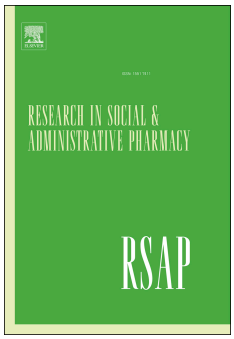

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Developing a Core Outcome Set for evaluating medication adherence interventions for adults prescribed long-term medication in primary care

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Abstract

Background: Approximately half of people prescribed medications do not take them as prescribed. There is a significant unmet need regarding the barriers to medication adherence not being addressed in primary care. There is no agreement on which outcomes should be measured and reported in trials of medication adherence interventions.

Objective: To develop a core outcome set (COS) for trials of medication adherence interventions in primary care for adults prescribed medications for long-term health conditions.

Methods: A list of potentially relevant outcomes from the literature was developed. Using a two-round Delphi survey of stakeholder groups representing patients and their carers; primary care staff; and academic researchers with an interest in medication adherence; each outcome was scored in terms of importance for determining the effectiveness of medication adherence interventions in primary care. This was followed by two consensus workshops, where importance, as well as feasibility and acceptability of measurement, were considered in order to finalise the COS.

Results: One hundred and fifty people took part in Delphi Round 1 and 101 took part in Round 2. Eight people attended the workshops (four attendees per workshop). Seven outcomes were identified as most important, feasible and acceptable to collect in medication adherence trials: Health-related quality of life, number of doses taken, persistence with medicines, starting (initiating) a medicine, relevance of the medication adherence intervention for an individual, mortality, and adverse medicine events.

Conclusions: This COS represents the minimum outcomes that should be collected and reported in all medication adherence trials undertaken in primary care. When developing and finalizing the COS, feasibility and acceptability of collection of outcomes has been considered. In addition to the COS, medication adherence trials can choose to include outcomes to suit their specific context such as the health condition associated with their medication adherence intervention.

Key words: Compliance, primary care, adults, long-term conditions, Delphi, workshops

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Introduction

An estimated one in two patients do not adhere to directions for prescribed medication to treat long-term conditions.[1] The World Health Organisation has identified medication non-adherence as an international priority as it presents a significant public health challenge that causes avoidable morbidity, mortality and resource utilisation.[2] A multicentre prospective cohort study of 1,280 older adults in the UK reported that one quarter of all medication-related harm is associated with non-adherence to long-term medication, and this translated into an estimated annual National Health Service (NHS) cost of £40 million in avoidable hospital readmissions alone.[3] Total avoidable NHS costs arising from further investigations and prescribing to mitigate the effects of non-adherence plus harm due to over or under usage of medication is estimated to be £500 million per annum with a further £300 million wasted on unused medication[4,5].

Efforts to address medication adherence have led to a plethora of interventions being designed and tested in differing patient populations. In 2014, a Cochrane review of randomised controlled trials of medication adherence interventions comprised 182 trials.[1] The interventions were largely complex in nature, most frequently including an education, reminder and regimen simplification component. A wide range of different patient populations, with differing health conditions were represented by the trials. However, the majority of trials focussed on one clinical condition with the most frequently represented conditions being HIV/AIDS, psychiatric disorders, chronic obstructive pulmonary disease, cardiovascular disease, hypertension and diabetes. This focus on a clinical condition may be due to the review only including studies if they reported a clinical outcome measure. The review included 46,962 participants thus offering the potential to generate high quality evidence in terms of the effectiveness of medication adherence interventions. However, the data could not be pooled in a meta-analysis due too much heterogeneity in the outcome measures despite studies only being eligible if they reported at least one medication adherence measure.

A Core Outcome Set (COS) is an agreed, standardised set of outcomes to be measured and reported in all clinical trials of a specific health condition or area of healthcare [6]. This enables comparison of results from similar trials as well as trial data aggregation in the future. It is widely accepted that a COS should be developed and used in all clinical trials testing the effectiveness of an intervention for a specific health condition or area of healthcare. A COS should only include outcomes that are fundamental, i.e., core to the evaluation of a treatment or intervention for a certain condition or area of healthcare, rather than every relevant or important outcome. [6,7] To ensure that a COS comprehensively includes both patient-centred and intervention-specific outcomes, at least one outcome from the core areas of 'death', 'life impact', 'pathophysiological manifestations' and 'resource use' [8] should be included.[8]

Whilst measurement of adherence may appear to be the most appropriate outcome measure for trials designed to address intentional patient non-adherence, the available tools largely have significant deficits in validity[9,10]. Furthermore, adherence is a measure of process and as such a predictor of future clinical benefit. Consequently, clinical outcomes provide a more patient-orientated picture of the effectiveness of medication adherence interventions. Prior to this study, there was no reported consensus as to which measures should be used within medication adherence focused interventions. This study aimed to develop a COS for use in all trials evaluating the effectiveness of medication adherence interventions in primary care for adults prescribed medications for long-term health conditions.

Methods

This study followed accepted conduct and reporting guidelines for developing a COS[6,11] (detail provided in Supplementary file 1) including registration on the COMET (Core Outcome Measures in Effectiveness Trials) database (https://www.comet-initiative.org/Studies/Details/2060). The methodology included three main stages: 1) identifying potentially relevant outcomes ; 2) two Delphi rounds, and 3) consensus workshops to finalise the COS.

The research team

The research team comprised academic researchers with pharmacy, health services research, medical statistics and health economics backgrounds. Two Patient and Public Involvement (PPI) members were part of the team and involved at all stages of research design, conduct and analysis. Our PPI members represented members of the public prescribed multiple medications with experience of accessing healthcare services. They provided insight into patient perspectives throughout the study and guided the team on approaches to support patients and their carers to participate in the study, including the development of plain English definitions for outcomes and advising on ways that participants could access the Delphi surveys (e.g., online, by telephone or by post).

Primary Care Influencer Group (PCIG)

A PCIG of senior voices representing professionals from healthcare, social care and local authorities, was established to work alongside the PPI members to provide oversight of the project.

Phase 1: Identifying and reviewing potentially relevant outcomes

Potentially relevant outcomes for medication adherence trials were identified through a search for Cochrane reviews and systematic reviews of medication adherence and published COS for similar topics, as recommended in published COS development guidance (add COMET ref). All potentially relevant outcomes were extracted from: a medication review COS [12]; a COS for hospital deprescribing trials for older people under the care of a geriatrician[13]; two Cochrane reviews regarding medication adherence interventions[1,14]; a systematic review of interventions for improving medication-taking for older people prescribed multiple medications[15]; and a paper examining persistence as a measure for medication adherence.[16] The research team, including our PPI members, also proposed additional outcomes. This list of outcomes was reviewed by the entire team for overlap, duplication and relevance and refined accordingly.

To develop plain English definitions for the potential outcomes, the literature and existing COS were reviewed and definitions extracted. Authors of the COS studies were contacted to request plain English definitions where these were not reported in manuscripts. For the remaining potential outcomes, research team members (JMK, DB, SS, DW, KK, DT) working with the PCIG and PPI members, developed definitions. All outcomes and definitions were reviewed and refined by the team, including our PPI members, to improve clarity and then similar outcomes were organised into domains: medication adherence; patient-reported outcomes; carer-reported outcomes; use of healthcare resources; death; adverse events; costs; and processes of care.

Phase 2: Modified Delphi

Participants

We planned to recruit participants representing five stakeholder groups: patients; informal carers; healthcare practitioners in primary care; primary care managers; and academic researchers involved in medication research.

Patients and carers and primary care staff stakeholder groups were in England and academics were worldwide. There is no set standard for the number of participants for a COS but it is generally agreed that higher numbers will increase the reliability of group judgments.[17] It has been suggested that a minimum number of participants should range from 10 to 18 per stakeholder group completing all Delphi rounds.[18] We planned to recruit 60 patients and carers, 60 practice staff and 30 academic researchers with a maximum of 150 participants. Estimating 20% attrition after Round 1, we anticipated approximately 120 participants completing both rounds, providing sufficient numbers overall and for each stakeholder group.[19,20] Participants provided demographic details including their stakeholder group, age, gender, location, ethnic background, professional role and years practising (primary care staff and academics only). It was not possible to report participation rates due to the use of gatekeepers for recruitment purposes.

Recruitment

General practices

General practices in England were contacted via research networks and asked to express an interest in identifying participants for the study, based on the eligibility criteria for staff and patients provided by the study team to gatekeepers. During this process, the practice identified a gatekeeper, which was a staff member who would be responsible for identifying staff and patients. Interested general practices were purposively selected based on the population socioeconomic deprivation score, proportion of patients aged ≥65 years, proportion non-white patients in the practice and whether the practice was located in an urban/non-urban area. This was to support inclusion of a range of views in order to develop a COS that was relevant to a diverse population.

Patients and carers

Patients were eligible to participate if they were aged ≥ 18 years, were responsible for managing their own medication and eligible to receive the NHS England structured medication review (SMR) service. The eligibility criteria for an SMR are[21]: people with complex and problematic polypharmacy, specifically those on 10 or more medications; prescribed medications commonly associated with medication errors; with an electronic Frailty Index score of >0.36; particularly isolated or housebound; two or more unplanned hospital admissions in previous six months and/or falls; or any other patients that the healthcare team think would benefit from an SMR. Individuals who are eligible to receive the NHS SMR service were identified as a population most likely to benefit from a medication adherence intervention.[21] Carers were eligible if invited by an eligible patient, aged ≥ 18 years and involved in managing an eligible patient's medications.

General practices identified eligible patients using an electronic search of their records. Patients deemed by the healthcare team as unable to provide informed consent were excluded. Study invitation packs containing the patient invitation letter with a link to an online expression of interest and a participant information sheet (PIS) were sent to eligible patients using the usual communication mode(s) adopted by the medical practice (electronic and/or post). If patients were willing to participate, they were advised to

complete an online expression of interest form (link contained within the invitation letter). The study team could be contacted by potential participants to discuss the study, and liaise with them regarding their preferred method of consent and questionnaire completion (online, telephone, paper).

Eligible patients were asked in the invitation to invite family members or friends aged ≥ 18 years, who were involved as informal carers in the management of their medications. Carers interested in participating followed the same process as patient participants to express an interest.

Primary care staff

Primary care staff were eligible if they had a role that included medication management (including general practitioners, clinical pharmacists, nurses), or were other practice staff (e.g., practice managers). Gatekeepers at each general practice distributed a letter of invitation (which included a link to an online consent form) with a PIS to identified primary care staff according to their usual communication procedures. If individuals were interested in taking part in the study, they were advised to complete an online consent form.

Academic researchers

Academic researchers were eligible to participate if they had an interest in medication adherence/medication management. Academic researchers were identified via the research team's networks. The team also contacted first, last or corresponding authors of medication adherence publications. All academic researchers were contacted by email with the PIS and a link to the consent form.

Delphi survey

A Delphi survey was hosted on Mantal,[22] an online research software platform. Two rounds of the Delphi were planned to approach consensus ahead of the workshops.[6] A hard copy of the Delphi surveys was provided to patient and carer participants who preferred not to participate electronically. Participants completing the Delphi this way could either complete

the form and return by mail to the research team or they could complete the Delphi survey over the telephone with a member of the research team. We worked closely with our PPI members to develop accompanying text that explained the Delphi process in understandable language for those who were completing the Delphi by telephone, online or by post.

In both Delphi rounds, outcomes were presented in their core areas of 'death', 'life impact', 'pathophysiological manifestations', 'resource use' [8] and 'other/processes' and within these areas, they were organised into domains[6] according to what is being measured e.g. medication adherence, adverse events or costs.

Participants assessed the outcomes presented to them in terms of their importance to measure in a research trial about medication adherence. The options were 'Yes', 'No' and 'don't know/not sure', with an opportunity to add comments for each outcome. We made the decision to use these options as we are aware that asking participants to rate outcomes on Likert scales can be confusing. In Round 1, participants were invited to suggest additional outcomes. These were reviewed by the research team to determine relevance and possible overlap with existing outcomes. New outcomes deemed relevant by the research team were presented in Round 2. Determinants, such as a person's knowledge about their medication, may be an enabler to medication adherence but are not an outcome as such. They are a measure of process to explain outcomes. Consequently, determinants were therefore not included in the Delphi process.

Participants received their Round 1 rating and the rating for their own and other stakeholder groups using histograms. The ratings of outcomes were then used to structure the consensus workshops.

Data analysis

Consensus to retain an outcome was defined *a priori,* if the outcome was rated as important (Yes) by ≥70% of participants in all three stakeholder groups and consensus to remove if the opposite were true.[6,18,19,23,24] Partial consensus to retain an outcome for the COS was met if the outcome was rated as important (Yes) by ≥70% of participants in at least one

stakeholder group. Non-consensus was declared if an outcome failed to achieve none of the above.

Outcomes that reached consensus as important progressed for discussion at the workshops (phase 3), those that reached consensus as not important, were removed from the study. Outcomes with partial consensus or no consensus at round 1 progressed to Round 2 for re-rating. For these outcomes, a participant's own Round 1 rating was presented along with histograms representing the average Round 1 rating for each stakeholder group.

Outcomes with partial consensus at Round 2 progressed for discussion at the workshops whilst non-consensus outcomes were removed from the study.

Phase 3: Consensus workshops

Two online 90-minute workshops were held with a sample of participants representing the three stakeholder groups. In the event that there was a large number of outcomes considered for inclusion in the COS after the two Delphi rounds, we planned a pre-workshop activity to ask participants to identify three outcomes that were most important to measure in medication adherence trials for each domain that had three or more outcomes. This ranking exercise was used to support discussion during the workshops, and outcomes were presented in terms of the proportion of participants that rated an outcome as one of their three most important outcomes.

Workshops were facilitated by research team members including PPI members, to support participation by patients and carers. Both workshops were audio-visually recorded and facilitators made notes of the discussions and decisions made. Recordings were reviewed after the workshops to ensure that all the decisions noted were accurate and reflected the discussions.

At Workshop 1, outcomes were organised into their relevant core area of 'death', 'life impact', 'pathophysiological manifestations', 'resource use' [8] and 'other/processes' to support discussion. This structure ensures for each core area that at least one outcome is included. 'Resource use' is an optional area, and there is no requirement to include a resource use outcome in the final COS [20]. Results from the pre-workshop activity were

presented and this formed the basis for discussion by workshop attendees to decide which outcomes in each area were most important. Later in the workshop, other core area outcomes were discussed in terms of importance for inclusion in a COS for medication adherence.

In Workshop 2, participants reviewed the outcomes identified by Workshop 1 participants as being most important to include in the COS. During this second workshop, outcomes were discussed in terms of importance, as well as feasibility and acceptability of measurement. To support evaluation of feasibility and acceptability, we presented tools that could be used for measuring each outcome to help guide their assessment (See Supplementary file 7). This was to ensure that the outcomes included in the COS were able to be collected in a trial setting. During this discussion, participants reviewed possible tools for measuring the outcomes to support decisions about how the outcomes could be measured and whether this would be acceptable and feasible in medication adherence trials.

Synthesis and review

Data from the study were reviewed by the research team and PCIG members to ensure that the COS is deliverable and includes only outcomes that are relevant and prioritised.

Results

Figure 1 summarises the process of developing the COS.

Phase 1 – identification of outcomes

One hundred and twenty-six outcomes were identified which were reduced to 46 outcomes through discussions between the research team to review for overlap and that each outcome was potentially relevant for medication adherence trials. Removal of 80 outcomes was due to duplication, overlap or being related to a determinant of medication adherence (Supplementary file 2 lists all outcomes and definitions included in Round 1 of the Delphi). For the measurement of medication adherence, the literature reported two measures:

Medication Possession Ratio (MPR) and Proportion of Days Covered (PDC), which are both similar and PDC was noted as being more accurate.[16] For this reason, we only offered PDC to the Delphi participants to reduce confusion.

[INSERT FIGURE 1 HERE]

Phase 2: Delphi survey

With lower than anticipated numbers of carers (n=3) and other practice staff (e.g., practice managers) (n=15) participating in the study led to two stakeholder groups being merged. Patients and carers were merged to become 'patients and carers'. Similarly for primary care practitioners and managers, the ratings of outcomes were similar during Round 1 and the decision was made to merge these to become 'primary care staff'. This resulted in three stakeholder groups rating outcomes representing service users, service providers and researchers. The reason for doing this is that in a Delphi survey, decisions are made on the proportion of each stakeholder group that rate an outcome as very important/critical (yes) or not important (no).

Participants

[INSERT TABLE 1 HERE]

Round 1 survey

Figure 1 provides the flow of outcomes rated in Round 1 (July – September 2022). Thirty of the 46 outcomes were rated as important by ≥70% of participants in all stakeholder groups and thus removed from Round 2; no outcomes met the criteria for exclusion. Participants proposed 34 additional outcomes (Supplementary file 3). However, when these were reviewed, they were either a determinant[25] (rather than an outcome) of medication adherence, a statement, or were already covered by an existing outcome. There was consistent feedback during this process about the need to collect and report clinical outcomes specific to certain medication or a particular health condition.

Round 2 survey

In Round 2 (September – October 2022), 16 outcomes were rated. Eleven outcomes reached consensus for consideration in the COS (providing 41 in total across the two Delphi rounds). The remaining five outcomes did not reach consensus to either retain or remove; these were rated as important by at least one stakeholder group (Supplementary file 4 and 5 summarise the ratings in Rounds 1 and 2).

Phase 3: Consensus workshops

The two consensus workshops were held in October-November 2022. Eight participants took part in workshops (four participants in each): Workshop 1 had two patients and two academics; Workshop 2 had two patients, one academic and one primary care staff member.

As the Delphi exercise excluded no outcomes for inclusion in the COS, all 46 outcomes were presented in Workshop 1, organised according to their pre-workshop activity ranking. Following discussion, nine outcomes were considered most important and considered for inclusion in the COS.

In Workshop 2, participants agreed that two of the nine outcomes considered important in Workshops 1 should be removed (see Table 2). All outcomes were discussed in relation to how the data could be collected, for example existing tools or whether a bespoke trial collection process was needed (see Supplementary file 7 for details). The outcome 'satisfaction with the intervention' was deemed to overlap with relevance of intervention for the individual', with the latter being considered more important. The outcome 'adverse medicine withdrawal event' was also removed because it may not to be applicable to all medication adherence trials. The original definition of this outcome was confusing and participants indicated that the return of symptoms from the condition after stopping a medicine was important, which appeared to be included in the original definition. The definition was revised to: A reaction caused by stopping a medicine, excluding return of the

health condition for which the medicine was prescribed. After revising the definition, participants agreed that this outcome should be excluded from the COS. However, adverse medicine withdrawal event could be captured, when relevant, by certain medication adherence trials, in addition to the COS.

Participants also recommended changes to the wording of one outcome that was included in the COS: 'number of medicines taken' was refined by the workshop participants to 'number of doses taken'.

[INSERT TABLE 2 HERE]

Final core outcome set

Table 3 summarises the seven outcomes retained in the COS and provides definitions and suggestions for measurement of these. Supplementary file 8 provides an overview of every outcome identified within the study and the decisions made throughout the study.

[INSERT TABLE 3 HERE]

Discussion

This study reports the development of a COS for medication adherence intervention trials in primary care for adults taking multiple medications for long-term health conditions. The COS contains seven outcomes that were the most important to all stakeholders and feasible and acceptable to be implemented in trials. These outcomes are the minimum that should be collected and reported by all medication adherence intervention trials in primary care for adults taking multiple medications for long-term conditions. The study also provides recommendations for measurement tools for the outcomes within the COS to support consistent measurement of the outcomes by future medication adherence intervention trials.

This COS addresses this gap. A strength of the COS is that the outcomes in the COS are not specific to particular medications or health conditions and are thus relevant to all medication adherence intervention trials in primary care for adults taking multiple medications for long-term conditions. For medication adherence intervention trials within a specific area, participants indicated the importance of measuring outcomes related to particular medications or health conditions. This has also been raised in a recent study exploring outcomes for medication adherence studies for rheumatology.[26] This is an important point and a COS does not preclude trials from measuring outcomes in addition to the COS according to the focus or context.[6,27] The use of this COS does not prevent researchers additionally seeking reasons for non-adherence.

Adoption of this COS by medication adherence intervention trials will result in consistency in the outcomes collected and reported which will enable comparison between trials and aggregation of data to determine the effectiveness of medication adherence interventions.[6] Trials will also be collecting outcomes that have been identified as important by patients and carers; primary care providers and academics.

During this study, the COS development process, in particular the Delphi surveys, did not remove any outcomes and did not distinguish 'core' outcomes from 'important' outcomes. It has previously been reported that a common limitation of the standard Delphi process is that many outcomes remain 'critically important'.[28] Before finalising the COS, participants also considered feasibility and acceptability of collection of the outcomes. This is not usual practice; recently published COS studies do not routinely report how to measure selected outcomes,[29] and searches for subsequent publications often reveals that this stage has not been published. A recent review reported that of 337 COS studies identified only 118 reported how to measure the outcomes in the COS. Without considering feasibility issues such as data collection burden or prohibitive costs, this is likely to lead to measurement variation between trials and trials not being able to collect core outcome data.[7]

Strengths and limitations

This study adhered to COS development and reporting guidance and has included input from three stakeholder groups: patients taking multiple medications and their informal carers; primary care staff; and academics with an interest in medication adherence/management. The outcomes within the COS are relevant to all medication adherence trials, with trials able to select additional outcomes to measure that reflect their context or health condition studied in relation to medication adherence. The study has considered not only the importance of outcomes but also feasibility and acceptability of measurement of the outcomes to increase the likelihood of adoption of the COS by relevant medication adherence intervention trials. However, despite following COS development guidance, the Delphi process did not remove any outcomes as 'not important', meaning that a large number of outcomes were considered in the workshops, where less people are involved in the final discussion and decisions. The study was limited to people who spoke English, and all participants except academics, lived in England. It was difficult to obtain a diverse range of participants in terms of ethnicity and location. The workshops were held online which may have been a barrier for some; however, online options also enable participation by a range of people without the need to travel.

Conclusions

This study has included key stakeholders to identify seven outcomes which are included within the COS and these outcomes should be collected and reported by all trials of medication adherence interventions in primary care for adults taking multiple medications for long-term health conditions. The implementation of this COS will address the variation in outcomes measured and reported by medication adherence trials, enabling comparison of results of intervention effectiveness across similar trials. It is recommended that in addition to the COS, medication adherence trials also consider measuring and reporting relevant clinical outcomes.

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Ethical approval

[Omitted for anonymised review]

Author contributions

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The authors declare that they have no competing interests.

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Supplementary file 1 - COS-STAR checklist

Supplementary file 2 - 46 outcomes (with definitions) rated in Delphi Round 1

Supplementary file 3 - New proposed outcomes from Delphi Round 1 participants

Supplementary file 4 – Delphi Round 1 ratings by stakeholder group

Supplementary file 5 –Delphi Round 2 ratings by stakeholder group

Supplementary file 6 – Outcomes as presented at Workshop 1

Supplementary file 7 - Tools presented in workshop 2 for measuring each outcome

Supplementary file 8 - Summary of all outcomes within the study

Supplementary file 9: Participant Information Sheets

Table 1: Characteristics of participants in the study

	Round 1		**Round 2**	
Patients & informal carers (n)	72		54	
Gender	Male	Female	Male	Female
N	32	40	25	31
Average age (years)	64		64	
Age (range; years)	31-88		35-88	
Ethnicity (%)	White	Non-white	White	Non-white
	97%	3%	96%	4%
Primary care staff (n)	53		28	
Academic researchers (n)	25		17	
TOTALS	150		101	

Table 2: Summary of decisions made in consensus workshops

Core area	Outcomes	Measurement tool considered in workshop 2	Important (Workshop 1)	Important (Workshop 2)	Feasibility	Acceptability	Included in COS?
Life impact	Health-related quality of life	EQ-5D Short form 8/36	✓	✓	✓	✓	✓
Pathophysiological manifestations	Adverse medicine event	Bespoke reporting process for the trial	✓	✓	✓	✓	✓
	Adverse medicine withdrawal event	Bespoke reporting process for the trial	✓	✗	✓	✓	✗
Death	Mortality	Not discussed at workshop; data available from Office of National Statistics (ONS)	n/a	n/a	n/a	n/a	✓
Other: Process outcomes	Satisfaction with the intervention	CSQ-8 client satisfaction questionnaire; Implementation outcome measures	✓	✗	n/a	n/a	✗
	Relevance of the intervention for an individual	CSQ-8 client satisfaction questionnaire; Intervention Appropriateness Measure (IAM)	✓	✓	✓	✓	✓

	Starting (initiating) a medicine	Bespoke reporting process for the trial	✓	✓	✓	✓	✓
	Number of doses taken (originally: Number of medicines taken)	Bespoke reporting process for the trial	✓	✓	✓	✓	✓
	Persistence with a medicine	Bespoke reporting process for the trial	✓	✓	✓	✓	✓

Table 3: Final COS with definitions, core area and suggested measurement tools

Outcome	Definition (plain English)	Core area	Suggested measurement tool
Health-related quality of life	A measure of how good a person feels their mental and physical health is.	Life impact	ED-5D
Adverse medicine event	An unwanted or harmful reaction caused by a person's medicine.	Pathophysiological manifestations	Bespoke reporting process for the trial
Mortality	The death of a person for any reason.	Death	Data from Office of National Statistics (ONS)
Relevance of the intervention for an individual	The extent to which a new way of helping people take their medicine as prescribed fits with a person's opinion of what they need.	Process outcome	Intervention Appropriateness Measure (IAM)
Starting (initiating) a new medicine	Whether a person begins taking their medicine.	Process outcome	Bespoke reporting process for the trial
Number of doses taken	For each medicine, the number of doses taken in a specific period of time.	Process outcome	Bespoke reporting process for the trial
Persistence with medicine	The length of time that a person continues to take their medicine as prescribed.	Process outcome	Bespoke reporting process for the trial

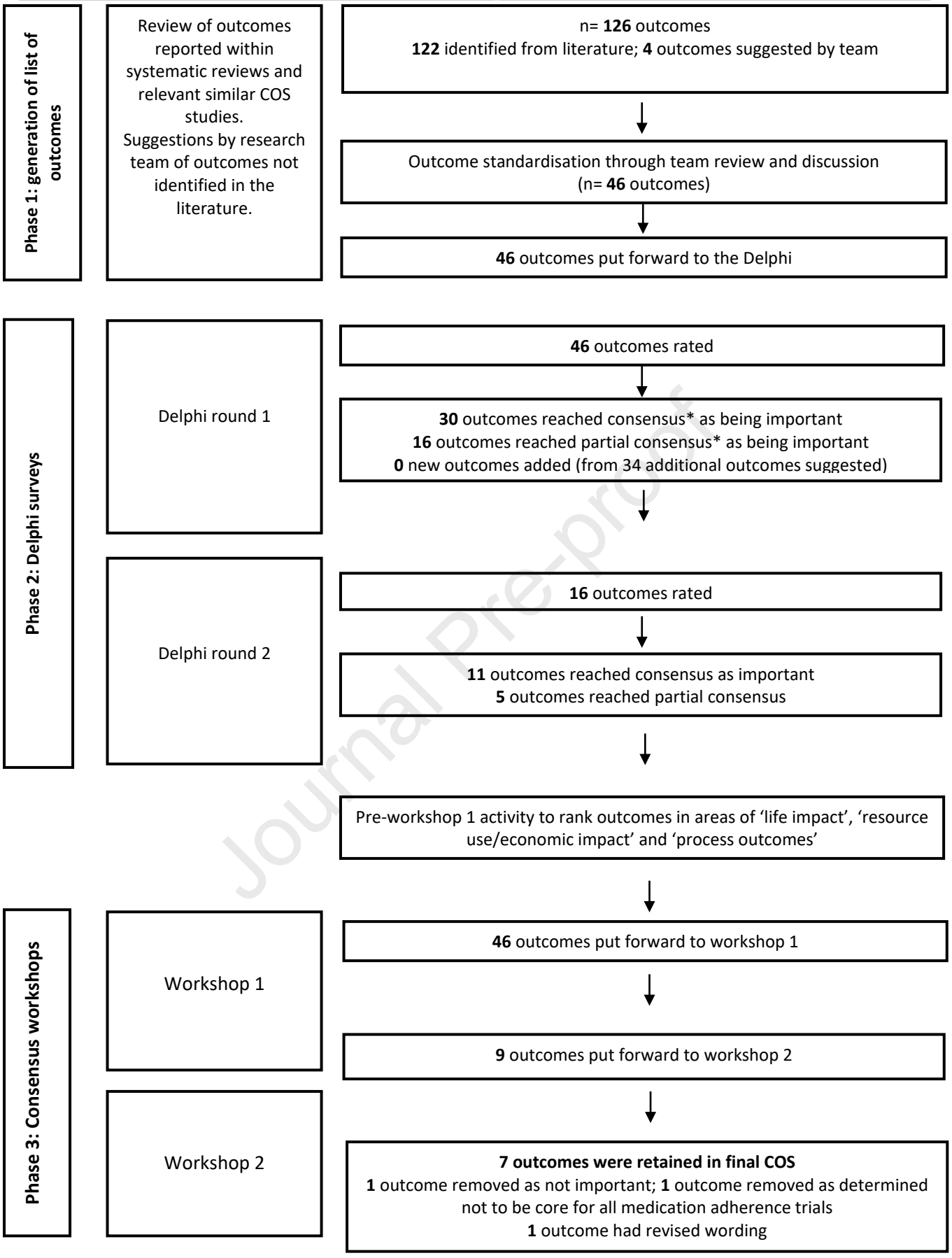

Figure 1: Overview of COS process

*Consensus: Rated as important or not important by ≥70% of participants in all three stakeholder groups

Partial consensus: Rated as important by ≥70% of participants in at least one stakeholder group

Highlights

- Core Outcome Sets enable trials to collect the same outcomes to enable comparison
- Seven outcomes were identified as most important for medication adherence intervention trials
- Considering feasibility and acceptability of outcome measurement increases adoption of the Core Outcome Set by relevant trials