

Cluster (group) randomized trials

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Cluster RCT

- Randomized experiment
- Unit of randomization=group
 - Natural aggregate
 - Organization
- Mostly used in pragmatic trials
 - Effectiveness in naturalistic setting

Examples of clusters frequently encountered in health-care research

- Primary care districts/doctors
- Hospital divisions
- Municipalities/regions
- Workplaces
- Schools/Classes/Teachers
- Temporal clusters

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Why cluster randomization?

- **Practical purposes**
 - Intervention can only be administered at cluster level (e.g. change in organization)
 - Wider reach
 - Increased compliance
 - Minimize contamination
 - Minimize ethical problems
- **Theoretical reasons**
 - Synergisms in the intervention (e.g. patients can be reached by the intervention only if staff is trained)
 - Need to study contextual variables (e.g. organization changes)

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What is so special with cluster-randomised trial?

- **The unit that is randomized** (the cluster)
→ e.g. the hospital division
- Is often the one at which the **intervention is delivered**
- But is not the same where the **outcome is measured**
→ e.g. patients
- Both ethical and methodological issues

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Ethical issue

- Individuals have a fixed probability to be included in a given intervention (given the cluster)
- In principle, they consent to data collection, not to be randomized
- What is the choice, if they opt-out?

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Methodologic issues



- Within each cluster, individuals tend to share some characteristics
- That may induce more similar trajectories of risk (outcomes) than
- Individuals belonging to different clusters

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På uppdrag av
Stockholms läns landsting



What do they have in common?

- **Primary care districts/doctors**
 - Patients
 - Age, treatments, advice
- **Hospital wards**
 - Patients
 - Treatments, equipments, staff composition, meals, physical environment
- **Municipalities/regions**
 - Residents
 - Air pollution, traffic
- **Workplaces**
 - Employees
 - Education, work-related exposures

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Shared characteristics may entail:



- Self-selection
 - E.g. behaviors, disease severity
- Shared exposures
- Spread of agents
- Mutual influences
- **Should be carefully documented!**

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Implications of the shared characteristics



- **Outcome variance of the recruited is the sum of**
 - Variance within the cluster : explained by individual variability
 - E.g. **Between individual patients in a primary care district**
 - Variance between the clusters: explained by cluster variability
 - E.g. **Between patients in different districts (e.g. due to staff)**
- **The more similar the individual in a cluster are the higher the cluster effect = intra-class correlation (ICC, ρ)**
- **The higher the ICC the less informative is the sample**

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Important consequences for:



- **Conduction of the trial (more challenging):**
 - Recruitment
 - Organisation
 - Standardization of the intervention
- **Internal validity**
 - Blindness often not possible
 - Power
 - Spurious standard error's estimate
- **External validity**
 - Selection at different levels (cluster and individual)
 - Implementation of the intervention

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Blindness



- **Intervention deliverer**
 - Often not possible
- **Individual participants (recipient of the intervention)**
 - Possible, but challenging
- **Outcome assessment**
 - Possible and often implemented

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Attrition (lost to follow-up)



- **Frequent both at cluster level and at individual level**

- **Cluster level drop-out**
 - Enormous loss of power
 - Almost always dependent on assignment to a particular intervention
 - And sometimes also on the group-level outcome

Example: staff may refuse continued cooperation because they find the intervention demanding

In a nutshell



- Cluster RCT should be carefully justified

- And carefully documented
 - Require own protocol and own reporting template
(CONSORT statement as in Campbel MK et al. BMJ 2012;345:e5661)

- **Be careful, out there!**



Thank you!
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