
**Core Outcome Measures in Effectiveness Trials**

www.comet-initiative.org

# Aims of the workshop

To identify and discuss challenges and potential solutions in the development and uptake of COS

# Reporting guideline

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## Core Outcome Set–STAndards for Reporting: The COS-STAR Statement

Jamie J. Kirkham[1], Sarah Gorst[1], Douglas G. Altman[2], Jane M. Blazeby[3], Mike Clarke[4], Declan Devane[5], Elizabeth Gargon[1], David Moher[6], Jochen Schmitt[7], Peter Tugwell[8], Sean Tunis[9], Paula R. Williamson[1]*

*PLoS Medicine* 2016; **13**(10):e1002148

Prinsen et al. Trials (2016) 17:449
DOI 10.1186/s13063-016-1555-2

Trials

RESEARCH Open Access

# How to select outcome measurement instruments for outcomes included in a "Core Outcome Set" – a practical guideline

Cecilia A. C. Prinsen[1*], Sunita Vohra[2,3,4], Michael R. Rose[5], Maarten Boers[1,6], Peter Tugwell[7], Mike Clarke[8], Paula R. Williamson[9] and Caroline B. Terwee[1]

**Abstract**

**Background:** In cooperation with the Core Outcome Measures in Effectiveness Trials (COMET) initiative, the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) initiative aimed to develop a guideline on how to select outcome measurement instruments for outcomes (i.e., constructs or domains) included in a "Core Outcome Set" (COS). A COS is an agreed minimum set of outcomes that should be measured and reported in all clinical trials of a specific disease or trial population.

**Methods:** Informed by a literature review to identify potentially relevant tasks on outcome measurement instrument selection, a Delphi study was performed among a panel of international experts, representing diverse stakeholders. In three consecutive rounds, panelists were asked to rate the importance of different tasks in the selection of outcome measurement instruments, to justify their choices, and to add other relevant tasks. Consensus was defined as being achieved when 70 % or more of the panelists agreed and when fewer than 15 % of the panelists disagreed.

**Results:** Of the 481 invited experts, 120 agreed to participate of whom 95 (79 %) completed the first Delphi questionnaire. We reached consensus on four main steps in the selection of outcome measurement instruments for COS: Step 1, conceptual considerations; Step 2, finding existing outcome measurement instruments, by means of a systematic review and/or a literature search; Step 3, quality assessment of outcome measurement instruments, by means of the evaluation of the measurement properties and feasibility aspects of outcome measurement instruments; and Step 4, generic recommendations on the selection of outcome measurement instruments for outcomes included in a COS (consensus ranged from 70 to 99 %).

**Conclusions:** This study resulted in a consensus-based guideline on the methods for selecting outcome measurement instruments for outcomes included in a COS. This guideline can be used by COS developers in defining *how* to measure core outcomes.

**Keywords:** COMET, Core Outcome Set, COSMIN, Delphi study, Guideline, Instrument selection, Outcomes research, Outcome measurement instrument

Williamson *et al. Trials* _####################_
DOI 10.1186/s13063-017-1978-4

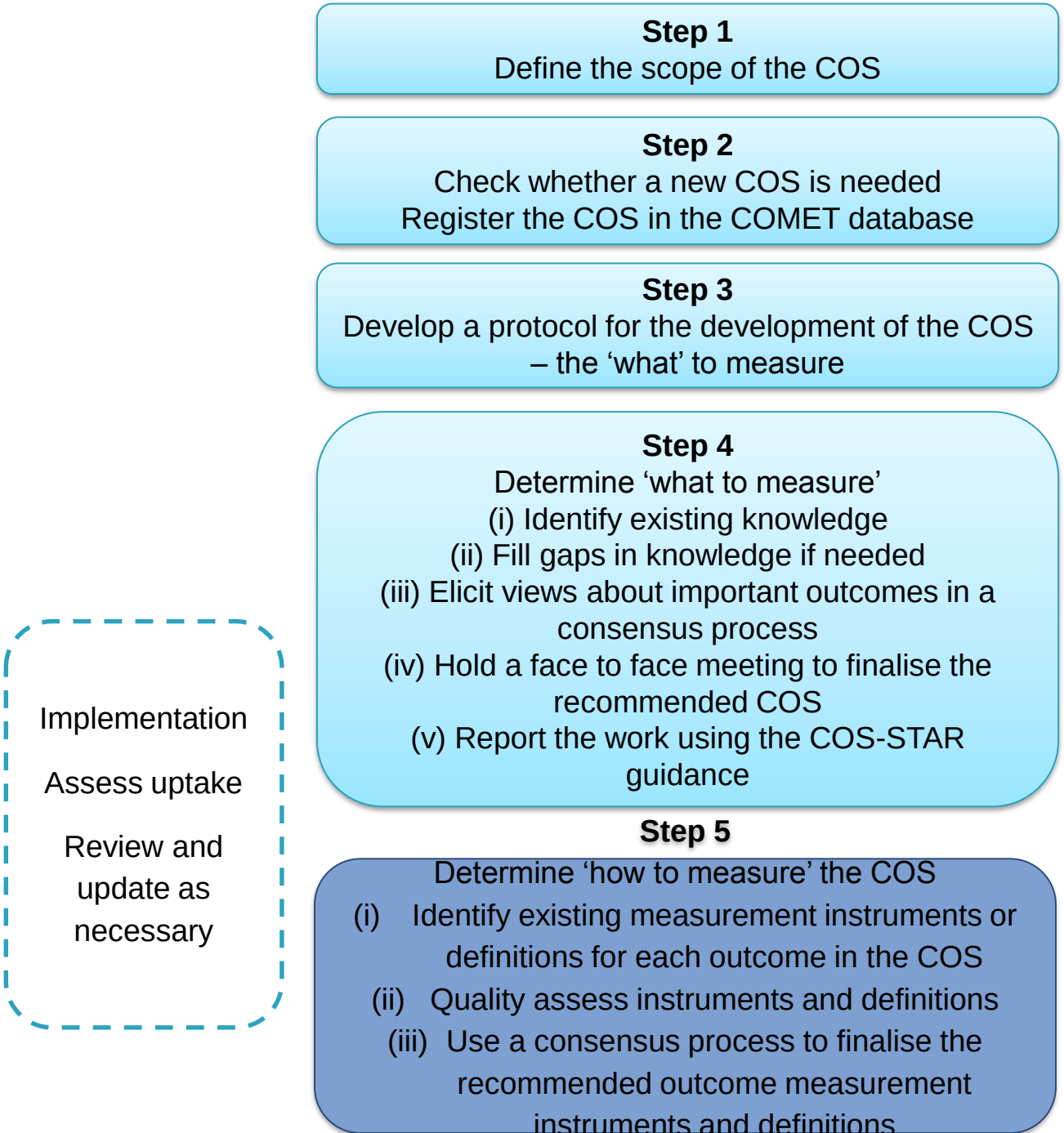
Trials

REVIEW Open Access

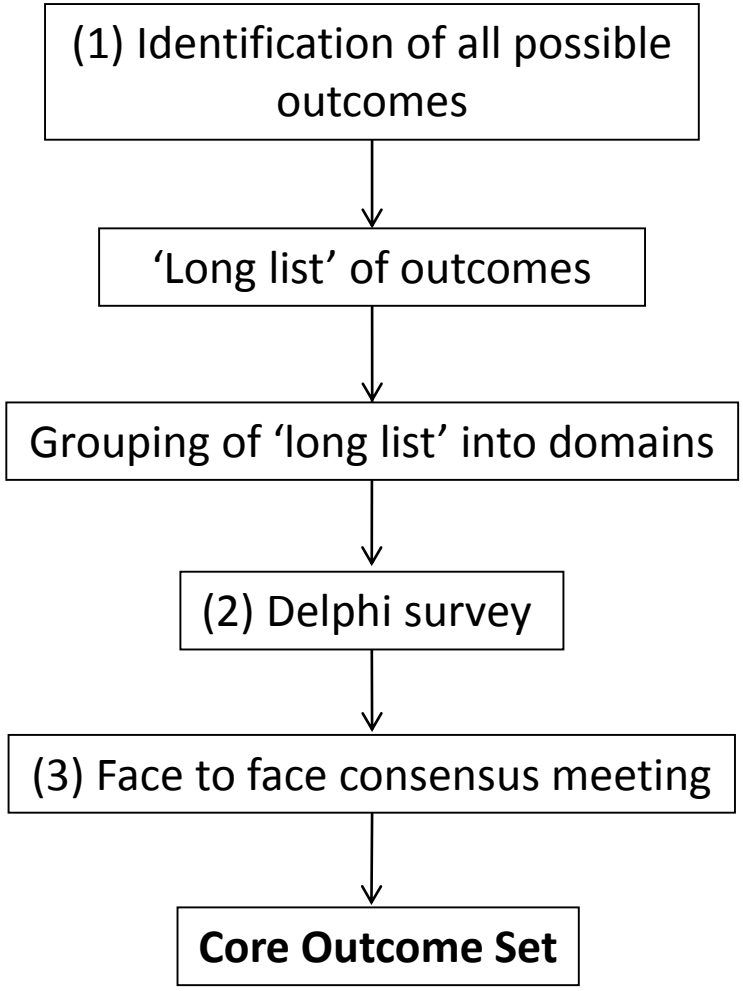
# The COMET Handbook: version 1.0

Paula R. Williamson[1*], Douglas G. Altman[2], Heather Bagley[1], Karen L. Barnes[1], Jane M. Blazeby[3], Sara T. Brookes[3], Mike Clarke[4,5], Liz Gargon[1], Sarah Gorst[1], Nicola Harman[1], Jamie J. Kirkham[1], Angus McNair[3], Cecilia A. C. Prinsen[6], Jochen Schmitt[7], Caroline B. Terwee[6] and Bridget Young[1]

**20th June 2017**


Step 1
Define the scope of the COS
Step 2
Check whether a new COS is needed
Register the COS in the COMET database
Step 3
Develop a protocol for the development of the COS – the 'what' to measure
Step 4
Determine 'what to measure'
(i) Identify existing knowledge
(ii) Fill gaps in knowledge if needed
(iii) Elicit views about important outcomes in a consensus process
(iv) Hold a face to face meeting to finalise the recommended COS
(v) Report the work using the COS-STAR guidance
Step 5
Determine 'how to measure' the COS
(i) Identify existing measurement instruments or definitions for each outcome in the COS
(ii) Quality assess instruments and definitions
(iii) Use a consensus process to finalise the recommended outcome measurement instruments and definitions
Implementation
Assess uptake
Review and update as necessary

# Three-stage approach



# Minimum standards for COS development

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## Core Outcome Set-STAndards for Development: The COS-STAD recommendations

Jamie J. Kirkham[1], Katherine Davis[1], Douglas G. Altman[2], Jane M. Blazeby[3], Mike Clarke[4], Sean Tunis[5], Paula R. Williamson[1]*

*PLoS Medicine* 2017; **14**(11):e1002447

Harman et al. Trials 2013, 14:70
http://www.trialsjournal.com/content/14/1/70

TRIALS

STUDY PROTOCOL Open Access

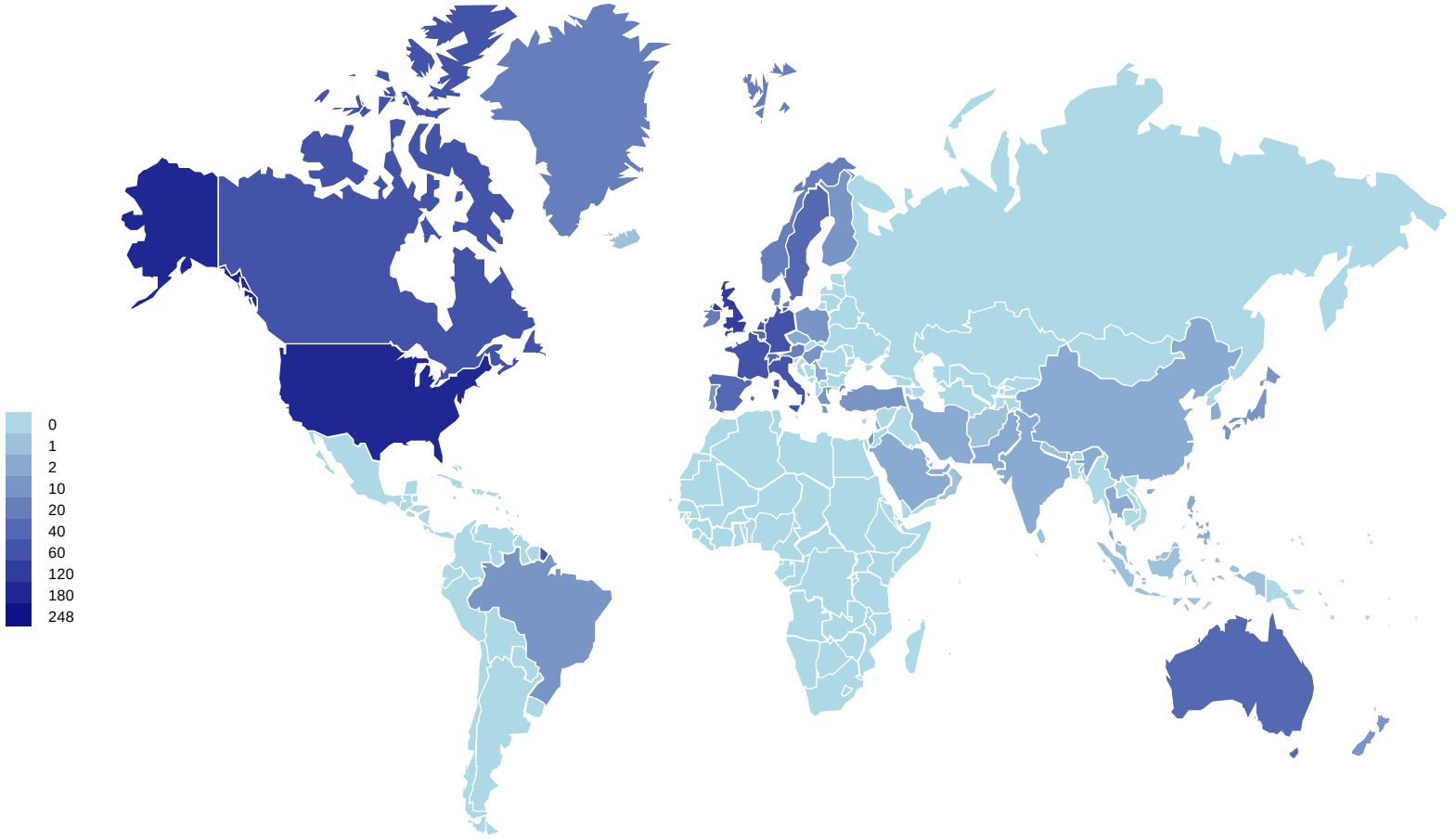
# MOMENT – Management of Otitis Media with Effusion in Cleft Palate: protocol for a systematic review of the literature and identification of a core outcome set using a Delphi survey

Nicola L Harman[1], Iain A Bruce[2], Peter Calley[3], Stephanie Tierney[3], Mohammad Owaise Sharif[4], Kevin O'Brien[1] and Paula R Williamson[4*]

# COS-STAP

Core Outcome Set-STAndards for Protocols

# Achieving global consensus



# Issues

- What will you write about generalisability?
- Practicalities: language and wording of outcomes, gathering opinions, finalising consensus, funding
- What – the same, How – differs (e.g. in lower income countries)
- Is this research? Need for REC approval

# Minimum standards for COS development

# Methods of COS development

- **'What' to measure** – minimum standards

- **How to select outcome measurement instruments for outcomes included in a 'Core Outcome Set'** – a practical guideline (Prinsen et al, 2016)

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# Core Outcome Set-STAndards for Development: The COS-STAD recommendations

DOMAINS

- Scope
- Stakeholders
- Consensus Process

| Domain | Standard number | Methodology | Notes |
|---|---|---|---|
| Scope specification | 1 | The research or practice setting(s) in which the COS is to be applied | COS developers should consider the details of the setting (e.g., for application in research studies or for use in routine care) that will be covered by the COS. |
| | 2 | The health condition(s) covered by the COS | COS developers should consider the details of the health conditions (e.g., treatment of rheumatoid arthritis or screening for cancer) that will be covered by the COS. |
| | 3 | The population(s) covered by the COS | COS developers should consider the details of the population (e.g., patients with advanced disease or children) that will be covered by the COS. |
| | 4 | The intervention(s) covered by the COS | COS developers should consider the details of the interventions (e.g., all interventions, drug therapy, or surgical interventions) that will be covered by the COS. |
| Stakeholders involved | 5 | Those who will use the COS in research | COS developers should involve those who will do the research that will use the COS (e.g., clinical trialists or industry). |
| | 6 | Healthcare professionals with experience of patients with the condition | COS developers should involve those healthcare professionals who would be able to suggest important outcomes (e.g., clinical experts, practitioners, and investigators with particular experience in the condition). |
| | 7 | Patients with the condition or their representatives | COS developers should involve those who have experienced or who are affected by the condition (e.g., patients, family members, and carers). |
| Consensus process | 8 | The initial list of outcomes considered both healthcare professionals' and patients' views. | COS developers should consider the views of healthcare professionals and patients (most likely identified from literature reviews or interviews) when generating an initial list of outcomes for inclusion in the consensus process. |
| | 9 | A scoring process and consensus definition were described a priori. | Although different consensus methods may be employed in different studies, to avoid any potential biases, COS developers should describe their consensus method a priori. |
| | 10 | Criteria for including/dropping/adding outcomes were described a priori. | COS developers should also prespecify criteria for including, dropping, or adding new outcomes to avoid potential biases. |
| | 11 | Care was taken to avoid ambiguity of language used in the list of outcomes. | COS developers should consider the language used when describing outcomes in front of different stakeholder groups. An example of 1 approach taken is to include both lay and medical terms, with these previously piloted with the stakeholders. |

COS, core outcome set.

https://doi.org/10.1371/journal.pmed.1002447.t002

*PLoS Medicine* 2017; 14(11): e1002447

# Scope of a COS

- Setting, Health condition, Population and types of intervention

## Setting

e.g. for application in research studies (RCTs) or for use in routine care

## Health Condition

e.g. treatment of rheumatoid arthritis or screening for cancer

# Scope of a COS

- Setting, Health condition, Population and types of intervention

## Population

e.g. in colorectal cancer, a COS might be developed for all patients or it may focus on patients with metastatic disease

## Interventions

e.g. in colorectal cancer, a COS may be created to use in trials of all interventions or surgery alone

# Stakeholder input

- **Healthcare professionals** that would be able to suggest important outcomes (e.g. clinical experts, practitioners, investigators with particular experience in the condition)
- **Patient representatives** (e.g. patients, public, participants who have experienced the condition, family members, carers)
- **Those who will do the research that will use the COS** (e.g. clinical trialists, industry)

- Those who will use the research that should have used the COS (e.g. systematic reviewers, guideline developers, policy makers, regulators)

- Stage of involvement may vary by group

# “Doctors know about the illness, but patients know about the impact”

- Berglas 2016: Review of 30 CADTH clinical guidelines

- Only 50% of the outcomes that patients said matter to them are captured in primary studies

# COMET People and Patient Participation Involvement and Engagement (PoPPIE) Working Group

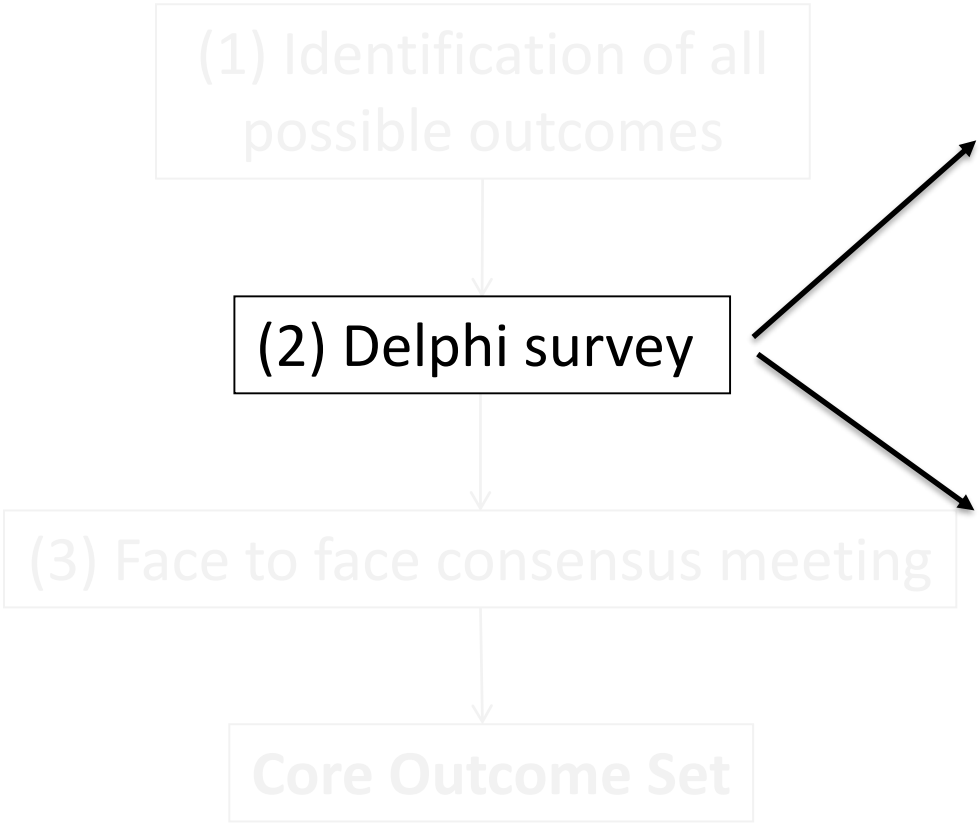
To lead and oversee the public participation, involvement and engagement work of the COMET Initiative, as set out in the COMET Public Involvement Strategy

# Transparent consensus process

- Initial list of outcomes consider *both* healthcare professionals' and patients' views
- Care is taken to avoid ambiguity of language used in the list of outcomes
- A scoring process and consensus definition is described *a priori*
- Criteria for including/dropping/adding outcomes are described *a priori*

# Delphi methodology

# Stage 2




- Structured technique
- Panel(s) of ‘experts’
- Sequential anonymised questionnaires
- Feedback
- Not face-to-face
- Enables large panel(s)

# Delphi surveys

- Published COS
- Original review 14%
- First update 29%
- Second update 55%
- Third update 55%

- Ongoing COS
- 167/188 (89%)

# Delphi surveys: Issues to consider

- Number of panels
- Group size
- Participant information
- Number of rounds
- Structure of the questionnaires
- Methods of scoring
- Nature of feedback presented between rounds
- Criteria for retaining outcomes between rounds
- Attrition (response bias) between rounds
- Consensus definitions
- How the degree of consensus will be assessed

# Number of panels

Single panel

- From one particular stakeholder group
  - COS informed by one stakeholder group only

- From multiple stakeholder groups (but ignore stakeholder status throughout process)
  - Retained outcomes dependent on mix of participants

# Number of panels

## Multiple homogeneous panels

- Distinct stakeholder groups retained
- Better when stakeholder opinions differ
- Outcomes taken forward may consist of:
  - (i) Outcomes deemed essential by all stakeholder groups
  - (ii) Outcomes deemed essential by any stakeholder group

# Number of rounds

- Typically 2 or 3 rounds
- Other considerations
  - time
  - costs
  - participant burden

# Outcome scoring

- Many approaches have been proposed
- Usually involves a VAS/Likert scale

| Importance | | | | | | | | | Don't know |
|---|---|---|---|---|---|---|---|---|---|
| Not that important for inclusion into the core outcome set | | | Important but not critical for inclusion in the core outcome set | | | Critical for inclusion into the core outcome set | | | |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

# Questions - Round 2

Please do not use the browser's back button. If you wish to go back to a page please use the dropdown list at the bottom of the page.

**You have answered: 0 out of 48 outcomes** **Page 1 of 51**

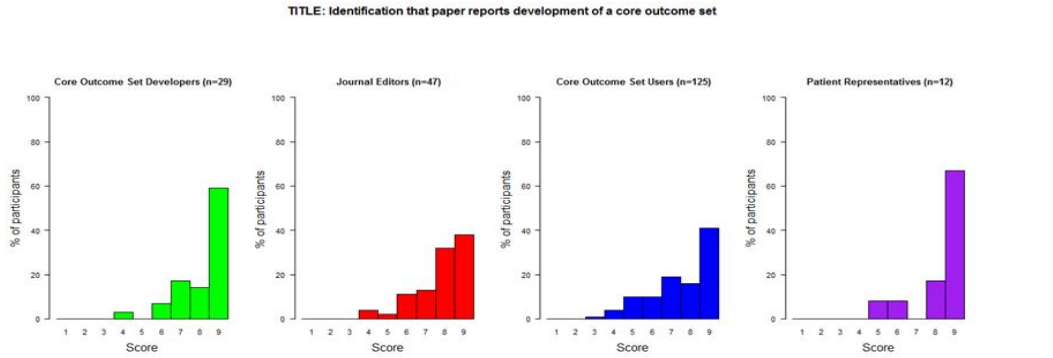
**Text for the questions page of round 2 should go here..**

If you would like clarification on a variable, please hold your cursor over the variable and a text box will be displayed with additional information or definitions where available.

## Identification that paper reports development of a core outcome set

Your score from Round 1 is highlighted in yellow.

**Summary of Round 1**




| Outcome | Not important | | | Important but not critical | | | Critical | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | Unable to score |
| **Title** | | | | | | | | | | |
| Identification that paper reports development of a core outcome set | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

**Please note**: You will only be able to save/move to the next page if you have answered **ALL** the questions on this page.

Save and Exit

Next Page

Questions - Round 2

# Group size

- Decision is not based on statistical power
- Choice is often pragmatic, may depend on:
  - condition
  - intervention
  - global representiveness
- Consider potential attrition
- Participants should have broad range of experience
- The more the better
- Pool stakeholder groups if numbers small and similar opinions expected

# Structure of questionnaire

- Involve stakeholders in the design and piloting
- Avoid jargon and technical terms
- Order of questionnaire items
  - May affect response rates
  - ‘Consistency effect’
  - Fatigue
- Additional open questions
  - At beginning or end of questionnaire
  - Pre-specified criteria for inclusion

# Retaining/dropping items

- Retain all items until end of final round
- Drop items according to pre-specified criteria
  - More inclusive criteria for retaining items in earlier rounds
  - Multiple panels: Criteria met by all or any panel?
- Holistic approach vs. burden
- May depend on initial number of items

# Consensus definition

- Many approaches…BUT important to specify the definition *a priori*
- For multiple panels – criteria met by all or any stakeholder group or some other combination?
- For example: Item retained if

  >70% of patients and >70% professionals scored 7-9

  Or >90% scored 7-9 by any single panel

# Information for participants

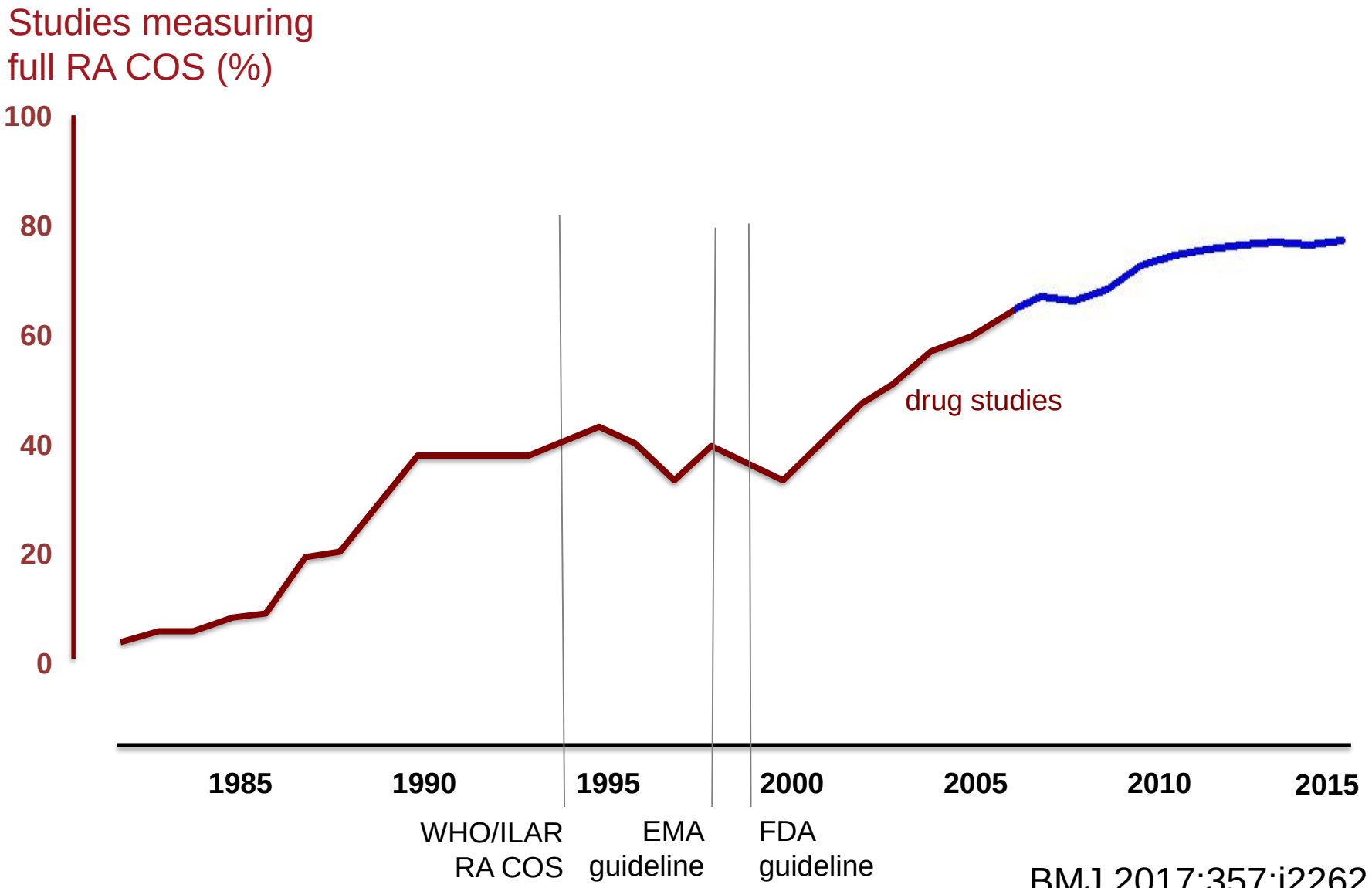
- Essential that all fully aware of purpose of Delphi/COS
  - Informed consent
  - Simplifies task, improves ability and motivation
- Information may differ across stakeholder groups
- Pilot information
- Reiterate the overall aim in each round
- Use of videos is increasing
- Plain language summaries available on the COMET Initiative website

# COS implementation

# COS implementation

- What is COMET doing?
- What are you doing?

# Improvements over time (Kirkham et al, *BMJ 2017*)




BMJ 2017;357:j2262

# COS Uptake and Endorsement

It is important to assess the uptake and use of COS in clinical trials, and other research, in order to avoid the development of these COS contributing to the research waste which their development aims to reduce. Assessing uptake can also highlight the benefits of measuring and reporting COS in trials while allowing review and feedback to ensure ongoing relevance, and removal of barriers and facilitators to uptake.

The following organisations actively endorse the use of COS and the COMET database.

## Trialists

- SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials

## Trial Funders

- National Institute for Health Research (NIHR), UK:Guidance Notes For Completing Full Proposals
- Horizon2020:
- http://ec.europa.eu/research/participants/portal/desktop/en/opportunities/h2020/topics/sc1-pm-10-2017.html
- Deutsche Forschungsgemeinschaft (DFG) German Research Foundation
- Proposal Preparation Instructions: Clinical Trials Programme – Draft Proposals
- Proposal Preparation Instructions: Clinical Trials Programme – Full Proposals
- Arthritis Research UK (ARUK)
- Health Research Board (HRB)

## Trial Registries

- ISRCTN

## Regulatory Authorities

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**Help, I want to...**

- Search COMET
- Send general feedback / enquiry
- Tell us about a new project/study
- Report a missing study
- Find out about how to measure
- COMET blogs

NIHR HTA guidance to applicants

*“Details should include justification of the use of outcome measures where a legitimate choice exists between alternatives. - Where established Core Outcomes exist they should be included amongst the list of outcomes unless there is good reason to do otherwise. Please see The COMET Initiative website at www.comet-initiative.org to identify whether Core Outcomes have been established”“*

# Save the date

We are pleased to announce the 7th Meeting of the COMET Initiative

## Thursday 15th and Friday 16th November 2018

## Rode Hoed, Amsterdam

*More details and registration to follow*

# Q&A


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