

EDITORIAL

Open Access



Improving the efficiency of trials using innovative pilot designs: the next phase in the conduct and reporting of pilot and feasibility studies

Lehana Thabane^{1*} and Gillian Lancaster²

Abstract

With continuously increasing costs of conducting trials, use of innovative approaches—such as pragmatic trials, registry-based randomised trials, adaptive trials, personalised medicine trials, platform trials, and basket trials—to the design and conduct of clinical trials has been advocated as one of the most promising solutions. In this editorial, we propose that the next wave of feasibility or pilot studies should focus on assessing the feasibility of trials using these designs, which we see as an imperative in order to unleash their potential to reduce trial costs and accelerate the drug development process and the search for best treatments, so that the right treatments can be delivered as soon as possible to the right patients.

Editorial

In this editorial, we welcome Professor Lehana Thabane as new co-Editor-in-Chief to work alongside Professor Gillian Lancaster. The journal has seen substantial growth over the past 18 months and with it the need for a second Editor-in-Chief. With all articles published in the journal indexed in PubMed, we look to the future and consider the next phase in the conduct and reporting of pilot and feasibility studies; we think about how innovative trial designs are contributing to improving trial efficiency.

Pilot and Feasibility Studies was launched in January 2015 to provide a dedicated place for the reporting of feasibility and pilot studies, and discussion of methodological issues around the planning, of future large-scale definitive trials and observational studies [1]. Led by the Working Group of the CONSORT Extension for Pilot and Feasibility Trials, the journal was established as part of the collective effort to change the practice of reporting of pilot and feasibility studies [2]. These efforts have also led to the publication of a framework

which clarifies the similarities and differences between a feasibility study and a pilot study. The former asks whether something can be done, if we should we proceed with it, and if so, how? In contrast, the latter asks the same questions, but it also has the specific design feature that a pilot study is a forerunner of a future study (or part of a future study) which will be conducted on a larger scale [3].

Then followed the publication of the CONSORT extension to pilot and feasibility trials, aimed at enhancing the transparency and completeness of reporting of pilot and feasibility randomised clinical trials, which are designed to inform the planning of future definitive trials [4, 5]. The methods and processes used to develop the CONSORT guideline have been described elsewhere [6]. Since its inception, *Pilot and Feasibility Studies* has received numerous submissions of pilot work, leading to over 140 publications—with 89 study protocols and 44 research reports of pilot and feasibility studies as the most frequent types of publication (Table 1). Clearly, the publication of pilot work in the journal is gaining momentum. This is also a sign of the growing recognition of the importance of reporting the design and results of pilot and feasibility studies.

* Correspondence: thabanl@mcmaster.ca

¹Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, ON, Canada

Full list of author information is available at the end of the article



Table 1 Type of publications in *Pilot and Feasibility Studies* since 2015

Article type	2015	2016	2017 (Jan–June)	Total
Study protocol	25	45	18	89
Research results	14	20	10	44
Editorial	2	0	0	2
Review	1	1	1	3
Methodology	1	3	1	5
Commentary	0	1	0	1
Letter	0	1	0	1
Update	0	1	0	1

Data from journal website on 13 June 2017

With rapidly rising costs of conducting clinical trials and limited funding [7], there has been some intense debate among stakeholders—funders, sponsors, clinical trialists, consumers and providers—on how to reduce trial costs. The use of innovative approaches to the design and conduct of clinical trials has been advocated as one of the most promising solutions. Examples of these approaches include pragmatic trials [8], observational trials [9], registry-based randomised trials [10], cluster randomised trials [11], adaptive trials [12], trials using Bayesian methods [13], small sample, biologically based trials (e.g. personalised medicine trials) [14], N-of-1 trials [15], platform trials [16], basket trials [17, 18] and umbrella trials [18]. In general, these innovations seem intuitively appealing. For example, registry-based trials—which use registries as the platform for data collection, randomization, and follow-up [10]—have even been described as *the next disruptive technology in clinical research* [19]; the platform trial, whose goal is to find the best treatment or management for a disease condition by simultaneously studying multiple treatments, has been characterised as *a vision for the future* [16].

Compared to standard clinical trial methodologies, these innovations offer many advantages. For example, because of their flexibility and efficiency, adaptive trial designs [12] offer the potential to cut drug development costs by allowing researchers (i) the opportunity to correct or update incorrect assumptions that were made at the start of the trial; (ii) to select the most promising treatment options as early as possible; (iii) to use emerging information that is external to the trial, in order to adapt the design; and (iv) the opportunity to react sooner to surprising results—for efficacy, safety or futility. These adaptations can shorten the development time and consequently speed up the development process, and lower costs. Another example is the use of basket trials in oncology [17, 18], which have the advantage of utilising novel designs that match patients with different cancer types (“baskets”) that have a rare genetic mutation, regardless of tumour histology, to a

drug that is expected to work through the mutational pathway.

However, there remain several uncertainties about the feasibility of some of these innovations in many clinical or health care settings. Therefore, assessing the feasibility and the prevailing uncertainties of the applications of these state-of-the-art technologies and strategies to clinical trials should be a top priority. These include feasibility of being able to recruit trial participants; implementation of intervention elements; assessment of outcomes; and evaluation of the acceptability and ethics of the designs; among others. As we look into the future, we can expect the next wave of pilot and feasibility studies to focus on these uncertainties, in order that the promise of reducing costs by using innovative trial designs can be realised. In fact, we have already seen a number of examples of pilot trials which have assessed the feasibility of different aspects of these designs. These have included the BRAVE pilot trial [20] which used a pragmatic design to assess the feasibility of a behavioural activation group therapy in reducing depressive symptoms and improving quality of life in patients with depression; a study aiming to determine the feasibility of using patient/disease registries to recruit subjects for clinical trials [21]; a pilot study using Bayesian methods in N-of-1 trials to assess the effect of Amitriptyline to relieve pain in juvenile idiopathic arthritis [15]; to mention only a few.

The application of innovative trial designs has the potential to reduce trial costs and accelerate the drug development process and the search for best treatments, so that the right treatments can be delivered as soon as possible to the right patients. But for these designs to have a substantial impact on how we develop new treatment strategies, our approaches have to start with assessing their feasibility, and adopting the right objectives and outcomes. Success in assessing feasibility will add to our evolving scientific knowledge base, and to our understanding of the ecology of patient care and the biology of human disease; and it will, hopefully, allow us to better design these trials to enhance the tailoring of more treatments to more patients in the future. As we move into the next phase of the new era in the conduct and reporting of pilot and feasibility studies, we look forward to continuing to work with the editorial team, to place *Pilot and Feasibility Studies* in the forefront of research innovation, and allow it to act as a useful forum for the dissemination and discussion of pilot or feasibility studies, particularly those that use innovative trial designs. We should mention that the journal is also a forum for publishing qualitative work and process evaluation alongside trial design in any pilot work [22]; and debates on topical issues related to the design, conduct and reporting of pilot and feasibility studies [23].

Acknowledgements

The Working Group of the CONSORT Extension to Pilot and Feasibility Trials are Professor Sandra Eldridge and Claire Chan, Queen Mary University of London; Professor Mike Campbell, Sheffield University; Professor Lehana Thabane, McMaster University, Canada; Professor Christine Bond, Aberdeen University; Dr Sally Hopewell, Oxford University; and Professor Gillian Lancaster, Keele University. We are grateful to Dr Stephen Walter for editing the manuscript.

Availability of data and materials

Not applicable.

Authors' contributions

LT wrote this Editorial. GL commented on and edited the draft. Both authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

Gillian Lancaster and Lehana Thabane are co-Editors-in-Chief of *Pilot and Feasibility Studies*.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Author details

¹Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, ON, Canada. ²Professor Gillian Lancaster, Institute of Primary Care and Health Sciences, Keele University, Keele, UK.

Received: 1 June 2017 Accepted: 13 June 2017

Published online: 06 July 2017

References

- Lancaster GA. Pilot and feasibility studies come of age! *Pilot Feasibility Stud.* 2015;1:1.
- Dolgin E. Publication checklist proposed to boost rigor of pilot trials. *Nat Med.* 2013;19(7):795–6.
- Eldridge SM, Lancaster GA, Campbell MJ, Thabane L, Hopewell S, Coleman CL, et al. Defining feasibility and pilot studies in preparation for randomised controlled trials: development of a conceptual framework. *PLoS ONE.* 2016; 11(3):e0150205.
- Eldridge SM, Coleman CL, Campbell MJ, Hopewell S, Thabane L, Lancaster GA, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. *Pilot Feasibility Stud.* 2016;2:64.
- Eldridge SM, Coleman CL, Campbell MJ, Hopewell S, Thabane L, Lancaster GA, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. *BMJ.* 2016;355:i5239.
- Thabane L, Hopewell S, Lancaster GA, Coleman CL, Campbell MJ, Eldridge SM. Methods and processes for development of a CONSORT extension for reporting pilot randomized controlled trials. *Pilot Feasibility Stud.* 2016;2:25.
- Roger C. Rapidly rising clinical trial costs worry researchers. *CMAJ.* 2009; 180(3):277–8.
- Thabane L, Kaczorowski J, Dolovich L, Chambers LW, Mbuagbaw L, et al. Reducing the confusion and controversies around pragmatic trials: using the Cardiovascular Health Awareness Program (CHAP) trial as an illustrative example. *Trials.* 2015;16:387.
- Berger ML, Dreyer N, Anderson F, Towse A, Sedrakyan A, Normand S-L. Prospective observational studies to assess comparative effectiveness: the ISPOR good research practices task force report. *Value Health.* 2015; 15:217–30.
- Li G, et al. Registry-based randomized controlled trials—what are the advantages, challenges, and areas for future research? *J Clin Epidemiol.* 2016;80:16–24.
- Puffer S, Torgerson DJ, Watson J. Cluster randomized controlled trials. *J Eval Clin Pract.* 2005;11(5):479–83.
- Kairalla JA, Coffey CS, Thomann MA, Muller KE. Adaptive trial designs: a review of barriers and opportunities. *Trials.* 2012;13:145.
- Ibrahim, et al. Bayesian methods in clinical trials: a Bayesian analysis of ECOG trials E1684 and E1690. *BMC Med Res Methodol.* 2012;12:183.
- Catenacci DVT. Next-generation clinical trials: novel strategies to address the challenge of tumor molecular heterogeneity. *Mol Oncol.* 2015;9:967–96.
- Huber AM, Tomlinson GA, Koren G, Feldman BM. Amitriptyline to relieve pain in juvenile idiopathic arthritis: a pilot study using Bayesian meta-analysis of multiple N-of-1 clinical trials. *J Rheumatol.* 2007;34(5):1125–32.
- Saville BR, Berry SM. Efficiencies of platform clinical trials: a vision of the future. *Clin Trials.* 2016;13(3):358.
- Redig AJ, Jänne PA. Basket trials and the evolution of clinical trial design in an era of genomic medicine. *J Clin Oncol.* 2015;33(9):975–7.
- Rashdan S, Gerber DE. Going into BATTLE: umbrella and basket clinical trials to accelerate the study of biomarker-based therapies. *Ann Transl Med.* 2016; 4(24):529.
- Lauer MS, D'Agostino Sr RB. The randomized registry trial—the next disruptive technology in clinical research? *N Engl J Med.* 2013;369(17):1579–81.
- Samaan Z, et al. A pragmatic pilot randomized trial to investigate the effectiveness of behavioural activation group therapy in reducing depressive symptoms and improving quality of life in patients with depression: the BRAVE pilot trial protocol. *Pilot Feasibility Stud.* 2015;1:39.
- Tan MH, Thomas M, MacEachern MP. Using registries to recruit subjects for clinical trials. *Contemp Clin Trials.* 2015;41:31–8.
- Schoultz M, Macaden L, Hubbard G. Participants' perspectives on mindfulness-based cognitive therapy for inflammatory bowel disease: a qualitative study nested within a pilot randomised controlled trial. *Pilot Feasibility Stud.* 2016;2:3.
- Cook JA, Beard DJ, Cook JR, MacLennan GS. The curious case of an internal pilot in a multicentre randomised trial—time for a rethink? *Pilot Feasibility Stud.* 2016;2:73.

Submit your next manuscript to BioMed Central and we will help you at every step:

- We accept pre-submission inquiries
- Our selector tool helps you to find the most relevant journal
- We provide round the clock customer support
- Convenient online submission
- Thorough peer review
- Inclusion in PubMed and all major indexing services
- Maximum visibility for your research

Submit your manuscript at
www.biomedcentral.com/submit

