Why and what are we controlling…?

Reflections on how to design and manage control groups in hybrid effectiveness-implementation trials

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Professor Nick Sevdalis

Academic Director, Centre for Behavioural & Implementation Science Interventions, NUS Yong Loo Lin School of Medicine

nick_sev@nus.edu.sg – bisi@nus.edu.sg

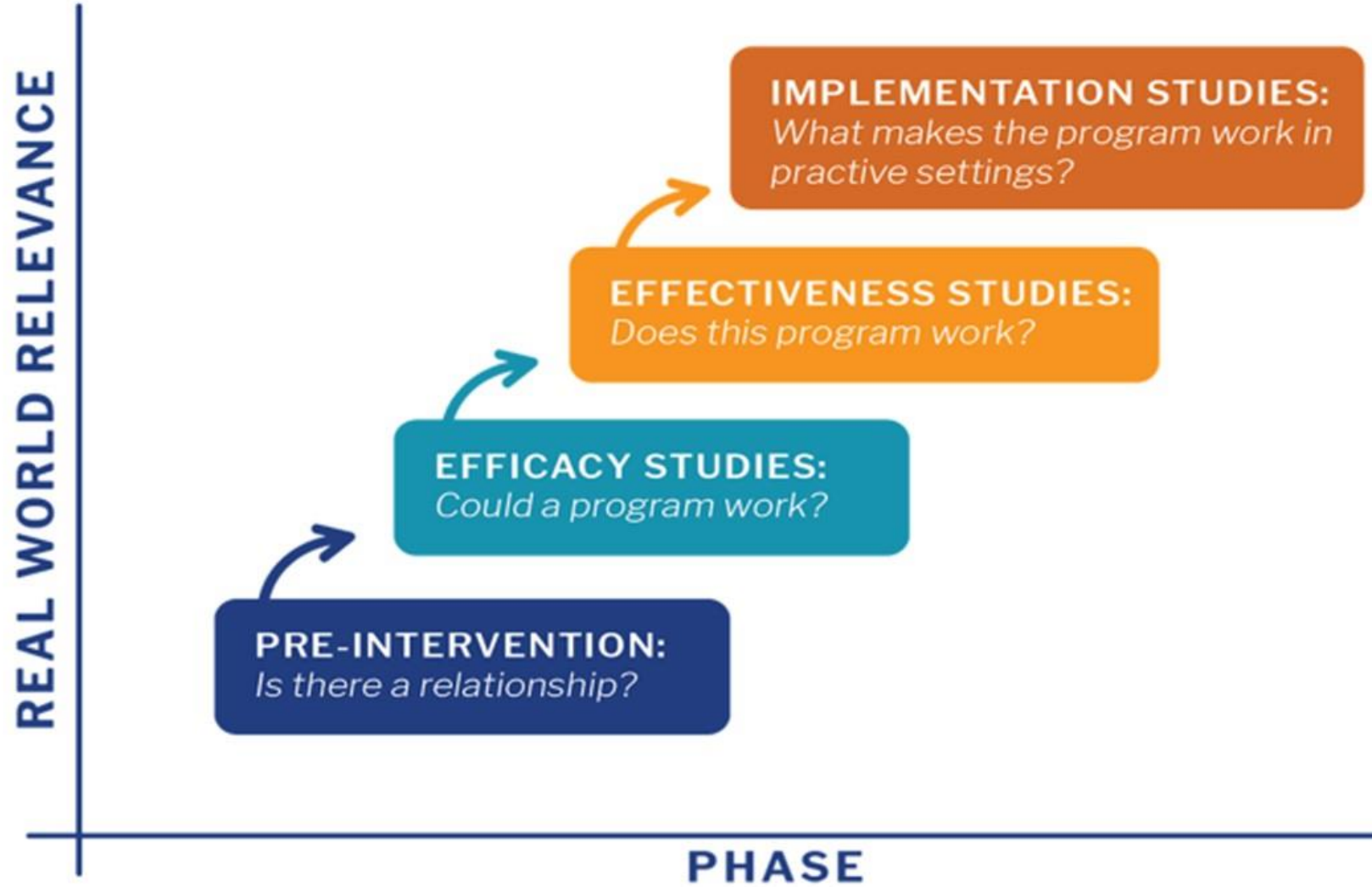
https://medicine.nus.edu.sg/bisi/

My aims today

- To offer an overview of the **nature of control groups** in effectiveness-implementation hybrid trials
- To articulate **what is being controlled and with what aims** and explore rationales for the choice of controls
- To present **illustrative case studies** of hybrid trials, demonstrating different considerations in selecting control groups
- To share and discuss my personal experiences of setting up and managing control groups, including **how to manage potential tensions arising in control arms** of hybrid trials

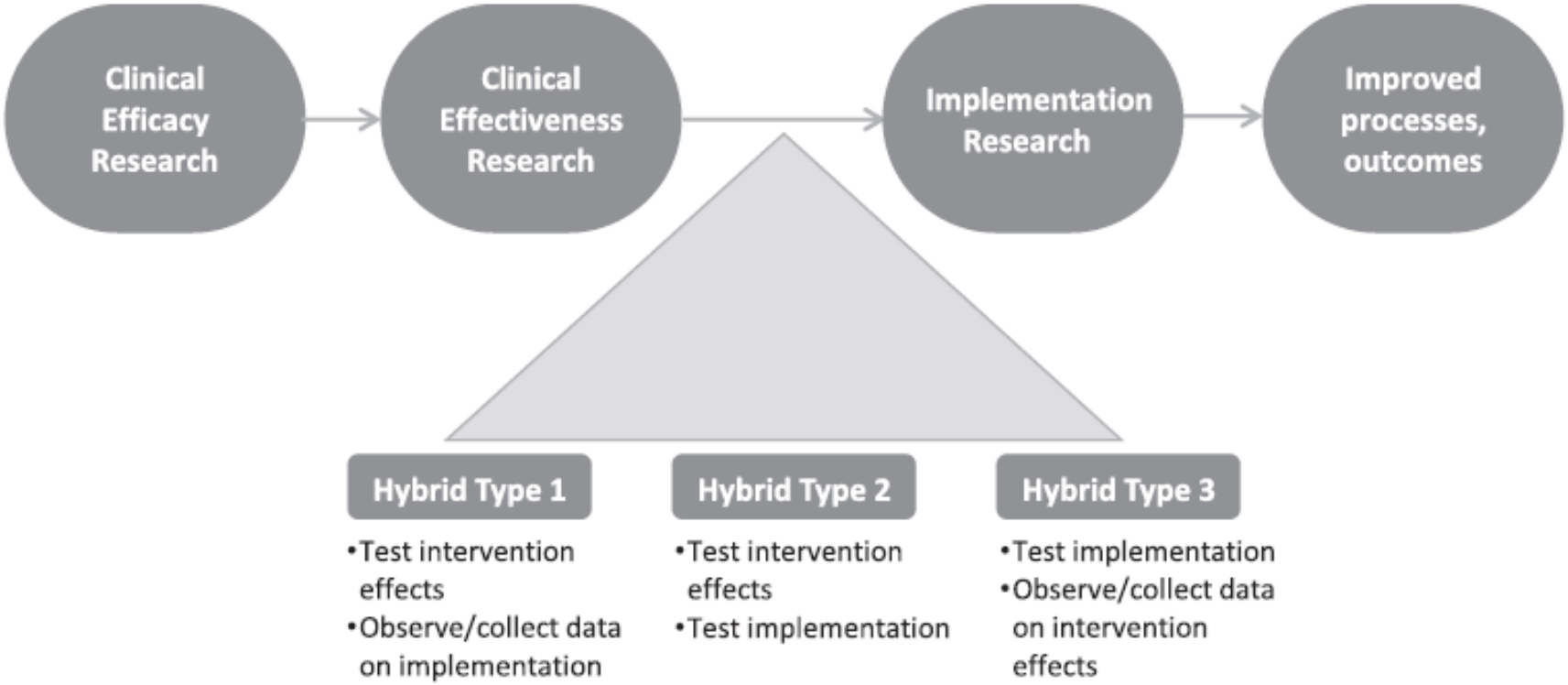
Essentially I would like to share a story of a challenge we faced in doing an implementation trial and seek your help…!

Translational pathway for research



HARVARD CATALYST

The concept of 'hybrid' RCTs



Curran et al, *Med Care* 2012;50:217-26
Schliep et al, *Evid Based Commun Assess Interv* 2017:11:82-98

What prompted my thinking about control groups in such trials?

The OASI care bundle: OASI1 trial

1. **Inform the woman** about OASI and what can be done to minimise her risk.

2. Documented use of **manual perineal protection** (MPP):
   - For spontaneous births, MPP should be used unless the woman objects, or her chosen birth position does not allow for it.
   - For operative vaginal births MPP should always be used.

3. When indicated, **episiotomy** should be performed **mediolaterally** at a **60-degree angle** at **crowning**.

Following birth, the **perineum should be examined** and any tears graded according to the RCOG guidance. The examination should include a **per rectum** check even when the perineum appears intact.

- Evaluated across 16 maternity units in the UK; N=55,060 live births
- Stepped wedge evaluation design, allowing controls: gradual implementation across 4 units at a time
- OASI rate 3.3% reduced to 3%
- Qualitative studies describe barriers and facilitators in using the care bundle

DOI: 10.1111/1471-0528.16396
www.bjog.org
Original Article
Intrapartum care

Impact of a quality improvement project to reduce the rate of obstetric anal sphincter injury: a multicentre study with a stepped-wedge design

I Gurol-Urganci,[a,b] P Bidwell,[b] N Sevdalis,[c] L Silverton,[d] V Novis,[b] R Freeman,[e] A Hellyer,[b,f] J van der Meulen,[a] R Thakar[g]

International Urogynecology Journal
https://doi.org/10.1007/s00192-021-04786-y

CLINICAL OPINION

The OASI care bundle quality improvement project: lessons learned and future direction

Magdalena Jurczuk[1] · Posy Bidwell[1] · Ipek Gurol-Urganci[1,2] · Jan van der Meulen[2] · Nick Sevdalis[3] · Louise Silverton[4] · Ranee Thakar[5]

The OASI care bundle: OASI2 trial

- Aim: to evaluate implementation strategies that will allow the OASI care bundle to be successfully implemented nationally
- We did not evaluate its clinical effectiveness (already shown) – so ALL study units received the care bundle
- Trial intervention: level of implementation support
- *Lean units (controls)*: receive booklets
- *Peer-supported units*: receive booklets + external OASI facilitator (from unit where OASI had already been implemented)

Study protocol

OASI2: a cluster randomised hybrid evaluation of strategies for sustainable implementation of the Obstetric Anal Sphincter Injury Care Bundle in maternity units in Great Britain

Jurczuk et al, Implement Sci 2021;16(1):55

Early control group design considerations

- Do we need a **controlled evaluation** in the first instance – i.e, should we not try to maximise uptake and scale-up based on OASI1 findings instead?
    - We do, *because we do not have good enough evidence for what works in terms of scale-up strategies*
    - *Funder well-informed about implementation science* and keen on generating high quality implementation evidence for national scale-up

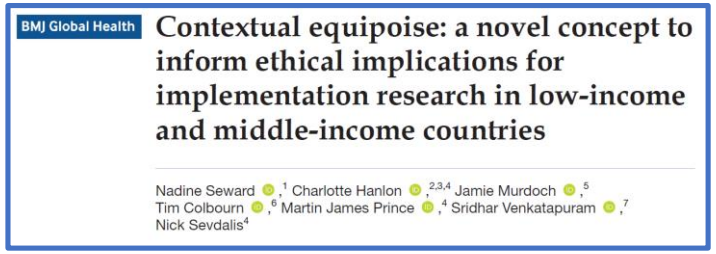
Early control group design considerations

- What would a **suitable control group** look like?

    - *Doing absolutely nothing was not an option*, because:
        I. It *did not seem representative of NHS reality* for guideline implementation
        II. It *risked making this a 'so what' project* (i.e. who would be surprised to observe better uptake compared to units with literally zero support?!)
        III. We hypothesised that peer-support would improve implementation, but that *high-quality manuals would also support it well-enough*

Wider issues regarding control group selection

- **Contextual equipoise**
  - Genuine uncertainty about whether known implementation strategies will support effective delivery of an evidence-based practice in a new context
  - We developed this concept in the context of global health research, but we feel it applies to several implementation research contexts


BMJ Global Health

Contextual equipoise: a novel concept to inform ethical implications for implementation research in low-income and middle-income countries

Nadine Seward [1], Charlotte Hanlon [2,3,4], Jamie Murdoch [5], Tim Colbourn [6], Martin James Prince [4], Sridhar Venkatapuram [7], Nick Sevdalis[4]

Seward et al, BMJ Global Health 2020;5:e003456

- **Ethical considerations**
  - We know that the OASI care bundle can improve women's outcomes, so would it be ethical to use a 'do nothing' control? – No!

- **Practical considerations**
  - Clinicians were very clear that a 'do nothing' control would make the trial unfeasible – i.e. already pressurized maternity units seemed to want something 'in return' for taking part in a complex research project

Mid-study control group management considerations

- Where is the defining line between **study management vs control group contamination**?
  - OASI2 was led by the *2 prime professional organisations* for maternity care in the UK, the Royal College of Midwives and the Royal College of Obstetricians and Gynaecologists
    - This was done intentionally, so that the OASI studies have senior national leadership and a good chance of their results informing national policy
  - Control sites were exposed to *news stories and commentary regarding the OASI care bundle*; they were getting in touch with the study team who they saw as national leaders for support in resolving implementation questions arising locally + queries and barriers regarding practicalities of the research (e.g., slow data collection, slow rate of recruitment, low staff availability etc.)
  - *From my point of view, I was not always clear where to draw the line between supporting the conduct of the research vs supporting the actual implementation process*

So what do control groups look like in the implementation science evidence base?

We studied (and shared) our challenges!

Phase 1: rapid narrative review

- Aim: to identify control group designs in the evidence base
- PubMed search (latest in Feb 2022)
- Search terms (in titles or abstracts of hybrid type III studies published in English)
    - Hybrid, effectiveness, implementation

Phase 2: comparative case study

- Aim: to consider a typology of control groups as revealed by the evidence base and reflect with their designers on their selection and implementation in studies
- Identified ‘exemplar’ study designs following Phase 1 findings
- Conducted brief structured telephone interviews with lead study authors
    - How were the controls selected, how were they managed throughout the study, how did they implement any improvements or adaptations to the implementation support materials

Phase 1 (review) results

- 670 study reports assessed
- Following screening, 45 reports of hybrid III studies with control groups reviewed
- Control group typologies:
  - **17 studies: A vs A+,** where A offers baseline implementation support and A+ offers baseline + some additional support
  - **26 studies: A vs B**, where two entirely different implementation support structures are compared
  - 2 studies: unable to classify

Phase 2 (comparative case study) results

Category of hybrid type-3 trial	Case	Clinical intervention	Site of implementation	Comparison/control arm	Intervention arm
A vs. B	P4AE1[a]	Physical activity programme	Secondary schools in New South Wales, Australia	Received no additional support/ materials	Internal facilitator trained to support each school throughout the study to implement a bundle of implementation strategies for programme roll out
A vs. A+	CATCHUP[b]	Insurance re-enrolment tool	Community Health Clinics in the US	Received educational materials only	Received educational materials + an external practice facilitator offering on-site, face-to-face trainings and support.
A vs. A+	OASI2[c]	Care Bundle to prevent childbirth injury	20 NHS maternity units in Great Britain	Received implementation toolkit and required to nominate two internal facilitators prior to study start	Received implementation toolkit, required to nominate two internal facilitators prior to study start, external experienced facilitator from within the same region to offer continuous support

P4AE1 study: Sutherland et al, BMC Public Health 2013;13:57
CATCHUP study: Hatch et al, BMC Health Serv Res 2020;20(1):428
OASI2 study: Jurczuk et al, Implement Sci 2021;16(1):55

Phase 2 (comparative case study) results

From the brief interviews

- Shared experiences:
  - Some *tension between 'hands off' management of control groups vs some support* to ensure study delivery
  - CATCHUP study team *organized meetings to respond to study site requests* for assistance (but then only signposted to the original educational materials provided) – so as not to render study unfeasible
  - The PA4E1 study team offered *reactive support to study implementation* to the schools that requested it
  - The OASI2 team initially received site feedback and *included edits to the implementation manuals*; these were kept unchanged during the 2nd half of the data collection
  - The OASI2 team also had *requests for the implementation manuals from non-study sites* – due to national publicity about the OASI care bundle. We disseminated the materials after all control sites had been enrolled

The full story here

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EDITED BY
Xiaolin Wei,
University of Toronto, Canada

REVIEWED BY
Jamie Murdoch,
King's College London, United Kingdom

*CORRESPONDENCE
Magdalena Jurczuk
mjurczuk@rcog.org.uk

†These authors have contributed equally to this work and share senior authorship

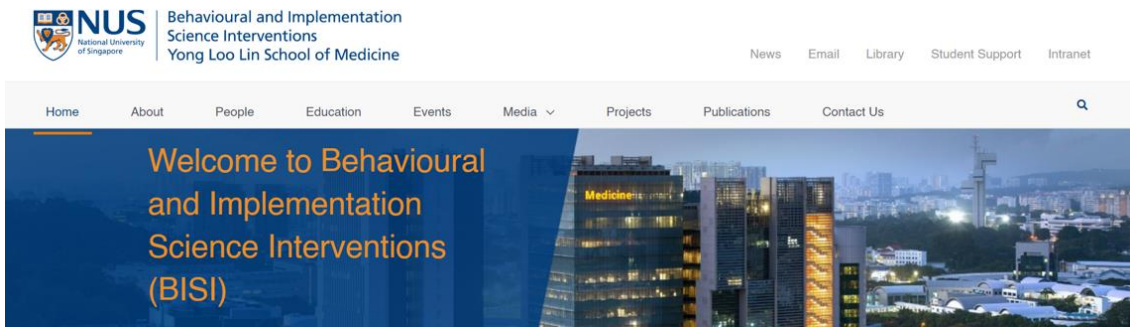
Design and management considerations for control groups in hybrid effectiveness-implementation trials: Narrative review & case studies

Magdalena Jurczuk[1*], Ranee Thakar[2], Fran E. Carroll[1], Lizzie Phillips[1,3], Jan van der Meulen[4], Ipek Gurol-Urganci[1,4†] and Nick Sevdalis[5†]

Jurczuk et al, Frontiers Health Serv 2023;3:1059015

Where do we stand? Questions for us to think about

- *What control group, if any, is ethically justifiable* in an implementation study?
- How do we balance the *need for internal study validity vs the need to pragmatically scale-up an intervention* of proven effectiveness (assuming the latter)?
- Are traditional controlled designs too static for some implementation questions – are *iterative study designs better suited to study implementation processes*?
- *Adaptations to interventions and/or implementation strategies seem to happen all the time, including in the context of RCTs* – is this your experience too?



Thank you

nick_sev@nus.edu.sg – bisi@nus.edu.sg

https://medicine.nus.edu.sg/bisi/