Author's response to reviews

Title: Meeting the challenges of recruitment to multicentre, community-based, lifestyle-change trials: a case study of the BeWEL trial.

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Response to Reviewers

Editorial suggestions

1) Please include the trial registration number at the end of your abstract. If your research article reports the results of a controlled health care intervention, please list your trial registry, along with the unique identifying number.
Done.

2) Please mention each author individually in your Authors' Contributions section.
Done.

Reviewer #1 (Peter Bower)

1) It would be helpful to have a more detailed section on the exact nature of the original sample size calculation.

The Methods section now starts with:

‘BeWEL’s sample size was calculated on the basis of a clinically important weight loss at 12-months of 7%, which at 80% power meant that 133 participants would be required to complete each arm of the study. The choice of 7% weight loss at 12 months was based on it being found to be effective for diabetes prevention [10]. Allowing for a drop out rate of 16% seen in the similar Bowel Health to Better Health (BHBH) study [11], meant that 158 participants were required for each arm, giving the recruitment target of 316.’

As suggested by the Reviewer, we have also added a small table containing the key recruitment assumptions together with the actual numbers achieved (the new Table 1). We have removed the text that mentioned estimates of between 22% and 67% consent rates, chiefly because the upper of these estimates is not actually a consent rate but the proportion of those attending screening who were eligible for the intervention being evaluated. The published study most similar to BeWEL was the Bowel Health to Better Health study, also led by Prof Anderson, and was the basis for the 70% consent rate estimate used for BeWEL. As we say later in our article, this estimate turned out to be optimistic. We have added some extra text to the Discussion to clarify where the estimate came from:
The estimated consent rate of 70% was based on the Bowel Health to Better Health (BHBH) trial [11], a trial similar to BeWEL. BHBH reported two consent rates: an overall rate of 51% and an 'initial' rate of 68%; the latter rate was the rate seen before a second Dundee-based trial started recruiting from the same patient pool. The 68% rate seemed to be a reasonable choice for BeWEL given the clear link between the fall in the BHBH consent rate and the start of recruitment by the second trial. As we found later, the overall BHBH consent rate would have been a better bet.

2) Consent rate of 49% seems high for primary care.

49% of people invited to take part did indeed respond saying they would like to do so. We were pleased with this although we would have been more pleased had it been nearer to our 70% estimate.

3) The basis of the original parameters should be discussed in more detail, both in the Methods and Discussion, as it raises some interesting issues about the basis of such calculations.

We have now explained where the original parameters came from in the Methods section (see response to Comment 1). We have also added a substantial new piece of text to the Discussion: see response to Comment 4.

4) The authors’ suggestions that a 50% threshold be applied is interesting, but seems a little arbitrary. I would be interested in their views on how those estimates can be improved.

The 50% is not completely arbitrary although we didn’t provide any justification at all in the original draft, which was a mistake. We have added a substantial new section of text to the Discussion in response to the Reviewer’s comment, which provides some justification for the 50% rule of thumb plus some thoughts on how trialists might improve their estimates as requested by the Reviewer.

‘Firstly, how should trialists estimate consent rates? One simple approach would be for trialists to estimate no more than 50% unless they have experience of higher consent from several studies in the same population being recruited in the same setting. This appears rather arbitrary but a study of recruitment in 207 breast cancer trials calculated the number needed to recruit one additional participant for the 69 trials that provided sufficient information to do the calculation and the result was remarkably consistent, with a median of two individuals being approached for every person recruited [18]. Gross et al. [19] found a median of 1.8 (range, 1-68) for their study of 172 trials, whereas Toerien et al. [20] in their study of 133 trials found that trialists assessed a median of 230% of their target number. A consent rate estimate of 50% is perhaps a reasonable rule of thumb in the absence of compelling evidence upon which to base it. More compelling evidence would comprise data from two or more studies that have recruited the same population, in the same setting, using the same sort of staff, for the same sort in intervention and all within recent history. Even
with these data trialists will need to make evidence-informed, judgement-based decisions about the similarity between earlier recruitment contexts and their own. It would be possible to put confidence intervals around consent rates from other studies, including pooled estimates, but it is context not statistical uncertainty that is likely to be the main driver of variability in consent rates. It is far from clear that taking the lower bound of the confidence interval would provide more reassurance than trialists (ourselves included) simply being more conservative when estimating consent rates, and many other parameters besides. The best approach to consent rate planning remains in-context pilot work prior to the full-scale trial.’

5) The second suggestion about qualitative research is an excellent one, although one potential block is ethics. Should trial teams build this in to ethics applications, to be activated if problems occur?

We have added the following text to the Discussion:

‘Indeed, given the commonplace nature of trial process problems, trialists would do well to build in the possibility of doing rapid, response-mode qualitative work into their initial ethics and other approval submissions.’

6) Can the team give an estimate of the time and cost for telephone reminders? They don’t seem very cost-effective. Similarly, the same could be done for site visits and home visits.

Unfortunately we cannot provide data on the time and cost of telephone reminders because no record was made of the time spent making the calls. Despite this, our gut-feeling, like that of the Reviewer, is that these were not cost-effective. We have not amended the text; we expect that readers will use their own gut-feelings and reach similar conclusions to the Reviewer and ourselves. We do already point out that both telephone reminders and visits to participants’ homes required substantial effort.

Similarly, we do not have records of the time spent on site visits. The study by Liénard and colleagues that the Reviewer mentions is the only study we are aware of that has looked at visits by trial teams and it only studied site initiation visits. The authors intended to look at repeat visits but the trial was terminated early and studying repeated visits was then not possible. The study did not find that site initiation visits increased recruitment as the Reviewer states.

7) Was there any discussion within the trial team of introducing any of these strategies on a randomised basis?

Not really. The strategies were implemented as quickly as possibly to try and increase recruitment and efforts transferred from one to another as experience with them, and of
their estimated effect, developed. There was no stomach, for want of a better expression, for building in embedded, randomised evaluations of recruitment interventions once the trial was underway. We expect this is a common sentiment. Evaluations planned before recruitment starts are an easier sell to trial teams; once the trial starts, it’s all hands on deck and enthusiasm and capacity for parallel methodological work is rather limited.

8) I would be interested in the team’s view of the relative importance of the strategies. Some strategies addressed practical problems that occurred or became apparent as the trial progressed (eg. approaching extra sites, adjusting the BMI cut-off at telephone screening, adding the possibility of home visits). Others were added to try and eek out a few more recruits from processes that were basically working but delivering fewer recruits than expected (eg. telephone reminders, brief participant information leaflets with NHS logos and local endorsement by a named consultant). The first of the remaining strategies, increasing site visits, seemed important to forge relationships between the trial team and the sites but whether this actually made a positive contribution to recruitment is debatable. With hindsight the efforts targeted at the new sites could have been better applied elsewhere given the very small number of recruits these sites returned and we discuss the issue of site selection at length in the Discussion. The final strategy, letters congratulating good recruitment was simple and cheap to do though we are not aware of clear evidence that it increases recruitment.

Some extra text has been added re. site visits at the end of Strategy 4: Frequency of visits by the trial manager to research nurses and on-site NHS staff increased to monthly:

‘Although supporting these relationships was considered essential for the success of BeWEL, there is very little published evidence regarding their effect on recruitment [4-6]. A single study has evaluated the effect of site initiation visits and found that they did not increase recruitment [13]. That study’s host trial was terminated early and the effect of repeat visits on recruitment could not be studied.’

..and re. consultants’ names towards the end of Strategy 6: The local consultants’ names and their endorsement of the study were added to the invitation letter:

‘This decision was based on a belief that potential participants would be more likely to respond to a letter signed by someone they recognised. There is no compelling evidence for such an effect [15] although the possibility of a small benefit is not ruled out completely. The strategy was, however, simple and cheap to implement.’
The Reviewer asked what our view of the relative importance of strategies is. Although we didn’t rank them (and still don’t), we do say in the Discussion that two strategies would have helped most: being better at estimating the consent rate and in selecting sites. Additionally, we are rather modest in our defence of the other strategies; in the first paragraph of the Discussion we say:

‘...it was clear that recruitment was not going as planned and a series of interventions to increase recruitment were implemented, including ones with evidence of benefit from systematic reviews (e.g. telephone reminders to non-respondents [4, 5]). While these probably helped..’ (new emphasis).

We don’t think we have enough information to rank the strategies in the way the Reviewer suggests but we are pretty confident that better consent rate estimation and site selection would have helped more than the telephone reminders and visits did.

9) The paper cites that 50% of studies fail to achieve their recruitment target. More recent figures by the same research group suggest slightly more positive figures of 45% (Sully, Julious et al. 2013).
We have updated the reference and numbers.

10) No-cost extensions.
We have have added the following sentence to start of the Discussion:

‘Despite the funder providing no additional funding, extending the trial by six-months was possible because of flexibility shown by contracted staff and because core-funded and other departmental staff contributed more time.’

Reviewer #2 (Ranjit Manchanda)

1) How were the 997 invitees to the trial selected? Please give details.

We have added the following text to the start of the Results:

‘Nine-hundred and ninety-seven letters of invitation were sent between November 2010 and April 2012 (17 months) to individuals who had undergone colonoscopy following a positive faecal occult blood test as part of the National Bowel Screening programme and had a diagnosis of adenoma confirmed by histopathology and were aged 50 to 74 years. To the best of our knowledge, this is all patients screened in the participating Health Boards for whom an adenoma was detected.’
2) **What are the characteristics of the 42 (9%) decliners - are there differences from the acceptors recruited?**

Unfortunately these 42 individuals changed their minds, or declined to take part before consenting to take part in the study so we had no ethical approval to ask, record or look for possible reasons behind their decisions.

3) **Is there anything that stands as different amongst the non responders?**

No, there was no obvious pattern. Our loss to follow-up was very low at only 21 (15 intervention, 9 control) of the 329 individuals randomised, which is well below the generally accepted threshold of 20% at which loss to follow-up compromises study validity.

3) **Did the authors use/ develop a customised database / trial management system.**

We did not use a trial management database. The trial manager had a series of spreadsheets to track recruitment and other trial management targets. Tayside Clinical Trials Unit, which supported some aspects of the BeWEL trial, does now offer a trial management database for tracking management processes although this is still very new.