Reviewer's report

Title: Did the trial kill the intervention? Experiences from a randomised controlled trial of a complex intervention.

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Reviewer: Morag Farquhar

Reviewer's report:

This is a clear and well-written paper describing the views of health care professionals and patients who participated in a randomised controlled trial (RCT) of a complex intervention of a rehabilitation programme for patients recovering after haematological malignancy and stem cell transplantation. This paper would be a useful addition to the literature on the design and evaluation of complex interventions and implicitly (rather than explicitly) highlights the need for the thorough development of complex interventions and piloting of RCTs of their evaluation prior to a definitive trial. It would benefit from the following revision and clarifications:

1) Major Compulsory Revisions:

1.1) The overall tenor of the paper (in both the title and the background section and elements of the discussion) implies that the RCT was the cause of difficulties encountered in the delivery of the complex intervention. The RCT did appear to play a role in the difficulties encountered, but it was not the only cause (and not the only cause cited): some of the practical difficulties of delivering the HPL programme and the organisational culture issues did not appear to be related to the RCT (the former appeared to be to do with the group format of the intervention and the latter may have been resolved by early involvement of all staff in the development of the intervention). A slight change in emphasis may therefore be required: it is more about the difficulties of developing, delivering and evaluating (by RCT) complex interventions.

1.2) The authors cite the MRC framework for the development and evaluation of complex interventions in the background section, but it is unclear whether they used the framework for the development and evaluation of this particular intervention. They state in paragraph 2 of the Background that the framework emphasises the need for ‘robust and rigorous evaluation of complex interventions’, but the framework also addresses their development. If they had used the framework then the early development work for the intervention (Phase I) and pilot RCT (Phase II) might have identified some of the difficulties reported which could then have been resolved, either by refining the RCT protocol (e.g. choosing a patient preference trial design, or altering the eligibility criteria in relation to the timing of the intervention etc.) or the intervention itself (e.g. the inclusion of massage, an individualised approach to the hospital chaplain’s information component, ironing out the logistical problems cited in paragraph 1 of ‘Practical difficulties of delivering the HPL programme’, identifying patients’
preparation for a further intervention etc.), before embarking on the definitive RCT. If they did conduct this early work then some reflection on why these issues were not identified would be useful. The authors should therefore be explicit as to whether any pilot work was conducted.

1.3) It would helpful to know if the self-managed rehabilitation programme (the SM programme) was standard care, or whether this was a further enhancement of standard care.

1.4) The authors refer to the non responders to the RCT, but not to any non responders to the qualitative interviews. Did all patients approached for the qualitative interviews agree to participate? If not, how many refused?

1.5) What percentage of the staff involved in the intervention and trial participated in the interviews? If not all, then how were they sampled and approached, and what was the response rate?

1.6) Why was the trial insufficiently powered (paragraph 2 of ‘Trial Design’ in Findings)?

1.7) There is a difference between intervention recruitment and trial recruitment, and these can be confused. In the last paragraph of ‘Trial Design’ (in Findings) the authors state that if staff had been able to reassure patients that participation in the rehabilitation programme would aid recovery ‘it is highly likely that recruitment would have been easier’: however, if patients were then allocated to the control arm (SM programme) their disappointment may have been greater and therefore compliance with the SM programme may have been different and the outcome of the SM programme different.

1.8) It only became clear to me in the third paragraph of the section headed ‘Standardisation of the Intervention’ that this was an intervention delivered in a group setting. This should be made clear earlier in the paper as this is an important element of the intervention design which impacted on some of the issues raised i.e. it may be this element of the design of the intervention (group rather than individualised) that led to some of the problems of limited flexibility. Complex interventions delivered on an individual basis can benefit from being tailored to individual needs by accessing a core set of defined component interventions as required; this is less possible in a group environment (so this issue is not just to do with the effects of the RCT).

1.9) The title of the section ‘Attempting to measure the true effect of an intervention’ is slightly misleading and may be better as ‘Timing of the intervention’ – or something similar.

1.10) Discussion, paragraph 1: were the staff involved in the design of the evaluation: the choice of RCT as a method, the type of RCT, the inclusion / exclusion criteria etc.?

1.11) End of paragraph 1 of Discussion: what was the method of patient recruitment to the RCT? Approaching patients by letter (from the health care professionals) and then consenting by the independent researcher can be helpful, rather than a verbal approach and consenting by health care professionals. Also, were the researchers independent of the intervention
delivery and clinical team (even if the patients find this distinction hard to see)?

1.12.) Paragraph 3 of Discussion: the ‘cultural expectations, both positive and negative’ affect how other people engage with the intervention as well as the trial, and this was clear here.

1.13.) Was more than one analyst involved in the qualitative interview analysis? If not, then this needs to be added to the study limitations.

1.14.) The paper would benefit from more recommendations for others e.g. last sentence of third paragraph of Discussion describes the ambivalence and lack of support – how could this have been addressed? Might earlier involvement of all staff in the decision to conduct and evaluation and the design of it have helped? If it was not used, then use of all stages of the MRC framework?

2) Minor Essential Revisions:

2.1.) Paragraph 1 of ‘Trial Design’ section in Findings: second last sentence should use ‘tested’ rather than ‘testing’.

2.2.) There are a series of inconsistencies in the referencing style: some references have full stops after initials, some don’t; some journal papers have ‘p’ before pages numbers, some don’t; use of ‘et al’ is inconsistent etc.

2.3.) There is a bit of interchangeable use of ‘organisational context’ and ‘organisational culture’ within the text and headings – that latter is probably the better term (more explicit).

2.4.) Paragraph 1 of Discussion cites ‘Lilford’ – shouldn’t this be ‘Edwards’ as the given reference [9] if for ‘Edwards, Lilford…’?

3) Discretionary Revisions:

3.1.) Views were collected after randomisation and, for those in the intervention arm, exposure to the intervention. It would have been interesting to know what the patients views were on equipoise and whether they felt they would benefit from either of the programmes, and their expectations of them, prior to their randomisation. Their retrospective responses may reflect the outcome of the intervention rather than their expectations of it.

3.2.) Last paragraph of ‘Trial Design’ in Findings: the authors state that ‘in order to be willing to take part in something that requires considerable effort and commitment on their part, patients may need to believe that the intervention will help them’ – but given the design of the control arm (a self-managed programme), both arms of the trial are likely to have required effort and commitment, with the latter perhaps also requiring greater self-motivation.

3.3.) Paragraph 1 of ‘Organisational Context’: much of this section relates to the views of staff in relation to the complex intervention, not the RCT – again, piloting and developmental work may have resolved this, or at least exposed this earlier.

3.4.) Most staff quotes come from S2 (n=6), with 3 from S3, 2 from S5, 1 from S1 and none from S4. Most patient quotes (n=4) come from the HPL group, only one from the SM group. This can sometimes simply reflect the nature of the qualitative interviews and data derived, but it may worth checking for selection
bias of quotes.

3.5.) End of paragraph 2 of Discussion: interpretability and making recommendations in such circumstances can be enhanced by defining the established core of an intervention (which may be a series of sub-interventions from which practitioners draw as patient need dictates). In reality interventions are rarely delivered in a consistent manner across settings – the role out of interventions to different settings and contexts inevitably leads to variation as local circumstances vary so much within the NHS.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

'I declare that I have no competing interests'