The Harmonising Outcome Measures for Eczema (HOME) implementation roadmap.

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HCW chaired the HOME core outcome set initiative from 2008 to 2021 and was involved in the development of the Patient Oriented Eczema Measure (POEM).

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- **What's already known about this topic?** Core outcome sets (COS) are standardized outcomes that should be measured and reported as a minimum in all clinical trials. COS can improve reporting of patient-relevant outcomes and enable comparison and combination of results to inform patient care. However, COS will only be as effective as their uptake into clinical trials. COS implementation involves strategies to increase their uptake into trials. Practical guidance on COS implementation in dermatology is very limited.
- **What does this study add?** The Harmonising Outcome Measures for Eczema (HOME) implementation roadmap is a pragmatic guide to COS implementation, that starts from COS development until completion. The HOME implementation roadmap is a starting point for a structured approach to COS implementation, to help fulfil the purpose of COS: the consistent use of relevant outcomes in clinical studies. This, in turn, enables and improves the quality of systematic reviews and meta-analyses to support therapeutic decisions.

Plain Language Summary

Outcomes are used to determine whether a particular treatment or intervention is effective in clinical trials (e.g., measuring itch in atopic dermatitis (AD) trials). Often, studies of the same disease select different outcomes or use multiple instruments to measure the same outcome. This makes it difficult to compare results between studies, which in turn makes it difficult to decide which treatments are best.

Core outcome sets (COS) are the minimal outcomes recommended in all clinical studies per condition. COS ensure that studies have a base set of comparable outcomes. The Harmonising Outcome Measures for Eczema (HOME) group developed a COS for AD via a meticulous multi-stakeholder process. Still, the HOME COS is not used in many AD studies, undermining its purpose. Motivating the research community to adopt COS in all clinical studies (i.e., COS implementation) is challenging, and practical advice on implementation is needed.

The HOME implementation roadmap aims to address this gap by providing pragmatic guidance for COS implementation. It was developed based on a review of the scientific literature, online resources, input from HOME lay and professional members, and the HOME executive committee's experience in COS development and clinical trials. The roadmap was designed to guide implementation throughout the COS lifecycle, starting at the initiation of COS development. The roadmap follows 3 stages. Stages 1 and 2 correspond to the COS development stage and focus on preparing for future implementation by ensuring the COS is considered scientifically credible and useful. Stage 3 takes place after the COS is complete, and is an iterative process focused on engaging stakeholders who can influence the selection of outcomes in trials, and ensuring the COS is easy-to-use and applicable to diverse patient groups. Step 3 starts by charting COS adoption into trials and gauging stakeholders' perceptions, followed by developing focused implementation projects, evaluating their impact on uptake, and adjusting them accordingly.

In summary, the HOME implementation roadmap supports efforts towards the consistent adoption of COS into clinical trials, to ultimately improve decision-making in patient care.

Abstract

Background: Core outcome sets (COS) are consensus-driven sets of minimum outcomes that should be measured and reported in all clinical trials. COS aim to reduce heterogeneity in outcome measurement and reporting, and selective outcome reporting. Implementing COS into clinical trials is challenging. Guidance to improve COS uptake in dermatology is lacking.

Objective: To develop a structured practical guide to COS implementation.

Methods: Members of the Harmonising Outcome Measurement for Eczema (HOME) executive committee developed an expert-opinion based roadmap founded on a combination of a review of COS implementation literature, the Core Outcome Measures in Effectiveness Trials (COMET) initiative resources, input from HOME members, and experience in COS development and clinical trials.

Results: The data review and input from HOME members was synthesized into themes which guided roadmap development: a. barriers and facilitators to COS uptake based on stakeholder awareness/engagement and COS features; b. key implementation science principles: assessment-driven, data-centered, priority-based, and context-sensitive.
The HOME implementation roadmap follows 3 stages. First, the COS uptake scope and goals need to be defined. Second, during COS development, preparation for future implementation is supported by establishing the COS as a credible evidence-informed consensus by applying robust COS development methodology, engaging multiple stakeholders, fostering sustained and global engagement, emphasizing COS ease-of-use and universal applicability, and providing recommendations on COS use. Third, incorporating completed COS into primary (trials) and secondary (reviews) research is an iterative process starting with mapping COS uptake and stakeholders' attitudes, followed by designing and carrying out targeted implementation projects. Main themes for implementation projects identified at HOME are stakeholder awareness/engagement; universal applicability for different populations; and improving ease-of-use by reducing administrative and study burden. Formal implementation frameworks can be utilized to identify implementation barriers/facilitators and to design implementation strategies. The effect of these strategies on uptake should be evaluated, and implementation plans adjusted accordingly.
Conclusion: COS can improve the quality and applicability of research and so clinical practice but can only succeed if used and reported consistently. The HOME implementation roadmap is an extension of the original HOME roadmap for COS development and provides a pragmatic framework to develop COS implementation strategies.

Introduction

Clinical trials have long displayed a wide variation in their choice of outcomes.[1] Heterogeneity limits comparison and data harmonization in meta-analyses and may introduce selective outcome-reporting. Outcomes should be relevant to key stakeholders, most importantly patients, and be measured using validated instruments. Core outcome sets (COS), which are consensus-based standardized sets of the minimum outcomes to be measured and reported in clinical trials,[2] aim to address these concerns.[3]

In dermatology, one of the first COS developed was the Harmonising Outcome Measures for Eczema (HOME) COS for atopic dermatitis (AD),[4] defining four domains (what to measure) as the minimum outcomes in AD clinical trials. HOME has agreed on a core set of instruments to measure these outcomes. Despite the success of the HOME COS development and its publication in major dermatology journals,[5–8] uptake and standardized reporting in AD clinical trials is still limited. In 2018, only about 60% and 20% of phase III/IV AD studies complied with HOME recommendations and used the Eczema Area and Severity Index (EASI) and the Patient-Oriented Eczema Measure (POEM) to assess signs and symptoms, respectively.[9] While EASI and POEM use in randomized-controlled trials (RCTs) between 2018-2022 improved to 94% and 60%, respectively, lack of standardized reporting across studies still hindered evidence synthesis.[10]

Low COS uptake is a universal problem.[11–13] Implementation research has broadened the understanding of the challenges facing COS implementation. Identified barriers include the level of understanding of the concept and purpose of COS, and awareness of the existence of a study-relevant COS.[11,12,14,15] COS which include domains, but don't provide recommended instruments or lack recommendations on how to apply these instruments, are harder to implement.[12] Concerns around patient burden from multiple outcome measurements, and trialists' own outcome preferences, are additional barriers. Implementation can be facilitated by making COS acceptable and easy-to-use. The wide-ranging research system can also increase COS uptake by influencing adoption of COS in trials[16] through stakeholders such as funding agencies and journal editors. Conversely, conflicting recommendations across major stakeholders, such as regulatory agencies, can lead to confusion and reduce uptake.[12] At the 2021 HOME IX meeting,[17] the main themes that may explain the limited uptake of the HOME COS were identified as stakeholder awareness and engagement, universal applicability of the COS for different populations, and administrative and study burden (ease-of-use). Upon launching the HOME implementation project in that meeting, the complexity of COS implementation became evident and with it a need for guidance. HOME previously designed a roadmap[18] to guide COS development. Here, we describe guidance on how to structure a COS implementation strategy in the form of an implementation roadmap.

Materials and methods

The HOME Executive Committee developed the roadmap in an iterative process based on a combination of literature searches, with expert and lay input on COS implementation processes. This committee has extensive experience in COS development[4] and as clinical trialists and systematic reviewers (YAL,HCW,LMH,LAAG,PS,JS,KST,CA,ELS,NK), serving in trial funding bodies (HCW), working with regulators, funding agencies, and Health Technology Assessment bodies (HCW,JS,CA,PS) and with the pharmaceutical industry (YAL,JS,CA,ELS).

The roadmap was developed as follows:

1. A selective PubMed search for publications on 'COS implementation' and 'COS uptake' was performed on 12/2021, with key papers extracted. The reference list of a recent comprehensive review on COS implementation[14] was reviewed for additional papers. Additionally, we conducted an online search for websites with implementation resources and of the Core Outcome Measures in Effectiveness Trials (COMET) initiative[3] website.
2. At the HOME IX[17] (virtual, 2020) and X (Montreal, 2021) multi-stakeholder meetings, HOME members identified HOME-specific implementation barriers and facilitators, and developed preliminary implementation strategies.
3. Opportunities for influencing COS uptake were then mapped throughout the course of a clinical trial and its subsequent use in systematic reviews and guidelines (Figure 1).
4. The data was integrated into the HOME implementation roadmap based on expert opinion. The roadmap was structured to follow the COS lifecycle, guiding implementation efforts for each phase.

Results

The literature search and input from HOME meetings were synthesized into two themes which informed the development of the roadmap:

a. **Barriers and facilitators to COS uptake,** categorized to form the main implementation avenues:
    i. Stakeholder awareness and engagement
    ii. Features of the COS affecting uptake
b. **A science-based approach to implementation**. Key principles were identified to guide the roadmap:
    1. Implementation outcomes should be defined and evaluated intermittently.
    2. Employ an empirical approach to designing interventions, building on scientific data.
    3. Prioritize the interventions that will have the most broad-ranging and rapid effect.
    4. Design context-sensitive interventions:[19] Avoid a 'one size fits all' approach and tailor the intervention to stakeholders.

The HOME implementation roadmap is presented in Figure 2. Future implementation should be considered right at the initiation of COS development, reflected in the first two stages of the roadmap. After the COS is developed, implementation methods and goals evolve in an iterative learning process, illustrated in the third stage of the roadmap.

Step 1: Define uptake scope and objectives

This step is focused on clarifying the implementation goals, to meet the roadmap principle of defining and evaluating uptake. The scope should specify the area of health/condition (e.g., AD) and the target trials specified by design (e.g., all clinical trials vs RCTs) and settings.

Next, define implementation objectives using selected uptake indicators within a specified time frame. For example: to reach 80% use of the COS in interventional clinical trials within 8 years of its development. While adoption in trials is the intuitive indicator, there are other possible implementation indicators such as acceptability, penetration, and user satisfaction.[20] Interim targets can also be defined to allow for adjusting implementation plans in real time, such as publication in leading journals, or endorsement by a specific stakeholder.

Step 2: Preparing for implementation during COS development

In the COS development stage, the implementation aim is to have the COS acknowledged as a credible and feasible consensus by a wide group of stakeholders. This stage corresponds to the main implementation avenues, as they manifest during COS development:

1. Stakeholder involvement and support
    a. ***Conduct a scientifically robust development process*** and adhere to a predefined methodology (e.g. HOME roadmap,[18] COS-STAndardised Protocol Items/STAndards for Development/ STAndards for Reporting,[21–23] COMET Handbook,[24] OMERACT handbook[25], or collaborate with the C[3] methods Group (Consortium for Harmonizing Outcomes Research in Dermatology and the Cochrane Skin COS Initiative).[26] To prevent redundant efforts and to engage with potential contributors, registration in the COMET (https://www.comet-initiative.org/Studies) database is helpful.
    b. ***Involve key stakeholders in COS development*** to contribute to credibility and create future advocates. Lack of key stakeholder involvement, especially patients, in COS development is a barrier to COS implementation.[12] It is important to involve key opinion leaders so that everyone has a voice at consensus meetings. HOME included patients, clinicians, researchers, methodologists, a regulator, and industry representatives.
    c. ***Foster sustained and global engagement.*** COS development is a lengthy process. Holding consensus meetings in different countries, disseminating interim results in meetings, high-impact journals,[5–8] and through social media[27] are all important for encouraging sustained global uptake.

2. Features of the COS: feasibility and acceptability for future large-scale use.
    a. ***Consider ease-of-use and universal applicability*** during COS development. For example, HOME stakeholders recommended a maximum of 4 domains to achieve a user-friendly COS. Other feasibility considerations are the time to complete the COS, avoidance of overlapping domains or instruments, and the cost and availability of instruments. There may be advantages to recommending instruments that are in the public domain or owned by academia. In the case of copyrighted instruments owned by commercial entities, it is important to ensure their availability to all trialists, regardless of their affiliation. The universal applicability of the COS to different populations is another key consideration.
    b. ***Minimize uncertainty in COS use*** by providing recommendations on how to measure and to report outcomes using the COS instruments. Lack of clear recommendations hampers uptake.[12] For example, HOME published a recommendation on standardized reporting of the EASI and the POEM.[28]

Step 3: Implementation post COS development

The implementation aim at this stage is to incorporate the COS into research, policy, education, and practice. Work in this stage was guided by the key roadmap principles: Assessment-driven, data-centered, priority-based, and context-sensitive. We suggest a pragmatic approach which is iterative in nature and broadly follows the plan-do-check-act (PDCA) cycle, a four-step framework for carrying out change.[29] The PDCA cycle should be repeated for continuous improvement. Similarly, implementation efforts involve repeated cycles of planning, executing, assessing, and recalibrating based on the results.

Step 3a: Data collection and analysis

This step explores the current COS uptake status, adhering to the implementation principle of utilizing scientific data as a foundation for implementation efforts.

- **Baseline uptake**

Assess baseline COS uptake by looking at the outcome domains and instruments used in target trials.[9] Trial registry data can efficiently provide current information,[36] as relying only on published papers may provide outdated information.[35]

It is useful to map COS uptake by stakeholders other than trialists. Uptake in this context means a requirement or an encouragement that trialists interacting with these stakeholders use the COS. Some stakeholders have a significant impact on outcomes selection by trialists and can serve as an effective means of enhancing COS adoption. Examples include funding bodies requiring COS use by applicants (e.g. UK NIHR[30] or German DFG[31]); regulatory bodies guidelines aligned with COS (e.g. the Food and Drug Administration and European Medicines Agency guidelines on rheumatoid arthritis)[32]; reporting guideline groups recommending COS use for trial outcome selection (e.g. SPIRIT[33]); trial registries guiding trialists to use COS when registering their trials (e.g. ISRCTN[34]); patient groups encouraging participation in trials which use COS; and professional journals requiring COS use in clinical trial publications (e.g. the British Journal of Dermatology[35] or the Journal of the American Academy of Dermatology[36]). Mapping uptake in these stakeholders can be performed by an online search of organizational guidelines and policy documents, or direct communication. We broadly prioritized the main stakeholders based on their anticipated uptake impact (Figure 3).

- **Identification of implementation barriers and facilitators**

Understanding why people aren't using the COS (barriers) and how to encourage them to use it (facilitators) is key to planning interventions for improving uptake.[14] Conceptual frameworks within implementation science[37] such as the Consolidated Framework for Implementation Research (CFIR)[38] can help guide the identification of factors which influence COS implementation. Examples for projects to improve understanding of these factors include:

1. Identify characteristics of trials with low COS uptake and temporal trends in uptake in relation to major events such as publication of the COS[9] or regulatory body guidelines supporting COS.[32]
2. Survey key stakeholders for their knowledge and attitudes regarding the COS.[11]
3. Discuss implementation barriers/facilitators within your COS group.[17,39] .

- **Identification of parallel implementation efforts and collaborations**

To minimize research waste and broaden implementation efforts, identify ongoing projects that may impact COS implementation. Methods include surveying the COS group members, reaching out to partner groups (e.g., COMET, C[3]) and other COS groups for collaborative work with major stakeholders (e.g., approaching regulators to endorse COS use in drug approval trials). Collaborations with professional groups can increase awareness of COS (e.g., incorporating outcome research into resident educational programs).

Step 3b: Develop implementation interventions

Building on the data gathered in the prior steps, develop implementation strategies. This step emphasizes the design of priority-based and context-specific interventions, in line with the key implementation principles.

Implementation research has identified different strategies, such as conducting educational meetings, intervening with patients to enhance uptake, and developing educational materials.[40] Methods for matching and adapting strategies to the identified barriers and facilitators have also been described, including concept mapping, group model building, conjoint analysis, and intervention mapping.[41] It is unknown which strategies and strategy-tailoring approaches are most effective.[42]

COS group workshops can advance the design and feasibility of implementation projects.[14,39] Example: group discussions in the HOME IX[17] meeting identified leading implementation themes, with corresponding working groups formed and advanced at the HOME X meeting.

The interventions developed in this stage target barriers/facilitators of COS adoption by the main implementation avenues:

- **Stakeholder awareness and engagement**

Mixed methods for stakeholder engagement are needed and include targeted information and use of social media. Behavioral science-based approaches for increasing COS uptake are under development,[43] building on behavior change frameworks such as the behavior change wheel.[44]

Stakeholder engagement projects should preferably focus on stakeholders with broad impact (figure 3) to maximize COS uptake, in line with the implementation principle of priority-based interventions. However, efforts should be weighed up against potential benefits. For example, while regulators are very impactful stakeholders, gaining their endorsement can be complex and resource demanding. Some stakeholders have global reach, such as trial registries and reporting guideline groups. However, many impactful stakeholders are region-specific (e.g., national/regional regulatory agencies, funding bodies, and patient groups). Galvanizing the COS community and its diverse regional representation, and identifying local champions in different geographical areas, may improve local uptake and support equality in healthcare.

Even when stakeholders endorse COS use, monitoring adherence to these endorsements is needed. Adherence monitoring can include projects like periodic assessments of trial registries for outcome selection, proactively approaching trialists to consider using COS, and encouraging peer-reviewers to request justification of outcome selection.

- **Features of the COS**
    - **Universal applicability**

Users of the COS require reassurance that the recommended instruments are applicable to people of different ages, cultures, skin tones and ability to understand the concepts being addressed. Additional content validity and cross-cultural validity studies may be required to

ensure applicability to different age groups and cultural settings.[45] Widescale use also requires availability of approved translations that conform to minimum standards, to ensure accuracy of translation and interpretation. A centralized repository of data from previous studies for different sub-groups of people can support the relevance and responsiveness for different target populations and can help inform trial design and sample size calculations.[46]

- **Ease-of-use**

Thinking through the feasibility of using the COS and how it impacts on different sorts of trials and stakeholder recommendations is key to acceptability and uptake.

Different methods can be used to minimize the burden (time and effort) and optimize the use of COS. Guidance is the starting point; information on how to best access the COS (including administration costs, approval for using instruments), organize data capture, collect, analyze, and interpret data of the COS is essential. A practical guide, infographic, education video for patients and up-to-date information on a website may prove very useful. Reducing overlap between instruments and/or the frequency of conducting questionnaires is another means of reducing COS burden. The question 'is the COS easy to use?' can be evaluated by a feasibility study. This includes not only the time to complete the COS, but also acceptability for patients and clinicians.

Step 3c: Carry out implementation projects

Given limited resources, prioritize the planned implementation projects which includes establishing a timeline. The HOME initiative found that allocation of leads and a team project manager can be instrumental in moving this stage forward.

Step 3d: Evaluate uptake against benchmarks

Uptake assessments need to be regularly assessed using consistent methodology to allow comparison over time. A useful way of periodically reviewing COS uptake is to assess their use in living systematic reviews and network meta-analyses of intervention trials.[10,47–49] Uptake can be assessed on multiple levels: are the COS domains being (partly or completely) measured (e.g., signs); are the COS instruments being used to measure these domains (e.g., EASI); and are the results reported as recommended (e.g., baseline and end of treatment mean and SD EASI for individual randomized groups).[28]

Step 3e: Recalibrate action plan

Implementation efforts may need to be recalibrated periodically. Some things will work better than others, and some might fail at the first hurdle, so an iterative learning process is needed.

Discussion

COS implementation in clinical studies is a difficult task which requires multi-stakeholder acceptance and engagement. The goal of this roadmap is to offer pragmatic guidance on *how* to implement COS throughout their development. Several key aspects of COS implementation are highlighted in this roadmap. First, we strongly recommend identifying implementation needs right at the start of COS development when the focus typically centers around research and development of the COS. Second, is the need for COS teams to be aware of the two main implementation avenues: methods for stakeholder awareness/engagement, and features of the COS which affect uptake, such as ease-of-use and universal applicability. Considering these avenues can aid in constructing implementation projects. Third, after the COS is developed, implementation efforts should be viewed as an iterative process, subject to evaluation and modification.

The HOME implementation roadmap promotes the design of implementation interventions based on scientific data, such as an examination of uptake barriers and facilitators.[14] It can complement the formal use of implementation frameworks,[37] in bridging the gap between scientific findings and their application – the "know-do" gap.[50] However, traditional data-driven approaches can be time-consuming and inflexible. Current trends towards semi-formalized and expert-based means to knowledge production may offer a quick and agile alternative.[51]

Implementation requires COS developers, who are often academic researchers, to step out of the comfort zone of data and analytics-based research to domains such as behavioral change, communication, and marketing. It can be advantageous to involve people with these skills early in the COS development process.

The HOME implementation roadmap, like the COS itself, is very much a work in progress as with all iterative projects. It is still unclear if our approach is superior to common implementation approaches,[14] which HOME implementation projects are effective, and whether such projects are generalizable to other fields of healthcare. This roadmap is a starting position that helps to structure the process and to start thinking about the practicalities of the implementation pathway within a finite resource envelope, that complements the HOME roadmap for COS development[18] nicely.

In summary, we hope this HOME implementation roadmap will help guide implementation efforts and improve COS uptake more generally beyond the field of AD, and complement established resources on COS implementation from the COMET group (https://www.comet-initiative.org/) and on COS in dermatology from the C3 group (https://www.c3outcomes.org/).

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Figure Legends

Figure 1: Implementation points of impact throughout the life of a clinical trial

Figure 2: The HOME implementation roadmap

Figure 3: Prioritization of main stakeholder groups by anticipated impact