A systematic review to collate the knowledge base for core outcome set development

Protocol

1 Background

The COMET (Core Outcome Measures in Effectiveness Trials) Initiative (www.comet-initiative.org) brings together people interested in the development and application of agreed standardised sets of outcomes, known as 'core outcome sets'. These sets represent the minimum that should be measured and reported in all randomised trials of a specific condition, and are also suitable for use in clinical audit or research other than randomised trials. The existence or use of a core outcome set does not imply that outcomes in a particular trial should be restricted to those in the relevant core outcome set. Rather, there is an expectation that the core outcomes will be collected and reported, making it easier for the results of trials to be compared, contrasted and combined as appropriate; while researchers continue to explore other outcomes as well. COMET aims to collate and stimulate relevant resources, both applied and methodological, to facilitate exchange of ideas and information, and to foster methodological research in this area.

As part of the COMET Initiative we are developing a publically available internet-based resource to collate the knowledge base for core outcome set development, as well as the applied work that has already been done according to disease area. This will be a useful resource for trial funders to refer to, for researchers to see what work has been done in their area of interest and for research funders who are looking to fund work in this area and wish to avoid unnecessary duplication. It will include planned and ongoing work as well as published accounts of core outcome set development. Keeping the database up to date is key to its value for users. This requires the development and application of an optimal, multi-faceted search strategy to identify work related to the development of core outcome sets (COS).

2 Aims

To identify studies that have been conducted to determine which outcomes or domains to measure in clinical trials

a. To identify the methodological techniques used in these studies
b. To identify COS developers/groups to include in a survey to explore methodological choices (separate study)

3 Methods

3.1 Criteria for considering studies for inclusion for this review

3.1.1 Types of studies

The following studies will be eligible for inclusion in the review:

1. Studies that developed or applied methodology for determining which outcome domains or outcomes should be measured, or are important to measure, in clinical trials

2. Systematic reviews of studies that developed or applied methodology for determining which outcome domains or outcomes should be measured, or are important to measure, in clinical trials

The following studies will be excluded from the review:

1. Studies relating to how, rather than which, outcomes should be measured (instruments, tools, scales, scores, outcome definition)

2. Studies reporting the design/rationale of a single trial

3. Studies reporting the use of a core outcome set*

4. Systematic reviews of clinical trials

5. Systematic reviews of prognostic studies

6. Studies (including systematic reviews and surveys) of outcomes measured in clinical trials (N.B although these will not be included in this systematic review, they will be eligible for inclusion in the COMET database)

7. Studies that elicit stakeholder group (e.g. patient or clinician) opinion regarding which outcome domains or outcomes are important or should be measured in clinical trials (including single perspective)

8. Studies identifying core outcome sets to evaluate the quality of care given by healthcare providers, or to guide the management of individual patients in clinical practice (e.g. minimum data sets for audit)

* reports relating to core outcome sets but not meeting inclusion criteria (e.g. where a core outcome set has been used) will be retrieved, so that their references can be checked for potentially eligible studies.

3.1.2 Types of participants

Studies relating to participants of any age and any conditions will be eligible for inclusion in the review.

3.1.3 Types of interventions

Studies relating to any intervention will be eligible for inclusion in the review. Studies that do not specify a specific intervention will also be eligible for inclusion.

3.2 Identification of relevant studies

3.2.1 Electronic searching

The following electronic databases will be searched:

1. MEDLINE via Ovid
2. SCOPUS
3. Cochrane Methodology Register

3.2.1.1 Search strategy

We will develop and apply an optimal, multi-faceted search strategy to search the databases using a combination of text words and index terms, adapting the search strategy as appropriate for each database. This will build on an appraisal of the searches from a previous review of studies that aimed to determine which outcomes to measure in clinical trials in children (1), a previous review of

studies using the Delphi technique to determine which outcomes to measure in clinical trials (2), and a previous review of studies addressing patients' priorities regarding outcomes (3).

The search strategy will combine three concepts of search terms (see Appendix 1) – 'randomised trial / systematic review', 'methodology' and 'outcomes'. All terms within each concept will be combined with the Boolean operator OR and then the three concepts will be combined using AND. Key search terms will also be targeted in title and abstract, which will be combined with the Boolean operator OR.

3.2.2 Hand searching

We will identify and review funded projects which included the development of a COS, including NIHR programme grant scheme reports and HTA reports.

We will search for known key authors and citations to key papers (e.g. the work of the OMERACT group), and reports will be sought and reviewed.

We will examine references cited in included studies, and relevant documents will be sought and reviewed.

We will examine references cited in studies relating to core outcome sets but not meeting inclusion criteria (e.g. where a core outcome set has been used), and relevant documents will be sought and reviewed.

We will identify and review regulator guidance documents.

3.2.3 Contact with Cochrane Review Groups

We will contact all Cochrane Review Groups across all areas of health care to request information on COS that they are aware of.

3.3 Selecting studies for inclusion

The records retrieved from the searching will be combined and duplicate reports will be removed. The titles and abstracts of all identified citations will be screened to assess eligibility (stage 1). The full text of potentially relevant articles will then be assessed for inclusion (stage 2).

Stage 1

One reviewer will independently screen the title and abstract of all citations. Each citation will be categorised as include, unsure, exclude, or exclude-references to be checked. Full papers will be retrieved for all those categorised as include, unsure, or references to be checked based on this screening of the title and abstract.

Full papers will be obtained for a 1% sample of the records excluded on the basis of the title and abstract and checked for correct exclusion by a second reviewer. If any studies are found to be incorrectly excluded, additional checking will be performed within the other excluded records.

Reasons for exclusion will not be documented at this stage, with the exception of abstracts that just miss out on being eligible for the review (e.g. Studies relating to how, rather than which, outcomes should be measured).

Stage 2

One reviewer will independently screen the full paper of all citations categorised as include or unsure based on the title and abstract. Full papers will be categorised as include, exclude or unsure.

Citations categorised as unsure will be reviewed by a second reviewer and a discussion will take place between the reviewers to reach consensus on its eligibility. A third reviewer will be consulted if agreement cannot be achieved.

Reasons for exclusion will be documented for each article judged to be ineligible in stage 2.

A second reviewer will review 5 % of excluded full papers to check for correct exclusion. If any studies are found to be incorrectly excluded, additional checking will be performed within the other excluded articles.

Full papers will be obtained for all records categorised as relating to core outcome sets based on the title and abstract but which do not appear to meet the inclusion criteria (e.g. where a core outcome set has been used). Reference lists will be checked, and relevant citations retrieved and assessed for inclusion.

The reference lists in the reports of all included studies will be checked, and relevant citations retrieved and assessed for inclusion.

The list of included studies will be sent to a network of researchers within the COMET Initiative to review for any omissions.

3.4 Data collection and extraction

For each included study, the following data will be extracted:

1. Health area
    a. Disease or health category (e.g. 'Lungs & airways' or 'Pregnancy & childbirth')
    b. Disease name (e.g. 'Asthma')

2. Target population
    a. Age
    b. Sex
    c. Nature/type of intervention

3. Method of development used, including
    a. Method of obtaining participant opinion (e.g. interviews, questionnaires, focus groups, Delphi)
    b. Detail of method (e.g. How the original list of outcomes was identified, questions asked of participants, level of anonymity, methods used to reduce number of outcomes, definition of consensus used)
    c. Participant response rate

4. Stakeholders involved in the process, including
    a. Who was involved (e.g. health professionals, patients, carers), including numbers and their geographical location
    b. Contribution of the different groups in the process
    c. Method for identifying health service users or their representatives (e.g. clinic, patient association, advocacy group, carer support group)
5. Participant eligibility criteria

6. Selected outcome domains and outcomes, indicating which are patient reported outcomes (PRO)

7. Geographical setting of the study

When information regarding any of the above items is missing or unclear, we will attempt to contact authors of the original reports to request further details.

It is anticipated that data extraction and follow up with authors will be done independently by one of two researchers. If there is disagreement about any extracted data, this will be discussed, with a third reviewer as necessary, to reach consensus.

3.5 Data analysis and presentation of results

Studies will be described in narrative form, and the findings will be provided in text and tables format. We do not anticipate conducting any statistical analyses to combine the findings of different studies.

3.6 References

1. Sinha, I., L. Jones, et al. (2008). "A systematic review of studies that aim to determine which outcomes to measure in clinical trials in children." PLoS Med **5**(4): e96.

2. Sinha, I. P., R. L. Smyth, et al. (2011). "Using the delphi technique to determine which outcomes to measure in clinical trials: recommendations for the future based on a systematic review of existing studies." PLoS Med **8**(1): e1000393.

3. Oliver S, Gray J. A bibliography of research reports about patients', clinicians' and researchers' priorities for new research. London: James Lind Alliance, December 2006

3.7 Appendices

Appendix 1 – search strategy for Medline via Ovid

# ▲	Searches
	RANDOMISED TRIAL / SYSTEMATIC REVIEW TERMS
1	Health Services/ut [Utilization]
2	registries/
3	systematic review.mp.
4	structured review.ti.
5	evidence based medicine.ab.
6	exp Clinical Trials as Topic/
7	clinical trial$.ab.
8	randomised controlled trial$.ti,ab.
9	randomised trial$.ti,ab.
10	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
	METHODOLOGY TERMS
11	workgroup$.mp.
12	standard$ outcome$.mp.
13	Practice Guideline/
14	clinical database.mp.
15	patient important outcome$.mp.
16	(standard$ adj3 reporting).mp.
17	congresses.pt.
18	Delphi Technique/
19	(recommend$ adj3 outcome$).mp.
20	consensus development conference.pt.
21	outcome$ reporting.mp.
22	priorit$ symptom$.mp.
23	(task force adj3 outcome$).mp.
24	appropriate outcome$.mp.
25	research design/
26	endpoint determination/
27	consensus development conference/
28	patient participation/
29	consensus.mp.
30	workshop.mp.
31	Consensus Development Conferences, NIH as Topic/
32	focus groups/

33	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32
	OUTCOME TERMS
34	outcome$.mp.
35	end point$.mp.
36	(core adj3 set).mp.
37	treatment emergent problem$.mp.
38	exp outcome Assessment Health Care/
39	Treatment Outcome/
40	Quality of Life/
41	34 or 35 or 36 or 37 or 38 or 39 or 40
	TITLE AND ABSTRACT TERMS
42	clinical-study design.mp.
43	patient$ perspective$.ti.
44	outcome$.mp. and delphi.ti.
45	(outcome$ and delphi).ab.
46	(perspective$ adj3 outcome$).ti.
47	core outcome$.ti,ab.
48	core set$.ti,ab.
49	clinical trial design$.ti.
50	design$ clinical trial$.ti.
51	(consensus and outcome$).ti.
52	42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51
	COMBINED SEARCH TERMS
53	10 and 33 and 41
54	52 or 53