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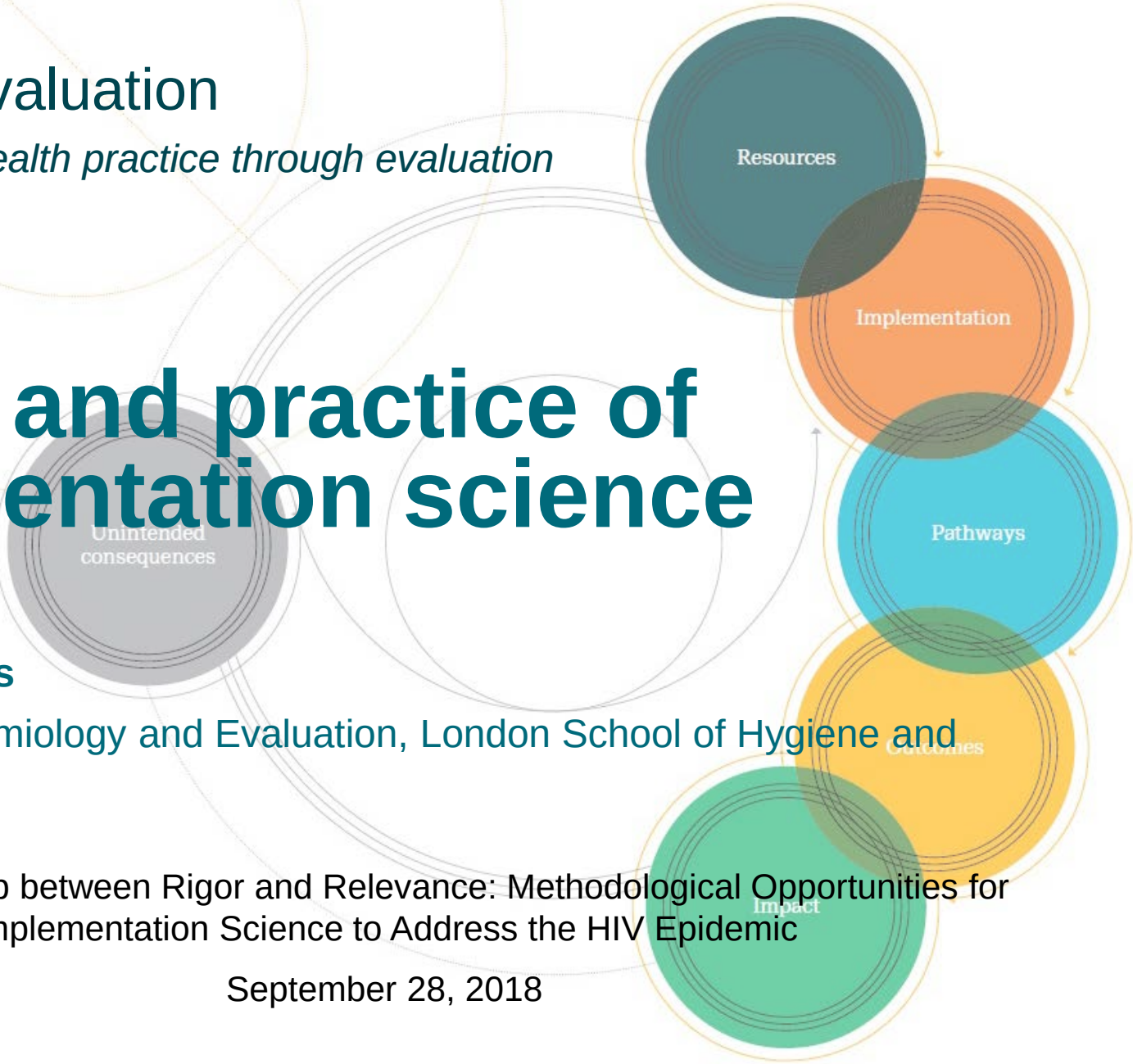
Improving global health practice through evaluation



Design and practice of implementation science trials

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Closing the Gap between Rigor and Relevance: Methodological Opportunities for Implementation Science to Address the HIV Epidemic

September 28, 2018

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

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Some biography and background

- Three overlapping interests:
  - HIV epidemiology and prevention in Africa
  - Social and structural inequalities in, and determinants of, health
  - Evaluation of ‘complex’ interventions

Implementation science and me

- Initial reservations
- Ongoing paper rejections, definitions …
- CROI: “the rules of RCTs” talk
- Evaluation = Implementation Science?
- Diving in a bit further, several talks (IAS, AHRI, AIDS 2018, here …)
- Stepped wedge trials
- “Learning more” work for Centre for Excellence in Development Impact and Learning (CEDIL)
- AIDS 2018 Rapporteur

What did we look for in Track E at AIDS 2018?

ART

Tests

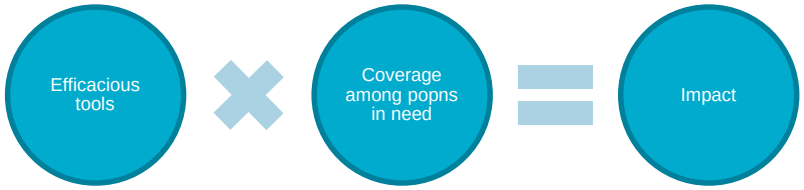
Condoms

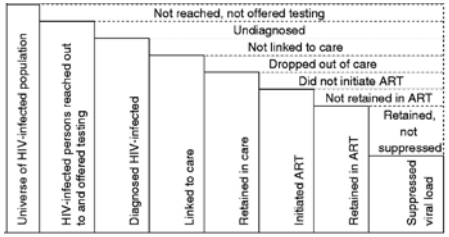
PrEP

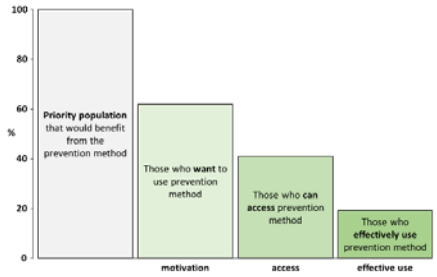
VMMC

Safe sexual behaviour

…







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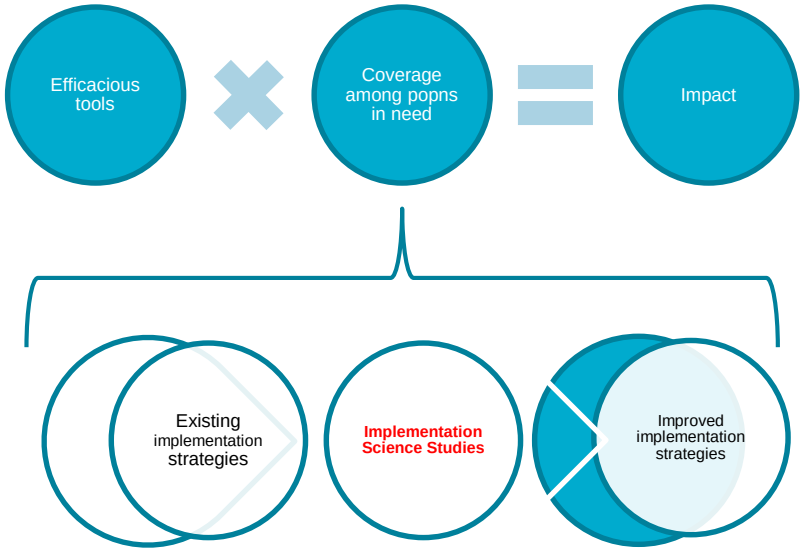
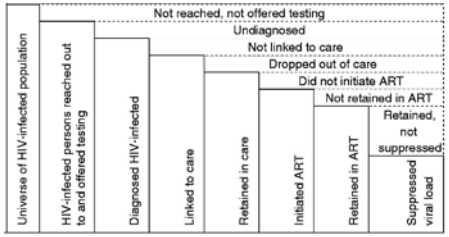
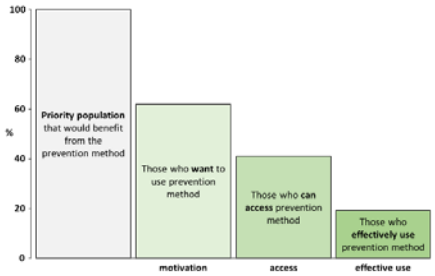
What did we look for in Track E?



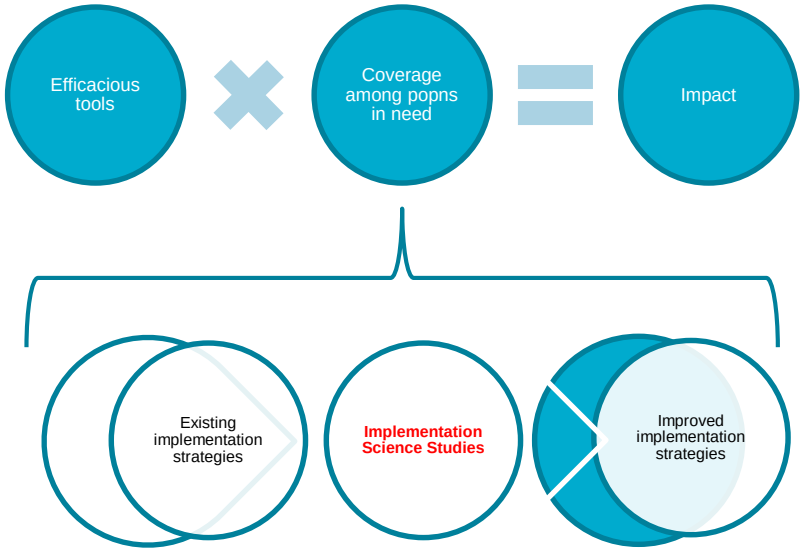


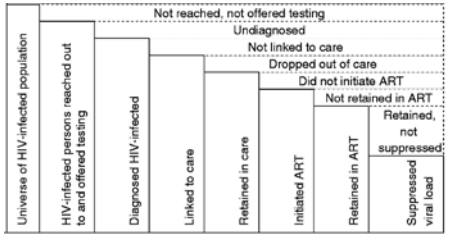


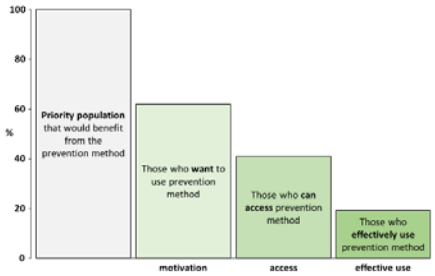
Implementation strategies are complex interventions:

- Targeting and differentiation
- Programme components
- Platforms for delivery
- Vertical / horizontal
- Intersectoral synergy
- Cost / financing
- Data systems
- Policy

What did we look for in Track E?







- Rigorous, pragmatic impact evaluations
- Process evaluation of programme implementation
- Costing / cost effectiveness studies
- Robust service delivery data to track the epidemic and drive the response
- Systematic Reviews of implementation studies
- Policy research and new policies relevant to implementation and financing

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And … what's missing?

And what did we find …

- Thin on the ground
  - Combination Prevention Implementation Science
  - Systematic reviews of Implementation Science
  - Innovative use of strong routine data
  - Costing and financing studies

- Developing agenda
  - Large UTT trials
  - Emerging PrEP agenda
  - Studies of implementation innovations in testing, linkage and retention

Ten issues in the design and practice of implementation science trials

Implementation science randomised trials: some views

- You shouldn't (Farmer, 2013 Lancet Global Health blog)
- You can't (Bonell, JECH 2013)
- Aren't appropriate (Bertozzi, Lancet 2008; some from social science)
- Are useless if they don't measure "hard", "biological" endpoints (various, World Bank)
- Should be quicker and cheaper than "research" trials (various)
- Should use routine data to measure outcomes (Padian, pers comm. 2018 – data not checked with respondent)
- Should be 'Realist' trials (Bonell, SSM)

CROI 2016: Implementation Science Trials – do the rules of RCTs apply?

- Rules of RCTs – **Yes, they apply*!**
    - Randomisation*, Pre-specification, Ethics, Reporting (CONSORT)
- Non-rules of RCTs
    - Expensive/Big, Highly controlled, Hard “biological” endpoints
- Four implementation science adaptations, with examples

Issues 1 and 2: Cluster randomised trials of complex to characterise interventions and questions

1. From individual randomisation (HPTN 052) to cluster randomisation (HPTN 071)

2. Defining interventions and framing questions

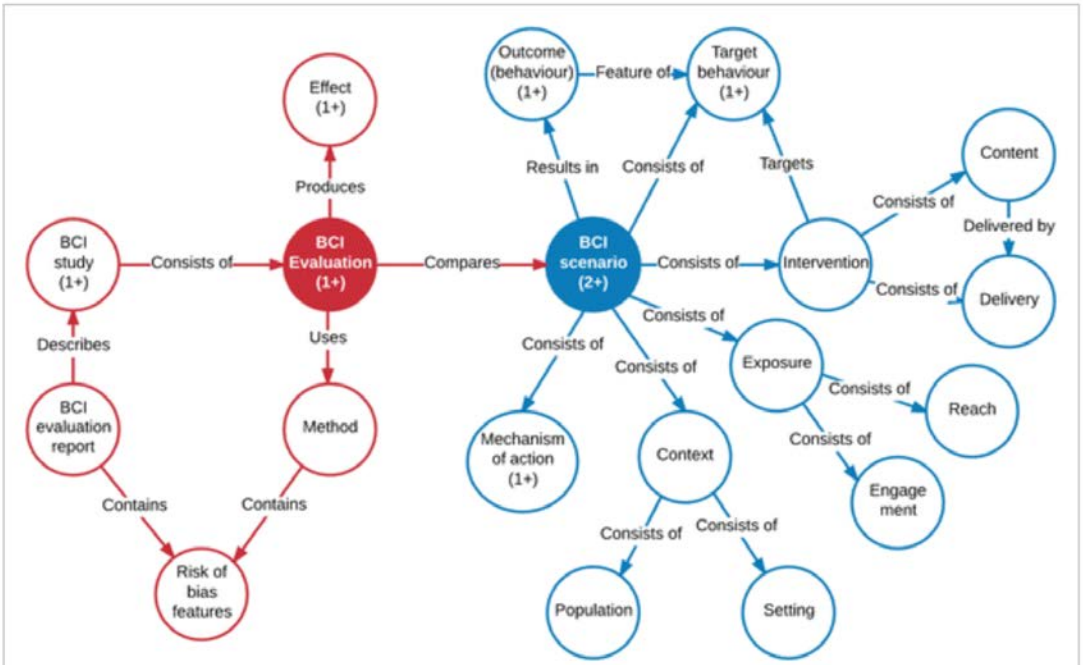


Fig. 1
Key upper-level entities and examples of relationships to be captured in the BCIO. Numbers in brackets refer to the number of entities required if not 1

Issues 3 and 4: Being pragmatic in intervention and control arms

3. Monitor as in real life and measure outcome among those intended to benefit - SAPPHIRE trial (Lancet HIV, 2018)

4. What's going on in the comparison arm (SEARCH, AIDS 2018)?

Summary

SEARCH
SUSTAINABLE EAST AFRICA RESEARCH IN COMMUNITY HEALTH

A community health approach with a patient- centered, multi-disease model rapidly increased population-level HIV suppression from 42% to 79% (intervention)-compared to control (68%) at 3 years

Improved Community Health	Reduced HIV incidence
↓ 21% HIV mortality	↓ 32% Annual HIV incidence within arm
↓ 59% HIV/TB year 3 annual incidence	↔ Cumulative HIV incidence between arms*
↑ 26% HT control	
Explanation: SEARCH intervention	*Explanation: Active control

Hypothesis: Community health approach with patient-centered, multi-disease model would reduce HIV and improve community health compared to SOC with baseline HIV testing
Study Design: 32 community RCT: N= 150,395 persons > 15 years rural Uganda/Kenya
Intervention: Baseline + annual health fair, Universal ART, Streamlined care for HIV/NCD
Control: Baseline health fair; ART by 2010,2013,2015 WHO guidelines

Issues 5 and 6: Evaluating processes and considering generalisability

5. Evaluating process is essential! Example: IMAGE trial (Lancet, 2006)

6. We need to "learn more" than just did this work here

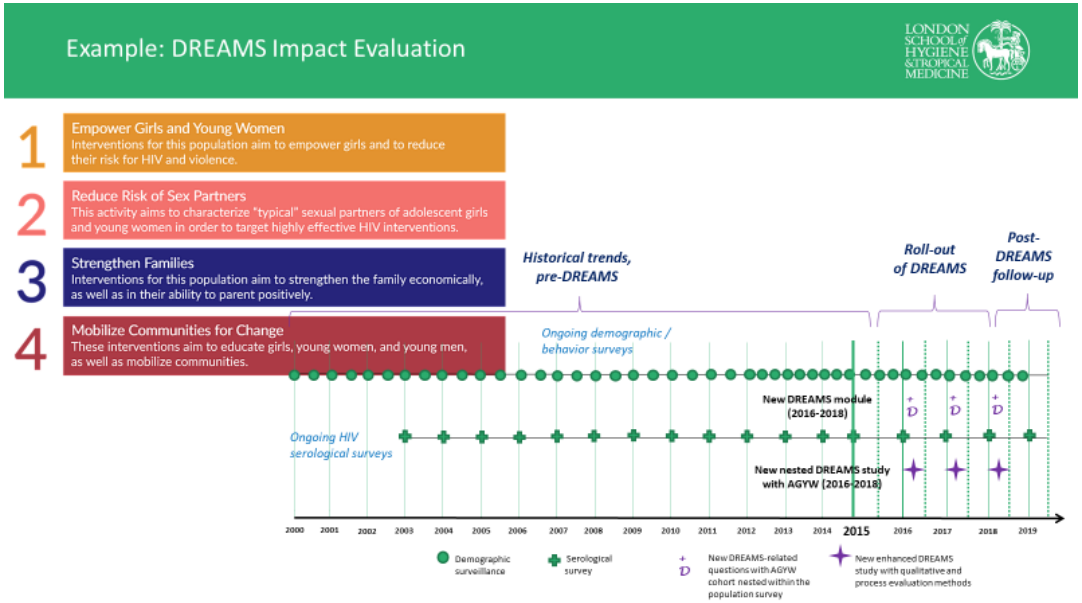
"Learning more" (forthcoming CEDIL working paper, Davey et al)

Intervention concepts	• Fidelity of form, feasibility of implementation and adaptation • Fidelity of function, and interventions as events in systems • Transferability, generalisability, external validity and transportability
Mechanisms and theories	• Context-mechanism-outcome configurations • Mid-range theories • Mathematical models of systems • 'Markers' of Context
Four evaluation approaches to inform action in new settings	1. Framing evaluation questions to test theories rather than interventions 2. Process evaluation with mixed methods 3. Leverage heterogeneity (i) to understand context 4. Leverage heterogeneity (ii) using case studies

Issue 7 and 8: Be innovative when randomisation isn't possible, and leverage opportunities to be

7. There are rigorous, transparent non-randomised designs available. Example: DREAMS Impact evaluation (2016…)

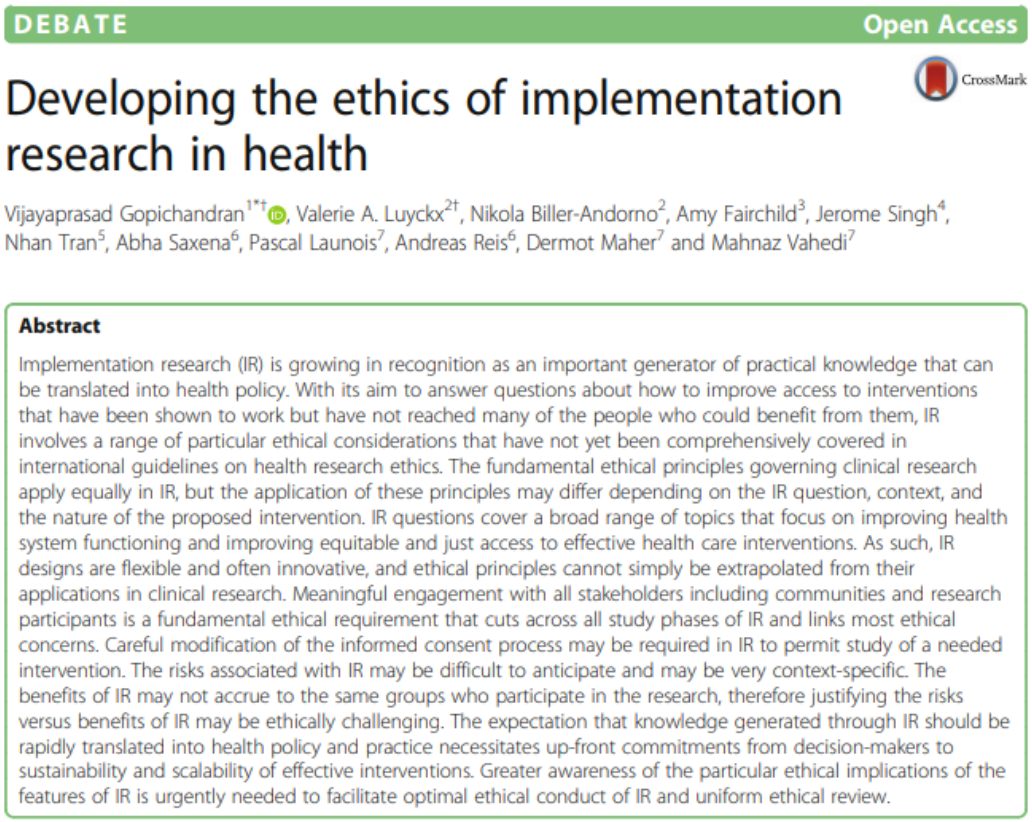
8. How do we ensure opportunities to be rigorous and learn are being realised?



Issues 9 and 10: Strengthen routine data and develop ethics frameworks for Implementation

9. Service delivery and behavioural data need to be strong to realise the promise of Implementation Science. MeSH Consortium (2014…)

10. Have we got the ethical frameworks right?



DEBATE Open Access

Developing the ethics of implementation research in health

Vijayaprasad Gopichandran[1*†], Valerie A. Luyckx[2†], Nikola Biller-Andorno[2], Amy Fairchild[3], Jerome Singh[4], Nhan Tran[5], Abha Saxena[6], Pascal Launois[7], Andreas Reis[6], Dermot Maher[7] and Mahnaz Vahedi[7]

Abstract

Implementation research (IR) is growing in recognition as an important generator of practical knowledge that can be translated into health policy. With its aim to answer questions about how to improve access to interventions that have been shown to work but have not reached many of the people who could benefit from them, IR involves a range of particular ethical considerations that have not yet been comprehensively covered in international guidelines on health research ethics. The fundamental ethical principles governing clinical research apply equally in IR, but the application of these principles may differ depending on the IR question, context, and the nature of the proposed intervention. IR questions cover a broad range of topics that focus on improving health system functioning and improving equitable and just access to effective health care interventions. As such, IR designs are flexible and often innovative, and ethical principles cannot simply be extrapolated from their applications in clinical research. Meaningful engagement with all stakeholders including communities and research participants is a fundamental ethical requirement that cuts across all study phases of IR and links most ethical concerns. Careful modification of the informed consent process may be required in IR to permit study of a needed intervention. The risks associated with IR may be difficult to anticipate and may be very context-specific. The benefits of IR may not accrue to the same groups who participate in the research, therefore justifying the risks versus benefits of IR may be ethically challenging. The expectation that knowledge generated through IR should be rapidly translated into health policy and practice necessitates up-front commitments from decision-makers to sustainability and scalability of effective interventions. Greater awareness of the particular ethical implications of the features of IR is urgently needed to facilitate optimal ethical conduct of IR and uniform ethical review.

Closing thoughts: What I want from my implementation science

- To be **defined by the questions** it addresses not the methods it deploys
- To rigorously answer relevant questions about what **strategies** will maximise the **population impact in the real world** of tools & know-how of "known" efficacy
- To **build iteratively through synthesis** of primary studies to inform decisions and/or research needs in relation to maximising programme impact in current and other settings
- To apply the highest, most appropriate **ethical standards**
- To be **empowering** for communities, providers and decision makers

- Implementation Science Trials can contribute to this agenda, but they will need to tackle with a range of design and practice issues to fulfil their promise

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