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Pilot vs feasibility studies: how to tell them apart?

The International Behavioural Trials Network
May 28-30, 2020

Lehana Thabane

Joint work with the PAFS Collaboration Group

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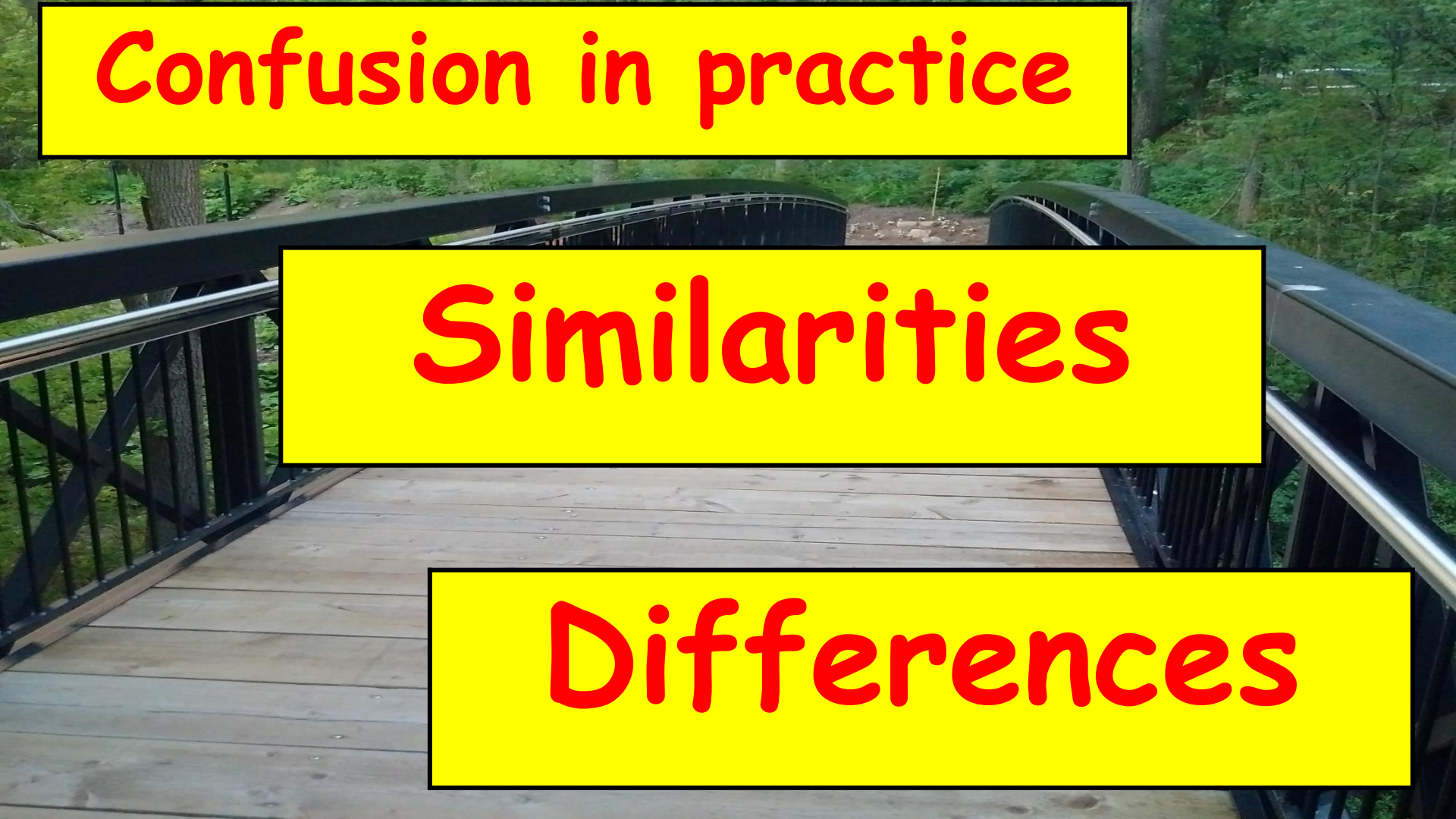
Keele University

McMaster University
HEALTH RESEARCH METHODS, EVIDENCE, AND IMPACT


Confusion in practice
Similarities
Differences

Confusion in practice

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

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

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

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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

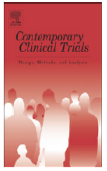
Lehana Thabane[1,2*], Jinhui Ma[1,2], Rong Chu[1,2], Ji Cheng[1,2], Afisi Ismaila[1,3], Lorena P Rios[1,2], Reid Robson[3], Marroon Thabane[1,4], Lora Giangregorio[5], Charles H Goldsmith[1,2]

Contemporary Clinical Trials 38 (2014) 130–133

Contents lists available at ScienceDirect

Contemporary Clinical Trials

journal homepage: www.elsevier.com/locate/conclintrial



Pilot and feasibility studies: Is there a difference from each other and from a randomised controlled trial?

Amy L. Whitehead, Benjamin G.O. Sully, Michael J. Campbell *

Design, Trials and Statistics Group, School of Health and Related Research, University of Sheffield, Regent Court, 30 Regent Street, Sheffield S1 4DA, UK

There was substantial variation in practice

- Studies are not reported consistently
- Terms are used interchangeably and inconsistently

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In research, words matter!

Most journals had no editorial policies on pilot studies

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]

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

Circulation. 2009;119:1694-1696

There's some evidence that editors often arm-twist authors to add "pilot" to acknowledge small samples in their studies

Rogue Editor

Desperate Author

Although there is an increasing number of pilot/feasibility studies in the literature, **the reporting is very suboptimal**

- Too much emphasis on hypothesis-testing
- No clear feasibility objectives/outcomes
- No progression criteria to the main study
- Inadequate descriptions of analytic plans
- **No explicit mention that they done to inform future studies**

Contemporary Clinical Trials 38 (2014) 130–133

Contents lists available at ScienceDirect

Contemporary Clinical Trials

journal homepage: www.elsevier.com/locate/conclintrial

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

Pilot and feasibility studies: Is there a difference from each other and from a randomised controlled trial?

Amy L. Whitehead, Benjamin G.O. Sully, Michael J. Campbell *

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

Others have worried that in the era of diminishing resources, PAFS could actually be a waste of resources

PLOS ONE

RESEARCH ARTICLE

Do feasibility studies contribute to, or avoid, waste in research?

Ben Morgan[1]*, Jennie Hejdenberg[1], Saba Hinrichs-Krapels[2], David Armstrong[3]

1 National Institute for Health Research Central Commissioning Facility, Twickenham, United Kingdom, 2 Policy Institute, King's College London, London, United Kingdom, 3 Department of Primary Care & Public Health Sciences, King's College London, London, United Kingdom

"We have estimated that …this may have saved the wider NIHR at least £20 million"

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Empirical evidence shows that lack of, or inadequate assessment of feasibility is the main reason why trials fail

Poor accrual is the primary reason for early trial termination

CIHR IRSC Canadian Institutes of Health Research Instituts de recherche en santé du Canada

Submitted by CIHR
Déposé par les IRSC

Clin Trials. Author manuscript; available in PMC 2016 January 31.

Published in final edited form as:
Clin Trials. 2015 February ; 12(1): 77–83. doi:10.1177/1740774514558307.

Unsuccessful Trial Accrual and Human Subjects Protections: An Empirical Analysis of Recently Closed Trials

Benjamin Carlisle, MA[1], Jonathan Kimmelman, PhD[1], Tim Ramsay, PhD[2], and Nathalie MacKinnon, BSc[1]

PLOS ONE

RESEARCH ARTICLE

Terminated Trials in the ClinicalTrials.gov Results Database: Evaluation of Availability of Primary Outcome Data and Reasons for Termination

Rebecca J. Williams[1]*, Tony Tse[1], Katelyn DiPiazza[2], Deborah A. Zarin[1]

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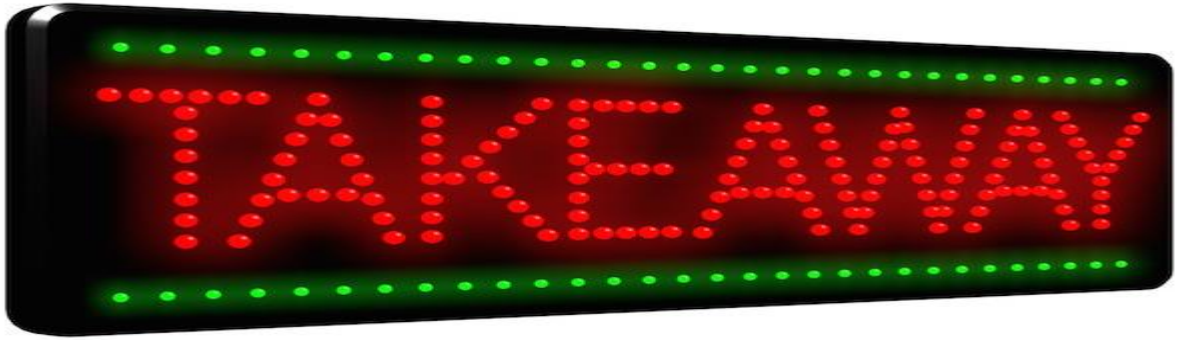

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The past practice in the conduct, analysis and reporting of pilot studies was inadequate

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We developed a conceptual framework to distinguish between pilot and feasibility studies

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PLOS ONE

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RESEARCH ARTICLE

Defining Feasibility and Pilot Studies in Preparation for Randomised Controlled Trials: Development of a Conceptual Framework

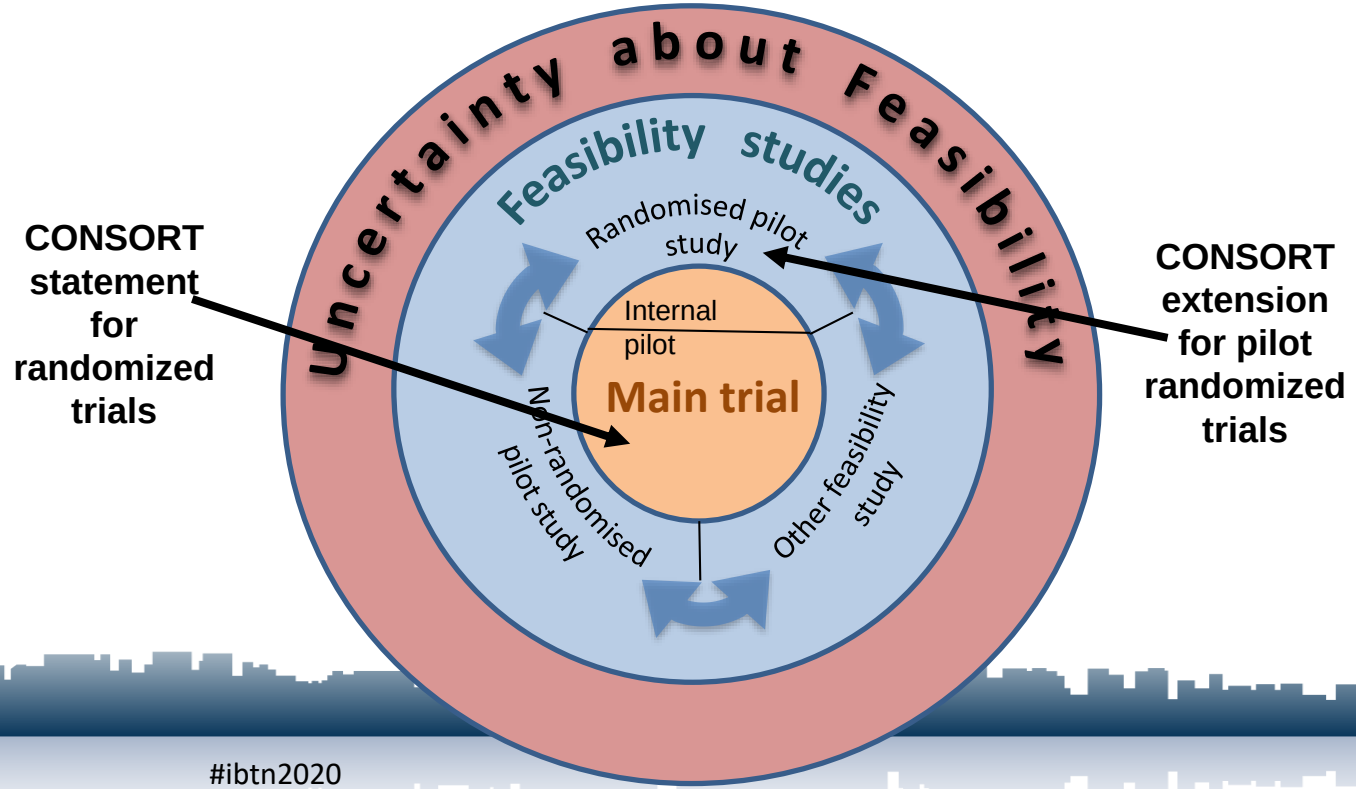
Sandra M. Eldridge[1]*, Gillian A. Lancaster[2], Michael J. Campbell[3], Lehana Thabane[4], Sally Hopewell[5], Claire L. Coleman[1], Christine M. Bond[6]

Definitions paper

We provide definitions for feasibility and pilot studies and define the conceptual framework

The framework and implications for reporting randomized pilot trials

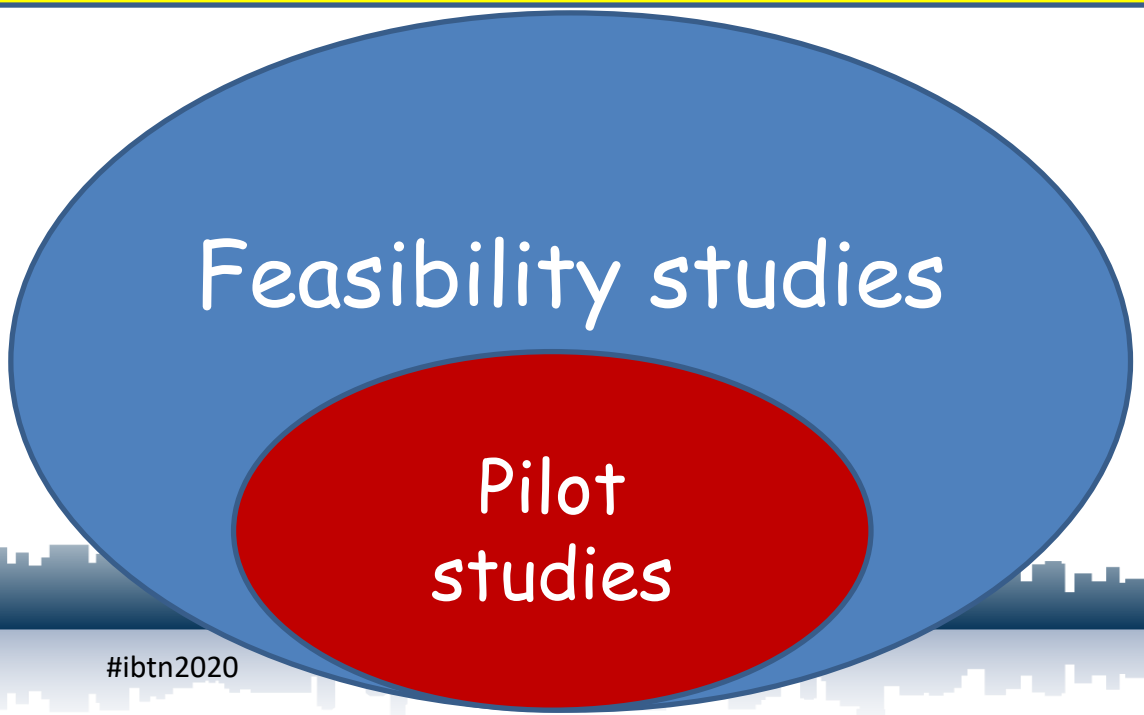
trials network



- ***A feasibility study*** asks whether **something** can be done, should we proceed with it, and if so, how.
- ***A pilot study*** asks the same questions but also has a specific design feature: in a pilot study a future study, or part of a future study, is conducted on a smaller scale.

Corollary

All pilot studies are feasibility studies but not all feasibility studies are pilot studies



Similarities:

All pilot studies are feasibility studies

Example 1: Randomized pilot study

Samaan *et al. Pilot and Feasibility Studies* (2015) 1:39
DOI 10.1186/s40814-015-0034-y

PILOT AND FEASIBILITY STUDIES

STUDY PROTOCOL Open Access

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

Zainab Samaan[1,2,3,4*], Kathryn Litke[2], Kathleen McCabe[1,2], Brittany Dennis[3], Jeff Whattam[2], Laura Garrick[2], Laura O'Neill[1,2], Terri Ann Tabak[1,2], Scott Simons[2], Sandra Chalmers[2], Brenda Key[1,2], Meredith Vanstone[3], Feng Xie[3], Gordon Guyatt[3,5] and Lehana Thabane[3,6,7,8,9]

To **assess feasibility** of RCT for management of depressive symptoms

- Recruitment rates
- Retention rate
- Data completeness rates
- Feedback on intervention
- Resources required to conduct main study

Example 2: Cluster-randomized pilot trial

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 rates
- ❑ Retention rates
- ❑ Participation rate
- ❑ Completion of action plans, feedback reports
- ❑ Completeness of data

Example 3: Non-randomized pilot study

AIDS Behav
DOI 10.1007/s10461-009-9540-3

ORIGINAL RESEARCH

Pilot Trial of an Intervention Aimed at Modifying Drug Preparation Practices Among Injection Drug Users in Puerto Rico

Hector M. Colon · Henriette A. Finlinson · Juan Negron · Irmaly Sosa · Eddy Rios-Olivares · Rafaela R. Robles

To **pilot an intervention** to avoid the use of syringes and contamination of materials amongst injecting drug users

- ✓ Adoption of each of four components
- ✓ Whether pre-post changes in blood residues indicated that intervention merited further testing

Example 4: Feasibility study, but not a pilot

BJR

HIP

The feasibility of performing a randomised controlled trial for femoroacetabular impingement surgery

A. J. R. Palmer,
G. E. R. Thomas,
T. C. B. Pollard,
I. Rombach,
A. Taylor,
N. Arden,
D. J. Beard,
A. J. Andrade,
A. J. Carr,
S. Glyn-Jones

From Nuffield

Objectives

The number of surgical procedures performed each year to treat femoroacetabular impingement (FAI) continues to rise. Although there is evidence that surgery can improve symptoms in the short-term, there is no evidence that it slows the development of osteoarthritis (OA). We performed a feasibility study to determine whether patient and surgeon opinion was permissive for a Randomised Controlled Trial (RCT) comparing operative with non-operative treatment for FAI.

Methods

Surgeon opinion was obtained using validated questionnaires at a Specialist Hip Meeting (n = 61, 30 of whom stated that they routinely performed FAI surgery) and patient opinion was obtained from clinical patients with a new diagnosis of FAI (n = 31).

To **determine feasibility** of RCT comparing operative with non-operative treatment for femoroacetabular impingement surgery

- ✓ Surgeon and patient opinion via a questionnaire

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Key Message

Pilot and Feasibility studies all focus on

feasibility as the primary focus to inform the design of a future main study

Differences:

Not all feasibility studies are pilot studies

Key Difference

Pilot studies are miniature versions of the main study, but feasibility studies do not necessarily need to have the same design as the main study

Example 1: Pilot Trial

Johnstone et al. Pilot and Feasibility Studies (2015) 1:19
DOI 10.1186/s40814-015-0013-3

PILOT AND FEASIBILITY STUDIES

Cook et al. Trials (2016) 17:377
DOI 10.1186/s13063-016-1495-x

Trials

STUDY PROTOCOL Open Access

*Pro*biotics: Prevention of *S*evere *P*neumonia and *E*ndotracheal *C*olonization *T*rial—PROSPECT: protocol for a feasibility randomized pilot trial

Jennie Johnstone[1,2,3], Maureen Meade[4,5], John Marshall[3,6,7], Daren K Heyland[8], Michael G Surette[4], Dawn ME Bowdish[9], Francois Lauzier[10], Lehana Thebane[5,11], Deborah J Cook[4,5*] and For the PROSPECT Investigators and the Canadian Critical Care Trials Group

Abstract

Background: Probiotics are defined as live microorganisms that may confer health benefits when ingested. Meta-analysis of probiotic trials suggests a 25 % lower ventilator-associated pneumonia (VAP) and 18 % lower infection rates overall when administered to patients in the intensive care unit (ICU). However, prior trials are small, largely single center, and at high risk of bias. Before a large rigorous trial is launched, testing whether probiotics confer benefit, harm, or have no impact, a pilot trial is needed. The aim of the PROSPECT Pilot Trial is to determine the feasibility of performing a larger trial in mechanically ventilated critically ill patients investigating *Lactobacillus rhamnosus* GG. A priori, we determined that the feasibility of the larger trial would be based on timely recruitment, high protocol adherence, minimal contamination, and an acceptable VAP rate.

Methods/design: Patients ≥18 years old in the ICU who are anticipated to receive mechanical ventilation for ≥72 hours will be included. Patients are excluded if they are at increased risk of probiotic-associated infection, have strict enteral medication contraindications, are pregnant, previously enrolled in a related trial, or are receiving palliative care. Following informed consent, patients are randomized in variable unspecified block sizes in a fixed 1:1 ratio, stratified by ICU, and medical, surgical, or trauma admitting diagnosis. Patients receive 1×10^{10} colony forming units of *L. rhamnosus* GG (Culturelle, Locin Industries Ltd) or an identical placebo suspended in tap water administered twice daily via nasogastric tube in the ICU. Clinical and research staff, patients, and families are blinded.

Discussion: The primary outcomes for this pilot trial are the following: (1) recruitment success, (2) ≥90 % protocol adherence, (3) ≤5 % contamination, and (4) ~10 % VAP rate. Additional clinical outcomes are VAP, other infections, diarrhea (total, antibiotic associated, and Clostridium difficile), ICU and hospital length of stay, and mortality. The morbidity, mortality, and cost of VAP underscore the need for cost-effective prophylactic interventions. The PROSPECT Pilot Trial is the initial step toward rigorously evaluating whether probiotics decrease nosocomial infections, have no effect, or actually cause infections in critically ill patients.

Trial registration: ClinicalTrials.gov. NCT01782755

Keywords: Critically ill, Intensive care, Probiotics, Infection, Pneumonia

RESEARCH Open Access

Probiotics: Prevention of Severe Pneumonia and Endotracheal Colonization Trial—PROSPECT: a pilot trial

Deborah J. Cook[1,2*], Jennie Johnstone[3,4,5], John C. Marshall[6,7], Francois Lauzier[8,9,10], Lehana Thabane[2], Sangeeta Mehta[5,7], Peter M. Dodek[11,12], Lauralyn McIntyre[13], Joe Pagliarello[13], William Henderson[14], Robert W. Taylor[15], Rodrigo Cartin-Ceba[16], Eyal Golan[5,7], Margaret Herridge[5,7], Gordon Wood[17], Daniel Ovakim[17], Tim Karachi[1], Michael G. Surette[1], Dawn M. E. Bowdish[18], Daphnee Lamarche[19], Chris P. Verschoor[18], Erick H. Duan[1], Diane Heels-Ansdell[2], Yaseen Arabi[20], Maureen Meade[1,2] and For the PROSPECT Investigators and the Canadian Critical Care Trials Group

Abstract

Background: Probiotics are live microorganisms that may confer health benefits when ingested. Randomized trials suggest that probiotics significantly decrease the incidence of ventilator-associated pneumonia (VAP) and the overall incidence of infection in critically ill patients. However, these studies are small, largely single-center, and at risk of bias. The aim of the PROSPECT pilot trial was to determine the feasibility of conducting a larger trial of probiotics to prevent VAP in mechanically ventilated patients in the intensive care unit (ICU).

Methods: In a randomized blinded trial, patients expected to be mechanically ventilated for ≥72 hours were allocated to receive either 1×10^{10} colony-forming units of *Lactobacillus rhamnosus* GG or placebo, twice daily. Patients were excluded if they were at increased risk of *L. rhamnosus* GG infection or had contraindications to enteral medication. Feasibility objectives were: (1) timely recruitment; (2) maximal protocol adherence; (3) minimal contamination; and (4) estimated VAP rate ≥10 %. We also measured other infections, diarrhea, ICU and hospital length of stay, and mortality.

Results: Overall, in 14 centers in Canada and the USA, all feasibility goals were met: (1) 150 patients were randomized in 1 year; (2) protocol adherence was 97 %; (3) no patients received open-label probiotics; and (4) the VAP rate was 19 %. Other infections included: bloodstream infection (19.3 %), urinary tract infections (12.7 %), and skin and soft tissue infections (4.0 %). Diarrhea, defined as Bristol type 6 or 7 stools, occurred in 133 (88.7 %) of patients, the median length of stay in ICU was 12 days (quartile 1 to quartile 3, 7–18 days), and in hospital was 26 days (quartile 1 to quartile 3, 14–44 days); 23 patients (15.3 %) died in the ICU.

Conclusions: The PROSPECT pilot trial supports the feasibility of a larger trial to investigate the effect of *L. rhamnosus* GG on VAP and other nosocomial infections in critically ill patients.

Trial registration: Clinicaltrials.gov NCT01782755. Registered on 29 January 2013.

Keywords: Critically ill, Infection, Intensive care, Probiotics

Example 1: Main Trial

Open access Protocol

BMJ Open

Evaluating probiotics for the prevention of ventilator-associated pneumonia: a randomised placebo-controlled multicentre trial protocol and statistical analysis plan for PROSPECT

Jennie Johnstone,[1] Diane Heels-Ansdell,[2] Lehana Thabane,[2] Maureen Meade,[2] John Marshall,[3] Francois Lauzier,[4] Erick Huaileigh Duan,[5] Nicole Zytaruk,[2] Daphnee Lamarche,[6] Michael Surette,[6] Deborah J Cook,[5] for the PROSPECT Investigators and the Canadian Critical Care Trials Group

To cite: Johnstone J, Heels-Ansdell D, Thabane L, *et al*. Evaluating probiotics for the prevention of ventilator-associated pneumonia: a randomised placebo-controlled multicentre trial protocol and statistical analysis plan for PROSPECT. *BMJ Open* 2019;**9**:e025228. doi:10.1136/bmjopen-2018-025228

► Prepublication history and additional material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2018-025228)

ABSTRACT

Introduction Ventilator-associated pneumonia (VAP) is the most common healthcare-associated infection in critically ill patients. Prior studies suggest that probiotics may reduce VAP and other infections in critically ill patients; however, most previous randomised trials were small, single centre studies. The Probiotics: Prevention of Severe Pneumonia and Endotracheal Colonization Trial (PROSPECT) aims to determine the impact of the probiotic *Lactobacillus rhamnosus* GG on VAP and other clinically important outcomes in critically ill adults.

Methods PROSPECT is a multicentre, concealed, randomised, stratified, blinded, controlled trial in patients ≥18 years old, anticipated to be mechanically ventilated ≥72 hours, in intensive care units (ICUs) in

Strengths and limitations of this study

- ► Randomized placebo controlled multicentre trial.
- ► Evaluation of the effect of probiotics on pneumonia, other intensive care unit (ICU)-acquired infections and diarrhoea in a large, adequately powered trial.
- ► International enrolment including patients over 65 years of age to enhance the generalizability of the findings.
- ► Characterisation of pre-hospital frailty to help understand the relationship between frailty, probiotics and ICU-acquired infections.
- ► Severely immunocompromised patients are excluded for safety reasons.

Comparison Pilot vs Main

Features	Pilot	Main
Title	The Probiotics: Prevention of Severe Pneumonia and Endotracheal Colonization Trial (PROSPECT)	The Probiotics: Prevention of Severe Pneumonia and Endotracheal Colonization Trial (PROSPECT)
Publication	▪ Pilot and Feasibility Studies (2015) 1:19 (Protocol) ▪ Trials (2016) 17:377 (Result)	BMJ Open 2019;9:e025228 (Protocol)
Primary Outcomes	Recruitment of trial patients; Adherence to protocol; Contamination; Ventilator associated pneumonia (VAP) rate	Ventilator-associated pneumonia (VAP)
Secondary Outcomes	Ventilator associated pneumonia (Clinical Primary); Other infections; C. difficile-associated diarrhea; Antibiotic-associated diarrhea; Diarrhea according to the Bristol Stool Chart; Duration of mechanical ventilation; ICU mortality and in-hospital mortality	Early VAP, late VAP and post-extubation pneumonia; Clostridioides difficile in the ICU; Any infection acquired during the ICU stay; Diarrhoea in the ICU; Antibiotic-associated diarrhoea in the ICU; Antimicrobial use in ICU; Duration: mechanical ventilation, ICU stay and hospital stay; ICU mortality and in-hospital mortality
Sample size	150	2650
Criteria for success of feasibility	Successful recruitment is defined as 150 patients in one year from all sites; ≥90 % protocol adherence; ≤5 % contamination; ~10 % VAP rate	
Hypothesis		Probiotic L. rhamnosus GG, compared with placebo, will reduce VAP and other clinically important outcomes in critically ill mechanically ventilated patients
Design: ▪ Arms ▪ Type	 ▪ 2 ▪ Multicentre Parallel group placebo controlled	 ▪ 2 ▪ Multicentre Parallel group placebo controlled

Example 2: Feasibility Trial

BJR

HIP

The feasibility of performing a randomised controlled trial for femoroacetabular impingement surgery

A. J. R. Palmer,
G. E. R. Thomas,
T. C. B. Pollard,
I. Rombach,
A. Taylor,
N. Arden,
D. J. Beard,
A. J. Andrade,
A. J. Carr,
S. Glyn-Jones

From Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences (NDORMS), University of Oxford, Oxford, United Kingdom

- A. J. R. Palmer, MA, BMBCh, MRCS, Clinical Research Fellow
- G. E. R. Thomas, MA, MBBS, MRCS, Clinical Research Fellow
- I. Rombach, MSc, Clinical Trials Statistician
- N. Arden, MSc, MD, FRCP, Professor of Rheumatology
- D. J. Beard, MSc, DPhil, Professor of Musculoskeletal Sciences
- A. J. Carr, FRCS, FMedSci, Nuffield Professor of Orthopaedic Surgery
- S. Glyn-Jones, MS, DPhil, FRCS, Consultant Orthopaedic Surgeon

Objectives
The number of surgical procedures performed each year to treat femoroacetabular impingement (FAI) continues to rise. Although there is evidence that surgery can improve symptoms in the short-term, there is no evidence that it slows the development of osteoarthritis (OA). We performed a feasibility study to determine whether patient and surgeon opinion was permissive for a Randomised Controlled Trial (RCT) comparing operative with non-operative treatment for FAI.

Methods
Surgeon opinion was obtained using validated questionnaires at a Specialist Hip Meeting (n = 61, 30 of whom stated that they routinely performed FAI surgery) and patient opinion was obtained from clinical patients with a new diagnosis of FAI (n = 31).

Results
Clinical equipoise was demonstrated when surgeons were given clinical scenarios and asked whether they would manage a patient operatively or non-operatively. A total of 23 surgeons (77%) who routinely perform FAI surgery were willing to recruit patients into a RCT, and 28 patients (90%) were willing to participate. 75% of responding surgeons believed it was appropriate to randomise patients to non-operative treatment for ≥ 12 months. Conversely, only eight patients (26%) felt this was acceptable, although 29 (94%) were willing to continue non-operative treatment for six months. More patients were concerned about their risk of developing OA than their current symptoms, although most patients felt that the two were of equal importance.

Conclusions
We conclude that a RCT comparing operative and non-operative management of FAI is feasible and should be considered a research priority. An important finding for orthopaedic surgical trials is that patients without life-threatening pathology appear willing to trial a treatment for six months without improvement in their symptoms.

Example 2: Main Trial

BJR

HIP

Protocol for the Femoroacetabular Impingement Trial (FAIT)

A MULTI-CENTRE RANDOMISED CONTROLLED TRIAL COMPARING SURGICAL AND NON-SURGICAL MANAGEMENT OF FEMOROACETABULAR IMPINGEMENT

A. J. R. Palmer,
V. Ayyar-Gupta,
S. J. Dutton,
I. Rombach,
C. D. Cooper,
T. C. Pollard,
D. Hollinghurst,
A. Taylor,
K. L. Barker,
E. G. McNally,
D. J. Beard,
A. J. Andrade,
A. J. Carr,
S. Glyn-Jones

From NDORMS, University of Oxford, Oxford, United Kingdom

A. J. R. Palmer, MA, BMBCh,

Aims

Femoroacetabular Junction Impingement (FAI) describes abnormalities in the shape of the femoral head–neck junction, or abnormalities in the orientation of the acetabulum. In the short term, FAI can give rise to pain and disability, and in the long-term it significantly increases the risk of developing osteoarthritis. The Femoroacetabular Impingement Trial (FAIT) aims to determine whether operative or non-operative intervention is more effective at improving symptoms and preventing the development and progression of osteoarthritis.

Methods

FAIT is a multicentre superiority parallel two-arm randomised controlled trial comparing physiotherapy and activity modification with arthroscopic surgery for the treatment of symptomatic FAI. Patients aged 18 to 60 with clinical and radiological evidence of FAI are eligible. Principal exclusion criteria include previous surgery to the index hip, established osteoarthritis (Kellgren–Lawrence ≥ 2), hip dysplasia (centre-edge angle < 20°), and completion of a physiotherapy programme targeting FAI within the previous 12 months. Recruitment will take place over 24 months and 120 patients will be randomised in a 1:1 ratio and followed up for three years. The two primary outcome measures are change in hip outcome score eight months post-randomisation (approximately six-months post-intervention initiation) and change in radiographic minimum joint space width 38 months post-randomisation. ClinicalTrials.gov: NCT01893034.

Arthroscopic hip surgery compared with physiotherapy and activity modification for the treatment of symptomatic femoroacetabular impingement: multicentre randomised controlled trial

Antony J R Palmer,[1] Vandana Ayyar Gupta,[1] Scott Fernquest,[1] Ines Rombach,[2] Susan J Dutton,[2] Ramy Mansour,[3] Simon Wood,[3] Vikas Khanduja,[4] Tom C B Pollard,[5] Andrew W McCaskie,[6] Karen L Barker,[1] Tony J M D Andrade,[5] Andrew J Carr,[1] David J Beard,[1,7] Sion Glyn-Jones,[1] on behalf of the FAIT Study Group

ABSTRACT

OBJECTIVE

To compare arthroscopic hip surgery with physiotherapy and activity modification for improving patient reported outcome measures in patients with symptomatic femoroacetabular impingement (FAI).

DESIGN

Two group parallel, assessor blinded, pragmatic randomised controlled trial.

SETTING

Secondary and tertiary care centres across seven NHS England sites.

PARTICIPANTS

222 participants aged 18 to 60 years with symptomatic FAI confirmed clinically and with imaging (radiography or magnetic resonance imaging) were randomised (1:1) to receive arthroscopic hip surgery

INTERVENTIONS

Participants in the physiotherapy group received a goal based programme tailored to individual patient needs, with emphasis on improving core stability and movement control. A maximum of eight physiotherapy sessions were delivered over five months. Participants in the arthroscopic surgery group received surgery to excise the bone that impinged during hip movements, followed by routine postoperative care.

MAIN OUTCOME MEASURES

The primary outcome measure was the hip outcome score activities of daily living subscale (HOS ADL) at eight months post-randomisation, with a minimum clinically important difference between groups of 9 points. Secondary outcome measures included additional patient reported outcome measures and clinical assessment.

Comparison Feasibility vs Main

Features	Feasibility	Main
Title	Femoroacetabular impingement Trial (Fait)	Femoroacetabular impingement Trial (Fait)
Publication	Bone Joint Res 2013;2:33–40	▪ Bone Joint Res 2014;3:321–7 (Protocol) ▪ BMJ 2019;364:l185 (Result)
Primary Outcomes	Surgeon opinion; Patient opinion	Hip outcome score activities of daily living subscale (HOS ADL)
Secondary Outcomes		HOS sport subscale; non-arthritic hip score (NAHS); Copenhagen hip and groin outcome score (HAGOS); Oxford hip score (OHS); and international hip outcome tool (iHOT-33); Quality of life, nature and location of pain, and psychological factors were evaluated using EQ-5D-3L; PainDETECT; hospital anxiety and depression score (HADS)
Sample size	23 Surgeons; 28 Patients	214
Criteria for success of feasibility	Not stated	
Hypothesis		Arthroscopic hip surgery improve patient reported outcome measures in patients with symptomatic femoroacetabular impingement (FAI) compared to physiotherapy and activity modification for improving
Design: ▪ Arms ▪ Type	Survey of surgeons and patients to assess whether it is feasible to conduct a RCT	▪ 2 ▪ Multicentre Parallel group

Example 3:

The CYCLE Study:
A case study of a complex rehabilitation intervention in the ICU

CYCLE

McMaster University HEALTH SCIENCES

CCCTG Canadian Critical Care Trials Group

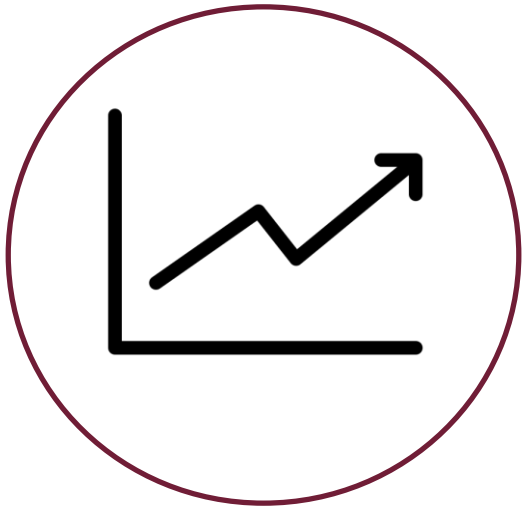
Chaires de recherche du Canada / Canada Research Chairs

Canada

CIHR IRSC

Why Physical Rehabilitation in the ICU?

behavioural trials network



- Increasing critical care demand[1]
- More critical illness survivors[1]

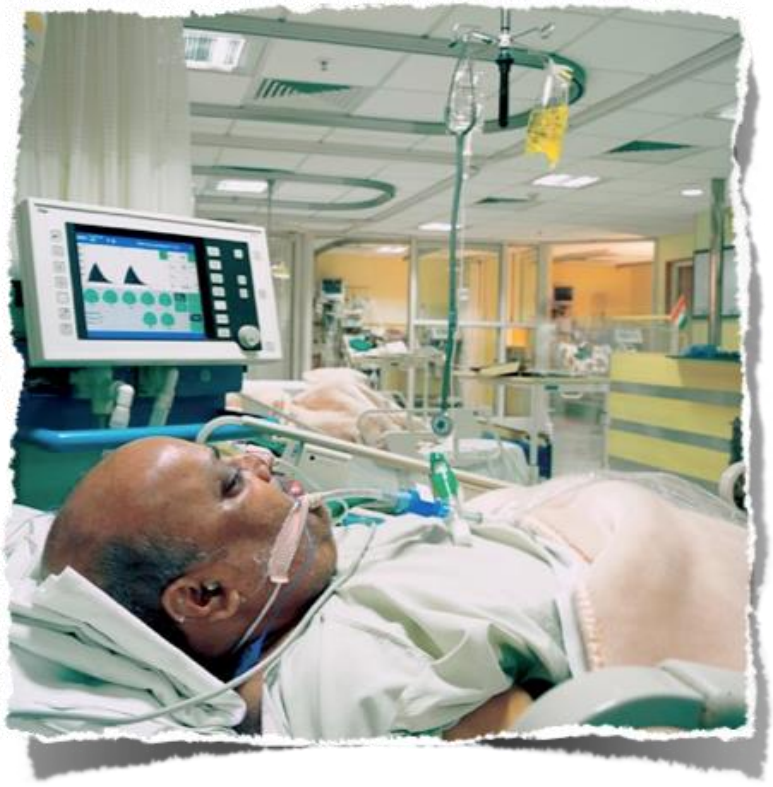
- Survivors at risk for disability[2]

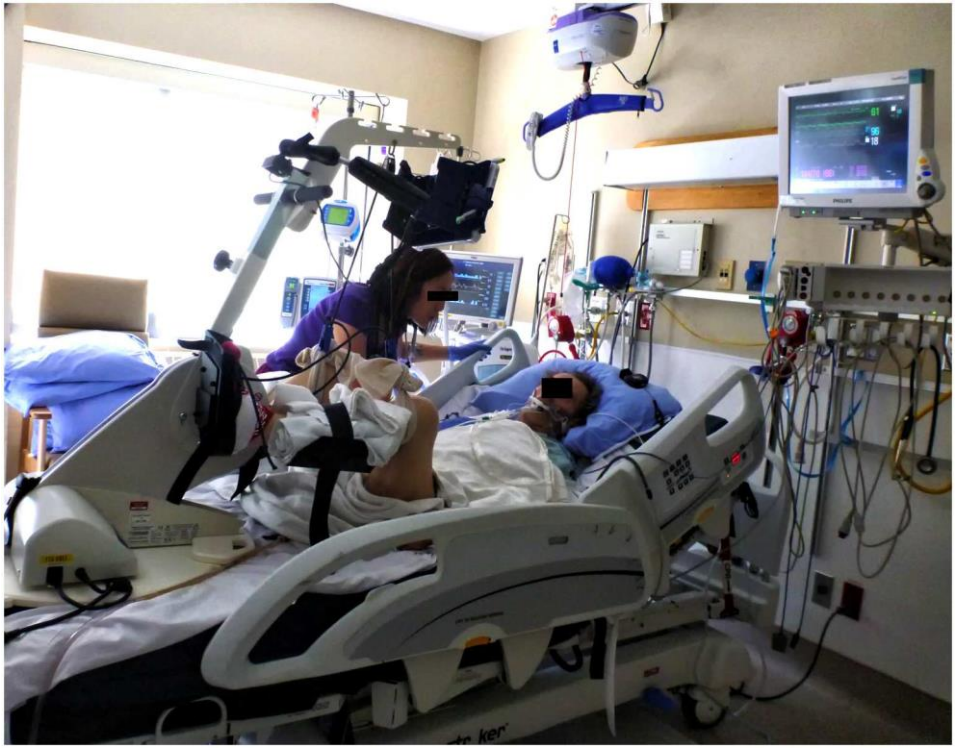
- ✓ PT and OT started @ 1.5 days[3]
- ✓ In-bed cycling started @ 2 weeks[4]

[1]Crit Care Med. 2005;33(3):574-9. [2]NEJM. 2011;*364*(14), 1293–1304.
[3]Lancet. 2009;373(9678):1874-82. [4]Crit Care Med. 2009;37(9):2499-505.

Graphics courtesy of H O'Grady.

Critically ill patients & exercise?





PLoS One. 2016;11(12):e0167561.

The CYCLE program included several feasibility studies and pilot (and vanguard) trials, all in preparation of the main trial

CYCLE: Critical Care Cycling to Improve Lower Extremity Strength

CYCLE
Preparation phase

ICAN Rehab

Survey development: pt, family, clinician satisfaction with rehab
Pilot & Feasibility Studies 2019

CYCLE-R

Systematic Review *In progress*

Uni-CYCLE

Retrospective chart audit ✓ *JCC 2015*

TryCYCLE:
Phase II
open label study

1 center, 33 pts
prospective cohort
- Design the intervention; select outcomes; assess fidelity, safety, satisfaction, and acceptability
✓ *PLoS One 2016*

CYCLE Pilot RCT:
Phase II pilot randomized trial

7 center, 66 pts
Feasibility ✓ *BMJ Open 2016 (protocol); BMJ Open Resp Res 2019*

CYCLE Vanguard
Pilot RCT *(added)*

6 center, 40 pts
Refinement;
Finished recruitment

CYCLE RCT:
Phase III randomized trial

Multicenter RCT
In progress

CYCLE$

Economic evaluation *In progress*

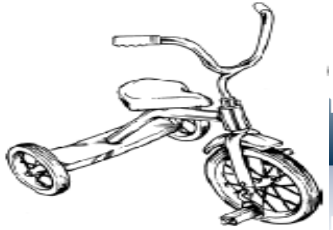
BICYCLE

KT Behavioural Intervention

Trial methodology questions:

Pilot RCT 5 lessons learned
Trials 2019

Barriers and facilitators to physiotherapist trial involvement
Pilot & Feasibility Studies 2019



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The PAFS group has worked hard to change practice including providing stakeholders with a platform to publish PAFS and share resources

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Gillian Lancaster, Editor-in-Chief

Gillian Lancaster is Professor of Medical Statistics at the Institute of Primary Care and Health Sciences, Keele University. She has been engaged in many multidisciplinary clinical investigations over the past 25 years, most notably the Working Group that developed the CONSORT extension guideline for reporting pilot and feasibility trials. Her research scopes many medical and social issues, with a specific interest in methodology for developing Patient Reported Outcome Measures and assessment tools for use on children and young people. More broadly she has served on a wide range of research review, pediatric ethics, funding, data monitoring and trial steering committees, has sat on the Council of the Royal Statistical Society and has been Associate Editor for the RSS Journal Series A: Statistics in Society.

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Lehana Thabane, Editor-in-Chief

Lehana Thabane is a Professor of Biostatistics and Associate Chair of the Department of Health Research Methods, Evidence, and Impact; associate member of the Departments of Pediatrics and Anesthesia at McMaster University (Hamilton, Ontario, Canada). He is the Director of Biostatistics at St Joseph's Healthcare—Hamilton (Ontario, Canada) and Senior Scientist at the Population Health Research Institute (PHRI) of the Hamilton Health Sciences and McMaster University. As a biostatistician and research methodologist, Professor Thabane's primary research interests include: i) design and analysis of clinical trials, pilot and feasibility trials, pragmatic trials, registry-based trials, and knowledge translation trials; ii) outcomes research; iii) evidence synthesis methods; and iv) mentorship in clinical trials. He is also interested in transparent reporting of trial findings, and he is a member of the Working Groups of the CONSORT extension to: a) Pilot and Feasibility Trials; and b) Cohort- and Registry-Based Trials.

All members of the Working group are founding editorial board members

We published the CONSORT extension to pilot RCT paper

Eldridge *et al. Pilot and Feasibility Studies* (2016) 2:64
DOI 10.1186/s40814-016-0105-8

Pilot and Feasibility Studies

international behavioural trials network

RESEARCH Open Access

CONSORT 2010 statement: extension to randomised pilot and feasibility trials

Sandra M. Eldridge[1*], Claire L. Chan[1], Michael J. Campbell[2], Christine M. Bond[3], Sally Hopewell[4], Lehana Thabane[5], Gillian A. Lancaster[6] and on behalf of the PAFS consensus group

RESEARCH METHODS AND REPORTING

OPEN ACCESS

CONSORT 2010 statement: extension to randomised pilot and feasibility trials

Sandra M Eldridge,[1] Claire L Chan,[1] Michael J Campbell,[2] Christine M Bond,[3] Sally Hopewell,[4] Lehana Thabane,[5] Gillian A Lancaster[6] on behalf of the PAFS consensus group

the bmj | *BMJ* 2016;355:i5239 | doi: 10.1136/bmj.i5239

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This website is designed to support those conducting pilot and feasibility studies using randomised and non-randomised designs and those carrying out methodological research on these types of studies.

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Points for discussion

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- Are trials with surrogate endpoints pilot trials?
- How concrete must the aspiration of a main trial be for a pilot/feasibility trial to be called a pilot/feasibility trial?
- Can one conduct a pilot/feasibility trial in the vague hope that someone else will run a main trial?


thank you
شكراً جزيلاً
ngiyabonga
рахмат
danke
謝謝
teşekkür ederim
Баярлалаа
mersi
kia ora
barka
welalin
spas
tack
mahalo
tapadh leat
спасибо
faafetai lava
vinaka
спасибі
blagodaram
dank je
misaotra
matondo
paldies
grazzi
gracias
kiitos
dankie
nanni
nandri
dhanyavad
mauruuru
köszönöm
hvala
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bayarlalaa
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