“Developing Core Outcome Sets for Pharmaceutical Care”

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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
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
COMET

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

**WP1:** Systematic review of evidence on medicine optimisation, stakeholder views, service specification

**WP2:** Identification of outcome measures/Core Outcome Set development

**WP3:** Development of Health Economic approaches

**WP4:** Develop and test training of pharmacist independent prescribers

**WP5/6:** Feasibility study/Pilot/RCT
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

<table>
<thead>
<tr>
<th>Area</th>
<th>Focus Groups</th>
<th>Participant type</th>
<th>Interviews</th>
<th>Participant type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aberdeen Scotland</td>
<td>3</td>
<td>GPs x 5 Pharmacists x 4 Residents/Relatives x 8</td>
<td>2</td>
<td>GPs x 1 Pharmacists x 1</td>
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<tr>
<td>Belfast N Ireland</td>
<td>3</td>
<td>GPs x 10 Pharmacists x 8 Care home staff x 2</td>
<td>4</td>
<td>GPs x 1 Care home staff x 3</td>
</tr>
<tr>
<td>Norfolk England</td>
<td>5</td>
<td>GPs x 7 Pharmacists x 8 Care home staff x 4 Care home managers x 3 Residents/Relatives x 6</td>
<td>0</td>
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</tr>
<tr>
<td>Yorkshire England</td>
<td>2</td>
<td>GPs x 2 Pharmacists x 5</td>
<td>7</td>
<td>GPs x 3 Pharmacists x 1 Care home managers x 3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>13</strong></td>
<td><strong>72</strong></td>
<td><strong>13</strong></td>
<td><strong>13</strong></td>
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</tbody>
</table>
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 Dephi (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

<table>
<thead>
<tr>
<th>Consensus classification</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Consensus IN</td>
<td>≥70% participants score outcome 7-9 AND &lt;15% score 1-3</td>
</tr>
<tr>
<td>Consensus OUT</td>
<td>≥70% participants score outcome 1-3 AND &lt;15% score 7-9</td>
</tr>
<tr>
<td>No consensus</td>
<td>Anything else</td>
</tr>
</tbody>
</table>
Online Delphi questionnaire format
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

- Literature (n=22)
- Stakeholders (n=41)
- Removal of duplicates/process outcomes → 29 outcomes
  - Included (n=12)
  - Excluded (n=0)
  - No consensus (n=17)
Results – cont’d

- Outcomes entered in Round 2 (n=20)
  - Included (n=2)
  - Excluded (n=0)
  - No consensus (n=18)

- Total outcomes meeting inclusion criteria (n=13)
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 \(\rightarrow\) 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:
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

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

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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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