Feasibility in all settings

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Overview

- Overview of some of the key issues
- Particular focus on “signs”, but applicable to all domains
- Interactive sessions and voting!
• What are we aiming for?
Enough to get the job done?
Types of trials

- **Early-phase trials** – high resource, frequent patient visits, often require careful monitoring of interventions and potential side-effects.

- **Phase IV, pragmatic** - comparative effectiveness trials – does the intervention work in “real life”? Long-term safety studies.

- **Large, multi-centre trials** – multiple assessors and potentially high turn-over of research staff.

- **Self-funded trials** – a clinician with a “good idea” and passion to answer the question, could be a collaborative network of volunteer clinicians / nurses.
“Core outcome” that can be used in ALL trial settings

Able to detect small differences?

Suitable for all severities & interventions

Quick & easy to complete in a clinic setting

Need an “objective” scale

Training requirements, inter-observer variability

Many investigators

Consistent & reliable over time

Are we measuring things of importance to patients, who completes the assessment?

Patient reported outcomes

Low resource

Data management, data entry, postal follow-up

Pragmatic trials

Open / unblinded trials

Long-term trials

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HOME III, San Diego 2013

6
BOTTOM LINE:
is the scale sufficiently simple for it to be included even if that outcome is not relevant to the study in question?
Three item severity scale

- Assess THREE signs at a “representative” site
  - Erythema (redness)
  - Excoriation (signs of scratching)
  - Oedema / papulation (swelling)

- These signs consistently been shown to associate with “worsening” of the disease

- Reasonably well validated, very quick and simple

Is it sufficient as a core outcome for eczema signs?
Trial of antihistamines versus no antihistamines in patients with moderate eczema

- 12 month, pragmatic trial
- Double-blind, participants seen in clinic at baseline then followed-up by post / on-line questionnaire

**Primary outcome:**
patient-assessed eczema severity assessed monthly by questionnaire (POEM scale?)

**Secondary outcomes:** use of topical therapy, other core outcomes for HOME (including eczema signs, long-term control and QoL)
PEST Trial

Behavoural intervention for the management of moderate to severe eczema

- 6 month RCT – clinic visits every 2 months.
- Assessor blind
- **Primary outcome:** eczema severity – assessed by blinded research nurses
- **Secondary outcomes:** other core outcomes for HOME (including eczema symptoms, long-term control and QoL)
What are we aiming for?
“What is eczema?”

“What improves as the eczema gets better?”
Focus on essential information

- What are we measuring and why?

  Bleeding, blistering, cracks in the skin, crusting, scratch marks on the skin, involvement of sensitive / visible body sites, lichenification, redness, dryness, flaking, sleep difficulties, soreness or pain, swelling, amount of body affected, tightness of the skin, weeping / oozing

- Are all items necessary?
Are all items necessary?

• Some chronic signs less likely to change quickly (e.g. lichenification)

• Acute signs may be more sensitive to change
  – Redness (erythema)
  – Scratching (excoriation)
  – Swelling (oedema / papulation)

• Dryness (depends when emollient last applied, best reported by patients?)
Doctor-assessed itch…….

“doctor-assessed itch?”

• Should severity assessment be made by patients?

• Independent observers can measure signs, but not symptoms.
Who assesses what?

- Our core domains currently focus on eczema signs and symptoms as separate domains

- Should this be interpreted as:
  - Investigator-assessed severity (signs only)
    (suitable for unblinded studies)
  - Patient-assessed severity (symptoms & QoL)
• Add question
Focus on essential information

• How are we measuring severity?
  
  Severity at a “representative site” x “area of involvement”
  or
  Severity assessed separately at multiple sites
  or
  Global assessment

• Each has pros and cons
How representative is a “representative site”?

• What is a “representative site”?  
  An area of the body that represents:
  – a “typical” patch of eczema for the patient
  – a “typical” patch of eczema for a particular sign (e.g. signs of scratching)
  – the worst patch of eczema for the patient
  – the worst patch of eczema for a particular sign

• Do all body sites get worse / better at the same time?  
• Are all sites equally important to patients?  
• Is the same “representative” site used for subsequent assessments?
• Discussion topic

• What does a “representative site” mean to you?
Vote

• Add question
Timeliness of the Core Set

• Do all domains need to be ready at the same time?
Conclusion

- Put your preconceptions / allegiances to one side
- Listen to all points of view with an open mind
- Enjoy the discussion
- Be prepared to make decisions
Disclaimer

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Combining data pre- and post- HOME

• Two of the most commonly used scales to date are:
  – SCORAD (includes Three Item Severity scale)
  – EASI (includes Three Item Severity scale)

• Meta-analysis of old and new trials?
  – How can we combine old and news trials to be in-line with core outcomes?
  – Could we encourage all to report TIS (3 signs) separately in all trials until final instrument has been decided?