



10th PCNE Working conference, Bled 2017

“Developing Core Outcome Sets for Pharmaceutical Care”

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PCNE 2017

Presentation outline

- Background
- COMET initiative
- COS development methodology
- Other COS initiatives
- COSs being developed in pharmaceutical care

Background

- **Outcomes**

- “What” we measure/report in studies
- Used as an assessment of effectiveness of interventions



Quality
of life

Mortality

GP visits

Falls

Adverse
drug
events

Gait
speed

Background

Assessment of effectiveness:

- Comparing results within/between trials
- Systematic reviews & meta-analyses
 - Evidence synthesis
 - Used to inform policy & practice

However...

Major challenge = **outcome heterogeneity**

(differences in outcome selection, definition, measurement & reporting between trials)

Outcomes in trials - challenges

- **Outcome selection:**
 - Are outcomes **meaningful?** (e.g. surrogate end-points)
 - Are outcomes **important** to all key stakeholders?



Too many different outcomes?

Heterogeneity → hinders comparison = barrier to evidence-based practice



BJCP British Journal of
Clinical Pharmacology



British Journal of Clinical
Pharmacology

Br J Clin Pharmacol (2016) ••••• 1

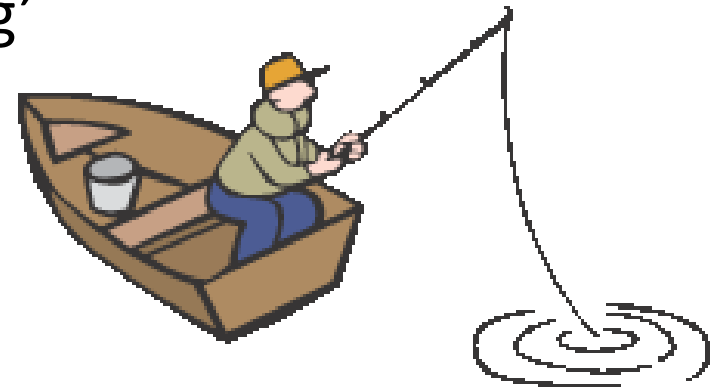
SYSTEMATIC REVIEW

A systematic review of the outcomes reported in trials of medication review in older patients: the need for a core outcome set

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Outcomes in trials - challenges

- **Reporting bias:** Outcome ‘switching’



Evidence of this in the top 5 medical journals: On average trials reported 58.2% of pre-specified outcomes and silently added 5.3 new ones

- **Publication bias:** ‘Positive’ outcomes more likely to be published

→ *Skewing of pooled evidence*

Solution?

Development & implementation of Core Outcome Sets (COSs)

*“A COS is a **standardised set of outcomes**, with international relevance, that represents the **minimum that should be measured and reported** in all trials within a specific area”*

COMET

- **Core Outcome Measures in Effectiveness Trials (COMET) Initiative:**
 - Established in 2010
 - Aims to bring together researchers interested in the development/application of COSs



COMET

- To raise awareness of current problems with outcomes in clinical trials
- To encourage COS development and uptake
- An international network of trialists, systematic reviewers, health service users, practitioners, editors, funders, policy makers, regulators
- To provide resources to allow practitioners to develop COS, e.g. COMET database

COMET

- www.comet-initiative.org

The screenshot shows the homepage of the COMET Initiative website. The browser address bar displays <http://www.comet-initiative.org/#>. The website features a navigation menu with links for Home, About COMET, Search, Events, Resources, Links, and Contact. The main content area includes a 'COMET Initiative' section with a detailed description of the initiative's purpose and a search box for the COMET database. A 'Core resource pack' section provides useful references for core outcome set developers. A 'Latest News' section highlights a recent article from September 21, 2016. The right sidebar contains social media links for Twitter and a 'Help, I want to...' section with various support options. The footer includes logos for the European Commission, Medical Research Council, and NHS, along with the text 'National Institute for Health Research'.

COMET INITIATIVE
Core Outcome Measures in Effectiveness Trials

COMET Initiative

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 843 references of planned, ongoing and completed work.

Enter Keyword

The keyword used for the search will be compared with study title, abstract and author's surname.

[View full search options](#)

To view a demonstration of how to search the 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, and things to think about once a COS is agreed. To read more, click [here](#).

Latest News

- Wednesday 21 September, 2016 - [How to select outcome measurement instruments for outcomes included in a "Core Outcome Set" - a practical guideline.](#)

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

EUROPEAN COMMISSION SEVENTH FRAMEWORK PROGRAMME

MRC Medical Research Council

NHS National Institute for Health Research

COMET

- Searchable database of completed and ongoing COS studies
- Available resources on COS development / reporting
- Links to other COS-related initiatives



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How to develop a COS (methodology)

Four key components of COS development:



Scope



Identify existing knowledge



Stakeholder involvement



Consensus exercise

1. Scope

- Define area of interest:
 - Health condition(s), population, type(s) of interventions
- Scope may be wide or narrow - should be guided by the volume of published literature

“A core outcome set for hip fracture trials.”

vs.

“A core outcome set for evaluating perioperative morbidity in the hip fracture population”

2. Identifying existing knowledge

- Aim – to generate a **‘long list’** of outcomes for consideration
- Review of previous trials/systematic reviews in an area can help identify a potential list of outcomes
- Qualitative research & stakeholder involvement → valuable source of potential outcomes

3. Stakeholder involvement

- Key stakeholders may include patients/carers healthcare professionals, other organisations/society representatives etc.
- Focus groups, interviews – can be used to ask:
“What do you think is important to measure in trials looking at the effectiveness of X?”

4. Consensus

- Delphi technique – most commonly used consensus method
- Sequential anonymous questionnaires; panel of participants with relevant ‘expertise’
- Participants ‘score’ outcomes based on perceived importance
- Responses fed-back to participants between rounds
- Pre-defined criteria for outcome inclusion

COS development – case study

- **CHIPPS study aim:**

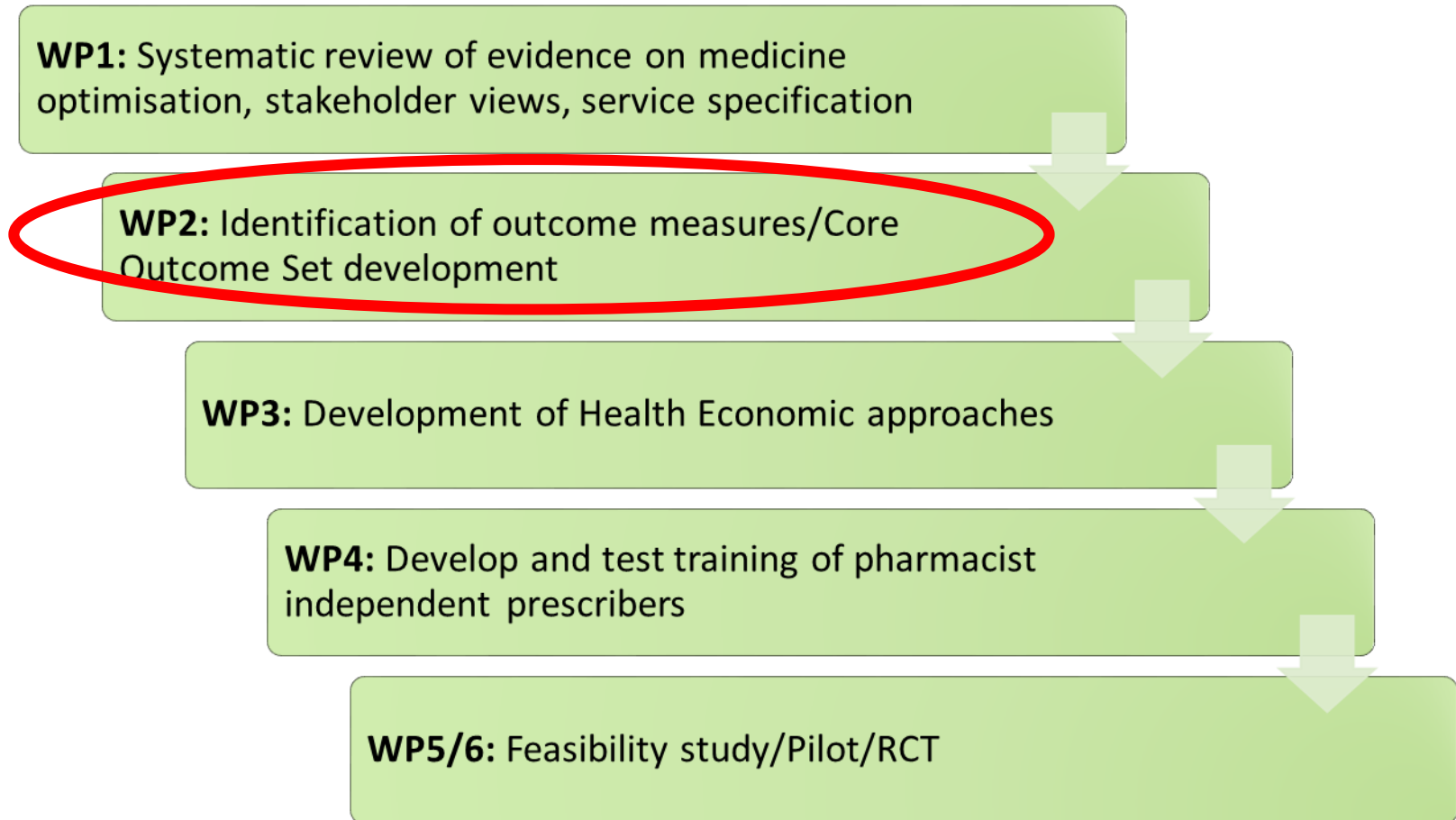
“To develop and deliver a cluster randomised controlled trial to assess the effectiveness and cost effectiveness of pharmacist independent prescribers (PIPs) assuming responsibility for medicines management within care homes compared to usual care”



UNIVERSITY OF LEEDS



CHIPPS study overview



CHIPPS COS development - overview

- **Phase 1: Identify all potential outcomes**
 - Review of relevant literature
 - Stakeholder involvement
 - Refinement of long-list
- **Phase 2: Delphi consensus exercise (2 rounds)**
 - Finalise COS → organise into outcomes / domains / categories

Identifying all potential outcomes

1. Review of relevant literature

- Identified all outcomes measured in the 12 studies included in relevant Cochrane systematic review:



2. Identifying potential outcomes: Stakeholder involvement

Area	Focus Groups	Participant type	Interviews	Participant type
Aberdeen Scotland	3	GPs x 5 Pharmacists x 4 Residents/Relatives x 8	2	GPs x 1 Pharmacists x 1
Belfast N Ireland	3	GPs x 10 Pharmacists x 8 Care home staff x 2	4	GPs x 1 Care home staff x 3
Norfolk England	5	GPs x 7 Pharmacists x 8 Care home staff x 4 Care home managers x 3 Residents/Relatives x 6	0	
Yorkshire England	2	GPs x 2 Pharmacists x 5	7	GPs x 3 Pharmacists x 1 Care home managers x 3
Total	13	72	13	13

Generate
long list of
outcomes

- Literature review
- Stakeholder involvement

Refine long
list

Delphi
consensus
exercise

Refining long-list of outcomes

- Pre-Delphi refinement of identified outcomes
 - Grouping similarly-worded outcomes (i.e. removing duplicates)
 - Removing outcomes suggested by stakeholders that were either:
 - Not relevant to the scope of COS
 - Or “process outcomes” i.e. descriptions of activity/intervention, not ‘true’ outcomes

Delphi consensus exercise

- Delphi exercise aim: to achieve consensus on outcomes of importance
- 2 round online Delphi (SurveyGizmo™) with expert panel (CHIPPS management team; n=19)

Scoring of outcomes - consensus

- Rated outcomes on a scale of 1-9 (where 9 = 'very important')
- GRADE working group scoring system

Consensus classification	Definition
Consensus IN	≥70% participants score outcome 7-9 AND <15% score 1-3
Consensus OUT	≥70% participants score outcome 1-3 AND <15% score 7-9
No consensus	Anything else

Online Delphi questionnaire format

The screenshot shows a web browser window displaying a SurveyGizmo questionnaire builder. The browser address bar shows the URL: <https://app.surveygizmo.com/builder/build/id/25c>. The page title is "WP2 Core Outcome Set Delphi Consensus Exercise".

The interface includes a navigation menu with options: BUILD, STYLE, TEST, SHARE, RESULTS, TOOLS, and ADVANCED. There is also a "Restore" button.

The main content area displays "Page 1: Thank you for taking part in this Delphi exercise." with a "Preview" button and editing icons.

The questionnaire content includes:

- A heading: "Below are the list of identified outcomes with brief explanations*." with an "Edit" button.
- A note: "*Please note: The explanations given are intended only to provide context for those who may be unfamiliar with the terms used. At this stage, these should not be interpreted as explicit definitions of how outcomes may be measured or reported."
- Instructions: "Instructions: Please indicate, on a scale of 1-9 (where 1 is 'not important' and 9 is 'critically important'), how important you think it is to measure the following outcomes in trials relating to optimising prescribing for older adults in care homes. If you are unable to offer an opinion on whether you think an outcome is important or not, you can select 'unable to score'."
- Outcome 1: "1. Number of medications (and associated costs)" with an "Explanation: A count of the number of medicines prescribed for care home residents (and the associated costs of these)." and a scale from 1 (Not important) to 9 (Critically important), plus an "Unable to score" option. Each scale point has a radio button. There are "Edit", "Move", "Copy", and "Remove" buttons for this item.
- Outcome 2: "2. Medication wastage (and associated costs)" with an "Explanation: Medication wastage refers to 'any medication which expires or remains unused throughout the whole medicines supply chain. Also refers to the unnecessary or inappropriate consumption of medications by patients, or the unjustified non-adherence to treatment guidelines by healthcare professionals' (West et al., 2015)." and the same scale and buttons as Outcome 1.

The Windows taskbar at the bottom shows various application icons and the system clock indicating 14:53 on 16/01/2017.

Online Delphi – example wording

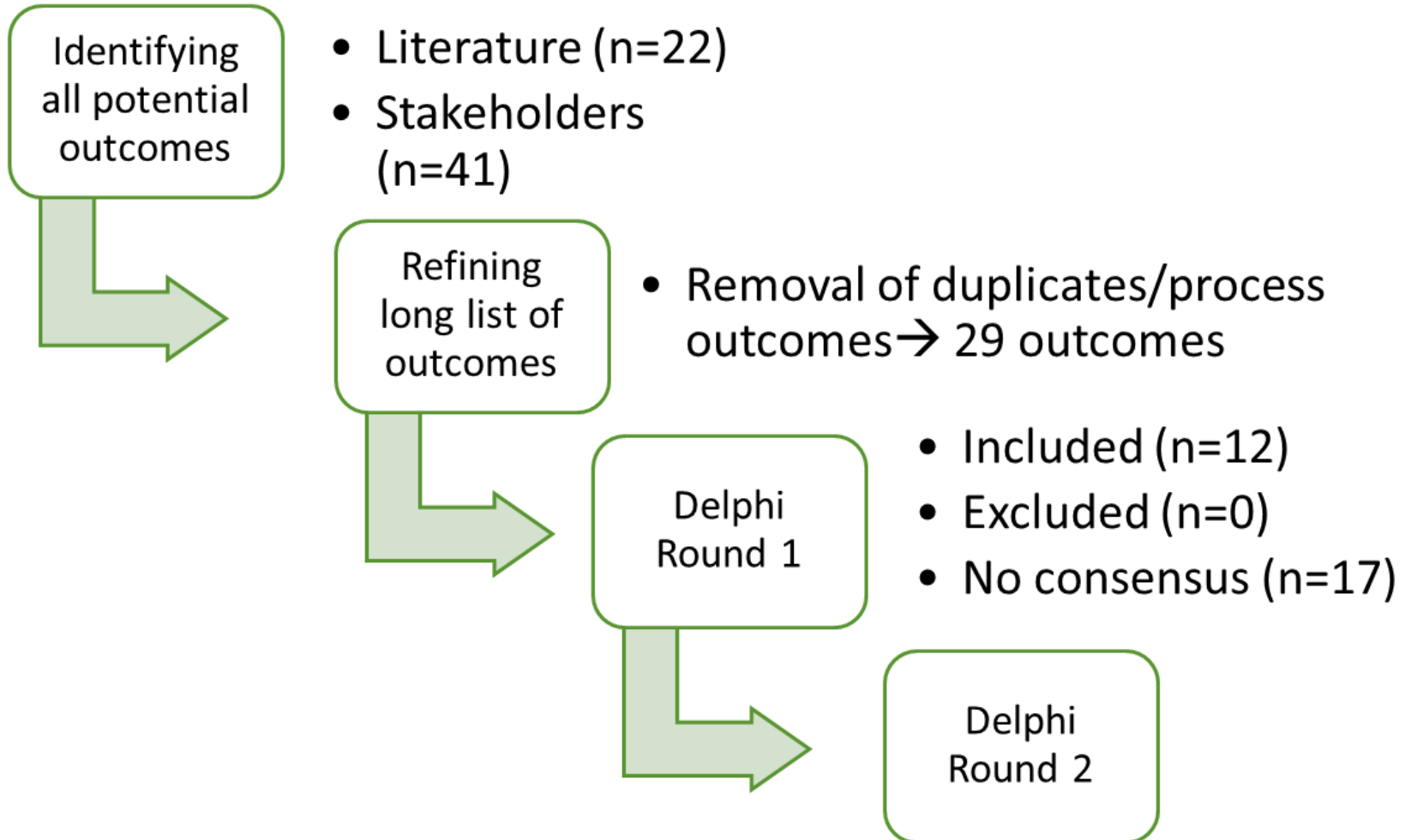
- Instructions: Please indicate, on a scale of 1-9 (where 1 is 'not important' and 9 is 'critically important'), how important you think it is to measure the following outcomes in trials relating to optimising prescribing for older adults in care homes. If you are unable to offer an opinion on whether you think an outcome is important or not, you can select 'unable to score'.

Falls

Explanation: Falls occurring amongst care home residents. A fall is “an event which results in a person coming to rest inadvertently on the ground or floor or other lower level” (WHO, 2012).



Results



Results – cont'd

Delphi Round 2



- Outcomes entered in Round 2 (n=20)

Delphi Round 2 results



- Included (n=2)
- Excluded (n=0)
- No consensus (n=18)

Final COS



- Total outcomes meeting inclusion criteria (n=13)

Organise outcomes

Final CHIPPS COS

3 categories → 7 domains → 13 outcomes:

1. Medication-related

- **Potentially inappropriate prescribing**
 - *Number of medicines*
 - *Duplicate drugs*
 - *Use of antipsychotics*
 - *Harmful interactions*
 - *Anticholinergic burden*
- **Adverse drug events**
- **Prescribing errors**

2. Patient-related

- **Quality of life**
- **Falls**
- **Mortality**

3. Healthcare utilisation-related

- **Admissions to hospital (and associated costs)**
 - *Admissions to A&E (and associated costs)*

Next steps...

- Determine 'how' outcomes should be measured/reported → To reduce heterogeneity in outcome *measurement*
- Medication appropriateness: STOPP/START; Beer's Criteria; MAI?
- Quality of Life: EQ-5D; SF-36; dementia-specific measures?

COSMIN initiative

- The COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) initiative
 - Aim: To aid selection of patient-reported outcome (PRO) measurement instruments



COSMIN

- Developed guideline that can be used by COS developers in defining how to measure core outcomes:



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

RESEARCH

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. Rose⁵, Maarten Boers^{1,6}, Peter Tugwell⁷, Mike Clarke⁸, Paula R. Williamson⁹ and Caroline B. Terwee¹
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Core Outcome Set–STAndards for Reporting: The **COS-STAR** Statement

- Checklist of 18 items considered essential for transparent and complete reporting in all COS studies

SECTION/TOPIC	ITEM No.	CHECKLIST ITEM
TITLE/ABSTRACT		
Title	1a	Identify in the title that the paper reports the development of a COS
Abstract	1b	Provide a structured summary
INTRODUCTION		
Background and Objectives	2a	Describe the background and explain the rationale for developing the COS.
	2b	Describe the specific objectives with reference to developing a COS.
Scope	3a	Describe the health condition(s) and population(s) covered by the COS.
	3b	Describe the intervention(s) covered by the COS.
	3c	Describe the setting(s) in which the COS is to be applied.
METHODS		
Protocol/Registry Entry	4	Indicate where the COS development protocol can be accessed, if available, and/or the study registration details.
Participants	5	Describe the rationale for stakeholder groups involved in the COS development process, eligibility criteria for participants from each group, and a description of how the individuals involved were identified.
Information Sources	6a	Describe the information sources used to identify an initial list of outcomes.
	6b	Describe how outcomes were dropped/combined, with reasons (if applicable).
Consensus Process	7	Describe how the consensus process was undertaken.
Outcome Scoring	8	Describe how outcomes were scored and how scores were summarised.
Consensus Definition	9a	Describe the consensus definition.
	9b	Describe the procedure for determining how outcomes were included or excluded from consideration during the consensus process.
Ethics and Consent	10	Provide a statement regarding the ethics and consent issues for the study.
RESULTS		
Protocol Deviations	11	Describe any changes from the protocol (if applicable), with reasons, and describe what impact these changes have on the results.
Participants	12	Present data on the number and relevant characteristics of the people involved at all stages of COS development.
Outcomes	13a	List all outcomes considered at the start of the consensus process.
	13b	Describe any new outcomes introduced and any outcomes dropped, with reasons, during the consensus process.
COS	14	List the outcomes in the final COS.
DISCUSSION		
Limitations	15	Discuss any limitations in the COS development process.
Conclusions	16	Provide an interpretation of the final COS in the context of other evidence, and implications for future research.
OTHER INFORMATION		
Funding	17	Describe sources of funding/role of funders.
Conflicts of Interest	18	Describe any conflicts of interest within the study team and how these were managed.

Examples of COSs under development

1. Medication review
2. Polypharmacy
3. Dementia
4. Bronchiectasis

1. Medication review COS



- COS for medication review in multimorbid older adults with polypharmacy
- Part of OPERAM study: OPTimising thERapy to prevent Avoidable hospital admissions in the Multimorbid elderly
- Method: Systematic review on medication review in older adults. Interviews with patients/caregivers. 3-round Delphi exercise with patients/carers/HCPs
- Four European centres: Belgium, Ireland, Netherlands, Switzerland

Developers: A Spinewine (PI), JB Beuscart, O Dalleur et al. Clinical Pharmacy research group, Louvain Drug Institute, Université Catholique de Louvain, Belgium



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2. Polypharmacy COS



- COS for interventions aimed at improving appropriate polypharmacy in older people in primary care.
- Current stage – Delphi Round 1
- Method: Cochrane Systematic Review, interviews with stakeholders. 3-round Delphi exercise (online) with public participants (n=40) and experts (n=120).
- Recruitment of public pts challenging

Developers: C Hughes, QUB (PI), A Rankin, QUB, Dr. Cristín Ryan, Royal College of Surgeons in Ireland (RCSI), C Cadogan, RCSI, S Smith, RCSI, B Clyne, RCSI

3. Dementia COS



- COS for medicines management interventions in people with dementia in primary care
- Current stage – Delphi exercise
- Method: systematic lit review, interviews with stakeholders, online Delphi with HCPs and academics (n=50)
- Challenges – few studies identified to extract outcomes from; decision to exclude patient participants from consensus exercise

4. Bronchiectasis COS



- COS for RCTs investigating the efficacy & safety of interventions for the long-term management of bronchiectasis in adults.
- Current stage – Delphi Round 2.
- Methods: Outcomes identified via Cochrane review & previous qualitative work. Online Delphi, Round 1 included 44 doctors, 8 nurses, 10 physios, 23 patients. Recruitment aided by:



ELF EUROPEAN
LUNG
FOUNDATION

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EMBARC

The European Bronchiectasis Registry

Summary

- COS development & implementation will help improve selection & reporting of outcomes in future trials
- COMET & other initiatives offer guidance to COS developers
- Numerous COSs in pharmaceutical care under development
- Uptake of these COSs in future research is key

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D.P. Alldred¹, A. Arthur², G. Barton², A. Blyth², C. Bond³, A. Daffu-O'Reilly¹, J. Desborough², C. Handford⁴, H. Hill⁴, C. Hughes⁵, J. Inch³, K. Lane², V. Maskrey², K. Massey⁵, P. Myint³, N. Norris², F. Notman³, F. Poland², L. Shepstone², I. Small⁶, AM. Swart², C. Symms⁷, D. Turner², A. Zermansky¹

1 University of Leeds; 2 University of East Anglia; 3 University of Aberdeen; 4 Public and Patient Involvement in Research, Norfolk & Suffolk; 5 Queen's University Belfast; 6 NHS North & East London Commissioning Support Unit; 7 NHS South Norfolk CCG.

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Hvala!

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