

The trials of trials: Negotiating the
methodological pitfalls of the randomised
controlled trial

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Overview

- The context - The ASyMS©-YG study
- Challenges encountered
- Issues with RCTs reported in the literature
- Tips for success

The ASyMS©-YG study



What is the ASyMS©-YG system?

- Advanced Symptom Management System for Young People
- A way of monitoring and supporting young people at home after they have had chemotherapy.
- Involves young people reporting their symptoms each day using a mobile phone/PDA.
- Worrying symptoms alert a nurse at the hospital. The nurse then rings the young person at home to check how they are and offer advice.
- Young people also receive text message advice on what to do about symptoms they report.

The ASyMS© System

Patient completes symptom questionnaire



Data is sent in real time from the mobile phone via the server to the nurse at the clinical site



Problematic symptoms immediately generate alerts on the dedicated pager system nurses carry



Patients receive a message with self-care advice in response to reported symptoms



Nurse views the patient's symptom data on the ASyMS-YG© website and contacts patient to offer advice



Patients can also view symptom graphs and information pages at any time



Example of the ASyMS©-YG questionnaire

ASyMS (Test Teenage)

Pain
Have you experienced any pain in the past 24 hours?

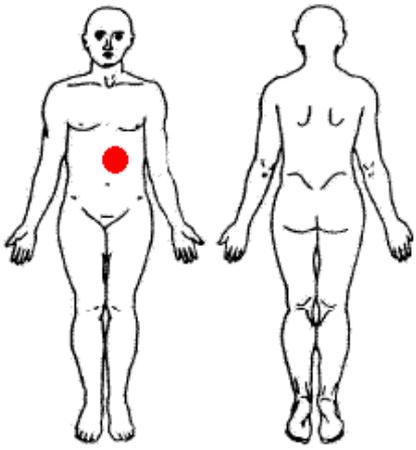
Yes

No

Back **Next** Discard

ASyMS (Test Teenage)

Where is your pain?



Back **Next** Discard

ASyMS (Test Teenage)

Pain
How severe was it?

Mild pain not interfering with normal activities

Moderate pain that has not gone away after taking painkillers or re-occurring pain

Unbearable pain, pain that is interfering with your ability to carry out normal daily activities

Back **Next** Discard

ASyMS (Test Teenage)

Pain
How much did it bother you?

Not at all

A little

Quite a bit

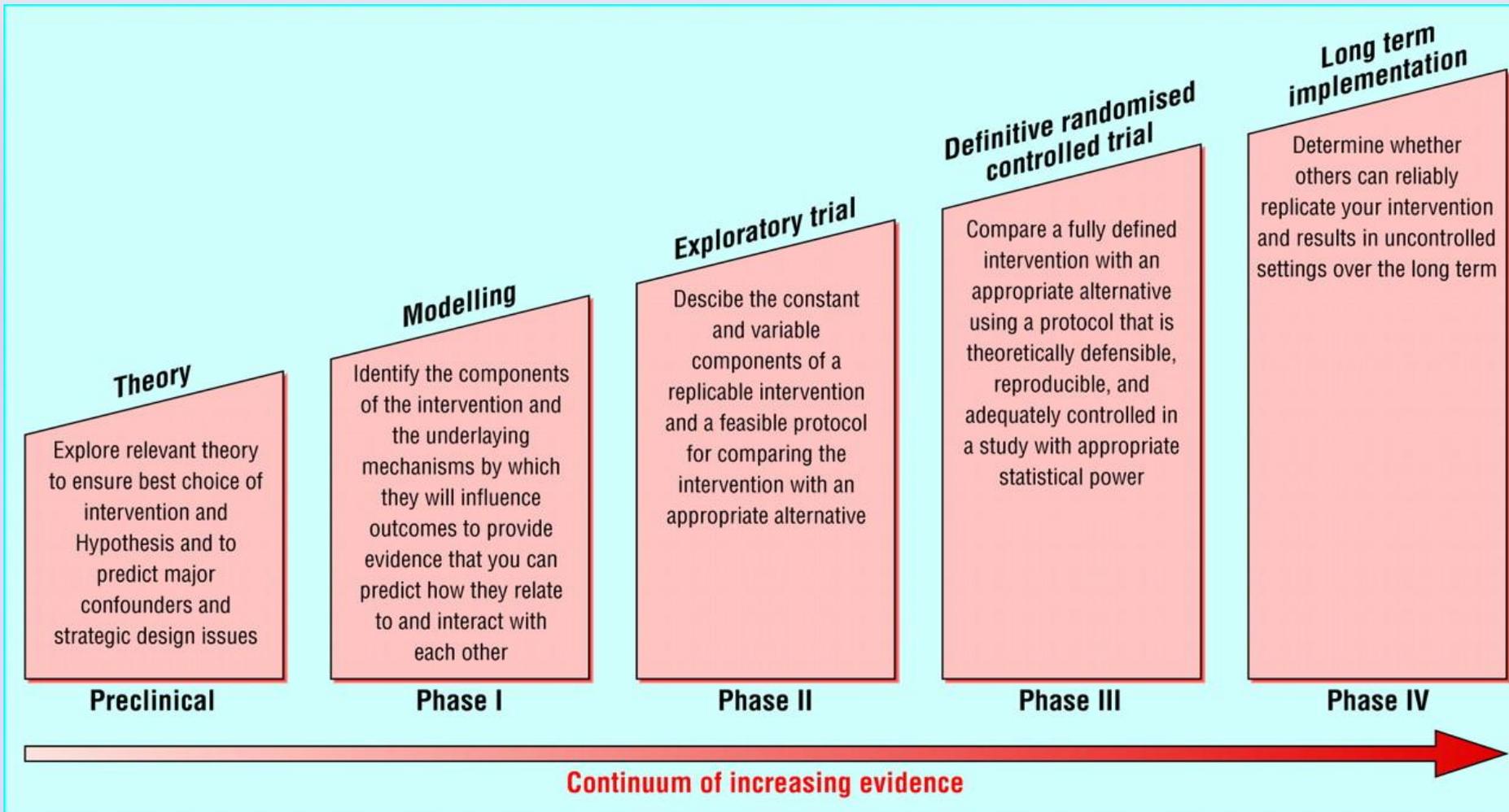
Very much

Back **Next** Discard

The ASyMS©-YG study

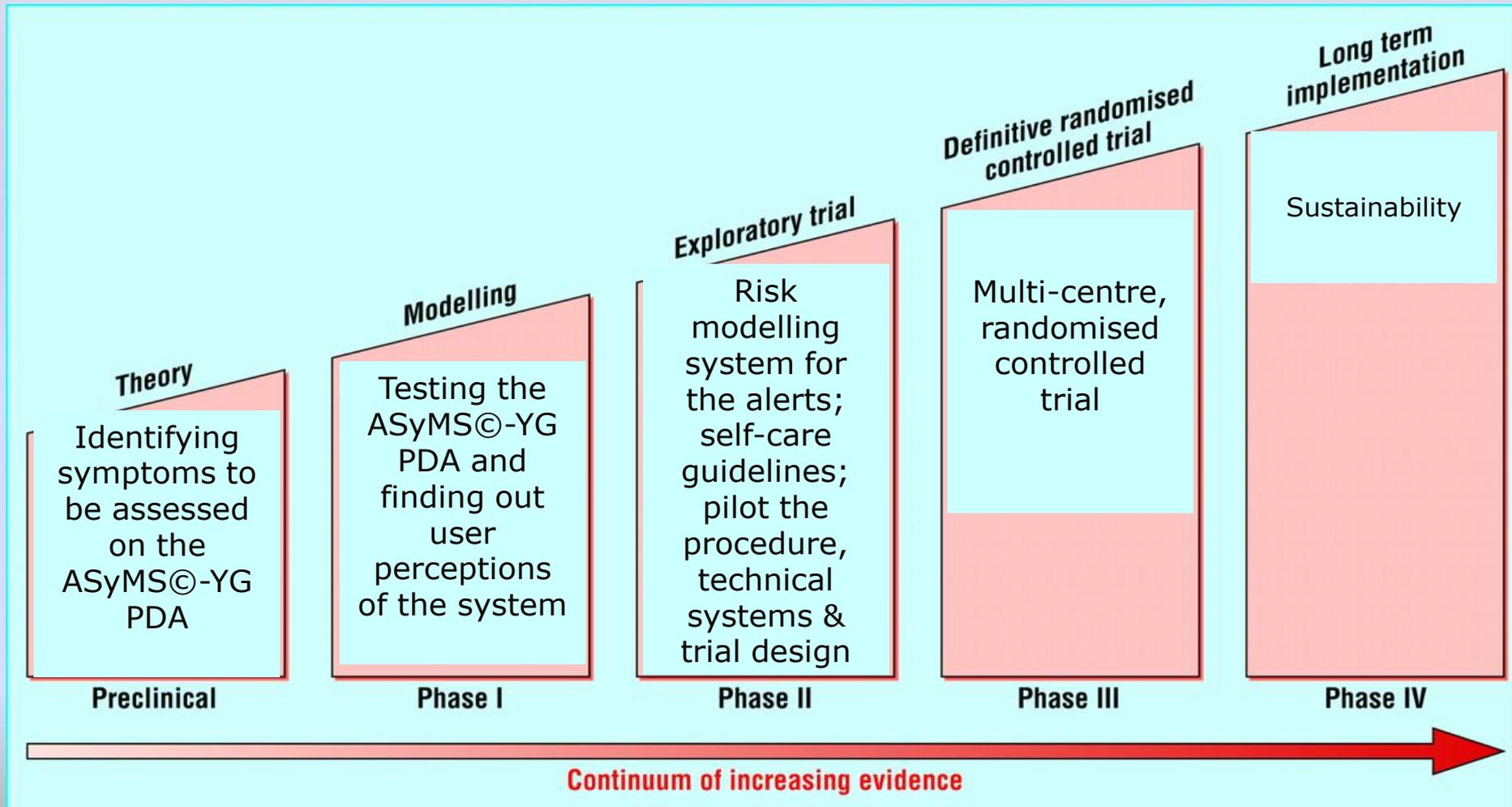
- Four phase development study.
- Based on the Medical Research Council framework for the development and evaluation of complex interventions (Craig et al 2008).

The MRC Framework



Campbell, M. et al. BMJ 2000;321:694-696

ASyMS©-YG development



ASyMS©-YG development

- Extensive involvement of young people and professionals in study development and design.
 - Very positive feedback from young people and professionals.
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- Aldiss, S., Taylor, R. M., Soanes, L., Maguire, R., Sage, M., Kearney, N., & Gibson, F. (2011) Working in collaboration with young people and health professionals. A staged approach to the implementation of a randomised controlled trial, *Journal of Research in Nursing*, vol. 16, no. 6, pp. 561-576.
 - Gibson, F., Aldiss, S., Taylor, R. M., Maguire, R., & Kearney, N. (2009) Involving health professionals in the development of an advanced symptom management system for young people: the ASyMS©-YG Study, *European Journal of Oncology Nursing*.
 - Gibson, F., Aldiss, S., Taylor, R. M., Maguire, R., Sage, M., & Kearney, N. (2010) Utilization of the Medical Research Council Evaluation Framework in the development of technology for symptom management: The ASyMS-YG Study, *Cancer Nursing*, vol. 33, no. 5, pp. 343-352.

The RCT

The aims were:

1. To determine changes in: chemotherapy toxicity, symptom distress, quality of life, anxiety and self-efficacy associated with the use of a remote PDA monitoring system for managing symptoms associated with chemotherapy.
2. To determine usefulness of information fed back to the patient under alert conditions.
3. To determine the use of self-management strategies as a result of self-care advice.
4. To determine changes in patient management as a result of generated alerts.
5. To evaluate the cost effectiveness of the ASyMS©-YG system.

Participants and recruitment

- Aged 13 - 24 years old.
- Diagnosed with lymphoma, bone tumour, soft tissue sarcoma or germ cell tumours.
- Being treated with chemotherapy.
- Four study sites.
- Potential participants identified by clinical team at each site.
- Study links gave information and took consent.
- Randomly allocated to control (standard care) or intervention group (use ASyMS©-YG PDA everyday throughout chemotherapy).

Outcome measures

- Measures of: self-efficacy, anxiety, quality of life, 'Life situation' (problems, symptoms, inconveniences relating to cancer and treatment).
 - Administered when entered study, at the end of treatment and six months after end of treatment.
- Perceptions of technology and ASyMS©-YG system questionnaire.
 - Completed when entered study, at the end of treatment.
- Paper version of PDA symptom questionnaire
 - Given at start of each chemotherapy cycle.

As the study progressed...

- Recruitment was extremely slow.
 - Despite contact with sites
 - By email and telephone
- We responded to their feedback
 - Following suggestions from the clinical teams the protocol was amended four times to try to increase recruitment.

Protocol amendments

What professionals told us...	What we did...
Teenage & young adult units take up to 24 years.	Changed the recruitment range from 13 – 24 years.
Increasing the age then involves other cancer types.	Germ cell tumours were added to the inclusion criteria.
Majority of young people were being randomised to the control arm.	Randomisation method was changed from minimisation to block.
There were difficulties recruiting after diagnosis: young person's mental state and the volume of studies they were being approached with at this time.	Recruitment can be at any time during the treatment trajectory.

Results

- Study withdrawn from two sites to concentrate recruitment on remaining two sites local to the research team.
- After 30 months the study was closed.
- 20 participants were recruited in total.
- Nine refusals to participate were documented.
- Six professionals from three study sites were interviewed to try to identify the challenges and barriers.

Challenges and barriers

Themes identified from the interviews:

- Burden of running a clinical trial
- General perceptions of research
- Views about ASyMS©-YG
- Perceptions of technology for supportive care
- Communication with young people.

The 'burden' running a clinical trial

- Unable to allocate time required to study procedures (consent, questionnaires, keeping track of chemotherapy cycles).
- Health professionals recruiting but not all trained in research conduct.
- Protocol violations, *'I'd forgotten when she was due in and then she missed that questionnaire and I had to give it retrospectively'*.
- Burden and complexities of the pager, *'I think I missed one alert because I was on holiday or I was somewhere that day. But we've made a choice not to involve the wider team, because it just seemed like too much work'*

General perceptions of research

- Hierarchy of research studies - drug trials taking precedence over any other, then other studies listed as if in order of preference, *'We have loads of other studies as well running at the same time... you know, we gave a bit more priority to... you're asking a young person about a clinical trial and say an adherence study...'*
- Views of the outcome measure, *'those horrible questionnaires'*.
- Number of research projects young people were approached to take part in, *'our patients at times, they feel like they're guinea pigs so not only are they on a clinical trial but this study is being done and this study is being done'*.
- Timing young people were approached to take part was important, i.e. not all at the point of diagnosis.

Views about ASyMS©-YG

- During the RCT it became apparent professionals perceived several issues with the system. (e.g. alerting system did not offer young people anything 'extra').
- Not always familiar with system (e.g. unaware of the graphs, still thought PDA questionnaire was restricted to start of chemotherapy cycles but actually completed every day).

Perceptions of technology for supportive care

- Development began in 2007 with 'hi-tech' PDAs - quickly outdated.
- Involvement of multiple technologies (PDA, web, pager) - overly complex.
- Pager viewed as outdated (often forgotten). Later removed from one site and text messages used.
- Felt threatened in their role – thought it could be seen as way of replacing nurses.

Communication with young people

- Differences between Trusts in how support for young people is provided.
- Patterns of communication with young people, ASyMS©-YG sometimes seen as conflicting or complementing.
- Contradictory statements about how easy/difficult it was for young people to contact the hospital team, *'there's three ward numbers and there's a day unit number. They also have access to their consultant's secretary, their social worker, me, a nurse consultant as I said before. So there are very, very different numbers. Eventually they would get hold of somebody...'*

What the literature says (1)

- RCTs are considered the 'elite' study design for evaluating the effectiveness of an intervention.
- But they can be complicated, expensive, time consuming and demanding for those involved.
- Often large numbers of participants required to provide adequate power to detect the effect of an intervention being tested.

What the literature says (2)

- Researchers conducting RCTs face numerous issues:

- Poor and slow recruitment.
- Retention of participants.
- Organisational obstacles.
- Maintaining staff interest.
- Gate keeping.
- Competing demands on clinical staff.

(Watson and Torgerson, 2006; Vedelo and Lonborg, 2010).

Other trial designs to consider

- Cross over trial
- Pragmatic trial
- Cluster RCT
- Zelen's design
- Factorial RCT

Tips for future success

1. An in-depth understanding of the context and services the intervention needs to fit in with, prior to commencing a project is vital.
2. Consider how the research sites will be supported (particularly when the core team is far away).
3. Include funding for appropriate personnel at each study site in applications.
4. Health professionals involved in research should be trained in research conduct - Good Clinical Practice training.

Tips for future success

5. Consider incentives for recruitment
 - a) Opt for inclusion in the National Institute for Health Research Clinical Research Network (NIHR CRN) Portfolio - research networks are assessed on their recruitment rates
 - b) Offer a per patient fee for recruitment.
6. Consider other 'novel' trial designs.
7. Implement methods to ensure professionals are informed and kept 'energised' about a study.

Tips for future success

8. Interventions using technology need to reflect the technology of the time.
9. Train researchers in research ethics pertaining to the rights of patients to make a choice (rather than assuming patients will feel overburdened and not approaching them to participate).
10. Facilitate local teams ownership of the study – so they feel they are part of the work rather than just data collectors.

Conclusion

- Trials are essential for establishing efficacy of an intervention; however they are complex and difficult to manage.
- It is important that preparatory work is thorough in order that the trial runs smoothly.
- Reflexivity is essential to enable amendments as necessary if things go wrong.