

## MEDICAL RESEARCH COUNCIL

MRC: IN CONFIDENCE

HSPHRB Nov 2006

### Complex Intervention Workshop Report – Revision of MRC Guidance

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#### 1. Background

An MRC PHSRN-funded workshop on Complex Interventions was held in May 2006 with the aim of discussing the MRC's 'Framework for Development and Evaluation of RCTs for Complex Interventions to Improve Health', and considering whether it needed updating. The workshop was organised by Paul Dieppe (Director, HSRC), Janet Darbyshire (Director, CTU) and Sally MacIntyre (Director, SPSU), with 30 delegates attending, including the authors of the original document.

The report from the workshop (Annex 1) summarises the day's recommendations, including the overall conclusion that the Framework needed updating. In discussion with the Office and the Board Chairman, the following next steps have been agreed in principle:

- Paul Dieppe has agreed to be responsible for taking forward the re-drafting of the Framework (Annex 2)
- Draft re-writes of Framework will be circulated to a subcommittee of Board members and others.
- The final version of the new Framework document would be submitted to the Board for endorsement within a year.

#### 2. Actions required

The Board is asked to:

- (i) To note and comment on the Complex Intervention Workshop report (Annex 1);
- (ii) To note and support the next steps being proposed (Annex 2); and
- (iii) To endorse, in principle, resources being allocated from the Board budget to take this forward.

#### 3. Annexes

Annex 1: Complex Intervention Workshop Report

Annex 2: Professor Paul Dieppe's letter outlining the writing group charged with the Framework revisions.

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DBMs: Professor David Armstrong  
Professor Max Parmar

LO'C/MB



- 3) *What are you trying to do and why?* The rationale for a complex intervention, including the use of theory and behavioural change theories in its development, needs careful thought. There may be lots of competing theories that should be considered, and the matching of theory to reality needs to be thought about. One approach is to use a logic model – if you cannot produce a simple diagrammatic logic model of what you are trying to do then you do not know what you are trying to do or why. (However, we recognised that there is an extensive literature about logic models that should be considered before they could be recommended for use in this context). We also need to consider the origin of the idea for a complex intervention. This might come from, amongst others:

- Policy makers
- New Technology
- Theory
- Service users
- An investigator
- A commercial interest

- 4) *What trial design are you going to use and why?* There are lots of options, including:

- The classical parallel group RCT
- Cluster randomised trial
- Step-wedge randomised designs
- Preference designs
- Pre-randomisation or modified Zelen designs
- n-of-1 trials
- The Wennberg design
- Others.

Different designs suit different questions.

You should randomise if at all possible, but it may not be possible to do that, in which case you should still think about the best ways to evaluate change, for example using objective measures and ensuring that you have good baseline data for before/after comparisons, or appropriate control groups.

- 5) *What outcome measures are you going to use, and how are you going to deal with them?* You need to think about primary and secondary outcomes, and how to deal with multiple outcomes, as well as their timing. Timing may be a critical factor in complex interventions (a logic path may help you predict when your outcome measures might change). You may have to use surrogate outcomes, or your outcomes may act as surrogates or mediators of other effects within complex systems. You also need to be aware of unpredictable outcomes and adverse events, and the need to try and capture them, as complex systems are likely to produce unpredictable change when an intervention is put into them. In addition, you should consider the possibility that different types of outcome may be of interest to different types of stakeholder. For example, for a dietary intervention, clinicians might be interested in a medical outcome measure such as bone density, but policy makers and politicians might want to know about changes in eating behaviours and the effects on local shops.

- 6) *Who needs to know about the result, and is the intervention you want to test 'implementable'?* You need to ask the question 'would it be possible to use this?' before embarking on a trial. In addition the whole issue of knowledge transfer after the trial is completed should be thought about 'up-front'. Work out who needs to know about the trial outcome in order to implement change that might be needed as a result of the trial outcomes. You should be prepared to work with those who might implement change resulting from the trial outcomes from the planning stage.
- 7) *What user involvement is there going to be in the trial?* In general appropriate 'users' should be involved at all stages of the development, process and outcome analysis of a complex intervention, as this is likely to result in better science and in more chance of the data being used appropriately at the end of the trial.
- 8) *Can you describe the intervention fully?* A complex intervention, however 'complicated' should be reproducible, which means that you need a full description of it, and an understanding of its components, including what bits are likely to be 'characteristic' (resulting from the intervention alone), what is 'incidental' (sometimes known as the context or placebo effects), and how the two categories do or do not overlap and interact. It is unlikely that a full description can be given in a scientific paper, so you may want to develop a manual to describe it. A relatively unrecognised (or not talked about) aspect of a complex intervention is the fact that it often changes with time, perhaps as a result of learning during the trial or for pragmatic reasons or change of external factors. 'Fidelity' is a key issue here, and investigators need to think about how much change or evolution of the intervention after design they would consider permissible. Any change of intervention needs recording, and process evaluation. It may be prudent and helpful to make sure that full details are available on a web site.
- 9) *Can you describe the context and environment in which the trial is being undertaken adequately?* Context is crucial, and needs to be stated clearly and the effect on external validity recognised. Furthermore, context may change after the trial has been designed or started, through, for example, the introduction of some new policy. Guidelines on how to describe a complex intervention fully within its context may be needed, both for trial manuals and for scientific reports.
- 10) *Is the trial ethical?* Ethical problems around complex interventions may have been overstated in the past, but obviously need clear consideration. Investigators need to think about the ethics of their design in terms of the autonomy of participants and informed consent, and think through the possible effects of their trial in terms of effects on communities, possible adverse events etc in as robust a way as possible. Complex or complicated trials, particularly if they are interfering with an unpredictable system, may have a variety of non-simple or unexpected outcomes that could have ethical implications.
- 11) *What will it cost and is it likely to be cost-effective?* The economic implications of the trial, and of implementation of the planned intervention need to be considered. It may be that the prohibitive costs of a large scale RCT to 'prove' the efficacy of an intervention mean that some other form of evaluation, such as a natural experiment needs to be considered.

- 12) *Have you done appropriate systematic reviews?* Systematic reviews need to be carried out at all stages of a complex intervention. However, this is a problem area, as the methodology of how to find, review and combine data from complex intervention trials and other study designs is not yet fully developed.
- 13) *What processes will be put in place to monitor and oversee the trial?* Any complex intervention trial should have an appropriate DMEC and Steering Committee, and should comply with local governance advice and legal requirements, as well as the relevant national laws, and with the EU Clinical trials Directive if it includes the evaluation of any medicinal product.

**Conclusion 2: There are some key areas of complex interventions that require further methodological research.**

These include:

- 1) *Systematic reviews and data synthesis.* In particular cross-design synthesis of data and the methods for combining data from different, but similar complex packages of care. Heterogeneity is a more difficult and different type of problem in complex –v- simple interventions.
- 2) *Definitions, descriptions and reporting of complex interventions.* There is lack of clarity about what constitutes a complex intervention (is it the intervention, the comparison, the outcome, the division into characteristic and incidental effects, or is it just that it is ‘complicated’?) A framework for thinking about this has been developed, but there are a variety of ways of describing or categorising complex interventions. Data presented at this meeting showed that reporting of complex interventions is poor. A modification of the CONSORT statement might help this. Guidelines for describing complex interventions, including their evolution would be of value.
- 3) *The application of complexity theory to complex interventions.* This topic includes the use of modelling to assess the likely impact of a complex intervention; how you recognise a complex system and explore its complexity; and how to explore issues such as likely sudden ‘phase changes’ within a system rather than a linear or ‘dose-related’ change in outcomes, as is usual in ‘simple trials’

**Conclusion 3: Complex interventions are of increasing importance to the developing world and to reduce health inequalities, as well as being used to assess the effectiveness of packages of care, policy interventions or behavioural change in the developed world**

The emphasis apparent in the current MRC framework, as well as in much of the literature, is on the use of complex interventions to test the efficacy or effectiveness of packages of care (such as rehabilitation programmes), behavioural interventions, or policy changes, in the developed world.

However, delegates to this workshop recognised the wider value of complex interventions and their potential to aid the reduction of inequalities in health and health care delivery, and in aiding developing countries to improve health. MRC might want to consider sponsoring further workshops or work on this agenda

**MRC PHSRN 2-DAY WORKSHOP ON COMPLEX INTERVENTIONS**  
**Monday 15 and Tuesday 16 May 2006**

London House, (Large Common Room), Goodenough College,  
Micklenburgh Square, Bloomsbury, London WC1N 2AB

**PROGRAMME**

**MONDAY 15 MAY 2006**

<b>11.00 - 11.30</b>	Coffee / Registration
<b>11.30</b> <b>PAUL DIEPPE</b>	Introductions / aims
<b>11.40</b>	<b>PART ONE: 'Complex Interventions: what are they and what do we know about them?'</b>
<b>PAT YUDKIN</b>	'Complex Interventions or Complex Trials?'
<b>SIMON LEWIN</b>	'Assessing health care interventions along the complex-simple continuum: a proposal'
<b>SARA BROOKES</b>	'Randomised trials of complex interventions - how often, and how well are they done?'
<b>DISCUSSION</b>	
<b>1.00 - 1.45</b>	Lunch
<b>1.45</b>	<b>PART TWO: Networks and Frameworks: the MRC framework and what is good and bad about it. The Canadian network and what it is trying to do.</b>
<b>RAY FITZPATRICK</b>	'MRC approach to complex interventions: framework or straight-jacket?'
<b>PENNY HAWE</b>	'An international collaboration on complex interventions'
<b>DISCUSSION</b>	
<b>Introduction to Group Sessions</b>	
<b>3.00 - 3.15</b>	Tea
<b>3.15</b>	<b>Two working groups:</b>  The MRC Framework - what is good about it, what is not so good, does it need to be modified, if so how and why?
<b>4.30</b>	Reports from working groups: General Discussion Discussants: Brian Oldenburg and Susan Michie
<b>7.30</b>	Dinner : Ciao Bella, 86-90 Lamb's Conduit St, Bloomsbury, WC1 3LZ

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**TUESDAY 16 MAY 2006**

<b>09.00</b>	<b>PART THREE: Developing interventions, designing trials, getting them done, some brief practical examples of what people have done to assess complex interventions</b>
<b>BRIAN OLDENBURG</b>	'Some Key ways to improve the implementation and evaluation of complex multi-level health interventions'
<b>RONA CAMPBELL</b>	'Modified Zelen designs and their role in the evaluation of complex interventions'
<b>MARK PETTICREW</b>	'Why evaluating complex interventions is complex : some examples'
<b>CHARLOTTE PATERSON</b>	'Characteristic and incidental (placebo) effects in complex interventions: distinct but not divisible'.
<b>11.00-11.30</b>	Coffee
<b>11.30</b>	<b>Analytical, economic and other practical issue</b>
<b>MIKE CLARKE</b>	'Complex interventions and systematic reviews: issues to consider'
<b>MIKE CAMPBELL</b>	'Can we learn anything from complexity theory?'
<b>ALAN SHIELL</b>	'Capturing the costs and consequences of changes in complex systems'
<b>1.00 - 1.45</b>	Lunch
<b>1.45 - 2.45</b>	Two group sessions. What needs doing next? Where do we go from here? What research priorities are there?
<b>2.45</b>	Tea
<b>3.00 - 4.00</b>	Reports from group sessions and general discussion Discussants : Alan Shiell, Janet Darbyshire

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I look forward to hearing your and the Board's response to these suggestions

With thanks and best wishes

Yours sincerely

A handwritten signature in black ink, appearing to read 'Paul Dieppe', with a long horizontal flourish extending to the right.

**Paul Dieppe**

*cc:\ Peter Craig, Chief Scientist Office, Scottish Executive Health Department, GE 10,  
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