randomised study within a trial. *BMC Medical Research Methodology.* 2016;16(1):1-8.

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Contributions:

VB designed and chaired the consensus development workshops. VB, SS, FS, JT and GR, facilitated the discussion groups. VB conducted the analyses, with comments on the guidance developed from SS, FS, JT, and GR. VB wrote the first draft of the paper and comments were provided from SS, FS, JT and GR. All authors agreed the final version.

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Table 1 Summary of evidence from the Cochrane systematic review of strategies to improve retention in RCTs, and qualitative study on the use of retention strategies in RCTs

Systematic Review Results							Qualitative Study Results
	Method of data collection	Number of RCTs in meta-analysis	Total number of participants in meta-analysis	RR 95% CI	P value	Absolute benefit based on 50% baseline response	
Effective retention strategies							
Monetary incentives							
Addition of monetary incentive vs. none (14-16)	Postal questionnaire	3	3166	RR 1.18; 1.09 - 1.28	P<0.0001	76 questionnaires per 1000 sent	Incentives are used in cash or voucher format given up front or on questionnaire completion. General agreement that small monetary incentives are viewed favourably by ethics committees. Uncertainty about effect of monetary incentives given up front or offered for questionnaire return.
Offer of a monetary incentive vs. none (17)*	Web based questionnaire	2	3613	RR 1.25; 1.14 - 1.38, heterogeneity P value = 0.14)	P<0.00001	100 questionnaires per 1000 sent	Offers of monetary incentives used.
Higher value monetary incentive vs. lower value monetary incentive (Bailey unpublished)	Postal questionnaire	2	902	RR 1.12; 1.04 - 1.22	P = 0.005	55 questionnaires per 1000 sent	£5- £20 monetary incentives used. Concern about coercion with higher valued incentives.
Strategies with some evidence of effect based on single RCTs							
Communication							
Total Design Postal Method (TDM) vs. customary postal communication (7)	Postal questionnaire	1	226	RR 1.43; 1.22 - 1.67	P < 0.0001	-	Some elements of TDM used to improve postal questionnaire response.
Recorded delivery vs. telephone reminder (8)	Postal questionnaire	1	192	RR 2.08; 1.11 - 3.87	P = 0.02	-	Recorded delivery used to send further copy of questionnaire / study materials. Mixed opinions on usefulness.
Methodology strategies							
Open vs. blind RCT design (18)	Postal questionnaire	1	538	RR 1.37; 1.16-1.63	P=0.0003	-	Open trial design not used to improve retention. Masking RCT participants to the intervention used to avoid bias associated with open RCTs.
Strategies with unclear evidence of effect							
New questionnaire strategies							
Short questionnaires vs. long (Edwards unpublished, Svoboda, unpublished (19, 20)*	Postal questionnaire	5	7277	RR 1.04; 1.00 - 1.08	P = 0.07	20 questionnaires per 1000 sent	Shorter follow-up questionnaires used with a second reminder. Long questionnaires thought to be off putting for participants.
More relevant questionnaires (i.e. those relating to alcohol use) vs. less relevant (20)*	Web based	2	3893	RR 1.07; 1.01 - 1.14	P = 0.03	-	No comments on the use of more or less relevant questionnaires.

Systematic Review Results							Qualitative Study Results
	Method of data collection	Number of RCTs in meta-analysis	Total number of participants in meta-analysis	RR 95% CI	P value	Absolute benefit based on 50% baseline response	
Non-effective strategies							
Non-monetary incentives							
Addition of non-monetary incentive vs. none (21-23)	Postal questionnaire	6	6322	RR 1.00; 0.98 t- 1.02, some heterogeneity (P value = 0.02)	P = 0.91	-	Gifts used as reminders about RCTs. Uncertainty about effectiveness.
Offer of a non-monetary incentive vs. no offer (24, 25)	Postal questionnaire	2	1138	RR 0.99; 0.95 - 1.03,	P = 0.60	-	Offers of gifts not mentioned as a strategy to improve retention.
Addition of monetary incentive vs. offer of prize draw entry (17)	Postal questionnaire	2	297	RR 1.04; 0.91 - 1.19	P = 0.56	-	Offers of entry into a prize draw seldom used but thought to potentially be useful.
Offer of monetary donation to charity vs. none (17)	Web based questionnaire	1	815	RR 1.02; 0.78 - 1.32	P = 0.90	-	Offers of donations to charity not mentioned as a way to improve retention.
Communication strategies							
Enhanced letter vs. standard letter (22, 26)	Postal questionnaire	2	2479	RR 1.01; 0.97 - 1.05	P = 0.70	-	Enhanced letter routinely used to improve questionnaire return.
Priority post vs. regular post (22, 23, 27)	Postal questionnaire	7	1888	RR 1.02; 0.95 - 1.09	P = 0.55	-	First class post routinely used to send post to participants.
Additional reminder vs. usual follow-up practices (28-31)*	Postal questionnaire	6	3401	RR 1.03; 0.99 - 1.06	P = 0.13	-	SMS text reminders thought useful for contacting young RCT participants. Thought similar system used for text reminders for NHS clinic appointments may improve follow-up in RCTs. Telephone reminders routinely used. Concerns about harassment with too many reminders. Email reminders thought useful for improving response.
Early vs. late questionnaire administration (22)	Postal questionnaire	1	664	RR 1.10; 0.96 - 1.26	P = 0.19	-	Questionnaires sometimes posted later in week to arrive at weekend.
Additional monthly reminder to RCT site vs. usual reminder (Land unpublished)	Return to research site	1	272	RR 0.96; 0.83 - 1.11	P = 0.57	-	Additional reminders to sites not mentioned as a way to improve retention.
Addition of telephone survey vs. monetary incentive plus questionnaire (32)	Postal questionnaire	1	700	RR 1.08; 0.94 - 1.24	P = 0.27	-	Telephone survey seldom used to improve retention. Telephone calls used by nurses to contact participants.
New questionnaire strategies							
Disease /condition questions before generic vs. generic questions before disease/condition questions (33)*	Postal questionnaire	2 quasi-randomised	9435	RR 1.00; 0.97 - 1.02	P = 0.75	-	Suggestions to improve questionnaire format include: < 10 pages, clear succinct questions, avoid repetition, include participant feedback section, use illustrations, colour coordinate questionnaires for each time point.
Long and clear questionnaires vs. shorter condensed questionnaires (34)	Postal questionnaire	1	900	RR 1.01; 0.95 - 1.07	P = 0.86	-	Shorter questionnaires used where possible.
Behavioural/motivational strategies							

Systematic Review Results							Qualitative Study Results
	Method of data collection	Number of RCTs in meta-analysis	Total number of participants in meta-analysis	RR 95% CI	P value	Absolute benefit based on 50% baseline response	
Behavioural/motivational strategies vs. standard information (35, 36)	Return to research site	2	273	RR 1.08; 0.93 - 1.24	P = 0.31	-	Not used, very negative about the usefulness of using behavioural strategies for retention.
Case management							
Case management vs. usual follow-up (37)	Return to research site	1	703	RR 1.00; 0.97 - 1.04	P = 0.99	-	Case management, seldom used, thought to be potentially useful for retention but expensive.

*Publication reports more than one retention RCT

Table 2 Consensus workshop characteristics and participants

	Discussion group	No of participants	Research roles of participants	Research areas represented
Workshop 1				
	Incentives	10*	Statisticians (n=5) Trial managers (n=1) Research assistants (n=1) Data managers (n=1) Clinicians (n=2)	Sexual health, alcohol reduction, e-health, learning disabilities, cardiovascular disease
	Communication	7	Research scientist / fellow (n=2) Clinicians (n=2) PhD students (n=2) Qualitative researchers (n=1)	Aging, e-health, mental health, smoking cessation, cardiovascular disease, primary care
	New questionnaire formats, and other strategies	9	Statisticians (n=2) Research assistants (n=4) Research fellows/associates (n=1) Clinicians (n=2)	Sexual health, smoking cessation, cardiovascular disease, primary care
Workshop 2				
	Incentives	19*	Statisticians (n=3) Trial managers (n=5) Trial assistants (n=2) Data managers (n=5) Research scientists / fellows (n=2) Clinicians (n=2)	Cancer, infectious diseases, statistical trial methodology
	Communication, and other	12*	Statisticians (n=6) Data managers (n=5)	Cancers, infections

	strategies		Clinicians (n=1)	
	New questionnaire formats	9	Statisticians (n=4) Data manager (n=1) Communication specialist (n=1) Research fellow/associates (n=1) Clinicians (n=2)	Cancers, infections

*More workshop participants expressed an interest in these discussion groups

ACCEPTED MANUSCRIPT

What is new**Key findings**

- Best practice guidance was agreed for the use of small financial incentives, 2nd class post, and relevant validated questionnaires in RCTs.
- Barriers for the use of effective retention strategies in RCTs were identified.

What this adds to what is known

- This is the first set of best practice guidance for the use of retention strategies in RCTs.

What is the implication, what should change now

- The extent of agreement on best practice is limited by the variability in the currently available evidence.
- There is some resistance to change existing retention practices thought to be effective.
- More evaluations of face to face and electronic follow-up technologies to improve retention in RCTs are needed.
- This guidance will need updating as new retention strategies are developed and evaluated.