
Article:
Julious, S.A. (2016) Pilot Studies in clinical research. Statistical Methods in Medical Research, 25 (3). pp. 995-996. ISSN: 0962-2802

https://doi.org/10.1177/0962280216651022

Pilot Studies in clinical research

Steven A Julious[1]*

University of Sheffield, UK

Steven A Julious, Medical Statistics Group, ScHARR, University of Sheffield, Regent Court, 30 Regent Street, Sheffield, S1 4DA, UK. Email: S.A.Julious@Sheffield.ac.uk

A well designed pilot study is important in the evaluation of therapies [1,2]. In this special issue, different aspects of pilot trials are reviewed in different research settings to practically illustrate the methodological issues with these studies.

One of the objectives of a pilot trial is to assess the feasibility of undertaking a large definitive assessment of efficacy. This is true for all pilot trials and Wilson and colleagues describes the challenges of undertaking pilot trials of complex interventions [3]. They highlight how the ideas developed for Phase II drug development could be extended to the assessment of complex interventions [4]. In particular they considered how the efficacy of complex interventions could be assessed in the context of current early phase feasibility or pilot studies.

In oncology the assessment of a new treatment in a Phase II trial includes an assessment of whether there are sufficient signs of effectiveness to justify being tested in a phase III trial [5]. Wason and Jaki highlight how there are a large number of recent methodological developments that have aimed to improve phase early phase oncology trials and they describenovel approaches that they believe should be considered as alternatives to traditional designs.

Hee and colleagues highlight how pilot studies are often done to serve a variety of purposes with little consensus on their design [7,8]. The reviewed the literature on methods for pilot studies that are based on the use of Bayesian decision theory and under took a systematic reviewing methodology to identify relevant published work in the area. Bayesian decision approaches are appealing as can help to inform decisions at the end of the pilot trial [9,10]. Decisions such as whether there has been sufficient has been discharged to enable to the start of the definitive trial [11]. Hee and colleagues contend that Bayesian decision-theoretic approaches to be appropriate for the design of pilot due to their role in informing decisions regarding further future clinical research

All trials need a sample size justification. Not all trials need a sample size calculation [12]. This is particularly true for pilot trials. Cluster randomised trials are a common study design in health services research [13-14]. Eldridge and colleagues highlight the issues in estimating the sample size for a cluster pilot trial [14]. They undertake simulations to provide the distribution of the expected number of clusters for the main trial under different assumptions and conclude that pilot studies will usually be too small to estimate parameters required for estimating a sample size for a main cluster randomised trial with sufficient precision.

For individually randomised trials a pilot sample size is usually recommended in terms of a flat rule of thumb [16]. Whitehead and colleagues discuss how when the outcome is continuous, the sample size estimation requires an accurate estimate of the standard deviation of the outcome measure and

how a pilot trial can be used to get an estimate of this [17]. They describe how an external pilot trial sample size can be chosen in order to minimise the sample size of the overall clinical trial programme - the pilot and the main trial added together - and propose stepped rules of thumb for pilot sample sizes.

In summary, this special issue covers many concerns with pilot trials from assessing health technologies to drug trials and from cluster trials to individually randomised trials with many practical recommendations.

1. Arain M, Campbell MJ, Cooper CL, et al. What is a pilot or feasibility study? A review of current practice and editorial policy. BMC Med Res Methodol 2010; 10: 67.
2. Lee E, Whitehead AL, Jacques RM, et al. The statistical interpretation of pilot trials: Should significance thresholds be reconsidered? BMC Med Res Methodol 2014; 14: 41.
3. Wilson DT, Walwyn REA, Brown J, Farrin AJ and Brown SR. Statistical challenges in assessing potential efficacy of complex interventions in pilot or feasibility studies. Statistical Methods in Medical Research 2015 doi: 10.1177/0962280215589507
4. Brown SR, Gregory WM, Twelves CI, et al. Designing phase II trials in cancer: A systematic review and guidance. Br J Cancer 2011; 105: 194–199.
5. Jaki T. Uptake of novel statistical methods for early-phase clinical studies in the UK public sector. Clin Trials 2013;10: 344–346
6. Wason JMS and Jaki T. A review of statistical designs for improving the efficiency of phase II studies in oncology . Statistical Methods in Medical Research 2015 doi: 10.1177/0962280215588247
7. Lancaster GA, Dodd S and Williamson PR. Design and analysis of pilot studies: recommendations for good practice. J Eval Clin Pract 2004; 10: 307–312.
8. Hee SW, Hamborg T, Day D, Madan J, Miller F, Posch M, Zohar S and Stallard N. Decision-theoretic designs for small trials and pilot studies: A review. Statistical Methods in Medical Research 2015 doi: 10.1177/0962280215588245
9. Stallard N. Decision-theoretic designs for phase II clinical trials allowing for competing studies. Biometrics 2003; 59: 402–409.
10. Stallard N, Thall PF and Whitehead J. Decision theoretic designs for phase II clinical trials with multiple outcomes. Biometrics 1999; 55: 971–977.
11. Julious, SA and Swank, DJ Moving statistics beyond the individual clinical trial: applying decision science to optimize a clinical development plan. Pharmaceutical Statistics 2005; 4(1) 37-46
12. Billingham S, Whitehead A and Julious S. An audit of sample sizes for pilot and feasibility trials being undertaken in the United Kingdom registered in the United Kingdom Clinical Research Network database. BMC Med Res Methodol 2013; 13: 104.
13. Eldridge S and Kerry S. A practical guide to cluster randomised trials in health services research. Sussex, UK: Wiley, 2012.
14. Eldridge SM, Ashby D, Feder GS, et al. Lessons for cluster randomized trials in the twenty-first century: a systematic review of trials in primary care. Clin Trials 2004; 1: 80–90

15. Eldridge SM, Costelloe CE, Kahan BC, Lancaster GA, and Kerry SM. How big should the pilot study for my cluster randomised trial be? Statistical Methods in Medical Research 2015 doi: 0.1177/0962280215588242
16. Julious SA. Sample size of 12 per group rule of thumb for a pilot study. Pharmaceut Stat 2005; 4: 287–291
17. Whitehead AL, Julious SA, Cooper CL and Campbell MJ. Estimating the sample size for a pilot randomised trial to minimise the overall trial sample size for the external pilot and main trial for a continuous outcome variable. Statistical Methods in Medical Research 2015 doi: 10.1177/0962280215588241