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Pilot Studies: What we need to know

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Sayem Borhan

April 25th, 2018

Michael G. DeGroote SCHOOL OF MEDICINE

McMaster University

Family Medicine

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Sayem Borhan

Biostatistician, DFM Research

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borhana@mcmaster.ca

@McMasterFamMed

Michael G. DeGroote SCHOOL OF MEDICINE

Learning Objectives

- Learn about the "what, why and how" of pilot studies;
- Gain knowledge about challenges and issues (e.g. sample size, ethics, publication etc.) related to pilot studies;
- Learn about new developments in pilot studies;

Randomized Controlled Trial (RCT)

- **RCT is a planned experiment designed to assess the efficacy of an intervention by comparing the intervention to a control**

- **Methodological steps**

- Design of trial
- Sample size
- Eligibility and enrolment
- Consent
- Randomization
- Follow-up
- Outcome
- Analyses

Key Paper

Lehana Thabane, PhD
Professor & Associate Chair
Department of Health, Evidence & Impact (HEI). McMaster University
Editor-in-chief, Pilot and feasibility studies

Thabane *et al. BMC Medical Research Methodology* 2010, **10**:1
http://www.biomedcentral.com/1471-2288/10/1

BMC Medical Research Methodology

COMMENTARY Open Access

A tutorial on pilot studies: the what, why and how

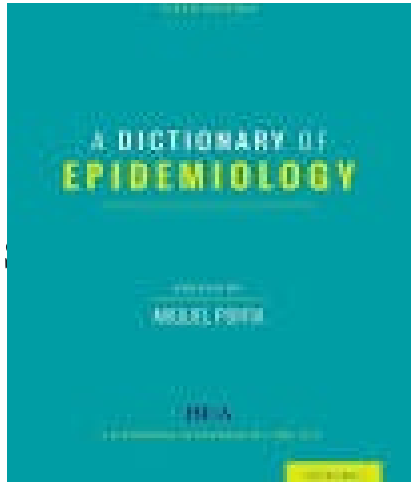
Lehana Thabane[1,2*], Jinhui Ma[1,2], Rong Chu[1,2], Ji Cheng[1,2], Afisi Ismaila[1,3], Lorena P Rios[1,2], Reid Robson[3], Marroon Thabane[1,4], Lora Giangregorio[5], Charles H Goldsmith[1,2]

Abstract

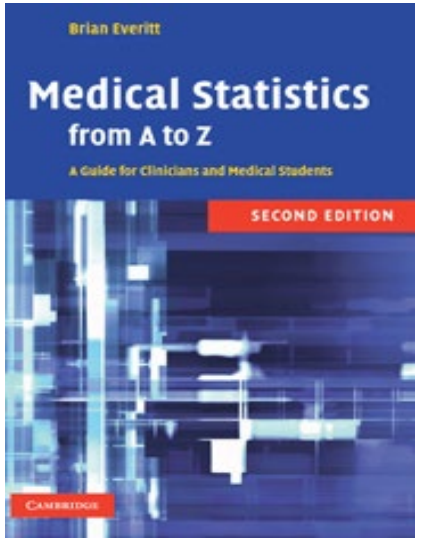
Pilot studies for phase III trials - which are comparative randomized trials designed to provide preliminary evidence on the clinical efficacy of a drug or intervention - are routinely performed in many clinical areas. Also commonly know as "feasibility" or "vanguard" studies, they are designed to assess the safety of treatment or interventions; to assess recruitment potential; to assess the feasibility of international collaboration or coordination for multicentre trials; to increase clinical experience with the study medication or intervention for the phase III trials. They are the best way to assess feasibility of a large, expensive full-scale study, and in fact are an almost essential pre-requisite. Conducting a pilot prior to the main study can enhance the likelihood of success of the main study and potentially help to avoid doomed main studies. The objective of this paper is to provide a detailed examination of the key aspects of pilot studies for phase III trials including: 1) the general reasons for conducting a pilot study; 2) the relationships between pilot studies, proof-of-concept studies, and adaptive designs; 3) the challenges of and misconceptions about pilot studies; 4) the criteria for evaluating the success of a pilot study; 5) frequently asked questions about pilot studies; 7) some ethical aspects related to pilot studies; and 8) some suggestions on how to report the results of pilot investigations using the CONSORT format.

Stat/Epi Dictionary Definition

- A small-scale **test of the methods and procedures to be used on a larger scale** if the pilot study demonstrates that the methods and procedures can work



- Small-scale investigation designed to **test the feasibility of methods and procedures** for later use on a large scale or **to search for possible effects and associations** that may be worth following up in a subsequent larger study



Different types of “pre”-studies

- Phase I/II trials
- Proof-of-concept studies
- Pilot studies
  - Qualitative
  - Quantitative

Pilot vs Proof-of-Concept Study

- **Proof-of-concept (POC) study**

  – to determine if a treatment (drug) is biologically active or inactive

Stat Med 2005;24:1815-35

- **Usually based on surrogate makers as endpoints**
- **Usually Phase I/II studies**

  –assessing safety, dose levels and response to new drugs

Proof of concept is not necessarily proof of feasibility

The Focus

- **Pilot studies for phase III RCT**
  - comparing two or more drugs or intervention strategies to assess efficacy and safety

J Eval Clin Pract 2004;**10**: 307-12

In Practice

Crit Care Med 2009 Vol. 37, No. 1 (Suppl.)

The design and interpretation of pilot trials in clinical research in critical care

Donald M. Arnold, MD, MSc (Epid); Karen E. A. Burns, MD, MSc (Epid);
Neill K. J. Adhikari, MD, MSc (Epid); Michelle E. Kho, BHSc (PT); Maureen O. Meade, MD, MSc (Epid);
Deborah J. Cook, MD, MSc (Epid); for the McMaster Critical Care Interest Group

- **Multiple terms used without clear distinction**

✓ Pilot work
✓ Pilot study
✓ Feasibility study
✓ Pilot trial

In Practice

Thabane et al. BMC Medical Research Methodology 2010, 10:1
http://www.biomedcentral.com/1471-2288/10/1

BMC Medical Research Methodology

COMMENTARY Open Access

A tutorial on pilot studies: the what, why and how

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Used pilot and feasibility study interchangeably

In Practice

Journal of Evaluation in Clinical Practice, 10, 2, 307–312

Design and analysis of pilot studies: recommendations for good practice

Gillian A. Lancaster MSc PhD,[1] Susanna Dodd MSc[2] and Paula R. Williamson PhD[3]
[1]Lecturer in Medical Statistics, [2]Research Assistant in Medical Statistics [3]Senior Lecturer in Medical Statistics,
Department of Mathematical Sciences, University of Liverpool, Liverpool, UK

- **Surveyed 7 journals: BMJ, Lancet, JAMA, NEJM, BJC, BJOG,BJS**

➢ Searched "pilot" or "feasibility" in title or abstract in 2000--2001

✓ 90 unique studies:**4/90 specifically stated that the pilot was in preparation for a bigger RCT**

➢ Contacted the editors of the 7 journals screened

✓ 4/7 indicated **no publication policy**

✓ 1/7 indicated the journal **did not publish pilot studies**

In Practice

Arain *et al. BMC Medical Research Methodology* 2010, **10**:67
http://www.biomedcentral.com/1471-2288/10/67

CORRESPONDENCE Open Access

What is a pilot or feasibility study? A review of current practice and editorial policy

Mubashir Arain[1], Michael J Campbell*[1], Cindy L Cooper[1] and Gillian A Lancaster[2]

- **Repeated Lancaster et al study for publications in 2007-8**

✓ contacted the editors of the journals screened

✓ 4/7 indicated **no publication policy**…

In Practice

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

Pilot Trials in Clinical Research: Of What Value Are They?
Joseph Loscalzo

Circulation. 2009;119:1694-1696

- **Editorial message**

✓ 41 pilot trials published in Circulation since 2004

✓ For most, **editors requested the term 'pilot' be added to the title to acknowledge small size and lack of generalizability**

Reasons

Reasons for conducting pilot or feasibility studies may be clinical, procedural or methodological

Feasibility of Procedures & Methods

JAMDA 15 (2014) 943–945

ELSEVIER

JAMDA

journal homepage: www.jamda.com

Brief Report

Implementing a Knowledge Translation Intervention in Long-Term Care: Feasibility Results From the Vitamin D and Osteoporosis Study (ViDOS)

Courtney C. Kennedy PhD [a], Lehana Thabane PhD [b], George Ioannidis PhD [a], Jonathan D. Adachi MD, FRCPC [a], Alexandra Papaioannou MD, MSc, FRCP (C) FACP [a,*] on behalf of the ViDOS Investigators

[a] Department of Medicine, McMaster University, Hamilton, ON, Canada
[b] Department of Epidemiology and Biostatistics, McMaster University, Hamilton, ON, Canada

- **Feasibility Outcomes**

✓ Recruitment rate
✓ Retention rate
✓ Participation rate
✓ Completion of action plans, feedback reports
✓ Completeness of data

Criteria for Success

- **It is always important to state the criteria for success or feasibility**

- **Outcome can be**

✓ Stop - main study not feasible;

✓ Continue, but modify protocol – feasible with modifications;

✓ Continue without modifications – feasible

- **The criteria should be based on key primary feasibility aims**

Criteria for Success

JAMDA 15 (2014) 943–945

ELSEVIER

JAMDA

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[a] Department of Medicine, McMaster University, Hamilton, ON, Canada
[b] Department of Epidemiology and Biostatistics, McMaster University, Hamilton, ON, Canada

Table 1
Feasibility Results for the ViDOS Trial

Measure	Target, %	Observed, %	Description
Recruitment	40	22	■ Acceptance rate was low; took several months ■ Accomplished target sample size (n = 40)
Retention	80	63	■ 7 INT homes withdrew active participation.
Participation	80	25–100	■ Overall: n = 164 participants from 12 active INT homes; 56% attended at least 2 meetings* **Key roles:** ■ ≥ 2 meetings: Director/assistant director of care†; pharmacist = 100%; medical director† = 92% ■ 3 meetings: Director/assistant director† = 83%; pharmacist = 92%; medical director† = 25%
Action plans	80	100	■ Completed by all homes
Feedback reports	80	100	■ Reviewed at all INT sessions (months 0, 6, 12)
Data completion	80	86–92	■ All spreadsheets: 86% control/92% INT homes

Sample Size for Pilot Studies

- **Sample Size calculations may not be required for some pilot studies**

✓ A pilot study may be used to generate information to be used for sample size calculations

- **Sample needs to be representative of the target population**

✓ It should also be based on the same inclusion/exclusion criteria

- **Sample used in the pilot may be carried to the main study**

✓ Caution is needed to ensure that the key features of the main study are preserved in the pilot (eg blinding in RCTs)

Stat Med 1990:9(1-2);65-71; discussion 71-2.

Ethics of Pilot Studies

- **Conducting underpowered trials is unethical**

Halpern SD et al. JAMA 2002; 288(3):358-362

- **Underpowered trials are ethical in only 2 situations:**

✓ Small trials of interventions for rare diseases

✓ Early-phase trials in the development of drugs or devices

- **Pilot studies of phase III trials are not addressed**

✓ Is it ethical to conduct a study whose feasibility can not be guaranteed?

✓ What obligation do we have to patients to disclose the feasibility nature of pilot studies?

- **Is it ethical to run phase III studies without piloting?**

✓ No, it's unethical to run phase III studies without looking into feasibility

Consent

- **Consent form should be explicit about the feasibility nature**

"The overall purpose of this pilot study is to assess the feasibility of conducting a large study to ...[state primary objective of the main study] . A feasibility or pilot study is a study that... [state a general definition of a feasibility study]. The specific feasibility objectives of this study are ...[state the specific feasibility objectives of the pilot study]. We will determine that it is feasible to carry on the main study if ...[state the criteria for success of feasibility] ."

Publication

- **Can I publish the results of a pilot study?**

✓ Yes, every attempt should be made to publish them

- **Why is it important to publish the results of pilot studies?**

✓ To provide information about feasibility to the research community

- **Most pilot studies do not show statistically significant results**

"no evidence of effect" is not "evidence of no effect"

BMJ 1995; 311: 485.

- The focus in reporting the results of a pilot should be on **feasibility, NOT statistical significance**

Other Important Issues

- **Can I combine data from a pilot with data from the main study?**

✓ Yes, provided the sampling frame is the same and so is the methodology

- **Can I combine the results of a pilot with the results of another study or in a meta-analysis?**

✓ Yes, same conditions as above

✓ Also depends on whether the main study is reported

- **Can a pilot ever exist on its own?**

✓ Yes, if the results show that it is not feasible to go to the main study or there is no funding for the main study

Other Important Issues

- **Can I apply for funding for a pilot study?**

✓ Yes, like any grant it is important to justify the need for piloting

✓ The pilot has to be placed in the context of the main study

- **Can I randomize patients in a pilot study?**

✓ Yes; to assess how a randomization might work in main study or whether it might be acceptable to patients

✓ In general, it is always best for a pilot to maintain the same design as the main study

Challenges with Pilot Studies

- **Most are not well designed**

  ✓ No clear feasibility objectives;

  ✓ No clear analytic plans;

  ✓ No clear rationale for piloting

  ✓ No clear criteria for success of feasibility

- **Most are not reported/published**

- **It can be dangerous to use pilot studies to estimate treatment effects**

✓ Estimates may be unrealistic/biased

Common Misconceptions

- **A small study that can be completed quickly**

✓ A small study done by a student/intern

- **A small study that does not require any funding**

✓ I don't have any funding to do a big study!

- **A small study that has limited funding**

✓ I have funding for only 10 patients!

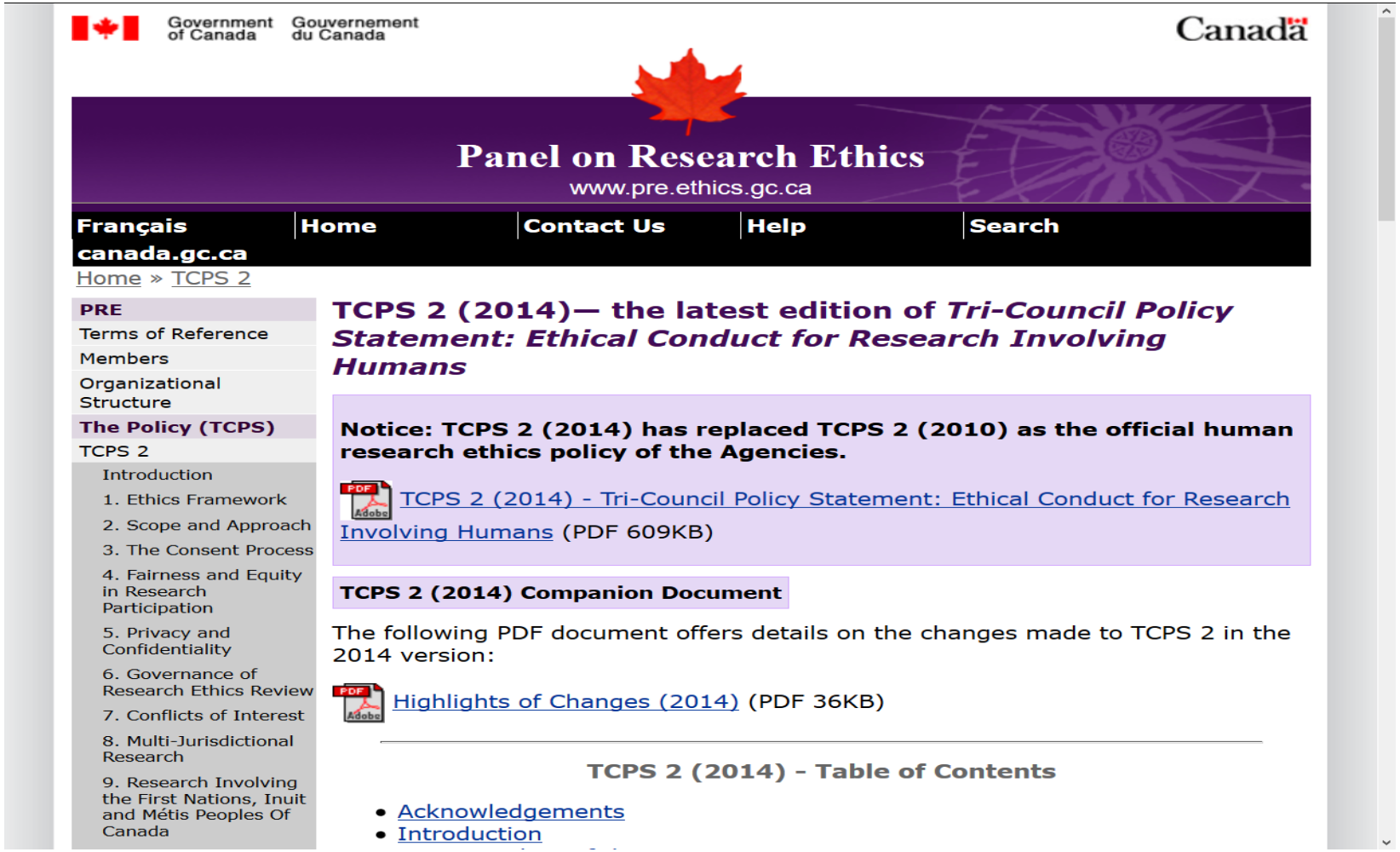
- **A small single centre study**

✓ I don't have the resources for a large multi-centre study!

- **A small study that is similar in size as someone else's published study**

✓ So-and-so did a similar study with 6 patients and got statistical significance – ours uses 12 patients (double the size)!

TCPS2



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  - 3. The Consent Process
  - 4. Fairness and Equity in Research Participation
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  - 8. Multi-Jurisdictional Research
  - 9. Research Involving the First Nations, Inuit and Métis Peoples Of Canada

TCPS 2 (2014)— the latest edition of *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*

Notice: TCPS 2 (2014) has replaced TCPS 2 (2010) as the official human research ethics policy of the Agencies.

TCPS 2 (2014) - Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (PDF 609KB)

TCPS 2 (2014) Companion Document

The following PDF document offers details on the changes made to TCPS 2 in the 2014 version:

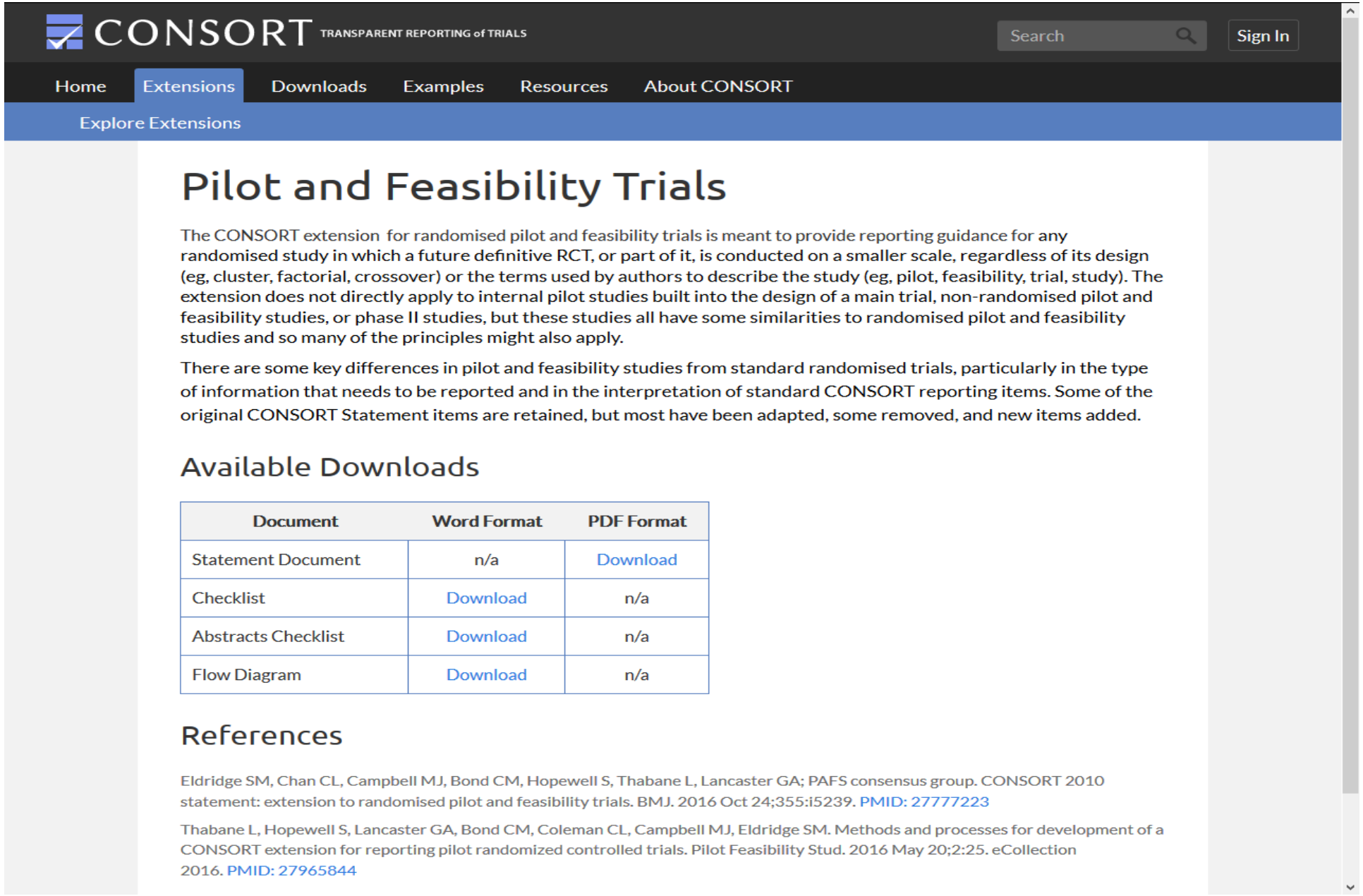
Highlights of Changes (2014) (PDF 36KB)

TCPS 2 (2014) - Table of Contents

- Acknowledgements
- Introduction

Pilot studies are covered in current version of TCPS2

CONSORT Extension



CONSORT TRANSPARENT REPORTING of TRIALS

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Pilot and Feasibility Trials

The CONSORT extension for randomised pilot and feasibility trials is meant to provide reporting guidance for any randomised study in which a future definitive RCT, or part of it, is conducted on a smaller scale, regardless of its design (eg, cluster, factorial, crossover) or the terms used by authors to describe the study (eg, pilot, feasibility, trial, study). The extension does not directly apply to internal pilot studies built into the design of a main trial, non-randomised pilot and feasibility studies, or phase II studies, but these studies all have some similarities to randomised pilot and feasibility studies and so many of the principles might also apply.

There are some key differences in pilot and feasibility studies from standard randomised trials, particularly in the type of information that needs to be reported and in the interpretation of standard CONSORT reporting items. Some of the original CONSORT Statement items are retained, but most have been adapted, some removed, and new items added.

Available Downloads

Document	Word Format	PDF Format
Statement Document	n/a	Download
Checklist	Download	n/a
Abstracts Checklist	Download	n/a
Flow Diagram	Download	n/a

References

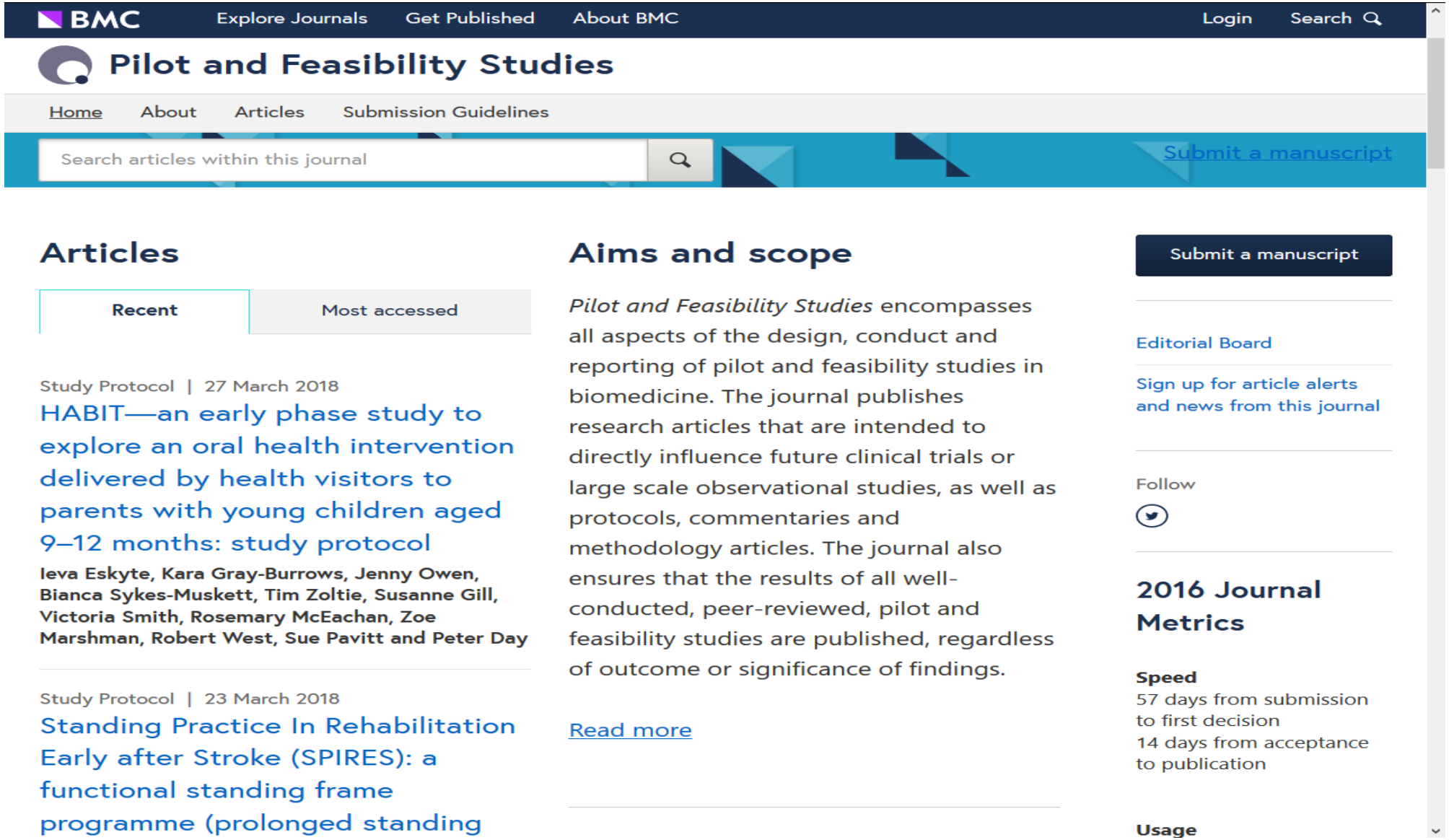
Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Thabane L, Lancaster GA; PAFS consensus group. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. BMJ. 2016 Oct 24;355:i5239. PMID: 27777223

Thabane L, Hopewell S, Lancaster GA, Bond CM, 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 May 20;2:25. eCollection 2016. PMID: 27965844

Section	Standard checklist item	Extension for pilot trials
Title and abstract		
1a	Identification as a randomised trial in the title	Identification as a pilot or feasibility randomised trial in the title
1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	Structured summary of pilot trial design, methods, results, and conclusions (for specific guidance see CONSORT abstract extension for pilot trials)
Introduction		
Background and objectives:		
2a	Scientific background and explanation of rationale	Scientific background and explanation of rationale for future definitive trial, and reasons for randomised pilot trial
2b	Specific objectives or hypotheses	Specific objectives or hypotheses of pilot trial
Methods		
Trial design:		
3a	Description of trial design (such as parallel, factorial) including allocation ratio	Description of pilot trial design (such as parallel, factorial) including allocation ratio
3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	Important changes to methods after pilot trial commencement (such as eligibility criteria), with reasons
Participants:		
4a	Eligibility criteria for participants	
4b	Settings and locations where the data were collected	
4c		How participants were identified and consented
Interventions:		
5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	

DRAFT

New Journal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Study Protocol | 27 March 2018
HABIT—an early phase study to explore an oral health intervention delivered by health visitors to parents with young children aged 9–12 months: study protocol
Ieva Eskyte, Kara Gray-Burrows, Jenny Owen, Bianca Sykes-Muskett, Tim Zoltie, Susanne Gill, Victoria Smith, Rosemary McEachan, Zoe Marshman, Robert West, Sue Pavitt and Peter Day
Study Protocol | 23 March 2018
Standing Practice In Rehabilitation Early after Stroke (SPIRES): a functional standing frame programme (prolonged standing
Aims and scope
Pilot and Feasibility Studies encompasses all aspects of the design, conduct and reporting of pilot and feasibility studies in biomedicine. The journal publishes research articles that are intended to directly influence future clinical trials or large scale observational studies, as well as protocols, commentaries and methodology articles. The journal also ensures that the results of all well-conducted, peer-reviewed, pilot and feasibility studies are published, regardless of outcome or significance of findings.
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Key Messages

- **Provide a good opportunity to assess feasibility of large full-scale phase III studies**

✓It can enhance the success probability of the main study

- **Pilot studies should be well designed**

✓Clear feasibility objectives

✓Clear rationale for piloting – needs to be linked to main study

✓Clear analytic plans

✓Clear criteria for determining success of feasibility

Key Messages

- **Pilot studies should be used cautiously for determining**

✓Treatment effects

- **They should be scrutinized the same way as full scale RCTs**

✓Require registration

✓They should also be published/reported in peer-review journals

THANK YOU ALL

McMaster University

Family Medicine

Department of Family Medicine
Michael G. DeGroote School of Medicine
Faculty of Health Sciences

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@McMasterFamMed