

Core Outcome Measures in Effectiveness Trials

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DMARD trials for rheumatoid arthritis

TRIAL	YEAR	PAIN	PT GLOB	SWOLLEN JOINT	TENDER JOINT	ACUTE PHASE	PHYSICIAN GLOB	FS	QOL	RADIOGRAPH
ERC	1960		Y			Y	Y	Y		Y
LEVY	1972				Y					
UROWITZ	1973			Y	Y	Y				Y
ANDREWS	1973	Y	Y		Y	Y	Y	Y		Y
CCC	1973					Y		Y		
SIGLER	1974					Y		Y		Y
DIXON	1975	Y				Y				
HUSKISSON	1976	Y			Y	Y				
MERY	1976		Y		Y	Y	Y			
SHIOKAWA	1977						Y			Y
WOODLAND	1981		Y		Y	Y		Y		
WILLIAMS	1983	Y	Y	Y	Y	Y	Y			
WARD	1983		Y	Y	Y		Y	Y		
ANDERSON	1985	Y	Y	Y	Y	Y	Y	Y		
WEINBLATT	1985		Y	Y	Y	Y	Y	Y		
WILLIAMS	1985	Y	Y	Y	Y	Y	Y	Y		
DOUGADOS	1988	Y	Y	Y	Y	Y		Y		
TUGWELL	1990	Y	Y			Y	Y	Y		
FURST	1990	Y	Y	Y	Y	Y	Y	Y		
DAVIS	1991			Y	Y	Y				
CLARK	1993	Y	Y	Y	Y		Y			
PINHEIRO	1993	Y			Y	Y		Y		
FORRE	1994	Y	Y	Y	Y	Y		Y		Y
ROZMAN A	1994		Y	Y	Y	Y	Y			

Source: Kirkham, J. J., M. Boers, et al. (2013). *Outcome measures in rheumatoid arthritis randomised trials over the last 50 years*, Trials 14(1): 324.

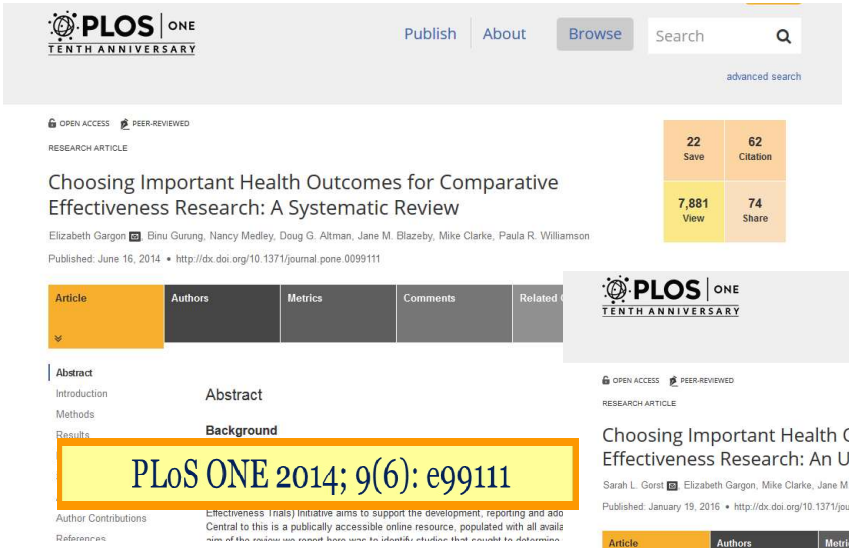
Core outcome set for trials

- An agreed standardised set of outcomes that should be measured and reported, as a minimum, in all clinical trials in specific areas of health or health care



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Systematic review of COS







- >300 published COS for trials
- 188 ongoing COS studies

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

Follow us on Twitter

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

Outcomes – from the very start

Clinical trials are only as credible as their outcomes
Tugwell, 1993

Equally true for systematic reviews as well

…and clinical guidelines

…and healthcare organisations

COS for routine care

- COS for clinical research: n = **229 studies** (87%)
- COS for clinical research and clinical practice: n = **35 studies** (13%)
- COS for registry: n = 6 studies
- COS for clinical practice and registry: n=3 studies
- **36%** ongoing COS studies are for research and practice

Focus of this talk

- **'What' to measure**

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

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

Consensus methods

Main methods	N
Semi-structured group discussion only	61
- Workshop	24
- Meeting	34
- Round table discussion	3
Literature/systematic review only	19
Unstructured group discussion only	18
Consensus development conference only	13
Delphi only	11
Survey only	3
Nominal Group Technique only	1
No methods described	20
Mixed methods	118
TOTAL	264

COS published between 1981 and 2016

Do methods matter?
Case study: Paediatric asthma

	SINHA ET AL	REDDELL ET AL		BUSSE ET AL			
				5-11 years		12+ years	
	TOP 6 PARENTS +/- CLINICIANS	ESSENTIAL	OPTIONAL	ESSENTIAL	OPTIONAL	ESSENTIAL	OPTIONAL
Symptoms	√	√				√	
Exacerbations	√	√		√		√	
QoL	√	√			√		√
Death	√		√				
Normal activities	√					√	
Exercise ability	√						
Reliever use		√				√	
Lung function		√		√		√	
Tx side effects		√					
Healthcare utilisation			√	√		√	
Biomarkers			√				
Hyper-responsiveness			√				

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

Minimum standards for COS development

PLOS | MEDICINE

GUIDELINES AND GUIDANCE

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

Scope of a COS

- Health condition, population and types of intervention

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

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

- Research or practice setting *or both*

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)

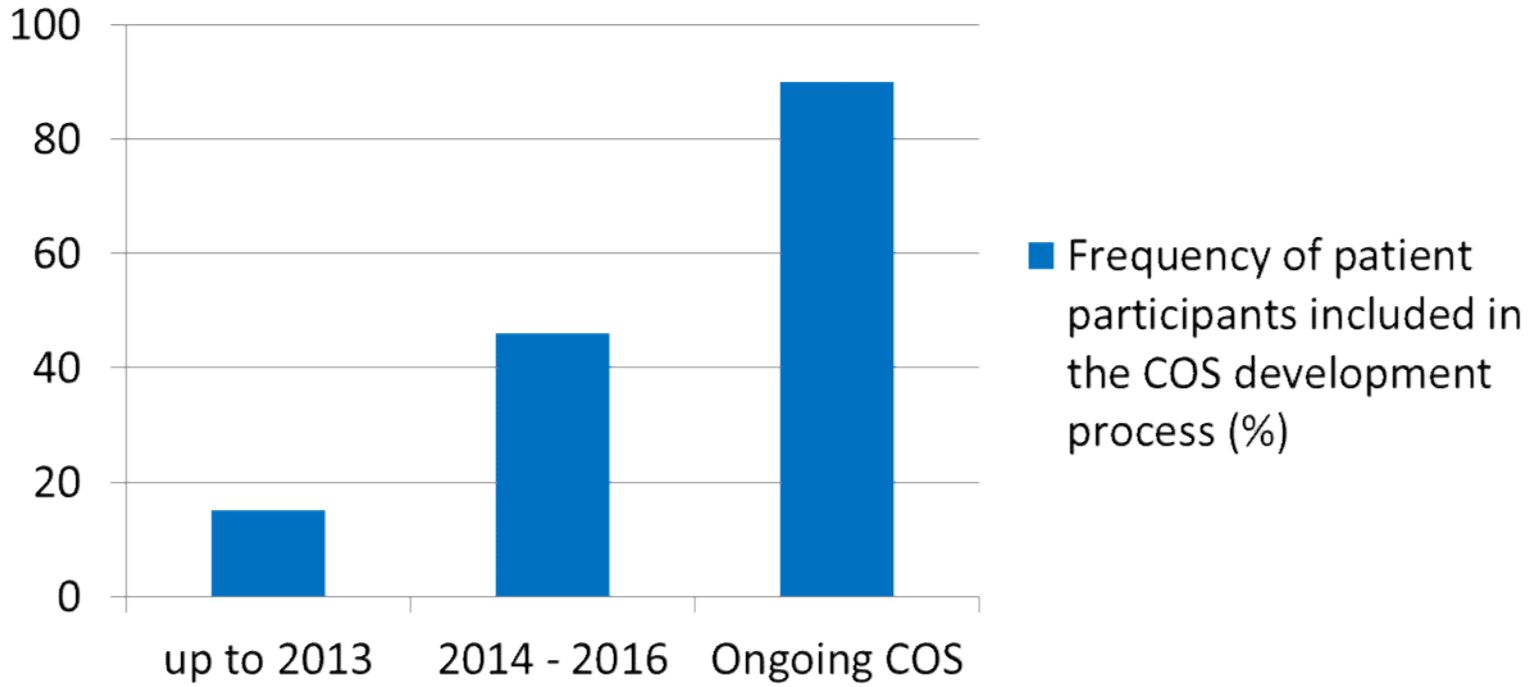
- Stage of involvement may vary by group

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

- Rheumatoid arthritis – **fatigue**
- Paediatric asthma – normal activities, exercise ability, death
- Only 50% of the outcomes that patients said matter to them are captured in primary studies (Berglas 2016)

Patient participation

- Patients, carers, patient support group representatives, service users

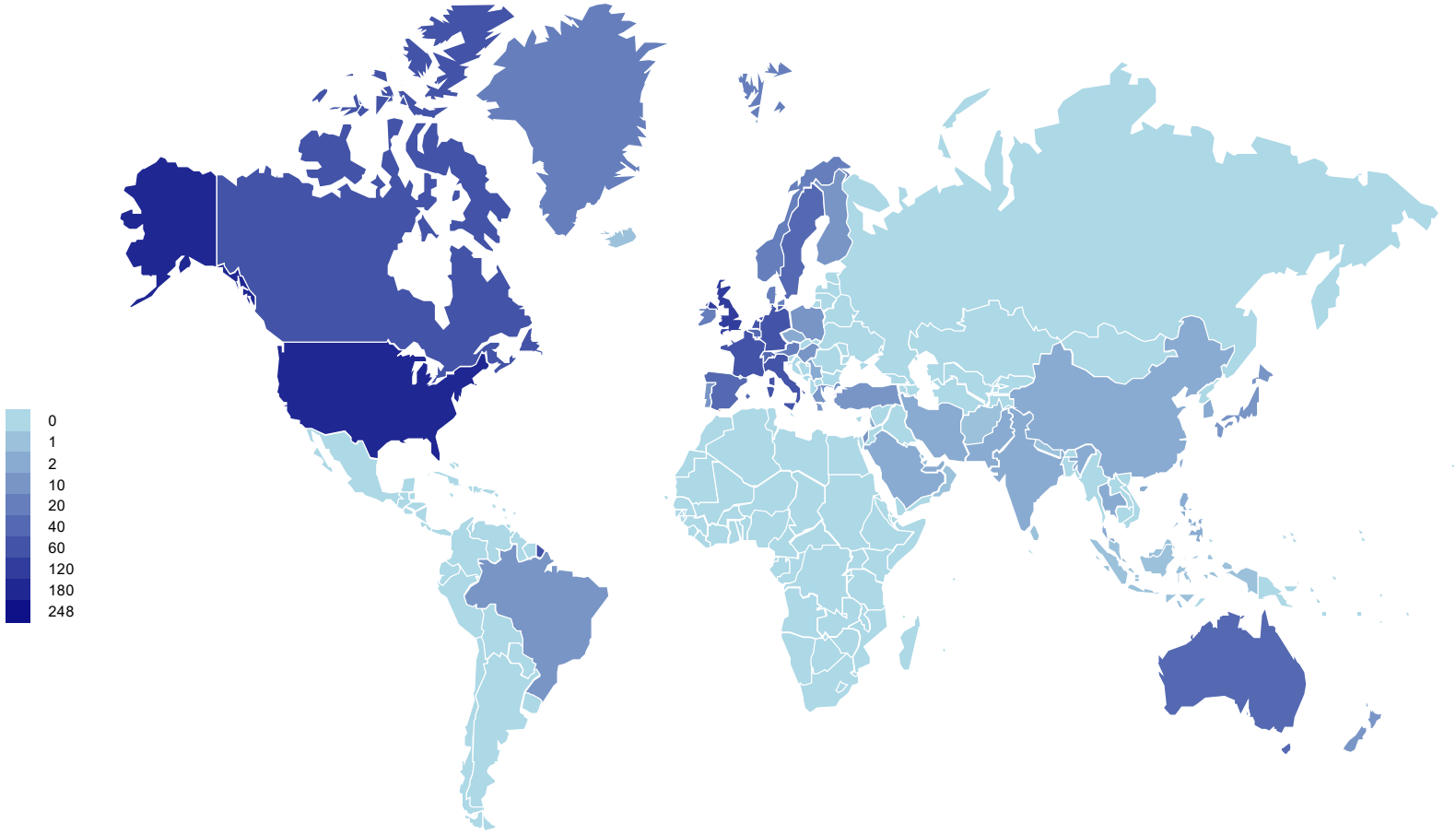


COMET People and Patient Participation Involvement and Engagement (PoPPIE) Working Group



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

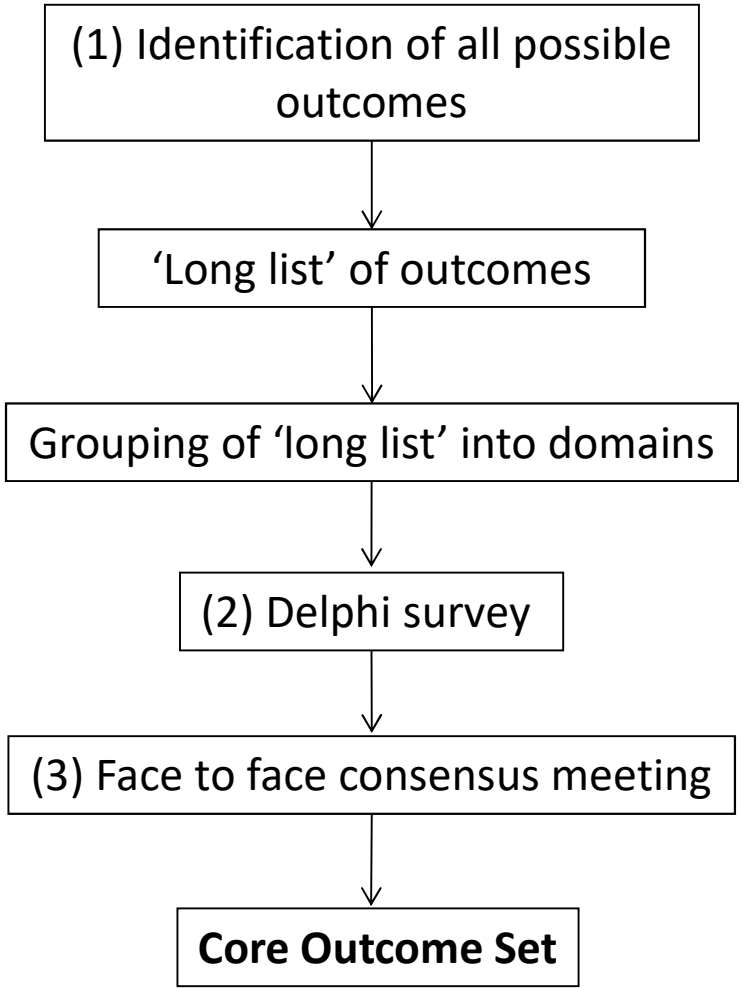
Achieving global consensus



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*

Three-stage approach

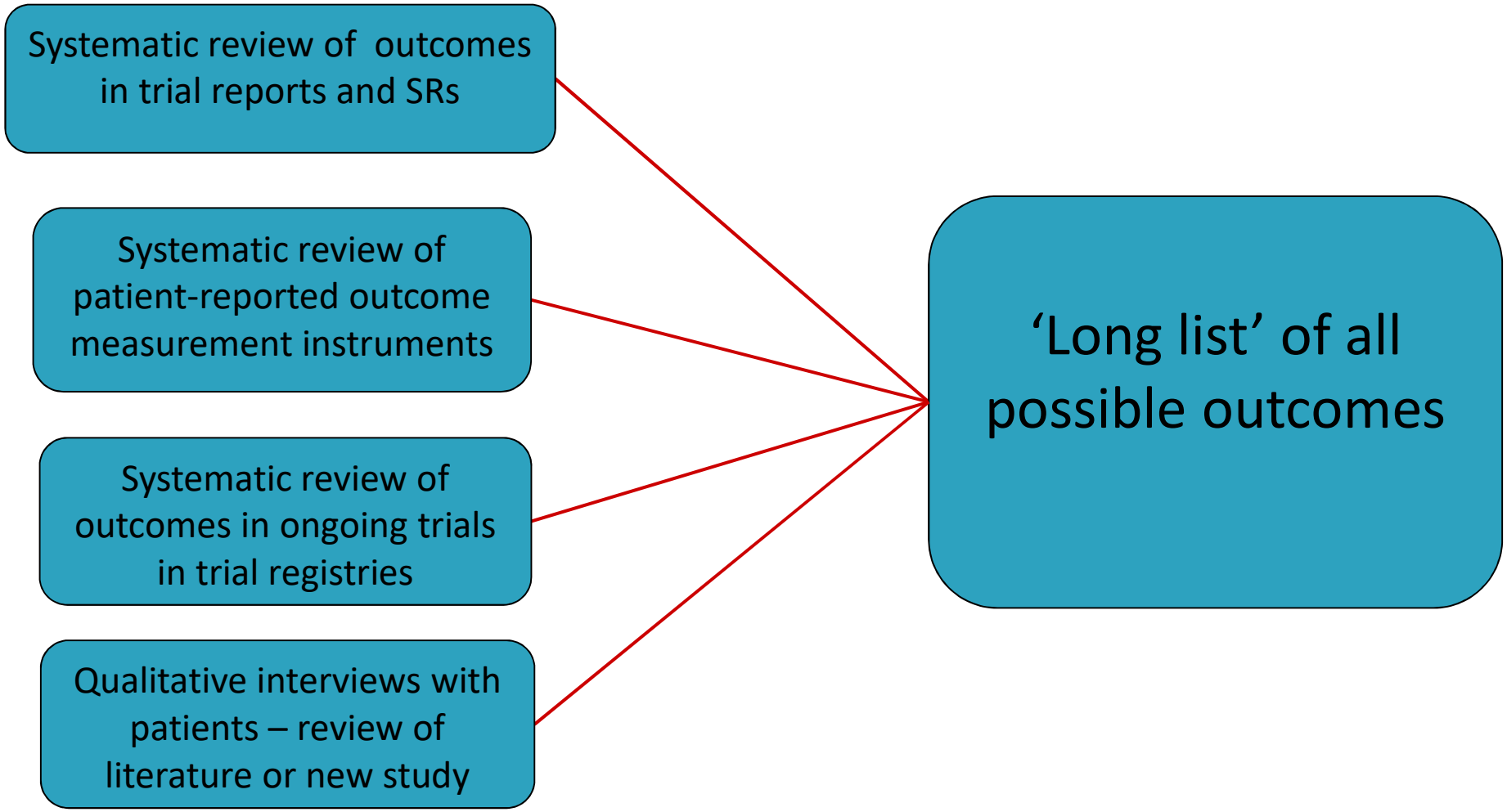


Delphi surveys

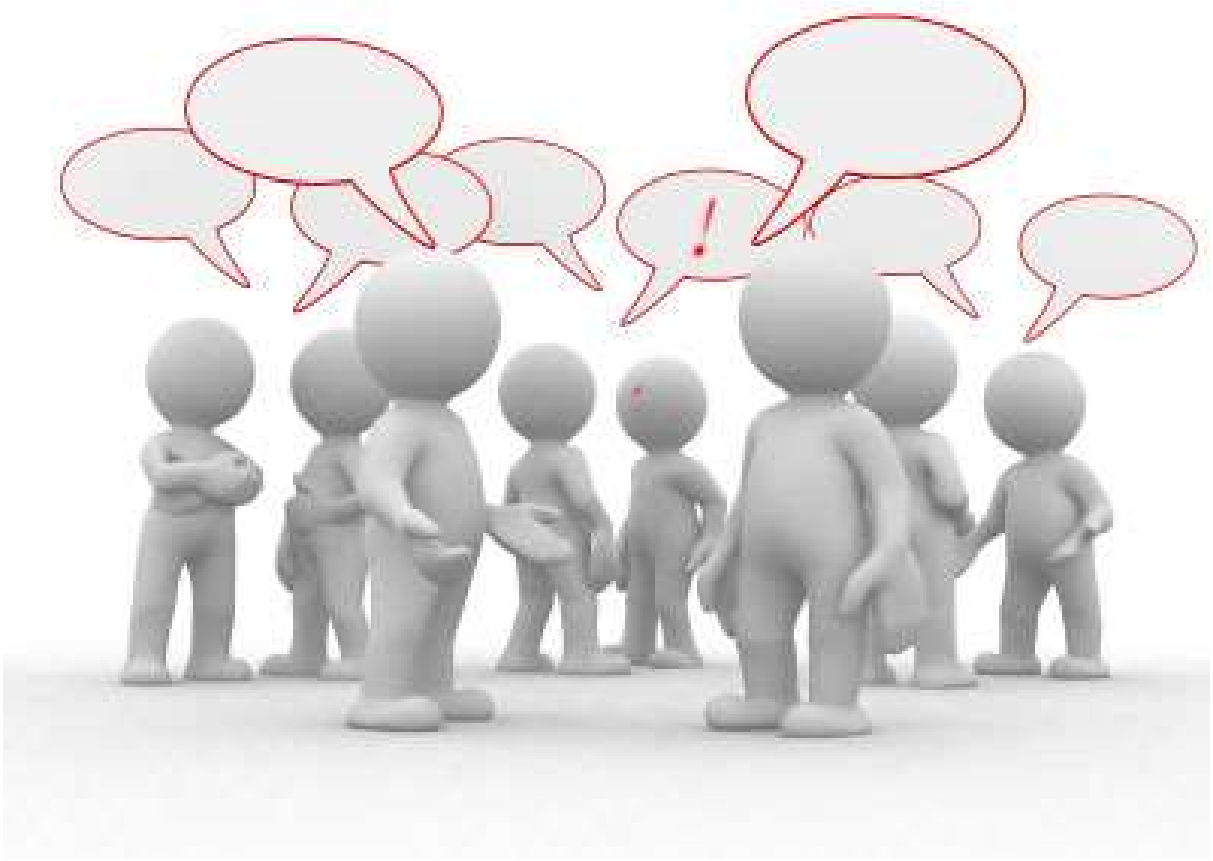
- Published COS
- Original review 14%
- First update 29%
- Second update 55%
- Third update 55%

- Ongoing COS
- 167/188 (89%)

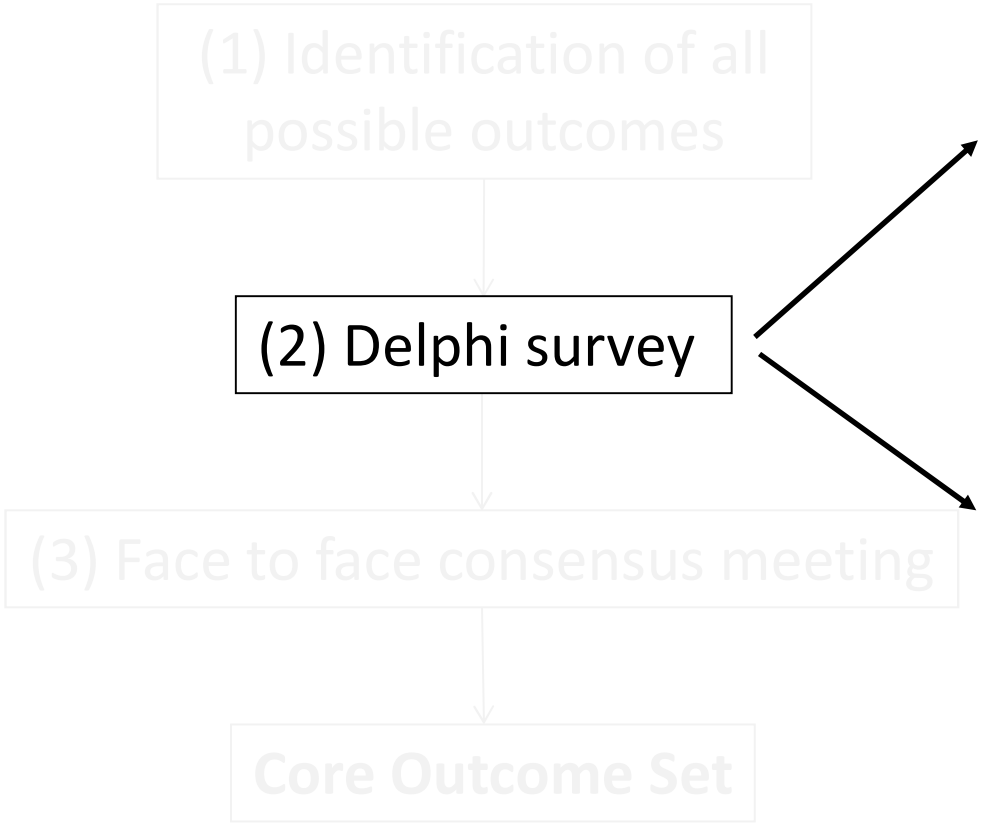
Stage 1: Information sources



Check items with patients and HPs



Stage 2



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

COMET INITIATIVE DelphiManager

Administration

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**

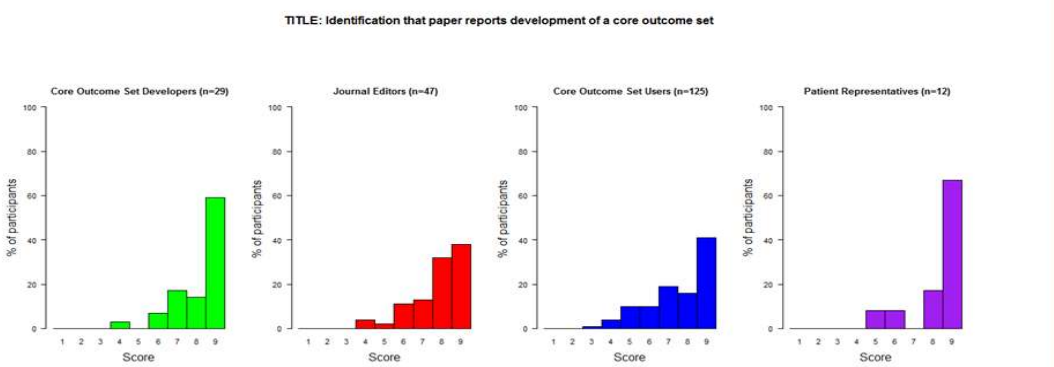
Text for the questions page of round 2 should go here..

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

Stage 3: Consensus conference

Issues to consider:

- May be needed before final COS agreed
- Who to invite? How many?
- Joint or separate meetings for stakeholders?
- Who will facilitate? What experience?
- What format?
- How will decisions be made?

Further issues to consider

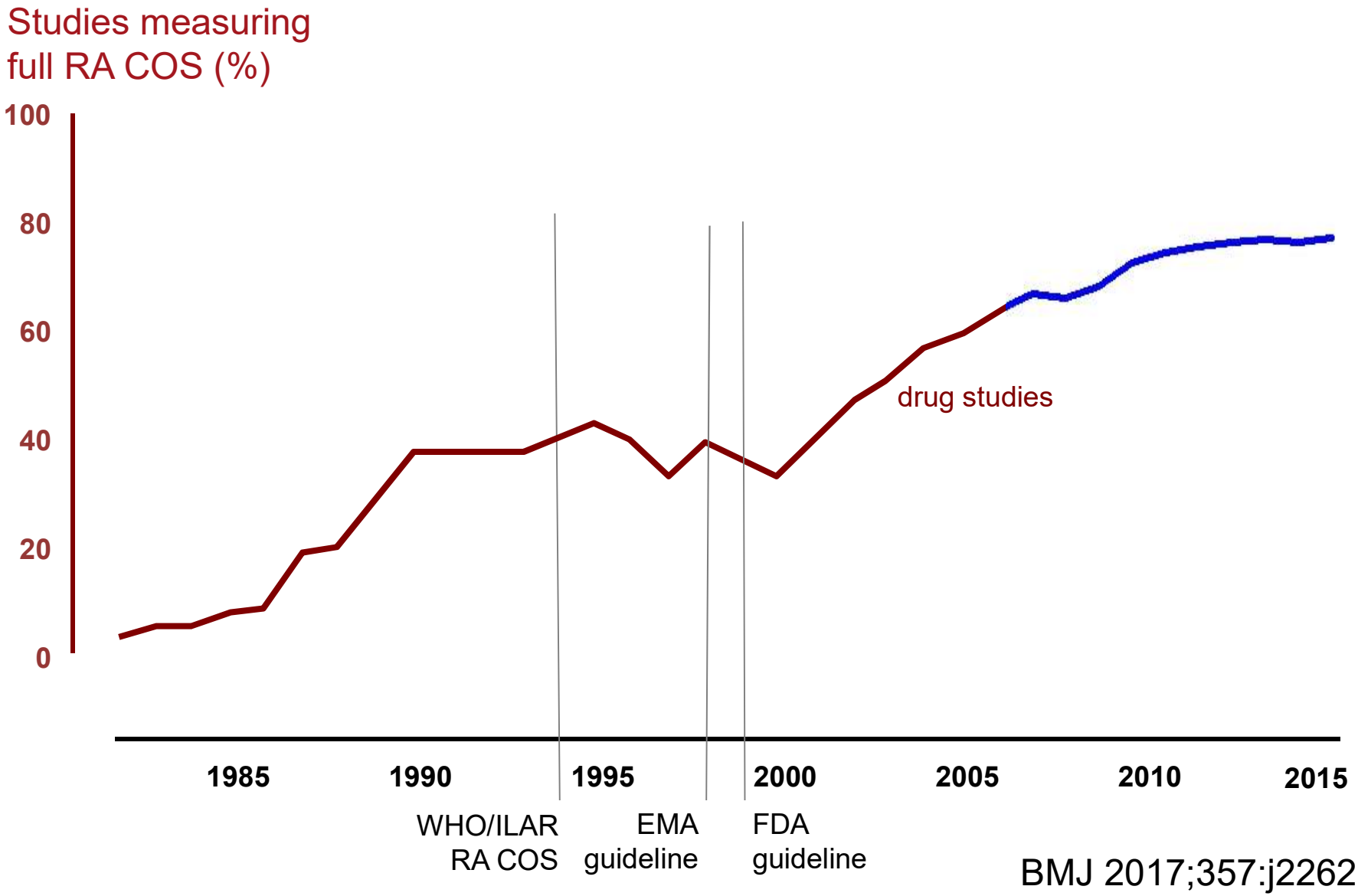
- Implementation

- development of a plan may help to identify relevant stakeholders (trials groups, funders, EHR and care providers, etc)

- Regular review, feedback, updating

- e.g. OMERACT RA COS and fatigue

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



BMJ 2017;357:j2262

COS for routine care

- THE 2017 EULAR RECOMMENDATIONS FOR A CORE DATASET TO SUPPORT OBSERVATIONAL RESEARCH AND CLINICAL CARE IN RHEUMATOID ARTHRITIS

(under consideration at the Annals of the Rheumatic Diseases)



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