MRC Network of Hubs for Trials Methodology Research Internal Pilot Workshop: summary

Workshop Title: Optimising the design and evaluation of internal pilot work to inform efficient randomised controlled trials. **Reference number:** R41

Workshop date: 24th March 2014 **Venue:** The Royal College of Surgeons of England, London

Overall aim: The workshop aimed to provide an engaging forum to discuss key issues to evaluate the use and success of internal pilot studies to optimally inform main trials.

Convenors: Dr Kerry Avery, Professor Jane Blazeby, Dr Peter Davidson, Professor Carrol Gamble, Dr Chris Metcalfe, Mrs Elaine O'Connell Francischetto and Professor Paula Williamson

Attendees: 30 attendees including trialists, funding body representatives, statisticians, methodologists and principal investigators.

Aims and objectives:

This one-day workshop aimed to bring together key specialist stakeholders, including funding body representatives, research methodologists, medical statisticians, clinicians and trialists, to develop guidance for funding bodies to evaluate the use and success of pilot work when considering progression to a main trial. The guidance is also planned to be of relevance to those involved in the design and conduct of pilot trials. The workshop will identify a research agenda for further research in this area. To achieve this aim, the workshop had the following objectives:

1. To develop a guidance document (publication) for funding bodies and other key stakeholders to use to evaluate the selection and success of pilot work when considering progression to a main trial.
2. To consider current evidence for the use of pilot work to inform main RCTs, and best methods for evaluating the success of pilot work. This will include consideration of existing guidance and findings from completed and on-going literature reviews undertaken by the ConDuCT-II and North West Hubs.
3. To produce a research agenda outlining priority areas requiring dedicated research activity to inform decision-making for: (i) the appropriate use of different types of pilot work, and; (ii) progression from pilot work to a main trial.
4. To facilitate discussion and exchange of ideas between key stakeholders.

The agenda incorporated presentations and vignettes/examples of RCTs with an internal pilot phase that aimed to facilitate targeted discussion around key areas related to internal pilot trials (please see Appendix 1 attached for a copy of the agenda).

What was actually achieved:

1. **Themes and ideas that emerged from the workshop:**
   - i. What is an internal pilot and what is it not? Including definition of an RCT with an internal pilot phase.
   - ii. Progression criteria in an RCT with an internal pilot phase - key issues to consider in the development of progression criteria during the design of an RCT with an internal pilot phase.
   - iii. Reviewing changing evidence during the internal pilot phase of an RCT
   - iv. Approaches to the development and review of progression criteria
   - v. Statistical considerations in developing and reviewing progression criteria
   - vi. Reporting of internal pilot trials

2. **Guidance document (publication)**

The grant co-applicants and members of the Internal Pilot Trials Workshop supported by the Hubs for Trials Methodology Research are currently in the final stages of preparing a publication for funding bodies and other key stakeholders to use to evaluate the selection and success of pilot work when considering progression to a main trial. This publication is currently in the final draft stages and the target journal for this publication

is 'Trials'. This paper summarises the key issues to consider in the development of progression criteria during the design of an RCT with an internal pilot phase. Priority areas requiring further research are also outlined.
The paper also lists the following 10 top tips for using progression criteria for internal pilot studies:

i. Pilot study recruitment sites should be representative of sites recruiting into the main study.
ii. A traffic lights system of green (go), amber (review) and red (stop) might be preferable to a simple stop/go approach when specifying progression criteria for internal pilot studies.
iii. Pre-specified progression criteria agreed with funders need to strike a careful balance between being firm enough to promote ambition in the trial team yet being flexible enough to allow opportunities to remedy early problems.
iv. Recruitment progression criteria should be based on rates per centre per month rather than reaching an absolute number by a specific date due to the unpredictability of opening sites.
v. When recruitment falls behind, it is essential to explore screening logs to determine whether insufficient participants are being approached, insufficient participants are passing eligibility criteria or insufficient eligible participants agreed to be randomised.
vi. The assessment of intervention adherence, crossover and outcome event rates should take into account the duration from randomisation to timing of primary outcomes if sufficient data are to be gleaned to inform progression.
vii. When assessing missing data, one should explore the degree of missingness within key outcomes as well as the percentage of participants with missing data.
viii. Trial teams should involve both their funders and their Trial Steering Committee in assessing their progression criteria.
ix. Trialists should always take the opportunity to assess whether changes in existing technologies have occurred since the original study was planned, so that new technologies can be considered with funders, such as using an adaptive design.
x. Pilot studies need to be reported fully and CONSORT extensions are now available for a range of such studies.

Next Steps:

- Publication of a manuscript entitled "Designing internal pilot studies to inform efficient randomised controlled trials: issues to consider when using progression criteria", reporting on the findings of this work (including details of the workshop). Status: draft manuscript currently under review by co-authors.
- Future research being considered within the pilot and feasibility theme of the ConDuCT-II Hub for Trials Methodology Research, including a PhD funded by the MRC HTMR Network (Katherine Fairhurst: Optimising the design and evaluation of pilot work to inform efficient RCTs in surgery. Oct 2015 – Sep 2018. Supervisors: Kerry Avery, Shelley Potter Jane Blazeby).