The Gift of the OMERACT Filter

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Outline

- What is a core set and why do we need them?
  - Issues with Trials
- Current initiatives to develop core sets
  - Outcome Measures in Rheumatology (OMERACT)
  - Core Outcome Measures in Effectiveness Trials (COMET)
- Existing definitions, conceptual structures and their history
- OMERACT proposal for core areas of measurement
Problems with trials

- Trials are done to evaluate whether an intervention is effective and safe
- Choice of measures to reflect benefit and harm
- In most areas choices not standardized
  - heterogeneity between trials
  - potential for bias (selective outcome reporting)
  - choice of measures less relevant to users
Solution

Development of trial core sets

- Minimum set of outcomes that should be measured and reported in all clinical trials of a specific condition

- What is an outcome?
- How to decide what belongs in a core set?
“Outcome MEasures in Rheumatoid Arthritis Clinical Trials”

Outcome Measures in Rheumatology*

- Informal, unofficial
- Group of health professionals and patient experts interested in outcome measures and endpoints in rheumatology

* www.omeract.org
Rheumatology, 1980-1990

*No consensus over which measures to include in RA trials*

- >25 different measures available
- 5 meetings: no single consensus
  - Confusion: purpose, focus of measurement, and selection of measures
  - Increasing recognition of the importance of sensitivity to change
- Transatlantic divide
OMERACT 1
Maastricht, 1992

- Core set for RA trials
- Minimum relevant improvement patients/trials
- Composite measures/improvement criteria
WHO/ILAR core set RA clinical trials

- global assessments patient & assessor
- pain
- painful joint count
- swollen joint count
- physical disability
- acute phase protein

- in studies ≥ 1 year: X-rays hands & feet
OMERACT 11  
(Pinehurst, 2012)

preconference symposium
- CAT/IRT

mini-module
- Psoriatic Arthritis

workshops
- Worker Productivity
- Acute Gout
- Ultrasound responsiveness RA
- Vasculitis
- OMERACT Filter 2.0
  - Truth: Areas/Domains
  - Truth: Instruments
  - Discrimination & Feasibility
  - Putting it all together
  - Patient Reported Outcomes
  - Imaging & Biomarkers

extra activities
- Fellow training
  - extended interest group
  - Flares in RA

special interest groups
- Myositis
- MRI-Juvenile Infl. Arthritis
- PROMIS
- Hand Osteoarthritis
- Equity
- Polymyalgia Rheumatica
- MRI-inflammatory arthritis
- Item Response Theory
- Hip Osteoarthritis
- Connective Tissue Disease/Interst. Lung disease
Bottom line

Achieving consensus over measures involves:

- Content
  - Education in methodology
  - Agreeing on:
    - Purpose
    - Domain(s)
    - Applicability of specific measures
- Iteration
Bottom line

Achieving consensus over measures involves:

- Content
- Process
  - Data-driven
  - Iterative, stepwise
  - Inclusivity
    - Important role for dissenters
    - Harsh data softened by political considerations
OMERACT Filter 1.0
OMERACT Filter
to select measures

To be applicable in its intended setting, a measure must be

- truthful
- discriminative
- feasible
OMERACT Filter

Truth

- free from bias
  - criterion, construct validity
- relevant
  - content, face validity
OMERACT Filter

**Discrimination**

- able to distinguish between states that are of interest:
  - at one time point
  - at different time points
  - reliability, reproducibility, sensitivity to change
OMERACT Filter

Feasibility

- time
- costs
- interpretability
OMERACT Filter

- Filter works best to select instruments once the **areas of measurement** have been decided on.
- Truth: “…measure what it’s supposed to…” but how to decide on the supposition?
- For any core set we need to decide in what areas we need to measure **core areas of measurement**.
WHO/ILAR core set for rheumatoid arthritis clinical trials

- Global assessments by patient & assessor
- Pain
- Painful joint count
- Swollen joint count
- Physical disability
- Acute phase protein

In studies ≥ 1 year: X-rays hands & feet
RA core set & outcome

- **Outcome:**
  “how a patient feels, functions or survives”
  - patient global
  - pain
  - physical function

- **Disease activity**
  - assessor global
  - swollen and tender joint counts
  - acute phase protein

- **Damage:** X-rays
Patient input in OMERACT started in 2002

- Core set is deficient because it does not include enough (patient-important) outcome measures
  - Fatigue
  - Sleep Quality

- …Content validity problem!
- …Core area problem!

- To decide on core sets, we need to define core areas first
OMERACT Filter 2.0
Core areas of measurement
Core areas of measurement

- Def.: areas that should always be addressed by measures included in a core set for trials aimed at a specific health condition
- to decide on core areas, we need:
  - a conceptual structure of health and health conditions
  - consensus on which areas in this structure are core
  - consensus on whether core areas are generic or specific to a certain health condition
Definitions

- health
- health intervention
- **core area:** aspect of a health condition that needs to be measured to appropriately assess the effects of a health intervention.
- **(sub)domain:** component of core area: a concept to be measured, a further specification of an aspect of health, categorized within a core area.
Definitions

- health
- health intervention
- core area: essential aspect of a health condition.
- (sub)domain: construct within a core area
- **outcome**: any identified result in a (sub)domain arising from exposure to a causal factor or a health intervention.
- **measurement instrument**: a tool to measure a quality or quantity of a variable.
Existing conceptual structures and their history

- WHO 2001
  International Classification of Functioning (ICF)
  - universal classification of human functionality, both positive and negative

```
health condition

body function & structure  activity  participation
```

contextual factors (environmental; personal)
# Core Areas for Measurement in Health Interventions

<table>
<thead>
<tr>
<th>Concepts</th>
<th>Impact of Health Conditions</th>
<th>Pathophysiological Manifestations</th>
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Core Areas for Measurement in Health Interventions

Concepts
- Impact of Health Conditions
- Pathophysiological Manifestations

Core Areas
- Death
- Life
- Resource Use/Economical Impact
- Pathophysiological Manifestations

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Core Areas for Measurement in Health Interventions

**Concepts**
- Impact of Health Conditions
  - Death
  - Life Impact
    - ‘lived experience of health’
    - AKA ‘Burden of Disease’

**Core Areas**
- Resource Use/
  - Economical Impact
    - Pathophysiological Manifestations
      - most ‘traditional’ trial measures
      - both physical and psychological

- Pathophysiological Manifestations
Core Areas for Measurement in Health Interventions

Concepts

Impact of Health Conditions

Pathophysiological Manifestations

Core Areas

Death

Life

Resource Use/

Economical Impact

Pathophysiological

Manifestations

Examples of specific Domains within Areas*

- disease
- intervention

* in all areas, domains can be generic or made more specific:
  eg. disease-specific, time specific (eg. short or long-term), specific for patient preference
Core Areas for Measurement in Health Interventions

**Concepts**

- Death
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- Resource Use/Economical Impact
- Pathophysiological Manifestations

**Core Areas**

- Impact of Health Conditions
- Pathophysiological Manifestations

**Examples of specific Domains within Areas**

- Disease
- Intervention
- ICF domains: activity and participation
- Quality of life
- Patient perception of health
- Loss of ability to work
- Psychosocial impact
- 2\textsuperscript{any} impact on family, caregivers
- Utility

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  - Disease-specific, time specific (e.g., short or long-term),
  - Specific for patient preference
Core Areas for Measurement in Health Interventions

**Concepts**

**Core Areas**

- **Death**
- **Life**
- **Resource Use/Impact**
- **Economical Impact**
- **Pathophysiological Manifestations**

**Examples of specific Domains within Areas***

- **disease**
- **intervention**

- **ICF domains: activity and participation**
- **quality of life**
- **patient perception of health**
- **loss of ability to work**
- **psychosocial impact**
- **2nd impact on family, caregivers**
- **utility**

- **societal**
- **individual**
- **health care**
- **direct/indirect (productivity)**
- **intangible costs**

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Core Areas for Measurement in Health Interventions

**Impact of Health Conditions**
- Death Life
- Resource Use/Economical Impact

**Pathophysiological Manifestations**
- ICF: body function and structure
- organ function (e.g., lung function)
- reversible manifestations
- irreversible manifestations
- biomarkers
- surrogate outcomes

**Core Areas**
- Death
- Life
- Impact
- Resource Use/Economical Impact

**Examples of specific Domains within Areas**
- disease
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- 2nd order impact on family, caregivers
- utility
- societal
- individual
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Impact of Health Conditions
Pathophysiological Manifestations

Core Areas

Concepts

Core Areas for Measurement in Health Interventions

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Impact of Health Conditions

Life

Resource Use/Economical Impact

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Adverse Events

AE’s are measured within the core areas, but are labeled separately to allow assessment of benefit and harm.

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Developing a Core Outcome Measurement Set

Core Areas
- Death
- Life Impact
- Resource Use
- Pathophysiological Manifestations

Setting/Contextual factors
- Adverse events

Stakeholder input

Draft Core Domain Set

Literature review
- List of Domains & Instruments
- Match Domains to Core Areas

All important stakeholders should be included from the start: patients and their proxies, caregivers, researchers, etc.

consensus

update cycle

agreement on what to measure at least one Domain from each Core Area
agreement on what to measure
at least one Domain from each Core Area
agreement on what to measure
at least one Domain from each Core Area

agreement on how to measure
at least one applicable Instrument per Domain
Developing a Core Outcome Measurement Set

Core Domain Set

- List of candidate Measurement Instruments per Domain

For each domain: covered by at least one Instrument?

- yes

- document applicability
  (for each available instrument: is it Truthful, Discriminative and Feasible?)

- yes

- When all Domains have at least one applicable instrument:

Candidate Core Outcome Measurement Set

- consensus

Core Outcome Measurement Set

agreement on how to measure at least one applicable Instrument per Domain
Developing a Core Outcome Measurement Set

Core Domain Set

Literature review

List of candidate Measurement Instruments per Domain

For each domain: covered by at least one Instrument?

- yes
- no

Document applicability (for each available instrument: is it Truthful, Discriminative and Feasible?)

Consensus

Preliminary Core Outcome Measurement Set

- develop new Instrument(s)
- validation studies
Developing a Core Outcome Measurement Set

**Core Domain Set**

- Literature review

List of candidate Measurement Instruments per Domain

For each domain:
- covered by at least one Instrument?
  - no
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Preliminary Core Outcome Measurement Set

- develop new Instrument(s)

validation studies

Candidate Core Outcome Measurement Set

- consensus

When all Domains have at least one applicable instrument:

**Core Outcome Measurement Set**

agreement on how to measure at least one applicable Instrument per Domain

update cycle
Thank YOU!
Questions,
Comments...