Extending MRC Guidance on Developing and Evaluating Complex Health Interventions

Laurence Moore
Kathryn Skivington
Peter Craig

Sharon Simpson
Lynsay Matthews
Workshop Structure

- Brief introduction to MRC Guidance and aims & structure of workshop (5 mins)
- Presentation on: (i) the Guidance update (ii) GUEST study and iii) INDEX study (15 mins)
- Small group discussions (40 mins)
- Key gaps identified to date (10 mins)
The 2000 MRC Guidance

Framework for design and evaluation of complex interventions to improve health

Michelle Campbell, Ray Fitzpatrick, Andrew Haines, Ann Louise Kinmonth, Peter Sandercock, David Spiegelhalter and Peter Tyrer

BMJ 2000;321:694-696
doi:10.1136/bmj.321.7262.694

A FRAMEWORK FOR DEVELOPMENT AND EVALUATION OF RCTs FOR COMPLEX INTERVENTIONS TO IMPROVE HEALTH

This document is a discussion document drafted by members of the MRC Health Services and Public Health Research Board. It is intended to provide a framework for individuals considering the evaluation of a complex intervention. It does not set out a set of required steps in carrying out trials in this area.

April 2000

Fig 1. Sequential phases of developing randomized controlled trials of complex interventions
Phases of RCTs of complex interventions: MRC April 2000

Preclinical
Explore relevant theory to ensure best choice of intervention and hypothesis and to predict major confounders and strategic design issues

Phase I
Identify the components of the intervention and the underlaying mechanisms by which they will influence outcomes to provide evidence that you can predict how they relate to and interact with each other

Phase II
Describe the constant and variable components of a replicable intervention and a feasible protocol for comparing the intervention with an appropriate alternative

Phase III
Definitive randomised controlled trial
Compare a fully defined intervention with an appropriate alternative using a protocol that is theoretically defensible, reproducible, and adequately controlled in a study with appropriate statistical power

Phase IV
Long term implementation
Determine whether others can reliably replicate your intervention and results in uncontrolled settings over the long term

Continuum of increasing evidence
Why update?

- Incorporate experience gained since 2000
- Address limitations in the 2000 framework
  - Better definition of complexity
  - A less linear model of the evaluation process
  - More attention to piloting/development work
  - Randomised trials and alternative methods
  - Need to understand process as well as outcomes
  - Importance of context
  - Case studies more persuasive than didactic recommendations
Developing and evaluating complex interventions: new guidance

New MRC guidance on evaluating complex interventions

Clarifying what interventions work by researching how and why they are effective

It is eight years since the publication of the Medical Research Council's original report on methods for developing and evaluating randomised controlled trials for complex interventions. Although presented as a "discussion document," the MRC framework and its companion paper have often been cited as authoritative guidance on methods. Other people, however, have found the definition of the complexity of interventions narrow and misconceived, and the suggested phases for developing and evaluating complex interventions as unhelpfully similar to commercial drug evaluation. However, the report can probably be credited with stimulating much of the ongoing debate about appropriate methods and concepts in healthcare evaluation—particularly when the intervention of interest is hard to define, hard to evaluate (using conventional experimental methods), or hard to explain.

The MRC has now updated its original report (www.mrc.ac.uk/complexinterventionsguidance) to reflect recent developments in methods and lessons learned in applying them. The guidance is summarised in the linked article by Craig and colleagues (doi:10.1136/bmj.a1053). It has a broader scope than the original version—it covers observational methods as well as randomised controlled trials and implementation as well as the development and evaluation of interventions; it also has a broader definition of complex interventions beyond the core dimension of having multiple components.

Prepared on behalf of the Medical Research Council by:
Peter Craig, MRC Population Health Sciences Research Network
Paul Dieppe, University of Oxford
Sally Macintyre, MRC Social and Public Health Sciences Unit
Susan Macleod, Centre for Customary Research and Evidence, University College London
Irvin Nazareth, MRC General Practice Research Framework
Mark Petticrew, Department of Public Health and Policy, London School of Hygiene and Tropical Medicine

www.mrc.ac.uk/complexinterventionsguidance
A less linear model

**Feasibility and piloting**
- Testing procedures
- Estimating recruitment and retention
- Determining sample size

**Development**
- Identifying the evidence base
- Identifying or developing theory
- Modelling process and outcomes

**Implementation**
- Dissemination
- Surveillance and monitoring
- Long term follow-up

**Evaluation**
- Assessing effectiveness
- Understanding change process
- Assessing cost effectiveness
Objectives: participants to learn about

- Key challenges in:
  - Developing and evaluating complex interventions
  - Conducting exploratory/feasibility research prior to a definitive study of effectiveness
- Plans and progress with INDEX and GUEST projects
- Variation in conduct and reporting of studies
- Key points to take account of in the development of the new guidance
- How to contribute further to the guidance development
Objectives: study team to learn

- Key challenges in:
  - Developing complex interventions
  - Conducting exploratory/feasibility research prior to a definitive study of effectiveness
- Variation in conduct and reporting of studies
- Plans and progress with INDEX and GUEST projects
- Key points to take account of in the development of new guidance
- Key challenges for us to produce useful guidance
- Key references (and case studies) that we should be aware of
- Who else we should involve and who would like to contribute later stages of guidance development
Questions to be addressed

- Can you think of any key projects we can use as case studies?

- Can you suggest any key publications for us to review?

- What do you consider to be the main gaps in the current guidance?
Identifying and assessing different approaches to developing complex interventions: An introduction to the INDEX Study

O’Cathain A, Hoddinott P, Duncan E, Yardley L, Turner K, Croot E, Sworn K, Rousseau N
Why is guidance needed?

- MRC guidance (2008) is brief
- Choice
  - MRC?
  - Behaviour Change Wheel?
  - Intervention mapping?
  - Co-production?
  - Other....Mixture...Addition...Bespoke/pragmatic
- Rapid development
Study design

Phase 1:
Systematic reviews

Phase 2:
Qualitative interview study: developers, funders, journal editors, policy makers n=20-25

Phase 3:
Consensus Exercise: Delphi exercise x 2 and workshop

1. Methodology review: Approaches to intervention development
2. Primary research: Review of context, mechanisms, strengths and weaknesses
3. Methods
4. Links between development and successful interventions
Continuum of intervention development

- Preparatory research (e.g., evidence synthesis, qualitative research)
- Intervention development
- Feasibility
- Evaluation
- Implementation

Refinement

Tailoring and adaptation to different contexts
Feasibility and piloting
- Testing procedures
- Estimating recruitment and retention
- Determining sample size

Development
- Identifying the evidence base
- Identifying or developing theory
- Modelling process and outcomes

Evaluation
- Assessing effectiveness
- Understanding change process
- Assessing cost effectiveness

Implementation
- Dissemination
- Surveillance and monitoring
- Long term follow-up
GUEST  Guidance for Exploratory Studies of complex public health interventions

L Moore, P. Craig, G Moore, S. Murphy, M. Robling, J. Segrott, S. Simpson, R. Turley, D. Wight, J. Pugmire, B Hallingberg, S Browne
Uncertainties....

- When should an exploratory study be conducted?
- What questions should an exploratory study answer?
- To what extent should an exploratory study focus on intervention design?
- What criteria should exploratory studies use to determine when to move onto a full effectiveness study?
- How is sample size determined and should an exploratory study seek to recover an estimate of effect size?
- Should the exploratory study be randomised?
Feasibility and pilot studies

- Standard definitions and practice (e.g., NIHR glossary) focus on refining, testing, and planning trial methods – sample size, recruitment, retention etc.
- Assumes some evidence of efficacy established and intervention is ‘ready’ for Phase III definitive trial.
- Highly problematic for complex interventions.
  - Massively variable practice in commissioning, design, assessment of feasibility/pilot studies.
  - ‘Exploratory trials/studies’ are first opportunity to assess acceptability, feasibility, system fit of the intervention and possible modification of the intervention for full trial.
- Progression to Phase III trial needs evidence related to the evaluation methods and intervention feasibility.
- Avoid well designed trials of underdeveloped interventions that won’t translate (too many done already!)
Exploratory trials of complex population health interventions

Developed the intervention using:
• Psychological / sociological etc understanding of how to bring about change
• Systematic review evidence / promising findings in other contexts

Test intervention’s:
• Acceptability, compliance (of/to target individual, organisation/setting/system fit....)
• Feasibility
• Mechanisms and intermediate impacts
• Barriers / facilitators / adaptations
• Cost
Also...

Test evaluation methods
- Measures
- Recruitment
- Response rates
- Randomisation
- Retention

- May be iterative, repeated, abortive
- Exploratory trials and their assessment highly variable!
Updating the MRC guidance

1. Gap analysis, based on scoping reviews to find publications that identify gaps and weaknesses in the existing guidance, or that provide more detailed guidance on specific topics
2. Convening a steering group to oversee the work, review and approve drafts, etc; and a writing group
3. Drafting the update and summaries
4. Designing and populating the online resource
5. A consensus meeting to review and agree the content and design of the online resource
6. Drafting the journal article and managing the publication process

October 2017

December 2018
What is a complex (social / public health) intervention?

- Complex interventions involve “multiple, synergistic components” [Bonell et al, 2012]

- They often address both social / environmental determinants and individuals’ knowledge and attitudes (i.e. “multi-level” approaches)

- Complex interventions interact with context

- There is therefore complexity both within the intervention model AND in its dependence on context, receipt, implementation; the wider system

- This presents challenges for RCTs as applied to relatively simple interventions
New MRC Process Evaluation Guidance is focused on “what works for whom in what context & why?”

Context
Contextual factors which affect (and may be affected by) implementation, intervention mechanisms and outcomes. Causal mechanisms present within the context which act to sustain the status quo, or lead to change.

Description of intervention and its causal assumptions
Logic model
Theory of action/change

Implementation
How delivery is achieved (training, resources etc..)?
What is delivered?
- Fidelity
- Dose
- Adaptations
- Reach

Mechanisms of impact
Participant responses
Intervention mediators
Unanticipated pathways / consequence

Outcomes

Moore et al 2015
<table>
<thead>
<tr>
<th>Simple</th>
<th>Complicated</th>
<th>Complex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flat pack furniture</td>
<td>Rocket to the moon</td>
<td>Raising a child</td>
</tr>
<tr>
<td>The components and instructions are essential</td>
<td>Formulae are critical and necessary</td>
<td>Formulae have limited application. Adaptation and flexibility are key</td>
</tr>
<tr>
<td>If all the bits are there and instructions are followed in order, the result is consistent</td>
<td>Sending one rocket to the moon increases assurance that the next will be okay</td>
<td>Raising one child provides experience but no assurance of success with the next</td>
</tr>
<tr>
<td>No particular expertise is required but helpful to be good with an allen key</td>
<td>High levels of expertise in a variety of fields are necessary for success</td>
<td>Expertise can contribute but is neither necessary nor sufficient</td>
</tr>
<tr>
<td>Produces standardised furniture</td>
<td>Rockets are similar in critical ways</td>
<td>Every child is unique and must be understood and responded to as an individual</td>
</tr>
<tr>
<td>The designed furniture will be reproduced</td>
<td>There is a high degree of certainty of outcome</td>
<td>Uncertainty of outcome remains</td>
</tr>
</tbody>
</table>
We need complex interventions that:

- Are resilient to contextual variation and therefore more transferable
  - Flexible
  - Standardised function, flexible form

and / or

- Have a clear program theory and thus a clear understanding of contextual dependencies, (target group, resources, system requirements etc) and system impacts

Or

- Take a whole system / complex systems approach
  - Multiple synergistic components
  - Each contributing but not sufficient
  - Feedback, non-linearity and emergence
CI Development needs to be informed by external (implementation) issues

- Preclinical: Explore relevant theory to ensure best choice of intervention and hypothesise how to predict major confounders and strategic design issues.
- Phase I: Identify the components of the intervention and the underlaying mechanisms by which they will influence outcomes to provide evidence that you can predict how they relate to and interact with each other.
- Phase II: Describe the constant and variable components of a replicable intervention and a feasible protocol for assessing the intervention in an appropriate alternative.
- Phase III: Compare a fully defined intervention with an appropriate alternative using a protocol that is theoretically defensible, reproducible, and adequately controlled in a study with appropriate evidence.
- Phase IV: Determine whether others can reliably replicate your intervention and results in uncontrolled settings over the long term.

Continuum of increasing evidence
Questions to be addressed

• Can you think of any key projects we can use as case studies?

• Can you suggest any key publications for us to review?

• **What do you consider to be the main gaps in the current guidance?**
Gaps in the existing guidance

- Definition of complex interventions
- Complex systems thinking
- Intervention development & pre-evaluation phase
- Intervention implementation
- Research priorities
- Programme theory evaluation approaches
- Economic evaluation
- Systematic reviews of complex interventions
- Patient public involvement
Complexity

‘Few interventions are truly simple, but there is a wide range of complexity.’

Some dimensions of complexity:

- Number of and interactions between components within the experimental and control interventions
- Number and difficulty of behaviours required by those delivering or receiving the intervention
- Number of groups or organisational levels targeted by the intervention
- Number and variability of outcomes
- Degree of flexibility or tailoring of the intervention permitted
Complexity - updated

A simple solution to a complex problem

http://www.luckyironfish.com/research
Complexity - updated

Effectiveness depends on

- Capacity to manufacture fish locally and cheaply
- Cultural meanings of fish, household cooking and storage practices
- Causes of anaemia (not all dietary)
- Chemical composition of the water used for cooking (may vary seasonally)
- Etc., etc.

➢ No intervention is truly simple, and there is a great deal of skill and judgement involved in deciding which dimensions of complexity are important
No intervention is truly simple, and there is a great deal of skill and judgement involved in deciding which dimensions of complexity are important:

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The nature and range of context-by-intervention interactions
Dealing with complexity

1) Implement ‘complex systems approaches’ to evaluation

‘Rhetoric urging complex systems approaches is only rarely operationalised in ways that generate relevant evidence or effective policies.’ (Rutter et al, 2017)

In the meantime...

2) Pay more attention to context

3) Do more replication studies in novel contexts (and fewer studies of novel interventions)

4) Do more realist trials and implementation studies

5) Other suggestions? Examples of case studies?
Over-emphasis on trials

References to RCTs as the ‘gold standard’ remain common, but misleading:

- Conflate ‘in principle’ benefits with what happens in practice
- Not empirically supported by systematic reviews of randomised vs non-randomised studies
- Assume that selection biases are more important than other threats to validity
- Redundant when randomisation is built into real life assignment
- Create a double standard that distorts decision-making (e.g. GRADE)

‘Researchers should beware of blanket statements ... and choose on the basis of specific characteristics of the study.’

Guidance on natural experimental approaches and risk of bias tools for non-randomised designs should level the playing field
Realist and programme theory

Examine the effects of intervention components separately and in combination

Examine pathways via which change occurs

Examine how effects vary by subgroups and with context more systematically

Draw on complementary quantitative and qualitative data to answer different RQs.

Build and test mid-level, program theories about how interventions work in context
There are numerous examples of other guidance that provide more detail than the existing complex intervention guidance e.g.:

- Using a theory-driven approach
- Identifying and delivering the mechanisms of change
- Co-production and prototyping of interventions
- Optimization of interventions

Feasibility and piloting: updates in this area drawing on more recent work on the use of exploratory studies:

- GUEST
- Evaluability Assessment
Intervention implementation

- Normalising interventions into routine practice as intended:
  - RE-AIM
  - Normalisation Process Theory (May, 2009)
  - Others?

- Wider aspects of implementation
  - Implementation in LMICs where there are issues around buying, storing, transporting equipment, for example.
  - Other examples of issues?
Deciding research priorities

- Emphasis is usually on seeking the views of evidence users (patients, clinicians, policy-makers, etc) and involving them in research funding decisions.

- Necessary, but not sufficient:
  - may generate wish lists of questions that can’t be answered;
  - may lead to a focus on gaps rather than on promising lines of enquiry.

- Needs to be supplemented by methods for selecting questions that can be answered at reasonable cost:
  - Value of information (VOI) methods
  - Evaluability assessments (EAs)
Economic evaluation

- Previous guidance on evaluating cost-effectiveness “disappointingly brief” but there have been few challenges to how standard methods of economic evaluation should be adapted for complex interventions.

- Incorporation of effectiveness evidence into models that decision-makers can use for themselves.
  - e.g. SCOTPHO Triple-I tool

- Potential to make use of other methods of evaluation e.g. Measure system change by analysing at a social network level.
- Need case studies that apply economic evaluation to complex interventions.