Core Outcome Measures in Effectiveness Trials

www.comet-initiative.org

DMARD trials for rheumatoid arthritis: Pre-OMERACT

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

- 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

COMET definition

Advantages of core outcome sets (COS)

- Increases consistency across trials
- Maximise potential for trials to contribute to systematic reviews of these key outcomes
- Much more likely to measure appropriate outcomes
- Major reduction in selective reporting

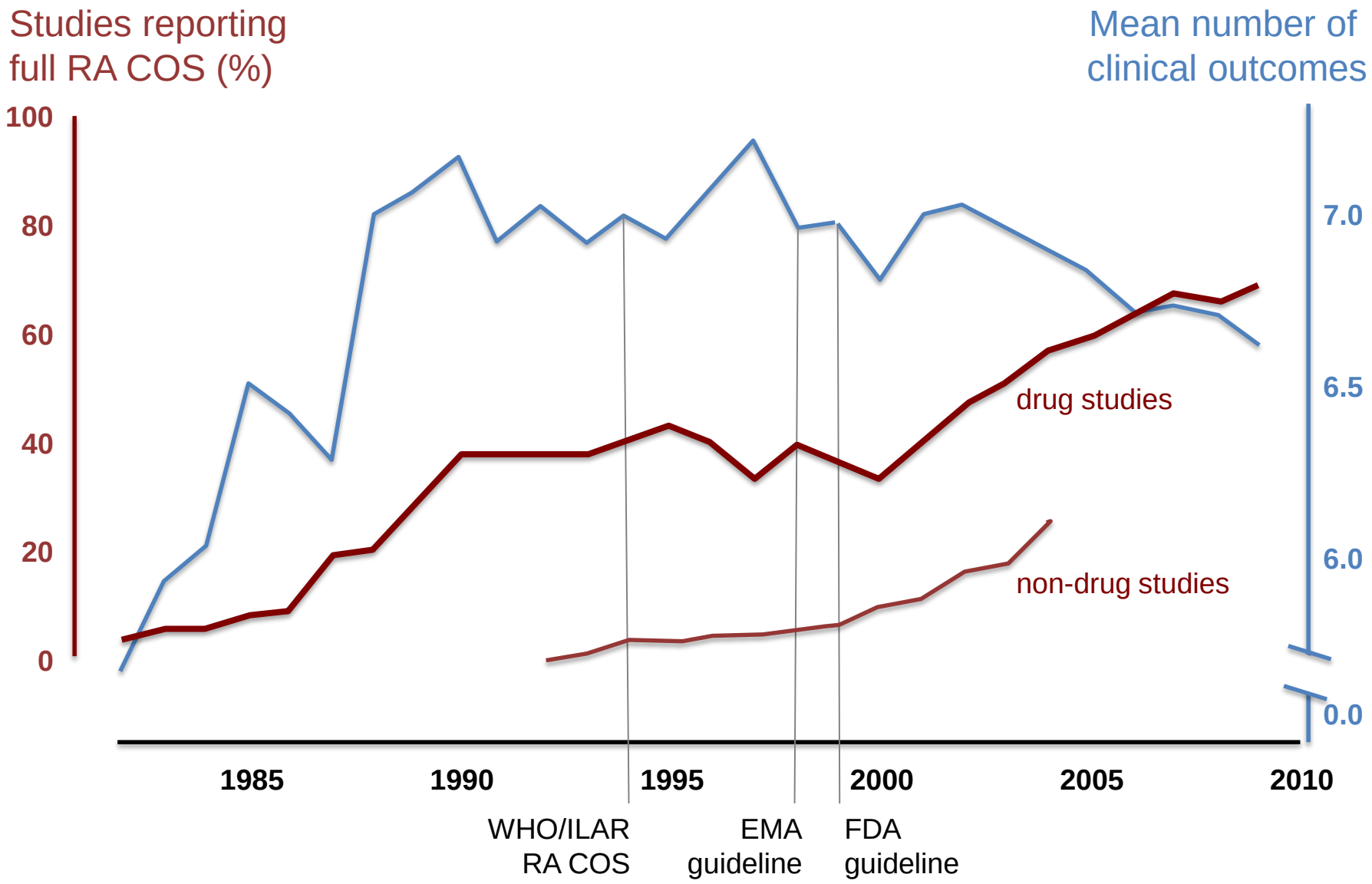
COS for RA (ILAR/WHO)

The Journal of Rheumatology

- Tender joints
- Swollen joints
- Pain
- Physician global assessment
- Patient global assessment
- Physical disability
- Acute phase reactants

Source: Boers M, Tugwell P, Felson DT, et al. *World health organization and international league of associations for rheumatology core endpoints for symptom modifying antirheumatic drugs in rheumatoid arthritis clinical trials*. J Rheumatol 1994;21 (suppl 41):86-9.

Improvements over time (Kirkham et al, *Trials* 2013)

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Core Outcome Measures in Effectiveness Trials
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The COMET (Core Outcome Measures in Effectiveness Trials) Initiative brings together people interested in the development and application of agreed standardised sets of outcomes, known as 'core outcome sets' (COS). These sets represent the minimum that should be measured and reported in all clinical 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.
When searching the COMET database, please note that a systematic review is currently underway to identify eligible material, and we are continually updating the database as we identify eligible studies. Therefore, the records retrieved by any search might increase on a daily basis.
Search COMET database
The COMET database currently contains 802 references of planned, ongoing and completed work.
Enter Keyword
Search
The keyword used for the search will be
COMET database click here
Core resource pack
Useful references for core outcome set developers.
This includes an overview of the problems with outcomes in trials, key issues to consider in the development of a core outcome set, examples of core outcome set development,
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SEVENTH FRAMEWORK PROGRAMME
NHS
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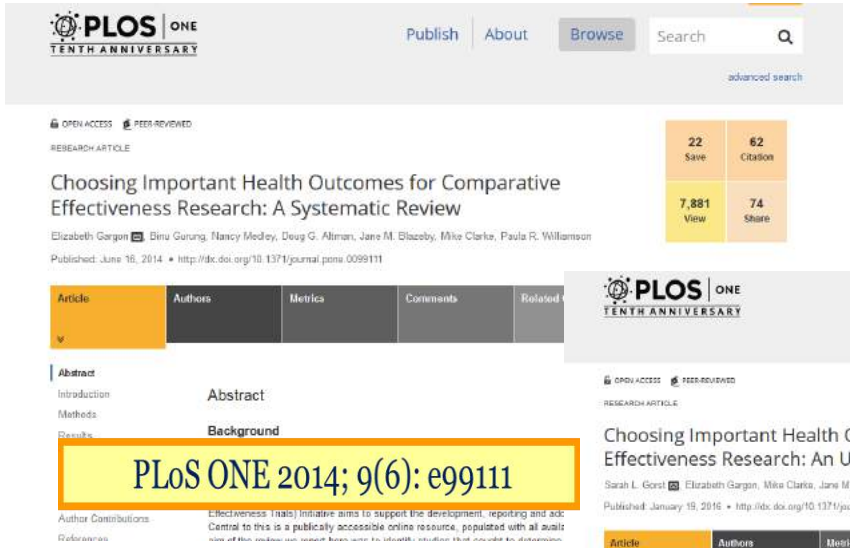
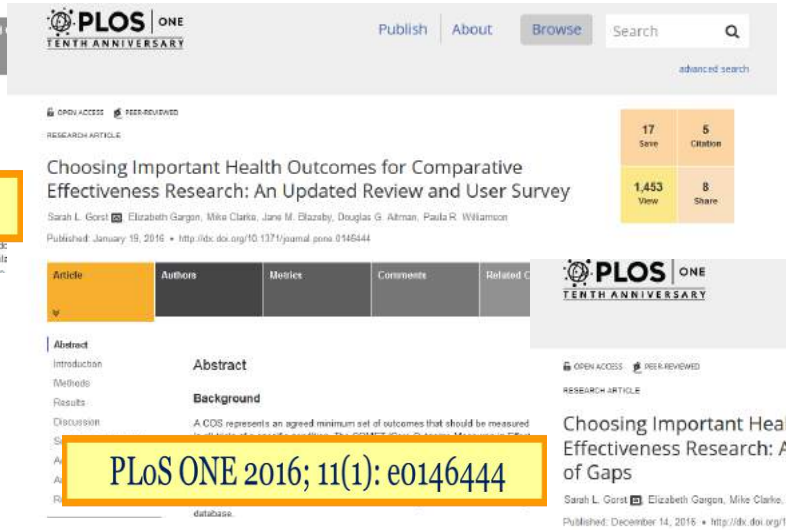
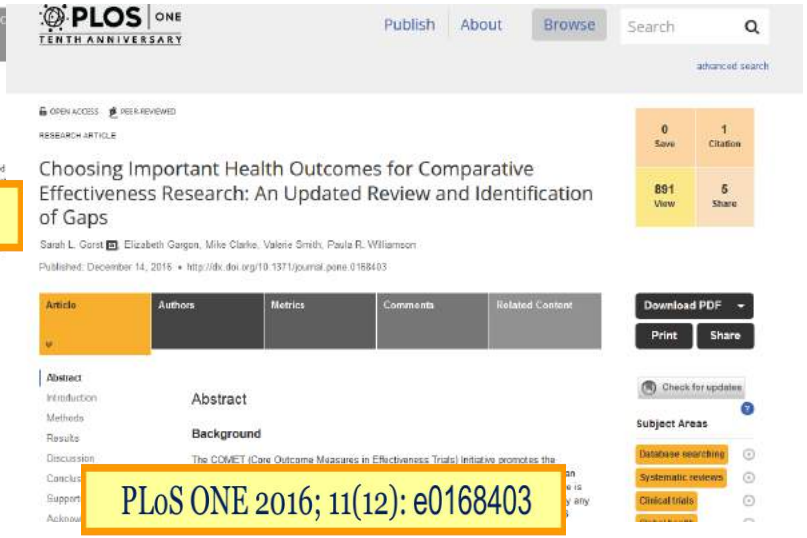
Systematic review of COS







COMET database

- >300 published COS
- >150 ongoing COS studies
- > 150 reviews of outcomes in trials
- > 50 studies of patients' perspectives

Promotion and collaboration

- Trialists - SPIRIT guidelines
- Trial funders - NIHR, ARUK, AMRC, HRB, Horizon 2020
- Industry – EFPIA
- Regulators – EMA, FDA
- Systematic reviewers – Cochrane
- Guideline developers – NICE, CMTP, GIN
- Journal editors – CROWN, COS-STAR guidelines
- Patients and the public – PoPPIE
- HTA bodies and payers – KCE

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COMET database launched to encourage use of core outcome sets in health research

Logon to the NIHR Portal Go

About The Portal
Portal Help

Professor Hywel Williams, Chair of the NIHR HTA Commissioning Board: 'Patients and professionals making decisions about health care need access to reliable evidence. The new COMET database will help researchers across the NIHR family and beyond when choosing the outcomes to include in the studies that will establish this evidence base'.

asthma, maternity care and pain. The work is funded by the MRC Network of Hubs for Trials Methodology Research.

Professor Paula Williamson, Director of the North-West Hub, noted 'A large amount of work has already been done to develop core outcome sets in a variety of conditions. We are helping people who are designing trials and reviews to find this information'.

Professor Hywel Williams, Chair of the NIHR HTA Commissioning Board added
'Patients and professionals making decisions about health care need access to reliable evidence. The new COMET database will help researchers across the NIHR family and beyond when choosing the outcomes to include in the studies that will establish this evidence base.'

- Videos
- Calls for Proposals
- Research Training Opportunities
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21/11/2011
International Rare Cancers Initiative launched

16/11/2011
TEWV NHS Foundation Trust wins the HSJ award for research

EMA guidance

Note for Guidance on Clinical Investigation of Medicinal 4 Products for Treatment of Asthma (EMA/CHMP/EWP/2922/01 Rev.1)

The use of core outcome sets (COS) is recommended to allow comparisons of the results across clinical trials when investigating controller medications. COS should include asthma control (symptom scores, exacerbations and change in lung function).

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Source: Boers M, Tugwell P, Felson DT, et al. *World health organization and international league of associations for rheumatology core endpoints for symptom modifying antirheumatic drugs in rheumatoid arthritis clinical trials*. J Rheumatol 1994;21 (suppl 41):86-9.

COMET website

- Since inception:

- 48,723 unique visitors from 168 countries

- 13,616 database searches

Focus of exercise

- ‘What’ to measure

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

TRIALS IMPACT FACTOR 2.12

Commentary

Highly accessed Open Access

Developing core outcome sets for clinical trials: issues to consider

Paula R Williamson*, Douglas G Altman, Jane M Blazeby, Mike Clarke, Declan Devane, Elizabeth Gargon and Peter Tugwell

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Trials 2012, **13**:132 doi:10.1186/1745-6215-13-132

Scope

Identifying existing knowledge

Stakeholder involvement

Consensus methods

Achieving global consensus

Regular review, feedback, updating

Implementation

Clear presentation

(1) 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

(2) Is a COS needed?

- Does a relevant core outcome set already exist? Search the COMET database
- If no, what is known about outcomes?
- from related COS
- in previous trials
- of importance to patients
- from HRQoL studies
- from a theoretical framework
- Is there an implicit COS?

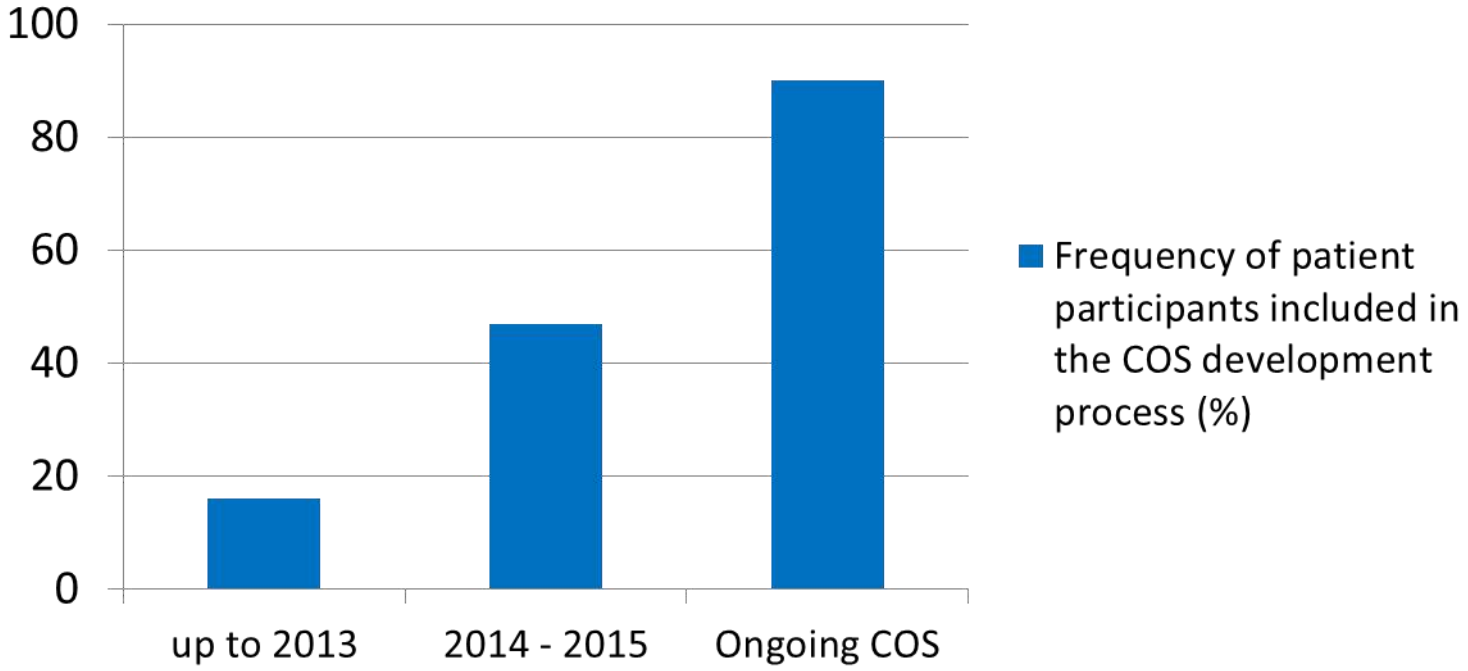
(3) Stakeholder involvement

- 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)
- 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)

- Stage of involvement may vary by group

Stakeholder involvement

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



(4) Consensus methods

Main methods	N
Semi-structured group discussion only	61
- Workshop	24
- Meeting	34
- Round table discussion	3
Literature/systematic review only	18
Unstructured group discussion only	18
Consensus development conference only	13
Delphi only	10
Survey only	3
Nominal Group Technique only	1
No methods	19
Mixed methods	106
TOTAL	249

Delphi Surveys

- Structured technique for reaching consensus
- Panel(s) of ‘experts’
- Sequential questionnaires
- Anonymised
- Feedback after each round

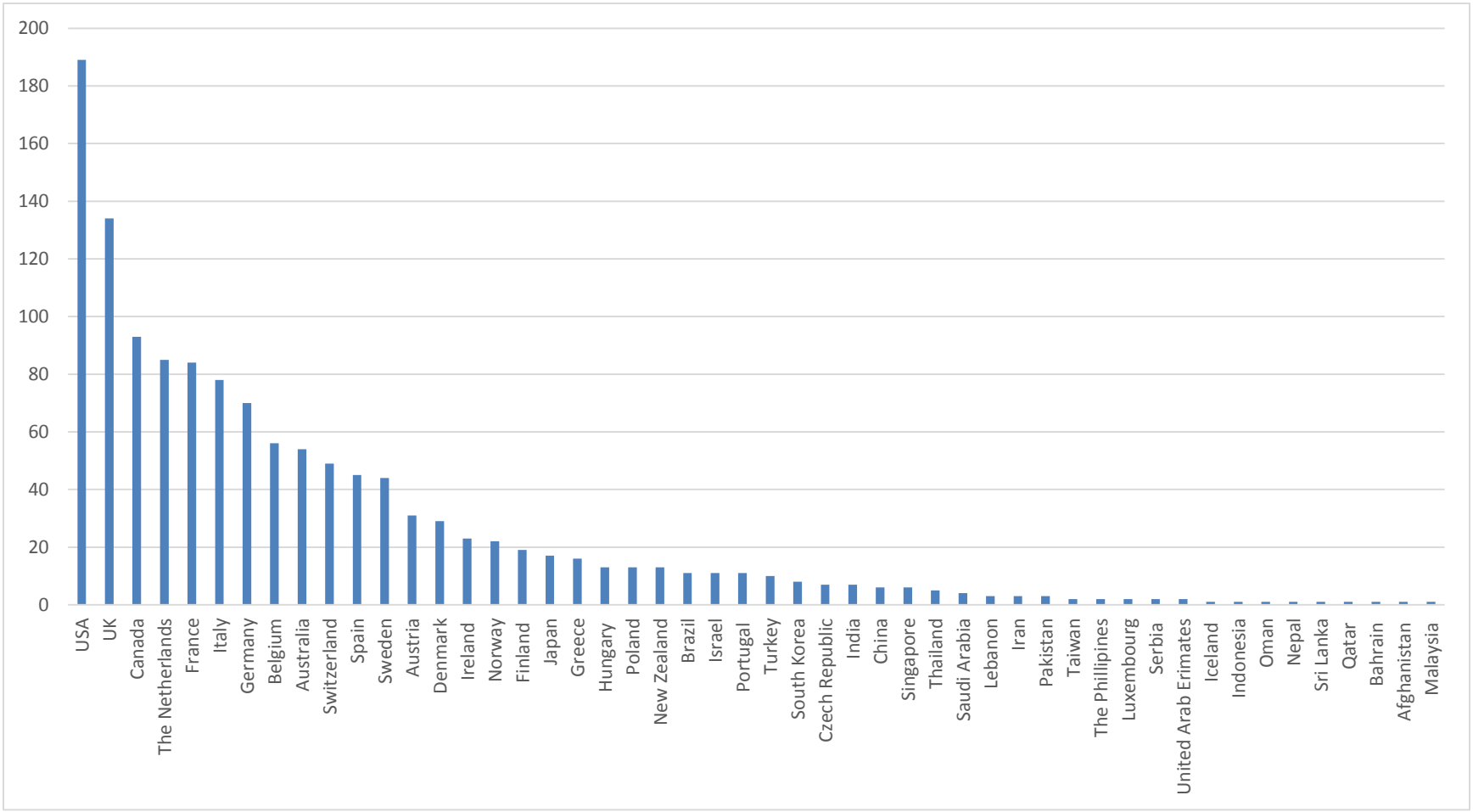
- Avoids problems of face-to-face interaction
- Enables use of large panel

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?

(5) Achieving global consensus



Advantages / Disadvantages

- Funding
- Geographical reach
- Language
- Wording (names for the outcomes)
- Gathering opinions
- Finalising consensus
- Reaching a genuine consensus
- Implementation

Issues to consider

- (6) Regular review, feedback, updating

- e.g. OMERACT RA COS and fatigue

- (7) Implementation

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

- (8) Clear presentation

- Use COS-STAR reporting guideline

COS-STAD: COS-STAndards for Development

- COS-STAD (set of ?? minimum standards for COS development)

- Closely linked to COS-STAR
  - COS-STAR is a reporting guideline (end stage)
  - COS-STAD is about standards for development (early stage)

PLOS | MEDICINE

:onsidered

GUIDELINES AND GUIDANCE

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):e100214

COS-STAD Development

- Establish a preliminary set of minimum standards (Stage 1).
  - Open survey involving COMET MG / COS-STAR CM attendees
- Conduct a 2-Stage Delphi survey (Stage 2).
- Hold a consensus meeting (Stage 3) or something similar????.
- Finalise minimum standards and a detailed E+E? (Stage 4).
- Post-development activities: pilot testing (Stage 5).
  - Miror training exercise!

Stakeholders

- COS developers
  - Lead authors of published COS (COMET database)
- Journal Editors
  - EiC of journals that have published COS (COMET)
  - EiC of CROWN journals (women's and newborn health)
- COS Users
  - Trialists (registered ongoing trials on clinicaltrial.gov)
  - Systematic reviewers (Cochrane CRG Co-Eds)
  - Clinical guideline developers (NICE, G-I-N)
- Patient representatives: PoPPIE (patient and public involvement in COS / COMET PPI events)

COMET VI registrants were also invited to take part

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

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Twitter: @COMETinitiative

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COS disease category