4th COMET Network Meeting

Date and venue

16th September 2014;
Department of Epidemiology and Biostatistics; VU University Hospital Amsterdam, Netherlands

Background

The aim of the meeting was to bring experienced developers of existing core outcome sets (COS) together to share experiences, identify best practices and reflect on resource building.

The meeting was organised by Maarten Boers. Sanne Prinsen and Alessandro Chiarotto of the Department of E&B helped prepare this report.

Programme

09:30	Refreshments
10:00	Welcome, Maarten Boers
10:10	COMET Initiative, Mike Clarke (includes summary of previous network meetings)
10.25	OMERACT initiative, Maarten Boers
	Presentations from core outcome set developers
10.40	Berthold Langguth: tinnitus
10.50	Piero Olliaro: cutaneous leishmaniasis
11.00	Finn Gottrup: non-healing wounds
11.10	Olivier Bruyère: acute low back pain
11.20	Davide Pareyson: Charcot-Marie-Tooth disease type 1A
11:30	Bio break
11.40	Peer Carsten Tfelt-Hansen: migraine
11.50	Alessandro Chiarotto: nonspecific low back pain
12.00	Round table discussion: sharing best practice for consensus techniques
13:00	Lunch
13.45	Round table discussion: Sharing best practice for selecting participants
14.45	Round table discussion: Sharing best practice for involving stakeholders: patients;
15.45	Refreshments
16:00	Round table discussion: implementation
17:00	Resource building
17.30	Meeting close

Attendees

Berthold Langguth	Ass Prof of Psychiatry and Psychotherapy	U Regensburg, DE
Piero Olliaro	Leader – Intervention & Implementation Research	WHO, Genève, CH
Finn Gottrup	Prof of Surgery	U of S Denmark, Copenhagen, DK
Davide Pareyson	Head of the Functional Department of Rare Diseases	C.Besta Neurological Institute, Milano, IT
Olivier Bruyere	Prof of Clinical Epidemiology & Geriatric Rehabilitation	U of Liege, B
Peer Carsten Tfelt-Hansen	Consultant Neurologist	Hilleroed, DK
Alessandro Chiarotto	Junior Researcher, Department of Health Sciences	VU University Amsterdam, NL
Caroline Terwee	Senior Researcher, Dept of Epidemiology & Biostatistics	VU University Medical Center, Amsterdam, NL
Sanna Prinsen	Post-doc, Dept of Epidemiology & Biostatistics	VU University Medical Center, Amsterdam, NL
Maarten Boers	Prof of Clinical Epidemiology	VU University Amsterdam, NL
Mike Clarke	Prof of Research Methodology	Queens University Belfast, N-Ir

Presentations

The first part of the day was spent on presentations. After introductions on COMET by Mike Clarke and OMERACT by Maarten Boers, each COS developer gave a brief presentation on his COS, with specific focus on the method for reaching consensus, selection of stakeholders, and implementation. A brief summary of the presentations is given at the end of this document.

Round Table discussions

The first discussion was ad-hoc, to get key issues on the table (and make sure these were covered). Then 3 topics were tackled: consensus technique, participant and stakeholder involvement, and implementation & resource building.

1. Consensus technique. Participants had used various combinations of Delphi and workshop discussions. Structured group techniques (e.g. nominal group) or newer methods (e.g. concept mapping) had not been used. Advantages and disadvantages of the different techniques were briefly elaborated. Participants felt the choice of a particular technique depends on scope and stakeholders, but there are no good criteria to choose the one over the other: thus there is a need to develop such criteria. A suggestion was made to study the development of diagnostic and classification criteria to see whether COS development could learn from their process of development, given that these diagnostic and classification criteria often become widely accepted. Also, participants felt the need for simple and accessible guidelines on how to apply a chosen technique to COS development. A general remark was that emphasis on "correct" methodology could itself become a barrier to develop a COS. In any case, COS developers should be explicit about the reasons for choosing a particular technique.

2. Participant & stakeholder involvement. Potential stakeholders include: patients (either as experienced or as experts), caregivers, health care providers, researchers (trialists and systematic reviewers were seen as different types of researcher – one is the person who measuring the outcomes in the first place, the other is the person who is trying to use what was measured), regulators, industry, payers, journal editors, trial registers, general public. It was recognized that participants are not the same as stakeholders: stakeholders might not participate in the COS development but be allowed to provide input at various stages. The idea is to enrich your consensus process with as much information as possible. Advantages of involving more stakeholders include: better consensus, better acceptance, and better implementation. As stated by Mike Clarke: "the people at the table are the ones who will implement your COS." The other stakeholders will ask: "was I consulted?" Or: "were the appropriate parties consulted." More and more, funders are looking to see whether patients or their proxies were adequately involved. The number of stakeholders and the level of involvement depend on the scope of the COS, and the advantages of involving them must be weighed against the disadvantages: practical issues, time, and costs. Also, the methodology of involvement is currently underdeveloped. Issues of identification (not only stakeholder

group but also specific persons; includes efforts needed to get at “the difficult to reach” groups and representativeness of the people who are approached or who agree to join the process), extent of involvement (e.g. participating and voting in Delphi vs. one-time consultation; involving disadvantaged groups, e.g. poor or illiterate), weighting of importance (equal voting, weighted voting, feedback by stakeholder group) are currently not solved. A key issue is the quality of information received from the participants. To start, participants must have a clear view of what is asked of them (e.g. what perspective should a clinician take: as disease expert or as someone seeing patients every day?). Most participants will need training to be able to fully participate in a consensus procedure. For example, OMERACT has a special training program for patients and for first-time participants. Special mention was made of the difficulties of getting regulators to participate. There are problems in finding the right persons, getting the organisation to agree they can come, funding their presence, and assessing the effectiveness of their participation.
As with the choice of consensus technique discussed under point 1, at this stage in the absence of good guidance or a “correct” methodology, it is important that COS developers are explicit about the choices made regarding stakeholder involvement.

3. Implementation and resource building. The following points were mentioned as factors predicting successful implementation: proximity to users and high perceived need, extensive stakeholder involvement. Success can be measured by number of citations, uptake in studies, wide translation of instruments endorsed by the COS. Future COS developers should write an implementation plan that could include the following items: wide circulation but also targeted circulation (users; “gatekeepers” such as ethical committees, funders; editors; registries); acceptance by authorities, scientific/professional societies; inclusion in RCT and other research guidelines (CONSORT, SPIRIT, Cochrane, specific guidelines put forward by professional societies) and guidelines from funding bodies and national ethical committees; and use in trial registries. The value of the COS can also be prospectively studied by the COS group, e.g. by monitoring the quality of the trials. In addition, COMET should look at ways to study the barriers that exist for successful implementation of COS.

In the discussion on resource building, several points were raised to increase awareness of COS development (and COMET): working to improve keywords so that COS work can be found more easily (this is especially important for new COS developers who need to know that resources already exist); promotional strategy aimed at the parties mentioned above under implementation; following Cochrane’s example to go to national funders to fund the infrastructure (website, database and search engine, guideline developers, train the trainers); training and maintaining a group of experts that are available to help other COS groups (this could work through a snowball effect: COMET provides an expert/trainer to a group on condition that at least one person of that group is willing to become an expert and help at least one other COS group). In addition, it was felt that COMET still looks very British. It should become truly global by expanding to other countries and continents, including low- and middle-income countries. Importantly, there are many neglected diseases for which the study of effective treatments is completely obstructed by the lack of good outcomes.

Summary of Presentations

Berthold Langguth – Tinnitus

Scope

International standards for patient assessment and outcome measurement in order to compare data from different clinical trials.
Goal 2006: to develop a first international standard that is feasible, flexible, inclusive, good input for clinicians/researchers

Stakeholders

Researchers clinicians, company reps, patient reps.

Methods for consensus

International tinnitus conference:
Consensus meetings, 4 workshops with 15 participants each (including patients consumers); aggregation of ideas and suggestions in a draft paper reviewed in 2 rounds by workshop participants.

Implementation

- Scientific publication
- Establishing an international database
- Consensus article for study methodology

Piero Olliaro – Cutaneous Leishmaniasis

Scope

Project underway. Improve and standardize methods to improve CL clinical trials especially concerning core outcome sets (core eligibility criteria; core outcome measures)

Stakeholders

CL researcher, health care providers and regulators to define relevant outcome measures and core eligibility criteria. Involving patients from this patients' population is challenging and will require a specific study.

Selection: not discussed

Methods for consensus

1. Generate awareness of the project
2. Delphi for stakeholder consultations, based on 2 Cochrane systematic reviews; plus patient interviews and regulators involvement.
3. Collaborative document revision of guidance paper.

Implementation: not discussed

Finn Gottrup – Non-healing wounds

Scope

Outcomes in wound healing, due to lack of high quality evidence.
Recommendations on the accepted level of precision on endpoint/outcome parameters, published in J Wound Care, 2010.

- 60% of the outcomes relates to healing

The objective is to find new outcomes.

Stakeholders
Patients were not involved up till now.
Clinicians (Medical doctors, nurses, podiatrists, physiotherapists), government, industry.

Selection: not discussed

Methods for consensus: not discussed

Implementation
- Translated to other languages in Europe
- Published paper on EWMA study recommendations on who to perform a good RCT, J Wound Care, 2014.
- Inviting national Med Tech industry organizations
- Meetings on a European level
- Monitoring

Olivier Bruyere – Acute low back pain
Scope
GREES: to produce a consensus document that may be used by regulatory authorities as a basis for drugs trials

Stakeholders
- Academic for university
- Scientists from industries
- Members of national and European drug licensing authorities

Selection: not discussed

Methods for consensus
- Systematic review
- One or two day meeting (presentations, general discussion, consensus by all participants)
- Draft paper and circulation of the draft paper
- If necessary, direct contact with first author, the president of GREES, and the member.
- No strict methodology to reach consensus
- Potential influence of key opinion leaders

Implementation
No involvement because still no guidelines on this topic from the EMA, but:
- Invitation from the EMA to discuss main issues

Davide Pareyson – Charcot-Marie-Tooth disease type 1A

Scope

Core outcome measures in Charcot-Marie Tooth (CMT) disease for ascorbic acid clinical trials
How to measure disease progression and intervention efficacy

Stakeholders

Clinical researchers, scientists, trial experts, epidemiologist, ascorbic acid expert patients.

Selection: not discussed

Methods for consensus

Workshop discussion in 2005 at the European Neuro Muscular Centre (ENMC), plus follow-up in 2009.
One weekend, 20 experts from different areas and countries.
Agreement on:

- Preparation of clinical trials, including core outcome measures, trial duration, frequency of assessment, drug dosages

Limitations:

- Arbitrary choices of topics and experts
- Limited number of participants
- Difficulty in solving all issues

Implementation

- Conclusions on the website
- Follow up in 2009
- Two papers (2006 and 2009)

Peer Carsten Tfelt-Hansen – Migraine

Scope

Problems in methodological guidelines (by International Headache Society) in migraine drug trials.

Stakeholders

41 participants; 6 from industry and 35 academics

Selection

- 75% by chairman as academics with practical experience in trials or statisticians
- Chairman asked national headache society for candidates

Methods for consensus

- Draft was circulated for comments before the committee meeting.
- 2-day committee meeting and consensus was reached after extensive discussions.
- Corrections / comments could be made via email.

Implementation

- No interest of FDA
- EMA elaborated in 2006 on … guidelines (2000 or 2002?)

Alessandro Chiarotto – nonspecific low back pain

Scope

Update of a core set for low back pain (LBP), focus on efficacy and effectiveness clinical trials for all health interventions for non-specific LBP

Stakeholders

Involved: health care researchers, clinicians, and patients. Industry and regulatory reps not involved.

Selection

- Members of the Steering committee (including all stakeholders), 6%
- Health care researchers (through systematic literature search, sampling, available email addresses), 50%
- Health care providers (sampling, available email addresses), 39%
- Patients (sampling, consent, booklet), 5%

N=280

Methods for consensus

1) Generation of a list of potential core domains (inclusion of: outcomes included in all clinical trials of 4 recent Cochrane reviews, categories of ICF core set, domains of a conceptual framework developed to characterize the burden of LBP),
2) Framing of potential core domains using the OMERACT Framework 2.0,
3) Delphi study to reach consensus on core domains.

Implementation

- Presentations at international conferences
- Multiple publications