# Ethics in cluster randomized trials

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ENGAGING SCIENCE.

# Why do CRTs pose ethical issues?

# 1. CRTs involve groups rather than individuals

## Individual randomized controlled trials:

- Involve individuals, commonly patients
- Ethics are well understood and aim to protect the liberty and welfare of individuals

## Cluster randomized controlled trials:

- Involve social groups, the moral status of which is not well understood
- Group interests may conflict with individual interests, complicates benefit-harm assessment

## 2. The units of randomization, intervention, and outcome assessment differ within any given trial

### Individual randomized controlled trials:

- Units of randomization, intervention and outcome assessment are the same

### Cluster randomized controlled trials:

- Complex and have multiple levels
- Complicates the identification of research participants
- From whom is informed consent required?

# 3. Clusters may be randomized before cluster members can be approached for informed consent

## Individual randomized controlled trials:

- Patients are identified and approached for consent prior to study participation

## Cluster randomized controlled trials:

- Clusters may be randomized prior to identification of individual cluster members
- Is consent to randomization required?
- May gatekeepers provide consent to randomization?

# 4. Intervention may be directed at the level of the individual or the level of the cluster

## Individual randomized controlled trials:

- Study interventions are directed at the patient

## Cluster randomized controlled trials:

- Study interventions may be directed at the individual or the cluster, or both
- Cluster-level interventions may be difficult for cluster members to avoid
- Refusal of study participation may be meaningless

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Guidelines and Guidance

# The Ottawa Statement on the Ethical Design and Conduct of Cluster Randomized Trials

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## Introduction

Cluster randomized trials (CRTs), also known as group randomized, place-based, or community intervention trials, are

systematically explored. As a result, researchers and research ethics committees (RECs) currently lack specific guidelines to help them design, conduct, and review CRTs according to interna-

tionally accepted ethical standards. Predictably, the lack of

# *Ottawa Statement* (2012)

1. Justifying the cluster randomized design
2. REC review
3. Identifying research participants
4. Obtaining informed consent
5. Gatekeepers
6. Assessing benefits and harms
7. Protecting vulnerable participants

# Who is the research participant?

# Research participants

- The units of randomization, intervention, and outcome assessment differ within any given trial
- Identification of research participants is logically prior to the application of protections

- Two errors:
  - Over-inclusive definition runs the risk of unduly burdening research
  - Under-inclusive definition will fail to provide protections to those who have a right to them.

# Research participants

- An individual whose interests may be affected by study interventions or data collection procedures
- A research participant is an individual…
  1. Who is the intended recipient of an experimental (or control) intervention; or
  2. Who is the direct target of an experimental (or control) manipulation of his/her environment; or
  3. With whom an investigator interacts for the purpose of collecting data about that individual; or
  4. About whom an investigator obtains identifiable private information for the purpose of collecting data about that individual.

# Research participants

- In public health studies in which an entire community is intervened upon, all community members may be research participants

- In knowledge translation studies, health professional who are intervened upon are research participants
- Patients of those health professionals are not research participants unless they are otherwise intervened upon, interacted with, or their private health information is collected.

# Research participants

Devon Active Villages Evaluation trial (cluster-cluster)

- Residents of villages (2+3)

Computerized guidelines for asthma/ angina (professional-cluster)

- Physicians (1)
- Patients (3+4)

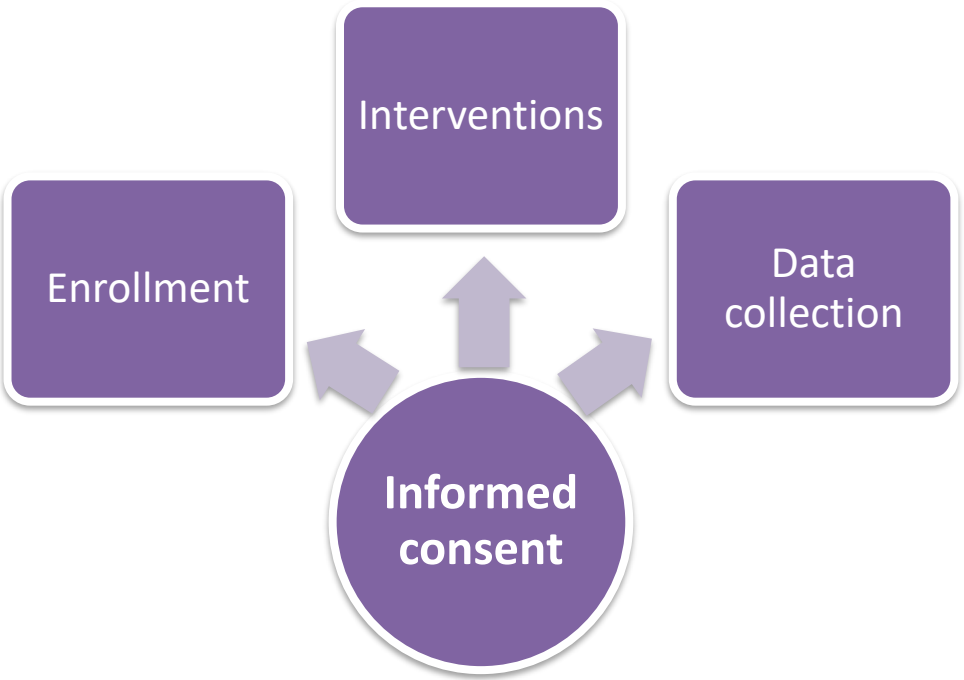
Cleansing of the umbilical stump (individual-cluster)

- Mothers (3) and neonates (1)

# Who must provide informed consent?

# Informed consent

- “Researchers must obtain informed consent from human research participants in a CRT, unless a waiver of consent is granted by a REC under specific circumstances.”
- Heuristic: “Get consent where you can.”



# Informed consent

- Health providers commonly research participants in CRTs
  - Knowledge translation interventions
  - Health services interventions
- Researchers and RECs may fail to recognize health providers as research participants
- Health professionals are entitled to the protection of REC review and informed consent (unless a waiver applies).

# Informed consent

- Waiving the consent requirement can only be justified when it is necessary to do so, and when the risk involved is minimal

- According to the *Ottawa Statement* a waiver of consent may be appropriate when participation poses only minimal risk and:
  - Cluster-level intervention is difficult or impossible to avoid; or,
  - Due to cluster size or other factors, requiring informed consent makes the study infeasible.

# Informed consent

Devon Active Villages Evaluation trial (cluster-cluster)

- Waiver of informed consent for study intervention
- Consent for postal survey

Computerized guidelines for asthma/ angina (professional-cluster)

- Informed consent is required from physicians
- Waiver of consent for patient records; consent for postal survey

Cleansing of the umbilical stump (individual-cluster)

- Informed consent from mothers.

# What is the role of gatekeepers?

# Gatekeepers

- “[A]n individual, body, or mechanism that can represent the interests of the cluster”

- Gatekeepers do not have the authority to provide proxy consent on behalf of cluster members, and CRTs should not proceed on the basis of such “consent”.

# Gatekeepers

- When a CRT may substantially affect cluster or organizational interests, gatekeepers may protect group interests
- Consultation with cluster members may protect group interests by subjecting the study to examination and discussion by those whose interests may be affected

- Permission is appropriately sought when a gatekeeper has the legitimate political authority to provide it; for example:
  - School principal may provide permission after considering staff availability, financial implications, and teachers/students willingness

# Gatekeepers

Devon Active Villages Evaluation trial (cluster-cluster)

- Community consultation and permission

Computerized guidelines for asthma/ angina (professional-cluster)

- Permission of practice manager

Cleansing of the umbilical stump (individual-cluster)

- Permission of public health/ community development authority.

# Ethics and Pragmatic RCTs Research Group