NPRI Workshop

Optimising the design and commissioning of trials of complex public health interventions: a structured discussion on pre-trial exploratory, feasibility, pilot work and what comes next
Optimising the design and commissioning of trials of complex public health interventions: a structured discussion on pre-trial exploratory, feasibility, pilot work and what comes next

4th December 2014
12:00 Laurence-Moore (University of Glasgow)
The importance of robust design in the intervention and trial design - getting the most from an exploratory phase

12:10 Gavin Malloch – MRC Programme Manager for Public Health Partnerships.
Funders perspective

12:25 Iain Crombie (University of Dundee)

12:40 Russ Jago (University of Bristol)

12:55 Discussion chaired by Laurence Moore to include Jeremy Segrott (Cardiff University) as discussant
The importance of robust design in the intervention and trial design - getting the most from an exploratory phase

Laurence Moore

Director, MRC/CSO Social and Public Health Sciences Unit
• Completed 7 large trials
  • ASSIST, NERS, FSBI, SHiP, FTS, EC
  • 2 ongoing ( SFP the biggest yet )
• 8 Exploratory trials
  • KT4LG, AWLPI, KAT, AHEAD, TAP, CHERRY, A-F, A-CAN
• NPRI and NIHR PHR Boards
Get the intervention right!

- Don’t rush to do the big trial
  - Do you really want to do a brilliant trial of a hopeless intervention?
  - There are lots of them!
  - Result of funding streams
  - Resulting in deficient evidence base
Evaluating complex interventions

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 Tyer

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 chaired by members of the MRC Health Services and Public Health Research Board. It is intended to provide a framework for individual or institution at the initiation 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 randomised controlled trials of complex interventions
Phases of RCTs of complex interventions: MRC April 2000

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

Phase I
- Modelling: Identify the components of the intervention and the underlying 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
- Exploratory trial: 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
• More funding / effort needed on:
  • Basic behavioural sciences, development
  • Feasibility / piloting
  • Adaptation of INTERVENTION

• Involve public, policy, practice stakeholders
• Develop logic model and program theory
Developing and evaluating complex interventions: new guidance

Prepared on behalf of the Medical Research Council by

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Irwin 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

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

**Implementation**
- Dissemination
- Surveillance and monitoring
- Long term follow-up
Feasibility studies
This is a definition that has been agreed by the EME, PHR, HTA and RfPB programmes.

Feasibility Studies are pieces of research done before a main study in order to answer the question “Can this study be done?”. They are used to estimate important parameters that are needed to design the main study. For instance:

- standard deviation of the outcome measure, which is needed in some cases to estimate sample size;
- willingness of participants to be randomised;
- willingness of clinicians to recruit participants;
- number of eligible patients, carers or other appropriate participants;
- characteristics of the proposed outcome measure and in some cases feasibility studies might involve designing a suitable outcome measure;
- follow-up rates, response rates to questionnaires, adherence/compliance rates, ICCs in cluster trials, etc.
- availability of data needed or the usefulness and limitations of a particular database;
- time needed to collect and analyse data.
Pilot studies
This is a definition that has been agreed by the EME, PHR, HTA and RfPB programmes.

- Pilot studies are a smaller version of the main study used to test whether the components of the main study can all work together. It is focused on the processes of the main study, for example to ensure that recruitment, randomisation, treatment, and follow-up assessments all run smoothly. It resembles the main study in many respects, including an assessment of the primary outcome. In some cases, this will be the first phase of the substantive study and data from the pilot phase may contribute to the final analysis; this can be referred to as an internal pilot. Or, at the end of the pilot study, the data may be analysed and set aside, a so-called external pilot.

We expect that when pilot or feasibility studies are proposed by applicants, or specified in commissioning briefs, a clear route of progression criteria to the substantive study will be described. Listing clear progression criteria will apply whether the brief or proposal describes just the preliminary study or both together. Whether preliminary and main studies are funded together or separately may be decided on practical grounds.
“Funders perspective”

Gavin Malloch,
MRC Programme Manager

4th December 2014
NPRI Funders perspective

Conduct of research

• Use best practice for clinical trials
  – independent TSC
  – ToR
  – DMEC
• Engage users and policy makers wherever possible and before starting – co-produce if possible
• Manage recruitment and delays pro-actively (don’t leave it too late and hope for an extension/supplement)
NPRI Funders perspective

Reporting of research

- Proper acknowledgement and attribution
- Report fully in Researchfish
- Publish outcomes even if not in journal
Support now available for early stage development

- Public Health Intervention Development Scheme (PHIND) supports early stage development of public health interventions
- Important UK or global public health issue
- Pipeline to NIHR schemes, DfID/MRC/WT Joint Global Health Trials
- Up to but not including pilot studies
- Up to £150k and max 18 months
- Rapid response streamlined scheme
- 3 deadlines a year
  - Next deadline 30th Jan 15
Feasibility of novel alcohol interventions

Professor Iain K Crombie
Dr Linda Irvine
Young women

- binge drinking in social groups
  - high risk of harms
- group intervention
- delivered by lay peers
Key feasibility issues

- develop acceptable intervention
- recruit and train lay peers
- recruit drinking groups
- fidelity of delivery
- retention, outcome assessment
Focus groups

- established patterns of drinking
  - careful planning
- strong motives for drinking
  - fun, socialising
- group encouragement to drink
- marked resistance to change
Intervention: Looking good, feeling great

- Three session tailored intervention (HAPA)
  - Organised around fun activities
1. Promoting motivation
   - Mocktail preparation
2. Setting goals
   - Make-up demonstration
3. Action and coping plans
   - Relaxation/ massage
Lay peers

❖ recruitment
  ➢ targeted at peers
  ➢ extended selection process

❖ training
  ➢ Motivational Interviewing
  ➢ role play: delivery of intervention
  ➢ user friendly manual

❖ findings
  ➢ motivated peers recruited
  ➢ role play extended
Participant recruitment

- **Marketing campaign**
  - local radio, buses, flyers, posters, NHS/university intranets

- **Outreach strategy**
  - community centres, shopping centres, gyms, parks, university, college

- **Findings**
  - target of 24 groups recruited
Delivering the intervention

- variety of venues
  - hotel, cocktail bar, community centres, university

- professionals
  - mixologist, beauty therapist, relaxation therapist

- findings
  - 92% completed 3 sessions
  - getting groups together difficult
Assessing fidelity

- **Monitoring**
  - recorded sessions
  - flipcharts collated
  - feedback with lay trainers

- **Findings**
  - enthusiastic engagement
  - decisional balance
    - advantages of less bingeing
  - 92% set goals to reduce consumption
    - no shots
Follow-up

- very challenging
  - participants willing, coordination hard
  - multiple attempts at contact
  - multiple methods

- findings
  - 86% completed follow-up
Post-study evaluation

- **acceptability**
  - more fun than expected
  - non-judgemental approach valued
  - group format important

- **benefits**
  - insight into extent of drinking
  - reduced drinking → more money, more time
  - goal setting used for other activities
Value of the feasibility study

- Methods successful
- Improvements made
  - training of lay peers
  - recruitment & follow-up of groups
- Modifications for full trial
  - over-recruit lay trainers
  - allow for sustained mentoring
  - more RA time for organising groups
Disadvantaged men 25-44 years: behaviour change in 160 characters

- **recruitment**
  - GP registers, community outreach

- **intervention**
  - engage, motivate
  - fidelity

- **retention**
Intervention development

- pre-study literature review
  - social cognition models, communication theory
  - intervention studies (text messages, alcohol)

- focus groups
  - discrepancy
    - binge drinking and social responsibilities
  - don’t preach
  - quotes from focus groups
Andy from Dundee says – “I cut back on drinking because my father-in-law died of it”. What would be a good reason for U to cut back? Text me back!

Motivate change
Can U think of someone who’d be happy if U made a change! What would U hear them say? Please text me your answer!

Views of others Reinforce intention to change
Content of the responses

- **Reasons for drinking less**
  - “I really wanna stay out of trouble and not become the person I can be after a few too many”

- **Money saved**
  - “£200 a month or more easy. That would be on carry outs and the pub.”

- **Buy with money saved**
  - “Trek 2.5 road bike - cost £1650.00 RR”

- **Benefits to others**
  - “My dad. Its good ur no phoning me for a lift at 2am!”
Summary

- exceeded recruitment target
- 96% retention
  - outcomes measured
- theoretically and empirically based text messages
  - in 160 characters
- high level of engagement
  - key components behaviour change strategy
Revisions for the full trial

- **Extended and modified intervention**
  - 36 texts → 110 texts
  - self-efficacy
  - action planning
  - long term maintenance

- **Multi-centre trial underway**
  - n=800
  - high level engagement
Value of feasibility studies

- develop intervention
- refine then test study methods
  - recruitment, intervention delivery, follow-up
  - provide evidence of success
- measures of fidelity
  - acceptability of intervention
  - engagement with behaviour change strategy
- estimate workload and sample size
Collaborators

Professor Iain Crombie  
Epidemiologist

Professor Rose Barbour  
Medical Sociologist

Professor Andrew Briggs  
Health Economist

Dr Carol Emslie  
Sociologist

Dr Josie Evans  
Epidemiologist

Professor Gerry Humphris  
Health Psychologist

Dr L Irvine  
Research Methodologist

Dr Claire Jones  
Software Engineer

Dr Ambrose Melson  
Health Psychologist

Professor John Norrie  
Statistician and Trialist

Dr Dennis Petrie  
Health Economist

Dr Peter Rice  
Consultant Psychiatrist

Professor Ian Ricketts  
Computer Scientist

Dr Peter Slane  
GP

Dr Falko Sniehotta  
Health Psychologist

Dr Vivien Swanson  
Health Psychologist

Professor Brian Williams  
Medical Sociologist
Action 3:30: Feasibility trial of an extra-curricular physical activity intervention

(Using information from a feasibility trial to refine an intervention prior to a definitive trial)
Study design

- Cluster RCT
  - 539 year five and six pupils, from 20 primary schools (max of 30 pupils per school)

- Two Teaching Assistants in each intervention school received a 5-day programme
  - Intervention schools (10) received a programme of 40 after-school PA sessions lasting 60 minutes taught by the TAs
  - Manual of 40 sessions plans were provided
  - The sessions aimed to enhance motor skills, confidence and enjoyment of PA in a wide group of children

- Primary outcome was accelerometer assessed MVPA assessed during last 3 weeks of intervention (T1) and 6-months later (T2)
Process and post-intervention qualitative methods

• Session attendance was recorded

• Costs were estimated

• Participants in intervention schools were asked to complete a survey that assessed reasons why they did not attend

• Interviews were held with participating Teaching Assistants (TAs) and school key contacts (KCs), and 10 focus groups were conducted in 10 intervention schools

• Interviews and focus groups examined how recruitment and session attendance might be improved
## Physical activity by trial arm – Both genders

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Intervention</th>
<th>I vs. C** adjusted difference in means (95% CI)**</th>
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<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
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<tr>
<td>MVPA/weekday (mins)</td>
<td>65.5</td>
<td>21.6</td>
<td>65.7</td>
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<td>MVPA/weekday after school (mins)**</td>
<td>13.0</td>
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<td>MVPA/weekday (mins)</td>
<td>55.3</td>
<td>22.7</td>
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<tr>
<td>MVPA/weekday after school (mins)**</td>
<td>11.7</td>
<td>7.4</td>
<td>11.0</td>
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</tbody>
</table>

** After school period =3.30 to 8.30 pm
** I = intervention; C = control
*Between group differences always compare to the intervention arm and are adjusted for baseline outcome value, IMD, school size, percentage of girls recruited, percentage of Y5 pupils recruited, LEA, and school-level clustering

Jago et al, Trials, 2013
Jago et al, IJBNPA, 2014
## Physical activity by trial arm – Boys

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Intervention</th>
<th>I vs. C†† adjusted difference in means (95% CI)*</th>
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<td></td>
<td>Mean</td>
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<tr>
<td><strong>MVPA/weekday (mins)</strong></td>
<td>72.3</td>
<td>23.8</td>
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<td>13.1</td>
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<td><strong>MVPA/weekday (mins)</strong></td>
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<td>26.5</td>
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<tr>
<td><strong>MVPA/weekday after school (mins)</strong>†</td>
<td>12.5</td>
<td>8.5</td>
<td>12.0</td>
</tr>
</tbody>
</table>

† After school period =3.30 to 8.30 pm

†† I = intervention; C = control

**Between group differences always compare to the intervention arm and are adjusted for baseline outcome value, IMD, school size, percentage of girls recruited, percentage of Y5 pupils recruited, LEA, and school-level clustering

Jago et al, Trials, 2013
Jago et al, IJBNPA, 2014
## Physical activity by trial arm – Girls

<table>
<thead>
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<th>Intervention</th>
<th>I vs. C** adjusted difference in means (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>MVPA/weekday (mins)</td>
<td>60.1</td>
<td>18.0</td>
<td>58.2</td>
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<tr>
<td>MVPA/weekday after school (mins)**</td>
<td>12.9</td>
<td>7.0</td>
<td>13.0</td>
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<tr>
<td>MVPA/weekday (mins)</td>
<td>49.2</td>
<td>16.9</td>
<td>49.1</td>
</tr>
<tr>
<td>MVPA/weekday after school (mins)**</td>
<td>11.1</td>
<td>6.4</td>
<td>10.4</td>
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Jago et al, Trials, 2013
Jago et al, IJBNPA, 2014
Delivery, attendance & costs

- Five of the ten intervention schools ran all 40 sessions.
- Three ran 39, one ran 38 and one ran 29 sessions

- Mean attendance over all club sessions in the 10 schools was 53% with considerable variation

- The indicative average cost of this intervention was £2,425 per school, or £81 per child during its first year, £1,461 per school or £49 per participating child thereafter

Jago et al, IJBNPA, 2014
Improving recruitment and attendance

TAs and key contacts felt that a taster session in which potential participants have the opportunity to participate in an Action 3:30 session would have been useful

TA: “So we thought perhaps we could’ve, do a taster session for all of our year 5s. To come along, have a go, see what they think, because I think, again, people just didn’t know …”

TAs and key contacts suggested that attendance could have been improved by asking the children to make an agreed commitment to attend the sessions

TA: “…I think maybe if there had been a charge or some sort of agreed commitment that made a difference…”
What worked well

The varied nature of the activities was enjoyed
Child: “...first of all I thought it would be a club that you do like one sport a day or something like that and then we done like a warm up a skill, and a proper activity so that was a real surprise for me, but that’s even better because you get more active”

The children enjoyed the autonomy of Action 330 sessions, particularly the ‘child led session’
Child: “...other clubs I've done, sporting clubs like football, tennis, they just say, right, we’re doing this, full stop. But in Action 330, we had choices and options.”

The children liked that they could have fun whilst being active
Child: “...I thought it was good, because it’s like fun to be active. And like, there’s no like running laps in the field or anything ... you just have a good time with your friends.”
Age appropriateness

Some of the sessions were not age appropriate, especially for year 6 girls

**Child:** “Yes, like that hop scotch game. It was just like babyish…”

**TA:** “…maybe to grab them that year earlier sort of year four / five, because while they’re still that little bit more open to suggestion and they’re not as worried to look a bit silly in front of their friends, and again the hormones just aren’t there. And they haven’t got the SATs.”
More work was needed to make the sessions appeal to girls

TA: “...some of the kids were, some of the girls in particular. It eludes me why they signed up in the first place ... they weren’t really that interested”.

Child (girl): “Yeah, and that the boys would never pass to the girls.”
Behavioural issues

Behavioural issues could disrupt the club & TAs said they would like more behaviour management training

Child (male): “Sometimes they [TAs] could be not strict enough and when somebody kind of goes off, they ... they kind of, um, not really know what to do that much.”

TA: “Maybe there wasn’t quite enough [training] in terms of how to ... what scenarios to do when you’ve got children that are difficult...”
Clearer session plans

TA: “maybe some of the games I didn’t quite understand....So, I have to get my head around that and then I would go email”

Additional resources (i.e. a video) would have been beneficial.

TA: “...it would be nice to have a DVD of the different activities and how they are because sometimes the games are not explained very clearly”
## Key changes before proceeding to a trial

<table>
<thead>
<tr>
<th>Source</th>
<th>Change</th>
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</thead>
<tbody>
<tr>
<td>TA</td>
<td>Identify the commitments of the children before selecting the days the club will run.</td>
</tr>
<tr>
<td>TA &amp; CFG</td>
<td>Revise programme to increase engagement of girls</td>
</tr>
<tr>
<td>TA, CFG &amp; KC</td>
<td>More age appropriate sessions</td>
</tr>
<tr>
<td>TA &amp; KC</td>
<td>Conduct intervention in Year 4/5 not 5/6</td>
</tr>
<tr>
<td>TA</td>
<td>Improve the clarity of the session plans</td>
</tr>
<tr>
<td>TA</td>
<td>Provide recordings of model sessions &amp; training</td>
</tr>
<tr>
<td>TA &amp; CFG</td>
<td>More behaviour management training</td>
</tr>
</tbody>
</table>

**Key**

TA = Teaching Assistant  
CFG = Child Focus Group  
KC = Key Contact
Acknowledgements

Co-applicants:
Prof Ashley Cooper – University of Bristol
Prof Ken Fox – University of Bristol
Prof Alan Montgomery – Nottingham Clinical Trials Unit
Prof Jane Powell – University of the West of England
Prof Janice Thompson – University of Birmingham
Dr Simon Sebire – University of Bristol

Team members (all University of Bristol)
Dr Mark Edwards & Dr Ben Davies (Project Managers)
Dr Lesley Wood (Statistican) University of Bristol
Kate Banfield, Jez Zahra, Carly Urbanski (Fieldworkers)

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