Designing trials within implementation laboratories

Discussion

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Outline

General thoughts & key themes from previous speakers

Outline future priorities

Lead discussion, based on priorities

General thoughts

RCTs in implementation labs need to move beyond basic two-arm parallel group RCTs

Much potential for more efficient designs: starting to be realised

- Answer multiple questions within single trials – complex factorial RCTs

UK example: **ENACT Enhancing NAtional Clinical audiT and feedbac*k***

'optimising content, format & delivery of feedback in national audits'

Web-based, **fractional factorial** screening experiment evaluating **six A&F modifications**

Uses subset of full factorial design

Statistical model predicts effects of all 6 A&F modifications & limited number of combinations

Evaluation across 4-5 audits: generalizable results; uptake across range of national audits

General thoughts (2)

Much potential for designing efficient trial implementation

- EHR / routine audit data offer advantages for trialists
  - Large numbers: patients & healthcare providers
    - High power
    - Ability to detect small effects
  - Low cost of obtaining outcome data

- But challenges too …
  - Handing missing data
  - Limited flexibility in data specification, timing etc

Standard & longitudinal cRCTs: key messages

- ‘Inspect power curve at design stage’ – **match design to best use of data**

  Think about

  Intended intervention effect; appropriate timing for primary outcome …

- Consider **advantages of longitudinal design** (pre & post repeated measures)

  ⇩ number of clusters (or power for important subgroups / smaller effects)

- Think about how to account for **learning & decay** effects

- Is **reliable data** available for complex sample size calculations?

- Remember **unduly restricting** number of clusters is risky

SMARTs: key messages

SMARTs are NOT **adaptive designs …**

… inform understanding of how to **adapt delivery** of implementation strategies

- **Robust design**
  - Large numbers – more nuanced understanding of implementation issues
  - Detection of delayed effects; protection against selection effects; retention for non-responding sites
- **Attractive to policy makers**
  - Decision makers can tailor more intense interventions for non- responders / poor adherers
  - Limited resources – results allow targeting to raise standards across the board

- **Challenging & complex designs to implement**
  - **Informed decisions up front:** which strategies to use & when, decision points, tailoring variables ….
  - Some relevant data may exist in EHRs, but some may not
  - Aligning decision points with available data across multiple sites at correct time points
- For clustered SMARTs, some **methods still in development**
- **End result: No classic evaluation** of the "best" adaptive implementation intervention

Multi-Arm Multi-Stage: key messages

Good potential to use these designs within implementation labs …

… but more work / adaption needed

- **Clustering**
  - Work required to adapt standard methods
- **Routine data**
  - Missing data? Bias?
  - No more issues than in regular trials … but adaptive approaches might help monitor more effectively for missing data issues
- **Drift over time** in standard of care and treatment effects
  - Causes issues in adaptive designs
  - Concurrent controls

Common methodological themes

Embedding trials within routine practice – how do we optimise designs?

➢ Strengths

- Efficient designs are feasible – ideally suited to answer relevant questions for policy-makers
- Large numbers of patients & sites available: high power; high external generalisability
- Low cost per patient evaluated

➢ Challenges

- How to adapt standard methods for clustering (adaptive trials, SMARTs)
- Large clusters: implications for power
- Limitations with use of routine data
- Outcome timing
- Learning/decay effects
- Effects in sub-groups
- Temporal effects

Future priorities …

- Methodological advances to **adapt methods** for use in implementation labs
- How to **maximize info** from trials – which design choices?
- How to **combine** adaptive design **AND** adaptive interventions?
- How to ensure implementation **laboratories talk to each other**?
  - 'Thoughtful' replication
  - Generalisability
  - Minimise research waste

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- Which methodological issues of most **relevance to healthcare organisations** to inform decision making?
  - Effect size: size? precision? identifying MCID? small change important?
  - Learning & decay effects?
  - Other issues?

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