



Outcomes and Endpoints in Clinical Pressure Ulcer Prevention Trials

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Pressure ulcer prevention background

2 part process (process cycles back and forth between parts)

1. risk assessment
2. based on the results of risk assessment, we implement preventative measures:
 - repositioning
 - early mobilization
 - support surfaces
 - preventative skin care
 - microclimate control
 - prophylactic

The clinical decision making of evidence-based pressure ulcer prevention takes into account:

- research results (published works and studies based on clinical trials)
- clinical expertise and patient preferences
- policy frameworks, legislation, reimbursement policies

How do we get the most helpful information out of research results/clinical trials?

Clinical trial construction

Clinical trial consists of 3 stages:

1. *Input*
 - External stimuli (e.g. environment)
 - Patient characteristics
 - Behaviors, tradition



- Exposures
- Treatments

Example: *Trying to figure out which support surface is better for prevention. Input is special support surface A compared to B for PU prevention.*

2. Processing

The “black box” – can be influenced by many individual differences, in addition to official input

Example: *Processing is patients being put on different surfaces and developing/not developing PUs. Affected by main input, but also by differences in individual structure and function, susceptibility, response patterns.*

3. Response

- What happened in the end?
- Outputs
- Outcomes
- Events

Example: *How many patients developed new pressure ulcers on each support surface.*

Mission critical: choosing the right outcomes to study

Clinical trial outcomes:

- Are fundamental to study design
- Must be related to population and intervention
- Reflect efficacy, effectiveness or harm
- Primary outcomes = main interest (sample size)
- Should be selected based on
 - Relevance
 - Validity
 - Reliability

Common outcomes chosen in PU clinical trials:



- (Non) occurrence of new pressure ulcers
- Pressure ulcer severity (category)
- Time to new pressure ulcer/pressure ulcer free period
- Quality of life
- Pain
- Length of (hospital) stay
- Costs
- Patient satisfaction

Outcome challenges

But even an outcome that looks simple and intuitive can be complex when you come to define it.

Example: Pressure ulcer incidence

Challenge #1: Case definitions

One ulcer per person? What about the number of ulcers per person?

What defines an incidence? Is it one PU that makes an incidence? Or one person an incidence, no matter how many PUs they develop?

Challenge #2: Inclusion criteria

Do we exclude subjects with an existing PU? Must you be free of PUs to be included in the clinical study? (reason to exclude: if they have a PU, they're more likely to get more)

Challenge #3: Location

- Where are you measuring the PUs?
- Does it matter where they are located on the body?
- Predilection areas only?
- Risk of misclassification



Challenge #4: Categories

- Skin redness (category I) to category IV, or II to IV?
- Only 'typical' pressure ulcers category III and/or IV?
- Is it appropriate to combine categories and locations?
- Risk of misclassification

Issue: Severe pressure injuries rarely occur in clinical trials.

If you want to compare one study to another, make sure the trial is BIG. Lots of patients. The sample size must be significant.

Solutions to the outcome challenges

Standardize pressure ulcer incidence measurement in all clinical trials

Report all categories separately

Alternative parameters?

Reported measures in vivo: thickness and structure (ultrasound, OCT), edema, erythema, perfusion, transcutaneous oxygen levels, temperature, stiffness, elasticity, interleukins, TEWL, SCH, sebum casual content...

Relevance unclear to unlikely (e.g. interface pressure)

Use core outcomes!

A **COS (core outcome set)** is an agreed standardized collection of outcomes, which should be measured and reported in all trials for a specific clinical area. (Williamson et al. 2012)

Outcome domain is the concept to be measured (what are we measuring?)



Outcome measurement instrument is the standardized way to measure the domain (how are we measuring?)

How do you develop a core outcome set?

1. Definition of scope and applicability
2. Development of outcome domains
3. Identification of all instruments (systematic review)
4. Identification of all validation studies (systematic review)
5. Quality appraisal of instruments
6. Testing, additional validation studies
7. Finalization and dissemination

Part of the Cochrane Skin Group Core Outcome Set Initiative is **OUTPUTs (The Outcomes for Pressure Ulcer Trials project)**.

OUTPUTs aims to develop an internationally agreed core outcome set for trials evaluating the efficacy or effectiveness of pressure ulcer prevention interventions.

Conclusions

- Various non-comparable outcomes used in PU research
- The use of heterogeneous outcomes limits trial results comparison
- Pressure ulcer incidence important and relevant endpoint, but challenging to measure
- No agreement on other potentially relevant and important outcomes
- Core outcomes may help to improve trial results comparability and evidence-based practice

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