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"Developing Core Outcome Sets for Pharmaceutical Care"

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2

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

SYSTEMATIC REVIEW

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

Correspondence Jean-Baptiste Beuscart, Institut de Recherche LDRI – CLIP, Université catholique de Louvain; Avenue E. Mounier 72 bte B1.72.02; 1200 Woluwe-Saint-Lambert, Belgium. Tel.: +32 2062 3494; Fax: +32 2062 6881; E-mail: jean-baptiste.beuscart@univ-lille2.fr

Outcomes in trials - challenges

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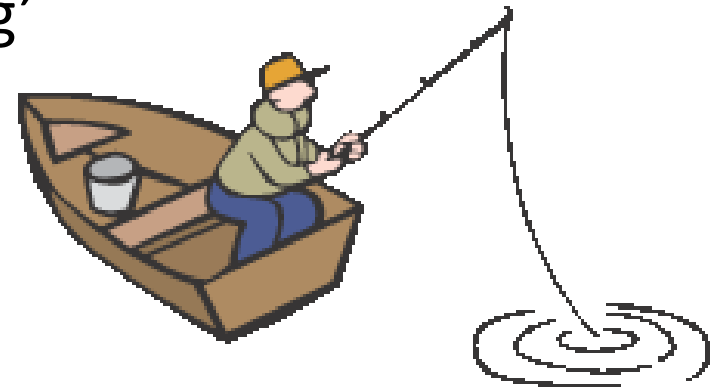
Evidence of this in the top 5 medical journals: On average trials reported 58.2% of pre-specified outcomes and silently added 5.3 new ones

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

→ *Skewing of pooled evidence*

Solution?

Development & implementation of **<u>Core Outcome Sets (COSs)</u>**

*"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 <u>you</u> 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
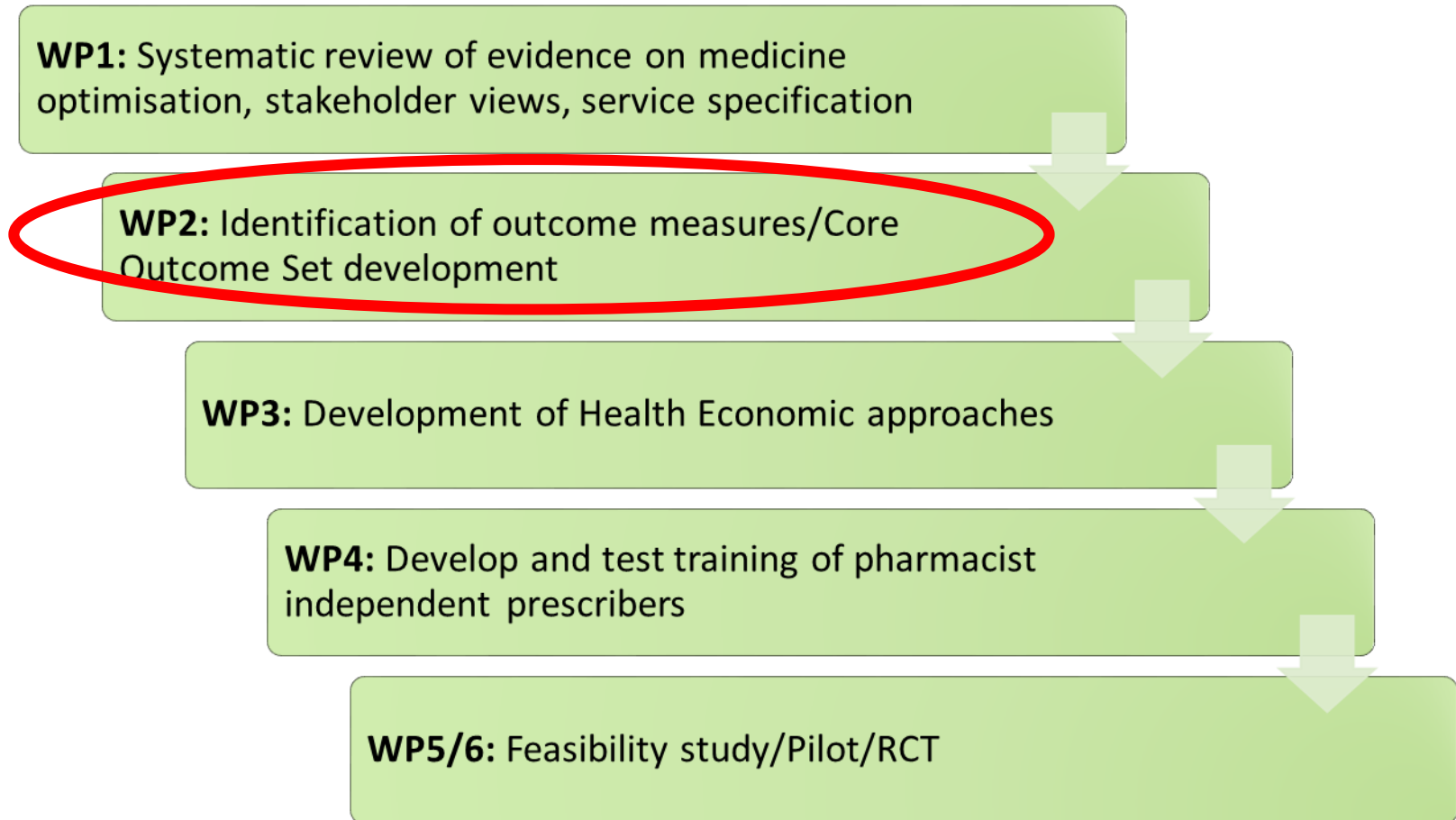
CHIPPS COS development - overview

- **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:

Cochrane Library

Cochrane Database of Systematic Reviews

Interventions to optimise prescribing for older people in care homes (Review)

Alldred DP, Kennedy MC, Hughes C, Chen TF, Miller P

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 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

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

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

Identifying all potential outcomes
- Literature (n=22)
- Stakeholders (n=41)

Refining long list of outcomes
- Removal of duplicates/process outcomes→ 29 outcomes

Delphi Round 1
- Included (n=12)
- Excluded (n=0)
- No consensus (n=17)
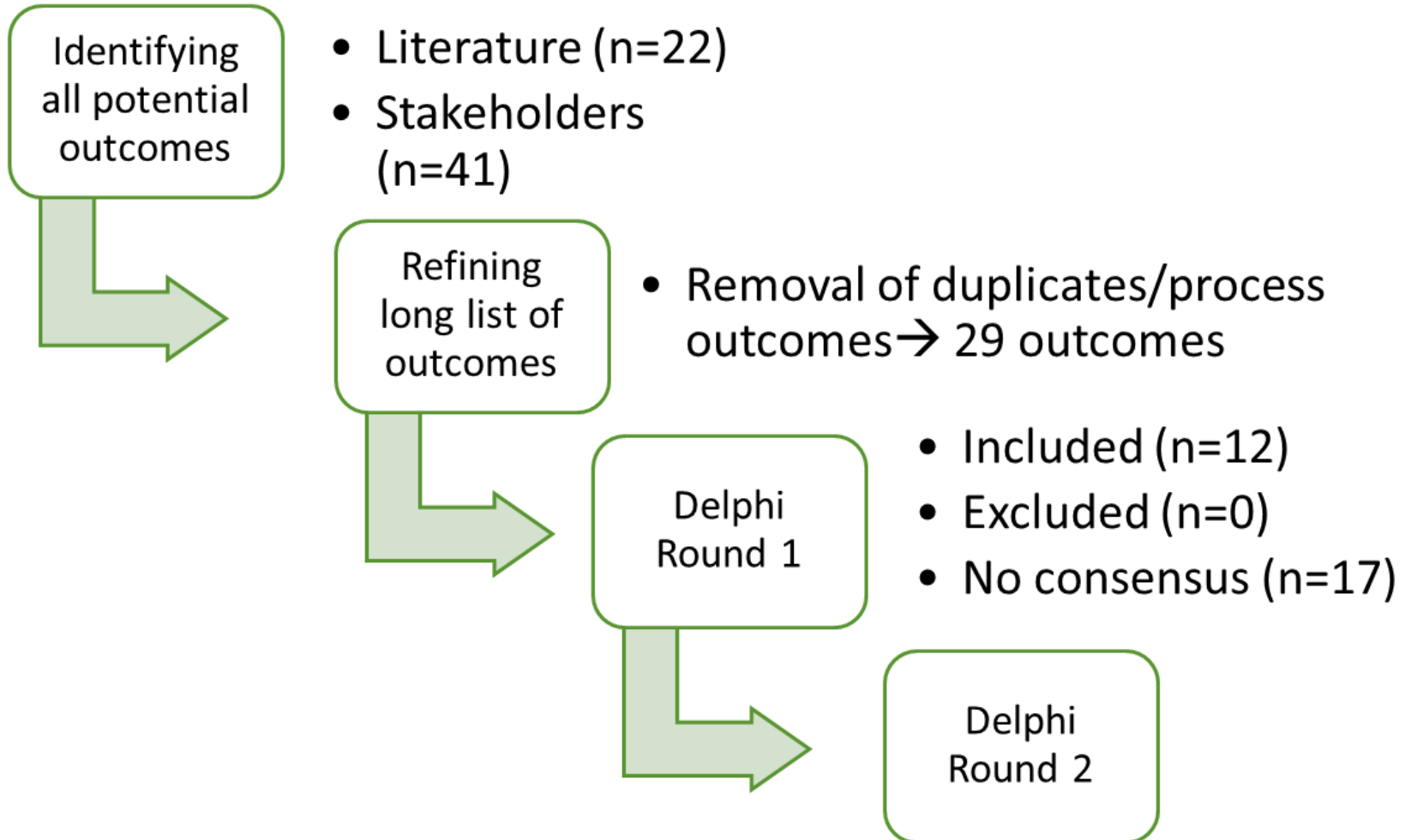
Delphi Round 2

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:

RESEARCH

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

Ceclia 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]

QUALITY of a HR-PRO

Reliability

Internal Consistency

Reliability (test-retest, Inter-rater, Intra-rater)

Measurement error (test-retest, Inter-rater, Intra-rater)

Validity

Content validity

face validity

Criterion validity (concurrent validity, predictive validity)

Construct validity

Structural validity

Hypotheses-testing

Cross-cultural validity

Responsiveness

Responsiveness

Interpretability

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

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

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Hvala!

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